Indian Journal of Anesthesia and Analgesia

Aims and Scope

The Indian Journal of Anesthesia and Analgesia (IJAA) is official peer-reviewed scientific journal addresses all aspects of anesthesia practice, including anesthetic administration, pharmacokinetics, preoperative and postoperative considerations, coexisting disease and other complicating factors, cost issues, and similar concerns anesthesiologists contend with daily. The Journal seeks a balance between outstanding basic scientific reports and definitive clinical and management investigations. The Journal welcomes manuscripts reflecting rigorous analysis, even if unusual in style and focus.

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Contents

Editorial

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Delirium in the Intensive Care Unit

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Delirium in the critically ill patients admitted in the Intensive Care Unit (ICU) is a challenge to the treating clinician. For most ICU patients, maintaining light sedation is associated with improved clinical outcomes including shorter duration of mechanical ventilation and shorter ICU stay. Ensuring critically ill patients free from pain, agitation, and delirium should not compromise with their clinical management goals, like cardiopulmonary stability and preserving adequate organ perfusion and function [1].

Delirium is a neuropsychiatric syndrome with acute onset of cerebral dysfunction characterized by fluctuating levels of cognition and inattention with disorganized thinking or an altered level of consciousness. It is usually triggered by underlying medical disorder and is more common in the elderly. The onset is usually rapid, occurring within hours or days and is often accompanied by sleep disturbances like daytime sleepiness and nighttime wakefulness. As the diagnosis of delirium is frequently missed, a high index of suspicion is required. Physiologically, delirium is characterized by derangement of cerebral metabolism with cerebral dysfunction and is usually caused by general medical illness, intoxication, or substance withdrawal [2]. In extreme cases, physical restraints may be needed for the patient to prevent harm to himself/herself or others.

DSM-V [3] (Diagnostic and statistical manual of mental disorders, 5th ed.) criteria for the diagnosis of delirium is.

A) A disturbance in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment).

B) The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day.

C) An additional disturbance in cognition (e.g., memory deficit, disorientation, language, visuospatial ability, or perception).

D) The disturbances in Criteria A and C are not better explained by another preexisting, established, or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal, such as coma.

E) There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e., due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies.

Delirium is common in the ICU especially in those on mechanical ventilation, ranging from 45% to 87%. It increases the length of hospital stay with higher risk of hospital acquired complications such as pressure sores and falls, causing increased morbidity and mortality. The one-year mortality rate associated with delirium is 35-40% [4]. Up to 60% of these patients have continued cognitive impairment with increased risk to develop dementia later [5].

Three clinical subtypes of delirium are described [6]: Hyperactive (restlessness, agitation, vigilance and aggression); Hypoactive (sleepiness, lethargy, reduced appetite and withdrawn state) and Mixed forms (move between two subtypes). Hypoactive and mixed delirium which are more difficult to recognize are common in the ICU. Hypoactive delirium occurs more frequently in older patients and has a worse prognosis.

Predisposing factors for delirium are age above

65 years, preexisting cognitive impairment or dementia, severe medical illness (renal or hepatic impairment, stroke, HIV infection), psychoactive drugs or alcohol/recreational drug dependency, decreased oral intake with dehydration or malnutrition and hip fracture. Precipitating factors include altered body chemistry, defective oxygenation and use of drugs affecting the central nervous system. Urinary / faecal retention and acute / chronic pain are other contributing factors.

Drugs (withdrawal/toxicity, anticholinergics)/ Dehydration

Electrolyte imbalance

Level of pain

Infection/Inflammation (post-operative)

Respiratory failure (hypoxia, hypercapnia)

Impaction of faeces Urinary retention

Metabolic disorder (liver/renal failure, hypoglycemia)/Myocardial infarction

ICU patients should be evaluated for the above risk factors for prompt interventions. Recent (hours or days) changes or fluctuations in behavior in a person at risk should alert the clinician for the diagnosis. Global or multiple deficits in cognition, disorientation, memory deficits and language impairment are common. There is usually inattention with difficulty in conversation and disorganised or incoherent speech. Altered behavior and level of consciousness with labile changes in mood with fear, paranoia, anxiety, depression, irritability, apathy, anger or euphoria are common. Altered sleep-wake cycle with daytime drowsiness, night insomnia, fragmented sleep is usual. Symptoms may have a fluctuating course of severity with lucid intervals in between with relatively normal behavior may occur.

The Confusion Assessment Method for the ICU (CAM-ICU) is a commonly used delirium monitoring tool in the ICU. It requires point 1 and 2 and either 3 or 4 of the following

1) Acute onset and fluctuating course

2) Inattention

3) Disorganised thinking

4) Altered level of consciousness (vigilant, lethargic / drowsy, stupor, coma)

Changeable course

Acute onset + Attention poor

Muddled thinking

Shifting consciousness

Differential diagnosis of delirium includes dementia, depression, mania, schizophrenia and hysteria. However, organic causes should be sought for and delirium excluded before making other diagnoses.

Benzodiazepine withdrawal usually manifests as anxiety, agitation, tremors, headache, sweating, insomnia, nausea, vomiting, myoclonus, muscle cramps, hyperactive delirium, and seizures. Stoppage of dexmedetomidine infusions after a few days can develop withdrawal symptoms with nausea, vomiting, and agitation. Withdrawal symptoms may result from abrupt discontinuation of illicit drugs, sedatives or opioids or chronic alcohol use.

Delirium due to drug or alcohol withdrawal usually manifests as hyperactive type. Symptoms of range from mild irritability and insomnia to life-threatening conditions such as Delirium Tremens (DT). It is characterized by central nervous system excitation (agitation, delirium, and seizures) and hyperadrenergic symptoms (hypertension, tachycardia, arrhythmias). Benzodiazepines and symptomatic support are the mainstay of treatment.

As delirium is often associated with severe underlying medical illness, identification and prompt treatment of the cause is important along with symptomatic and supportive care including psychological support and calm atmosphere. Pharmacological management is needed for patients whose symptoms are uncontrollable and harmful to themselves or others. Oral route is usually preferred and all medications have to be reviewed every 24 hours. The starting dose is based upon the age, body size and degree of agitation and titrated until the desired sedation achieved up to the maximum daily dose, preferably with the help of a psychiatrist.

Oral haloperidol 0.5-1mg up to a maximum of 5 mg in 24 hrs is usually preferred in the elderly. Younger and healthy patients may require higher doses, daily maximum of 30 mg [7]. In those who cannot take orally and those requiring quick control of symptoms, haloperidol is given intramuscularly daily max 5 mg in the elderly and upto 18 mg in the younger patients. Peak effect of haloperidol by oral and intramuscular routes are 4-6 hrs. and 20-40 mins respectively.

Haloperidol should not be given in those with elongated QTc (>470 ms) in ECG. Patients should be monitored with respiratory rate, pulse oximetry, BP, and Temperature. Haloperidol may cause acute dystonic reactions which may require treatment with benzodiazepines or procyclidine.

Olanzapine 2.5 - 5 mg orally 2 hourly, daily max 20mg (10mg in elderly) can be used in patients with dystonia. Benzodiazepines are preferred in those with Parkinson's disease/parkinsonism, seizures, elongated QTc and alcohol withdrawal states. Lorazepam 0.5 – 1 mg oral/IM 1-2 hourly, max 4 mg daily is often prescribed.

Continuous IV infusions of dexmedetomidine is a valuable adjunctive for patients with delirium in the ICU unrelated to alcohol or benzodiazepine withdrawal.

Delirium may be a disease-induced syndrome (e.g., organ dysfunction in severe sepsis), for which timely management of the cause or causes is essential in order to reduce the incidence, severity, and duration of delirium. Iatrogenic (e.g., exposure to sedative and opioid medications) or environmental (e.g., prolonged physical restraints or immobilization) factors may also contribute to delirium in ICU patients. ICU patients should be evaluated for identifiable and avoidable risk factors, and therapeutic interventions should be assessed in terms of their likelihood of either causing or exacerbating delirium in individual patients. Delirium prevention strategies can be categorized as nonpharmacologic (e.g., early mobilization), pharmacologic, and combined pharmacologic/ nonpharmacologic approaches. Monitoring critically ill patients for delirium with valid and reliable delirium assessment tools enables clinicians to potentially detect and treat delirium sooner, and possibly improve outcomes.

Up to one third of cases of delirium is preventable. Delirium prevention strategies can be nonpharmacologic (early mobilization), pharmacologic, and combined approaches Patients at risk of delirium should be assessed for factors that may contribute to delirium within 24 hours of admission and treated promptly [8].

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Book Review

Introducing "Synopsis of Anesthesia"

Through this review we hereby introduce 1st edition of Synopsis of Anesthesia, as concise textbook of anesthesia by Red Flower Publishers Pvt Ltd. The first edition of synopsis of anesthesia aims to provide a single textbook, short yet comprehensive to provide efficient and rapid revision of concepts to meet the clinical needs of anesthesia residents.

A physician has to learn and update knowledge because of constantly evolving advances in management. There is an exhaustive amount written on anesthesia and critical care as subject is vast and varied, but not always readily accessible. We have aimed to keep the chapter's short and highly relevant thereby providing simple yet informative knowledge about the topics. This book has been prepared as per the curriculum and requirement of anesthesia degree courses in India. It has been prepared and written in a systemic manner and opts a simple approach in presenting the text. Utmost efforts have been made to cover all necessary important aspects of the subject including recent advances wherever required.

Thoroughly updated, this edition has sections on Physics in anesthesia, History of anesthesia, pulmonary function tests, topics in critical care such as nutrition, fluid therapy, electrolyte disorders, arterial blood gases disorders, high flow nasal cannula, brain dead, acute respiratory distress syndrome, recent advances in anesthesia, early recovery from anesthesia and surgery, dealing with difficult airway, statistical analysis, cardio-pulmonary exercise testing, etc. Various standard flow charts with references have been added for quick reference guide. The book also features numerous figures and tables to highlight key points and writing style is simple yet effective.

It is well organized with 33 chapters covering the basics such as physiology, and systemic approach to anesthetic management of geriatric, bariatric, obstetric, pediatric, patients with liver/kidney disorders, burns, cardiac, respiratory, neurosurgery and for day care surgeries. It gives step-by-stepteaching for patient management, as well as an in-depth analysis of ancillary responsibilities and problems.There are also chapters on physics, history of anesthesia, CPET and pain management, which usually ignored by students while preparing for final examination.

This book has been designed to cater to the needs of post graduate residents and senior residents who are preparing for various exams such as theory and practical examination, multispecialty (multiple choice based) examinations, EDAIC, etc. It is also helpful for undergraduate students who have keen interest in the subject and want to acquire knowledge about the same in limited frame of time.

We express our sincere gratitude to all those who helped us in completion of this book. Any suggestions from the faculty and students will be highly appreciatedfor further improvement in future editions.

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Original Research Article

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Sevoflurane Induction of Anaesthesia in Critically ill Patients Undergoing Emergency Laparotomy

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Abstract

Sevoflurane has characteristics of rapid inhalational induction of anaesthesia in 60 secs while maintaining spontaneous respiration, bronchodilatation, haemodynamic stability with rapid recovery in elective scenario. This retrospective study analysed 40 (n=40) critically ill patients undergoing induction of anaesthesia with sevoflurane in emergency laparotomy. Standard methods and techniques were used in patient induction and management. Patients were optimized prior to sevoflurane induction were in ASA-III E (72.5%) and ASA-IV E (27.5%) status. Clinical outcome of sevoflurane anaesthesia induction analysed in terms of any airway managment complication and haemodynamic stability. Statistical analysis of haemodynamics done by ANOVA (analysis of variance). Incidence of airway complication such as laryngospasm, aspiration were nil and none of patient required abandoning or modification in induction process. Patients Spo2 improved postinduction (only 2.5% SpO_2 between 85%-90%) even in comorbid COPD and smoker patients showing beneficial effects of sevoflurane induction. Induction of anaesthesia with sevoflurane is associated with significant changes ($p < .05$) in MAP and pulse peaking at 3 minutes postinduction as sevoflurane induction unable to attenuate intubation response on haemodynamics. None of the patient had bradycardia (HR < 60 bpm), hypotension (MAP < 60 mmHg) and arryythemias or required additional vasopressor support post induction and throughout perioperative period. None of patient required postoperative ventilation due to delayed recovery. Study concludes sevoflurane induction is without airway complications and haemodynamic unstability is suitable induction agent in emergency laparotomy in optimized critically ill patients while taking measure to prevent aspiration though unable to inhibit adrenergic endotracheal intubation responses.

Keywords: Sevoflurane; Induction of Anaesthesia; Emergency Laparotomy; Haemodynamic stability; Airway complications; safety; Critical patients.

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Introduction

Management of induction of anaesthesia in critically ill is challenge to any anaesthesiologist. Apart from time tested anaesthetic agent, more recently introduced sevoflurane (1990) has established itself as induction agent in elective patients [1]. Sevoflurane is a potent, non-pungent,

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haemodynamically stable volatile anaesthetic agent. In high concentration sevoflurane is haemodynamically stable with rapid uptake and elimination (blood gas partition coeffcient 0.62) without awareness while maintaining spontaneous respiration. This is of value in unanticipated difficult airway and haemodynamically unstable emergency critical patients [2]. Increasing the concentration of sevoflurane [3] relatively slow passage of sevoflurane through the excitatory stage 2 of anaesthesia will be passed more rapidly. Induction time is less than 60s have been demonstrated and reported without awareness. Incidents of increased airway secretions or laryngospasm rarely occur with minimal coughing or breath-holding during induction with sevoflurane [4]. 8% sevoflurane has been shown to offer good haemodynamic stability even in patients with poor cardiovascular reserve and arrythymia [5]. There is no biochemical evidence of associated hepatotoxicity and concerns of potentially nephrotoxic have been largely discounted [6].

Aims and Objective

1. To examine safety and efficacy of induction of general anaesthesia with sevoflurane in emergency laparotomy in critically ill patients.
2. To evaluate any airway complication and haemodynamic stability during sevoflurane induction and perioperative period in critically ill patient undergoing emergency laparotomy.

Material and Methods

This retrospective study was undertaken after institutional ethics committee approval. Standard technique material and methods were used for patient management. Patients managed with sevoflurane induction only included in this retrospective analysis were 40 (n=40). Informed consents were obtained as routine [7]. All patients were investigated and evaluated to know their physiological metabolic status and clinical diagnosis. This includes haemoglobin, Complete blood count (CBC), serum electrolytes and blood sugar, liver function test, kidney function test, x-ray chest and abdomen, Ultrasonography (USG) and arterial blood gas analysis (ABG). Haemodynamic management based on clinical and noninvasive vital parameter and on ABG. Table 2 showing distributution of clinical diagnosis of patient. After gaining intravenous access with wide bore cannula of 16 G and 18 G patients were optimized haemodynamically with intravenous fluids, colloids, blood product, oxygen with or without requirement of dopamine/noradrenaline (15% Table 3). Patients optimized prior to sevoflurane induction were in optimized American society of Anesthesiology ASA-III E (72.5%) and ASA-IV E (27.5%) status (Table 4). After optimization patient were taken for surgical intervention under general anaesthesia. Non invasive perioperative monitoring including noninvasive blood pressure (NIBP), electrocardiography (ECG), oxygen saturation (SpO_2) applied. Patients were premedicated with inj tramadol, inj pantoprazole, inj metoclopramide, inj ondansetron, inj glycopyrolate. Inj midazolam. 03 to .05 mg/kg given with preoxygenation with 100 percent oxygen for 5 minutes. All measures were taken to prevent aspiration including ryles tube aspiration of gastric content, intravenous pantropazole and sellick's maneuver as appropriate and preparation to deal with if any regurgitation of gastric content occurs.

Sevoflurane Induction Technique [Sevoflurane vaporizer Intermed Penlon Sigma Delta Vaporize]- Patients were explained and visually shown to breath gently after a full expiratory breath to residual volume comfortably and regularly till loss of conscious and eyelid reflex. Anaesthesia machine (oracle S505) closed breathing circuit primed with 100 percent oxygen and 8 percent sevoflurane for 3 to 5 minutes. Patients were asked to take forced exhalation to residual volume breath as explained followed by breath gently regular breath with oxygen flow at 80 to 100ml/kg/ minutes on Mapalson D circuit. Sevoflurane vaporizer set to 1% and increased after every 2 breaths, in sequence 1,2,4 and 8% [8]. Concentration of sevoflurane limited to 6% in patients above 65 years (12.50% Table 1).

Time to induction of anaesthesia taken from when the vaporizer was at 8% to the time when the eyelid reflex lost to central pupil [9]. In late stages 50% nitrous oxide mixed to enhance the induction to minimize agitation. Analgesic properties of nitrous oxide may enhance quality of induction of anaesthesia [9]. Time to loss of conscious defined as the interval from induction time to loss of eyelid reflex. It usually takes 60 to 70 sec to loss of consciousness and eyelid reflex after 3 to 6 breath [10]. With lose of eyelid reflex and consciousness in 50 to 70 secs, patient were given inj. succinylecholine 1 mg/kg and intubated in 60 secs. Patients maintained on intermittent positive pressure ventilation (IPPV) with sevoflurane 1.6 to 3% with oxygen - nitrous oxide and closed circuit sodalime

with minimum positive end expiratory pressure (PEEP) of 2-4 mmHg [12]. Perioperative monitoring included pulse rate, NIBP, ECG, endtidal carbondioxide ($EtCO_2$), tidal volume, Inspiratory :expiratory (I:E) ratio, repiratory rate, temperature and urine output. Neuromuscular relaxation ensured with inj atracurium and vecuronium as appropriate. Vitals were recorded non invasively at 3 to 5 minutes interval. NIBP, pulse rate and SpO_2 were taken at 1, 3, 5, 10, 15, 30, 60 minutes and 10 minutes post extubation and statistically analysed. Surgical intervention performed lasted 90 minutes to 180 minutes (Table 5) and patients extubated after neuromuscular reversal on table as haemodynamics were stable and assessment was possible. Appropriate analgesics were ensured and patient put on oxygen and 24 hrs intensive care unit (ICU) monitoring. Routine investigations were checked postoperatively were within normal limits Patients were given intensive and routine care and discharged from hospital without any increase in morbidity.

Statistical analysis

Statstical analysis was done with the help of statistical package for social sciences (SPSS) version 21. Demographic data and distribution were analysed. Haemodynamic variable analyzed using a Analysis of Variance method (ANOVA) for intergroup analysis. $p<0.05$ considered statistically significant.

Result

This retrospective study analysed 40 (n=40) patients undergoing emergency laparotomy management by standard methods and techniques of sevoflurane induction only. Patient distribution analysed according to age and gender (Table 1), disease (Table 2), cormorbid and physiological status (Table 3), ASA-E status (Table 4), duration of surgical anaesthesia (Table 5). Haemodynamic variable of this patient population analysed by ANOVA depicted in Table 6, 7, 8 & 9 and graphics representation in Graph 1, 2, 3. Table 10 showing incidence of complication during perioperative period.

Majority of patient were male (67.50%). Of all patients 45% were smoker and 45% anaemic. Age varied between 18 to 76 yrs, 77.50% in 18-65 years (Table 1). All patients were referred from distant areas or bought as first medical contact to our medical college hospital in late ASA 4 E (65%) status (Table 4). More than 50% of patients presented with duodenal perforation peritonitis (Table 2) and 90% were in comorbid state of sepsis (Table 3). 10% were in acute haemorrhagic shock require 2 or more units of blood transfusion. Patient were optimized before induction to improve ASA status (Table 4). Despite preinduction optimization, 5% patients remained in Spo2 between 85% to 90%, 5.12% remained in mean arterial pressure (MAP) range of 50-60 mmHg (Table 3). 6% of patients had required dopamine/noradrenaline support to maintain

Table 1: Age with gender distribution of Patients

Group	Male	Female	Age (Years)		
			>65	18-65	8-18
n	27	13	5	31	4
%	67.50%	32.50%	12.50%	77.50%	10%

Table 2: Disease wise distribution of Patients

S No.	Disease/Surgical condition	n=40	%	Surgical intervention
1	Duodenal ulcer perforation peritonitis	23	57.50%	Graham's Omentopexy
2	Tubercular perforation peritonitis	2	5%	Ileostomy/Resection & Anastomosis
3	Appendicle perforation	3	7.50%	Appendectomy
4	Idiopathic peritonitis perforation	1	2.50%	Exploratory Laparotomy & Lavage
5	Traumatic Intestinal perforation	3	7.50%	Ileostomy
6	Perforated Hepatic abscess with peritonitis	1	2.50%	Lavage and Drain of abscess
7	Multiple bleeding polyp jejunum	1	2.50%	Resection Anastomosis
8	Inguinal hernia gangrene	1	2.50%	Herniorrhaphy with Resection & Anastomosis
9	Intestinal obstruction	3	7.50%	Resection Anasttommosis
10	Caecum perforation peritonitis	1	2.50%	Limited Right Hemicolectomy
11	Ruptured ectopic pregnancy	1	2.50%	Right Salpigiectomy Oophrectomy

MAP >60 mmHg (Table 3) Resuscitation lead to optimization of patients with 72.50% patients in ASA-3 E status and 27.50% patients remain in ASA 4 E status (Table 4) with tachycardia, tachypneoa, decreased urine output, requiring repeated ABG correction despite optimization. These patients were induced with sevoflurane. None of the patient required abandoning/modification of the induction due to coughing, aponea <20 secs (5%), agitation or dystonia or had hypotension, vomiting or aspiration, bronchospasm or arrythemias (Table 10). Only 2.5% had SpO_2 between 85%-90%

Table 3: Co morbid and Critical Physiological Status of Patient

S. No.		N=40	%
1	COPD	4	10%
2	SEPSIS	36	90%
3	Haemorrhagic shock	4	10%
4	Ischaemic Heart Disease	0	0%
5	Smokers	18	45%
6	Anaemia(Hb 10 or<10gm%)	18	45%
7	Dopamine?Noradrenaline	6	15%
8	Spo2 Opti PreIND (85-90%)	2	5%
9	Mean BP Opti. PreIND (51-60 mm)	3	5%

Table 4: American Society of Anesthesiology (ASA) Distribution of Patients

ASA – E Status	I-1	II- 2	III-3	IV-4	V-5	E
Pre Optimized	0	0	14	26	0	40
%	0	0	35%	65%	0	100%
Optimized	0	0	29	11	0	40
%	0	0	72.50%	27.50%	0	100%

Table 5: Duration of Surgical Anesthesia

Time- Minutes	80-120	121-150	151-180
N=40	32	6	2
%	80%	15%	5%

Table 6: Descriptive analysis of Preinduction with Mean Arterial Pressure, Pulseand Spo2 values.

Variables	Mean	S.D.	Minimum	Maximum
Optimized Preinduction MAP	*80.84*	*6.41*	*68.67*	*91.33*
1 min.PIND MAP	78.71	5.97	66	88
3 min.PIND MAP	85.17	4.85	74.33	93.33
5 min.PIND MAP	88.16	4.19	72.33	91.33
10 min.PIND MAP	82.11	4.42	70	90.67
15 min.PIND MAP	82.46	4.35	69.33	90
30 min.PIND MAP	82.54	3.81	77.33	90.67
60 min.PINDMAP	82.15	3.48	72	88
10 min.PETBMAP	84.9	4.09	76	94
Optimized Preinduction Pulse	*107.28*	*6.62*	*90*	*120*
1 min.PIND Pulse	105.05	6.21	90	122
3 min.PIND Pulse	109.75	5.99	96	125
5 min.PIND PULSE	104.92	4.62	93	114
10 min.PINDPulse	102.88	4.4	92	110
15 min.PIND Pulse	101.2	3.85	93	108
30 min.PINDPulse	101.5	3.55	93	108
60 min.PIND Pulse	97.5	5.76	90	112
10 min.PETB Pulse	102.42	3.43	96	108
Optimized Preinduction SpO_2	*96.05*	*2.54*	*90*	*99*
1 min.PIND SpO_2	94.52	14.07	90	99
3 min.PIND SpO_2	97.4	3.54	92	95
5 min.PIND SpO_2	97.2	1.8	92	99
10 min.PIND SpO_2	96.75	4.63	96	99
15 min.PIND SpO_2	97.95	1.43	94	100
30 min.PIND SpO_2	97.68	1.47	94	99
60 min.PIND SpO_2	97.5	1.37	94	99
10 min.PETB. SpO_2	96.18	1.8	91	99

PIND-Postinduction, PETB-Postextubation

Showing preinduction Mean BP of 80.84 mmHg. None of post induction values was less than this except at 1 minute 78.71 mmHg. None of values was below 66 mmHg.

postinduction as compare to 5% before induction. Duration of surgical anaesthesia management lasted 80 to 120 minutes in 80% of patients and 5% lasted for between 150-180 minutes (Table 5).

Preinduction optimize MAP changed significantly at 1, 3, 5, 10, 15 min. postinduction (Table 7) peaking at 3 minute postinduction (Table 6) remained above preinduction optimized basal level all the time. At preinduction 5.12% of patients had optimize MAP in range of 50-60 mmHg (Graph 1). Minimum mean MAP observed was 66 at 1 min. postinduction (Table 6).

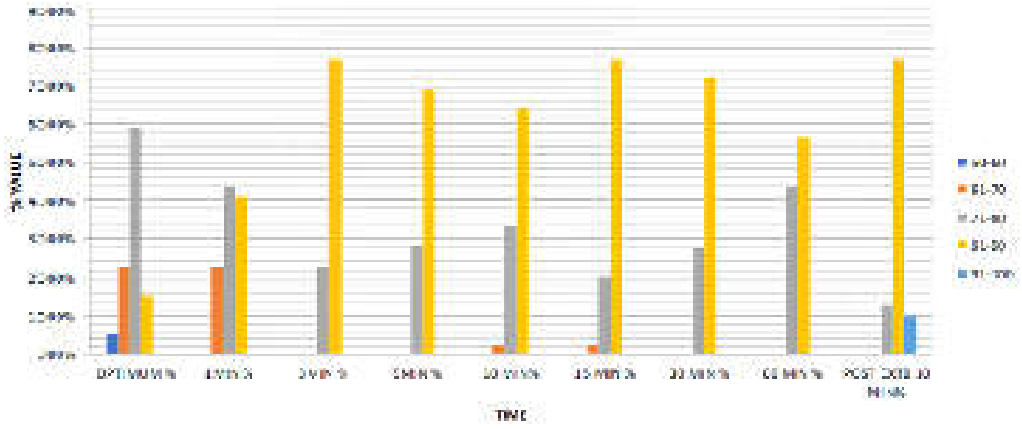
Graphic colour representation (Graph 1)showing % distribution of preinduction optimize and post induction peak MAP changes.

Changes in mean pulse values were significant at 1, 3, 5, 10 & 30 minutes postinduction as compare

Table 7: Analysis of variance between reference preinduction value of Mean Arterial Pressure (MAP) with different timing

Timing	Group	Sum of Squares	d.f	Mean Square	F	Sig.
1 min PIND MAP	Between Groups	1360.023	20	68.00	41.09	0.000
	Within Groups	31.442	19	1.66		
	Total	1391.465	39			
3 min. PIND MAP	Between Groups	835.139	20	41.76	9.63	0.000
	Within Groups	82.399	19	4.34		
	Total	917.538	39			
5 min PIND MAP	Between Groups	568.273	20	28.41	4.52	0.001
	Within Groups	119.373	19	6.28		
	Total	687.646	39			
10 min PIND MAP	Between Groups	660.929	20	33.05	6.15	0.000
	Within Groups	102.159	19	5.38		
	Total	763.088	39			
15 min PIND MAP	Between Groups	544.567	20	27.23	2.66	0.019
	Within Groups	194.804	19	10.25		
	Total	739.37	39			
30 min PIND MAP	Between Groups	367.758	20	18.39	1.74	0.116
	Within Groups	200.482	19	10.55		
	Total	568.24	39			
60 min PINDMAP	Between Groups	226.011	20	11.30	0.86	0.626
	Within Groups	248.402	19	13.07		
	Total	474.414	39			
10 min PINDMAP	Between Groups	451.143	20	22.56	2.13	0.053
	Within Groups	201.698	19	10.62		
	Total	652.841	39			

Table 7 showing significant changes in mean arterial pressure observed at 1,3,5,10 and 15 minutes post induction (PIND) as compare to preinduction. Changes were insignificatent at 30,60 postinduction and 10 min post extubation(PETB)



Graph 1: % distribution of Patients MAP in time variable
EXTB-Extubation, Optimum-Optimized or Basal preinduction

to optimize values (Table 8). None of values are less than 60 at any time. Optimize preinduction pulse depicted in (Table 6) showing peaked post induction rise at 3 minute postinduction (Table 6).

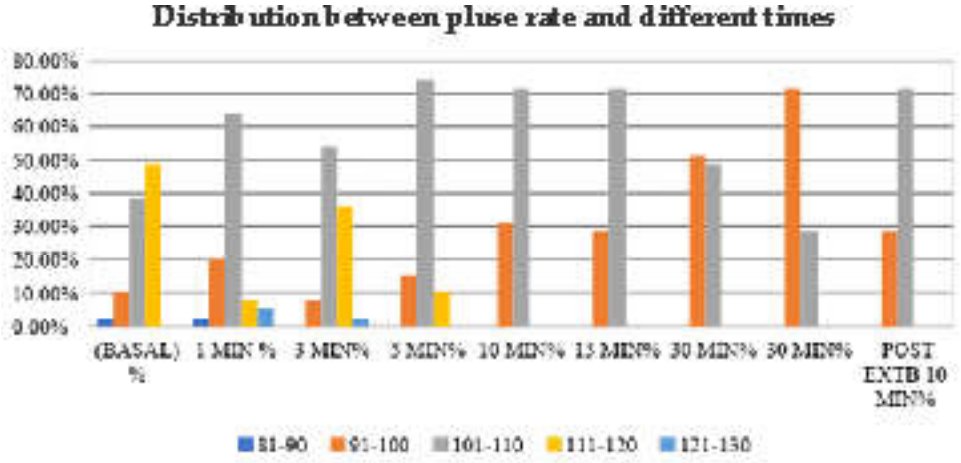
Except at 1 amd 15 min. changes in mean SpO_2 were significant at all times (Table 9) As compare to 5% preinduction only 2.50% of the patient had SpO_2 between 85%-90% range postinduction (Graph 3).

No airway complication reported (Table 10) except cough and apnonic episodes of <20 sec in 5% of patients without any modification or abandoning of induction process.

Table 8: Analysis of variance between preinduction pulse with different timing

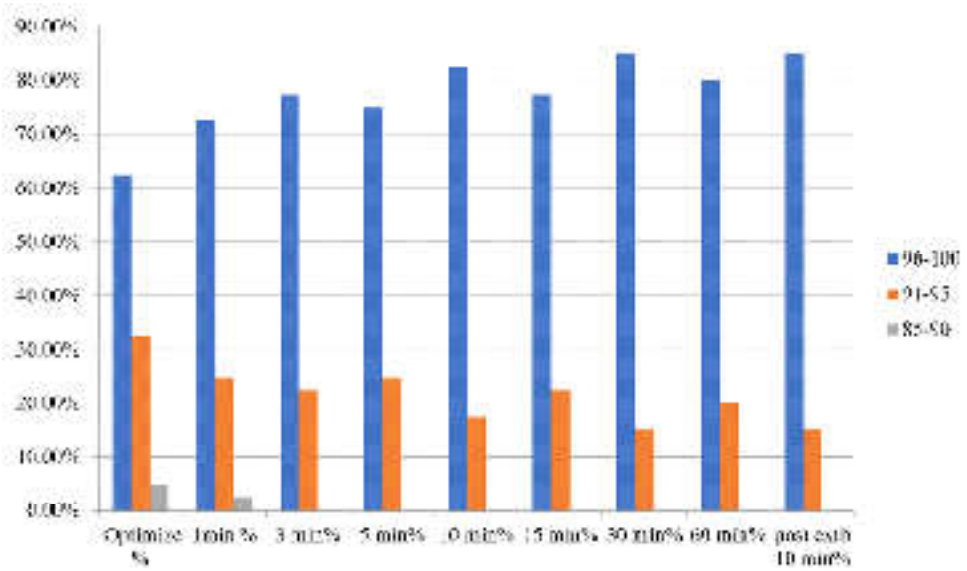
Timing	Variable	Sum of Squares	df	Mean Square	F	Sig.
1 min.PIND Pulse	Between Groups	1402.67	15	93.51	21.33	0.000
	Within Groups	105.23	24	4.39		
	Total	1507.90	39			
3 min.PIND Pulse	Between Groups	1228.82	15	81.92	11.52	0.000
	Within Groups	170.68	24	7.11		
	Total	1399.50	39			
5 min.PIND Pulse	Between Groups	716.54	15	47.77	9.86	0.000
	Within Groups	116.23	24	4.84		
	Total	832.78	39			
10 min.PIND Pulse	Between Groups	599.63	15	39.98	6.12	0.000
	Within Groups	156.75	24	6.53		
	Total	756.38	39			
15 min.PIND pulse	Between Groups	323.23	15	21.55	2.03	0.059
	Within Groups	255.17	24	10.63		
	Total	578.40	39			
30 min.PIND Pulse	Between Groups	321.23	15	21.42	2.98	0.008
	Within Groups	172.77	24	7.20		
	Total	494.00	39			
60 min.PIND Pulse	Between Groups	425.27	15	28.35	0.78	0.685
	Within Groups	870.73	24	36.28		
	Total	1296.00	39			
1 0 min.PETB Pulse	Between Groups	191.59	15	12.77	1.14	0.374
	Within Groups	268.18	24	11.17		
	Total	459.78	39			

Table 9 showing significant changes in pulse at 1, 3, 5, 10, 15 and 30 minutes as compare to preinduction optimize values. None of the time pulse rate was less than 60bpm.
PIND-Post Induction, PETB-Postextubation, min-minute



Graph 2: % Distribution of patient pulse rate in time variables

BASAL-Optimized Preinduction, Min-Minutes, EXTB-Extubation



Graph 3 % Distribution of patients spo2 in time variables

Min-Minutes, Extb.-Extubation, Optimize-Optimize Preinduction or Basal

Table 9: Analysis of variance between preinduction SPO2 with different timing

Timing	Variable	Sum of Squares	df	Mean Square	F	Sig.
1 min.PIND Spo2	Between Groups	1097.876	8	137.24	0.64	0.737
	Within Groups	6628.099	31	213.81		
	Total	7725.975	39			
3 min.PIND Spo2	Between Groups	239.419	8	29.93	3.71	0.004
	Within Groups	250.181	31	8.07		
	Total	489.6	39			
5 min.PIND Spo2	Between Groups	109.388	8	13.67	24.92	0.000
	Within Groups	17.012	31	0.55		
	Total	126.4	39			
10 min.PIND Spo2	Between Groups	160.508	8	20.06	0.92	0.514
	Within Groups	676.992	31	21.84		
	Total	837.5	39			
15 min.PIND Spo2	Between Groups	59.938	8	7.49	11.64	0.000
	Within Groups	19.962	31	0.64		
	Total	79.9	39			
30 min.PIND Spo2	Between Groups	58.454	8	7.31	8.61	0.000
	Within Groups	26.321	31	0.85		
	Total	84.775	39			
60 min.PIND Spo2	Between Groups	44.555	8	5.57	5.86	0.000
	Within Groups	29.445	31	0.95		
	Total	74	39			
10 min.PETB Spo2	Between Groups	102.797	8	12.85	16.48	0.000
	Within Groups	24.178	31	0.78		
	Total	126.975	39			

Significant changes in SpO_2 at all time except 1 and 10 minute postinduction.
PIND-Postinduction, PETB-Postextubation, SpO_2-Oxygen Saturation

Table 10: Postinduction -Perioperative Complication/Critical Incidence

Complication/ Critical incidence	Coughing/ Apnea<20s	Hypotension MAP<60 mmHg	Spo2<90%	Dystonia /Vomiting	Additional intervention	Abandoning/Modify Induction
Patients N=40	2	NIL	1	NIL	NIL	NIL
%	5%	0	2.5%	0	0	0

Discussion

Rationale of study is to utilize inhalational induction charateristices of sevoflurane i.e. non pungency and low blood gas solubility [1] and haemodynamic stability. Within 60 secs loss of eyelid reflex and conscious occurs with sevoflurane standard techniques of induction [10]. This retrospective study analysed sevoflurane induction of anaesthesia in critically ill patient undergoing emergency laparotomy. Most of the patients were in ASA 4 E status (65%). As table-1 showing majority (67.50%) were male, 77.50% patients were in age group of 18 to 65 years. Age affects MAC of sevoflurane and in critically ill patient require adjustment of % MAC is desirable particularly above 60 years. 6% sevoflurane instead of 8% above 65 years (15%) in critically ill at induction. 57.50% patients were of duodenal perforation peritonitis (Table 2) may be chornic smoking (45%) contribution to high incidence. Associated comorbid state sepsis (90%), haemorrhagic shock (10%), chronic smoker (45%) COPD (10%) and anaemia (45%) (Table 3). None had coronary artey disease or arrythemias clinically.

These patients were resuscitated to optimize their physiological and comorbid status from ASA4 E (65%) before induction to ASA 3E (72.50%) post optimization (Table 4) with fluid, colloids, blood and ionotrops like dopamine and noradrenaline. 5% patient had Spo2 85%-90% before induction (Table 9) Dopamine or noradrenaline required before induction in 6% of patients to maintain MAP 60 or above though 5.12% had MAP between 50-60 mmHg preinduction despite optimization before induction (Table 10).

Sevoflurane induction done using Mapelson D circuit with flow rate 80 to 100 ml/kg. This low flow compare to 100 to 200 ml/Kg allowed rebreathing to occur to maintain spontaneous respiration for faster induction [10]. This has the advantage that it allows ventilation to be sustained when consciousness is lost and specific maneuvre such as breath - holding or vital capacity breaths are not required to facilitate induction of anaesthesia as patients were critically ill [8]. After preoxygenation with 100% oxygen, stepwise increase addition of sevoflurane in increment of 1%, 2%, 4% and 8% every 2 breath allows an anaesthetist to assess airway patency and assist ventilation [2]. In such high concentration in emergency patients [14] inhalational induction of anaesthesia may parallel the speed of intravenous induction [10]. Induction with an initial concentration of 8% sevoflurane produces more rapid passage through the excitatory stage possibly resulting in fewer adverse events [15]. Maintainence of spontaneous ventilation is definitive advantage of sevoflurane particularly with potentially difficult airway in such critically ill patients [2,15]. Patient that had airway complication (Table 9) as coughing, laryngospasm, apnoea <20 sec (5%) resulting in abandoning or modifying induction were nil in our study indicating smooth induction charateristics of sevoflurane (Table 10) Nitrous oxide may add little to the efficacy of inhalational induction [16] though we have added 50% nitrous oxide to induction after achieving 8% sevoflurane concentration. Sevoflurane may be delivered in high inspired concentration without much airway complication may be attributed to a more rapid passage to a deeper plane of anaesthesia not associated with awareness [10]. Bronchodilator properties of sevoflurane have additional advantages in patients with COPD (10%) and chronic smoker (45%) and not associated with increased secretions, allergy and anaphylaxis. Only 2.5% had SpO_2 between 85%-90% postinduction as compare to 5% before induction Post induction only 2.5% of patient had SpO_2 in between 85 to 90% that to improved after 1 minute post induction showing beneficial effects of sevofluration induction (Graph 3). This improvement in SpO_2 observed due to its bronchodilatation properties, loss of pain, improving ventilation, application of PEEP and or positive pressure ventilation with improve oxygenation in basal atelectic lungs suggesting sevoflurane induction does not influence SpO_2 adversly if oxygenation ventilation is maintained during induction. Changes in SpO_2 were significant at perioperative period except 1 minutes and 15 min. though none of patient had SpO_2 less than 90% post induction anytime after one minute during perioperative period. Sevoflurane do affect ventilation perfusion significantly in hypoxic conditions [17]. Whether this result of SpO_2 fluctuation during perioperative period after 1 minute though within normal limits in patients is due to peripheral vasoconstriction or dilatation or changes in patient temperature reason is largely speculative critical ill.

As SpO_2 never below 90% after 1 min post induction. No active intervention required and positive pressure ventilation maintained with low PEEP of 2-4 mmHg with 35%-50% oxygen with nitrous oxide during perioperative management of patients.

Most intravenous anaesthetic agents as thiopental, propofol, midazolam may associated with haemodynamic instability in critically ill

patients. 90% patient were in sepsis and 10% in haemorrhagic shock in our study. In heart of septic rats maximal cardiac work dysfunction occurred in the order ketamine -6%, < etomidate -< 17%, midazolam 38% < profofol -50% as reported by Zausig et al. [13]. Etomidate has good haemodynamic induction profile but associated with adrenal suppression [13].

Ketamine is associated with undesirable psychotomimetic effects like illusion, delirium and disturbing dreams making assessment difficult after extubation and in ICU which is not observed with sevoflurane due to faster recovery from anaesthesia without any residual sedation or psychomimatic effects.

Postinduction mean MAP remain above preinduction mean values (except 66 mmHg at 1 min.) throughout peri-operative period. 5.12% of patients were in MAP 50-60 mmHg range before induction though none had MAP <60 mmHg (Table-9) post induction (Graph 2). This study found that changes in Mean Arterial Pressure (MAP) response were significant (Table 7) at 1 to 15 minutes post induction of anaesthesia. MAP peaked at 3 and 5 minutes post induction suggesting sevoflurane unable to inhibit adrenergic response of intubation though none of patient had MAP below 66 mmHg at any time showing haemodynamic stability with sevoflurane. Changes in pulse from optimize preinduction value to postinduction at 1 to 30 minutes post induction were significant (Table 8) peaking at 3 min postinduction. None of pateint had bradycardia or arrythemias (Table 10).

Sevoflurane induction result in increase in MAP and heart rate (Table 6,7,8) due to uninhibited sympathoadrenal responses of endotracheal intubation as though sevoflurane itself does not affect haemodynamics. At 1.5 MAC sevoflurane do not prevent haemodynamic response of incision. None of patient had bradycardia or MAP <60 mmHg. There is no increase in requirement of dopamine or noradrenaline support after induction of anaesthesia with sevoflurane. Its non arrythemogenic properties is particular value in critically ill patient with high catecholamine levels levels. Haemodynamic effects of sevoflurane voatile anaesthetic with N_2O are minimal compared with those of equi-MAC alone [12]. A CVP guided haemodynamic management, more potent short acting analgesic like fentanyle [18,19] may have more optimize anaesthetic management with sevoflurane induction attenuating haemodynamic responses in such patients though we did not find any hypotension or bradycardia or arrythemias or increased requirement of vasopressors with sevoflurne induction in such critically ill. Incidence of postoperative ventilator requirement or metabolic derangements which may likely to occur due to haemodynamic instability and residual sedation may be reduced. Sevoflurane has faster recovery characteristic as compare to ketamine, opiates and no adrenal suppression as compared to etomidate. Thus rational of sevoflurane has advantage of faster induction, haemodynamic stability [5], no adrenal suppression and quick recovery in emergent situations minimizing use or additional vasopressors to maintain haemodynamices in critically ill [13].

Conclusions

Sevoflurane has advantages of rapid inhalational induction, bronchodilation and relative haemodynamic stability and faster recovery [20,21]. This study concludes that sevoflurane likely to be agent of choice for anaesthetic induction and management of critically ill patients in emergency with rapid induction without airway complications, minimum haemodynamic disturbances, least requirement of vasopressors, early recovery in emergency laparotomy with all prophylaxsis to prevent aspiration. Sevoflurane unable to attenuate adrenergic responses of laryngoscopy and endotracheal intubation.

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Comparison of Epidural Levobupivacaine 0.125% with Fentanyl 2 mcg/ ml and Levobupivacaine 0.125% Alone for Postoperative Pain Management

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Abstract

Introduction: The aim of the study was to compare effectiveness of single dose epidural 0.125% levobupivacaine with fentanyl 2 mcg/ml and 0.125% levobupivacaine alone in patients undergoing elective lower limb orthopaedic surgery. *Methodology:* We designed a prospective, randomized, double blind study, in which 60 patients with ASA1 and ASA2 were scheduled to undergo elective lower limb orthopedic surgery. Group A received single epidural block with 8 ml of 0.125% levobupivacaine and Group B received epidural block with 8 ml of 0.125% levobupivacaine and 2 mcg/ml fentanyl. Duration of analgesia, Quality of analgesia, Degree of motor blockade, sedation score, hemodynamic changes and side effects were assessed. *Results:* Duration of postoperative analgesia for group B (366±39.70 min) was longer as compared to group A (236±34.99 min). Quality of anaesthesia was significantly better in group B as compared Group A. *Conclusion:* We conclude that addition of fentanyl 2 mcg/ml to epidural 0.125% levobupivacaine produces significantly better quality and longer duration of postoperative analgesia, good hemodynamic stability and no side effect as compared to 0.125% levobupivacainealone in patient undergoing elective lower limb orthopedic surgeries.

Keywords: Levobupivacaine; Fentanyl; Postoperative Pain.

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Introduction

Lower limb orthopedic surgeries are common in many elderly patients and these surgeries are considerably more painful than other general surgeries. The pain can cause immense suffering to the patient and also alter physiological functions induced by hormonal changes. The increased sympathetic nervous system activity can stress the heart due to high blood pressure and/or rapid heart rate. This can increase the risk of myocardial ischemia because the myocardial oxygen

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demand exceeds its supply. For this reason, early postoperative pain control should improve the outcome of lower limb orthopedic surgery.

The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain and reduced cost of care. The failure to provide good postoperative analgesia is multifactorial. Insufficient education, fear of complications associated with analgesic drugs, poor pain assessment, and inadequate staffing are among its causes. Poorly controlled acute postoperative pain may be an important predictive factor in the development of pathologic long-term chronic pain after surgery [4,5]. Control of acute postoperative pain may improve long-term recovery or patient-oriented outcomes (e.g., quality of life). Patients whose pain is controlled in the early postoperative period (especially with use of continuous epidural or peripheral catheter techniques) may be able to actively participate in postoperative rehabilitation, which may improve short- and long-term recovery after surgery [6,7]. Epidural analgesia is one of the most effective regimens for post-operative pain relief after lower limb surgeries. Epidural infusion of local anesthetic alone may be used for postoperative analgesia. However, epidural local anaesthetic administered alone have never become widely used for routine postoperative analgesia because of the significant failure rate resulting from regression of the sensory block and the unacceptable incidence of motor blockade and hypotension [8]. A variety of adjuvants may be added to epidural infusions to enhance analgesia while minimizing the side effects and these include mainly Opiates, Ketamine, Clonidine, Benzodiazepines etc. But no single drug has proved to be devoid of any side effect. Search for an ideal adjuvant still continues that could result in reliable prolongation of postoperative pain relief without side effects. Levobupivacaine is a pure 5 - enantiomer of racemic bupivacaine [9]. They were developed mainly to overcome the fatal cardiotoxicity associated with bupivacaine, which is a well-established local anaesthetic whose one of the main use is postoperative pain management through epidural route. The benefits of addition of opiate to postoperative epidural levobupivacaine infusion is controversial. Fentanyl has emerged as a suitable opioid for infusion into epidural space. Advantages of fentanyl over other opioids are that it easily crosses lumbar dura and quickly penetrates the lipid phase of underlying tissue of the cord as it is more lipophilic. Since not many studies have been done to compare the effects of adding fentanyl to epidural levobupivacaine 0.125% for postoperative analgesia after major orthopedic surgery. Therefore we conducted this study in order to evaluate epidural levobupivacaine 0.125% with fentanyl 2μg/ml is compared with levobupivacaine 0.125% alone with regard to the effectiveness in postoperative analgesia, onset of action and hemodynamic changes in patient undergoing elective lower limb orthopaedic surgery.

Aims and Objectives

To compare the effectiveness of epidural 0.125% levobupivacaine with fentanyl 2μg/ml and 0.125% levobupivacaine alone in patients posted for elective major orthopaedic surgeries regarding: Duration of analgesia, Quality of postoperative analgesia, Hemodynamic changes: blood pressure and heart rate, Any adverse effects.

Material and Methods

This prospective randomized double blind study was conducted on 60 patients aged between 20-60 years of either sex belonging to ASA class I and class II posted for elective major orthopedic surgeries at M.G.M. Medical College, Kamothe, Navi Mumbai were selected for the study. The study was conducted from January 2016 to January 2017. The study population was randomly divided into two groups with 30 patients in each group (n=30). Group A: Epidural block with 8 ml of 0.125% levobupivacaine, Group B: Epidural block with 8 ml of 0.125% levobupivacaine + 2 μg/ml fentanyl. Preoperative assessment was done for each patient and informed consent was taken. Intravenous line was obtained with 18 G i.v cannula and was preloaded with ringer lactate 500 ml half an hour before anaesthesia. The patients were randomly divided into two groups as designed above and demographic data was noted. Baseline vital parametres were noted. After pre anaesthetic checkup patient were kept fasting from previous night and premedicated with tablet ranitidine 150 mg and tablet alprazolam 0.5 mg. Patients were placed in sitting position. Under aseptic precautions, epidural space was identified at L2-L3 using 16G Tuohy's needle by loss of resistance technique, epidural catheter inserted into the epidural space and fixed 3 cm inside epidural space. The epidural catheter will be tested for intravascular or subarachnoid placement

with 3 ml of 2% lidocaine containing 1:200000 epinephrine. After epidural catheter insertion, spinal anaesthesia was given with 0.5% hyperbaric bupivacaine 10-12 mg. Once surgery is completed patient was shifted to postoperative room, pain was assessed using visual analogue scale (0= no pain till 10= maximum pain) and motor blockade assessed using modified Bromage scale. Once the patient gives VAS score as 4, the test drug was injected through epidural catheter. Now patient is evaluated for post-operative pain at rest and upon movement using VAS score. Sensory block was assessed bilaterally by pin prick method with a short bevelled 27G needle. Haemodynamic changes and motor blockade checked every 5 mins upto 30 min and every half hour thereafter. The following parameters were assessed postoperatively At the end of the operation, the quality of analgesia was assessed according to the VAS score: Time taken for reappearance of VAS score 4 from the time of injection was considered as total duration of post-operative analgesia. Degree of Motor Blockade was assessed according to modified Bromage scale. Modified Bromage scale. The level of sedation was assessed using the sedation score described by Chernik et al a follows: Grade 0: Wide awake, Grade I: Sleeping comfortably, responding to verbal commands., Grade II: Deep sleep, but arousable, Grade III: Deep sleep, not arousable. The parameters such as heart rate, non invasive blood pressure, ECG and Spo2 were periodically monitored every 5 mins upto 30 min and every half hour thereafter.

Statistical Analysis All the collected data was entered in Microsoft Excel sheet and then transferred to SPSS software ver. 17 for analysis. Qualitative data was presented as frequency and percentages and analysed using chi-square test. Quantitative data was presented as mean and SD and compared by t-test. P-value < 0.05 was taken as level of significance.

Results

Table 1: Preoperative hemodynamic parameters amongst different study population

Preoperative	Group A	Group B	P value
SBP	124.73 ± 9.8	125.3 ± 6.4	0.38
DBP	78 ± 9	80.83 ± 5.9	0.17
Pulse	80.3 ± 9	85.13 ± 10	0.056
RR	13.37 ± 1.3	12.87 ± 0.9	0.101
SpO2	99.53 ± 0.73	99.43 ± 0.7	0.597

Both groups were comparable in respect to mean age, sex, height, weight, ASA grading. There was no significant changes in systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and peripheral oxygen saturation (SpO_2) of the patients in both groups pre and post operatively (Table 1).

Table 2: Duration of action amongst different study population

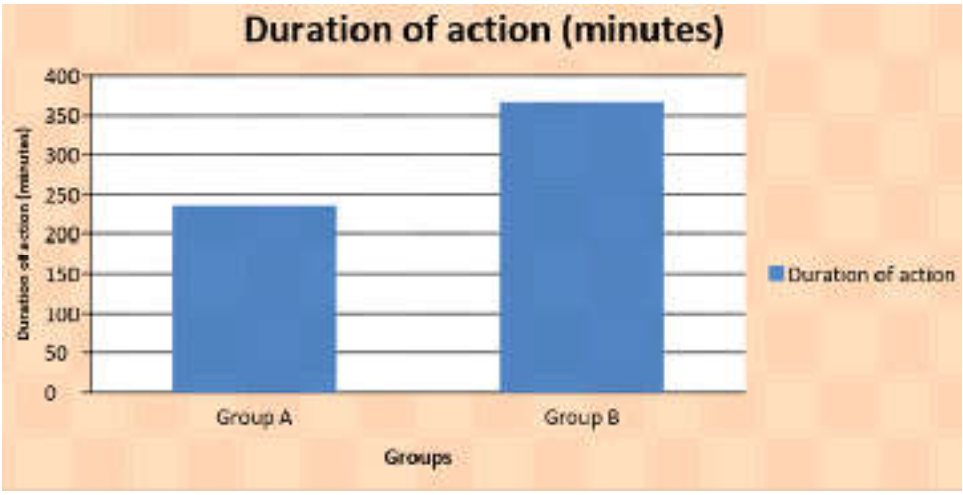
Duration of action	Group A	Group B	P value
Duration of action	236.00 ± 34.99	366 ± 39.7	0.0001

As seen in the above table 2, duration of action was significantly longer in group B (366±39.70 min) as compared to Group A (236±34.99 min). (Graph 1)

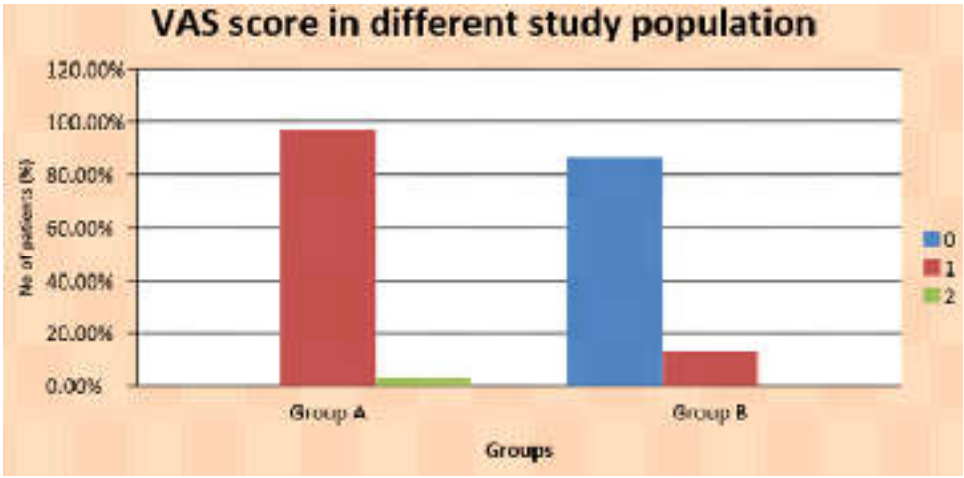
Table 3: Quality of analgesia amongst different study population

VAS Score	Group A	Group B	Total
0	0 (0%)	26 (86.7%)	26 (43.3%)
1	29 (96.7%)	4 (13.30%)	33 (55%)
2	1 (3.3%)	0 (0%)	1 (1.7%)
Total	30 (100%)	30 (100%)	60 (100%)

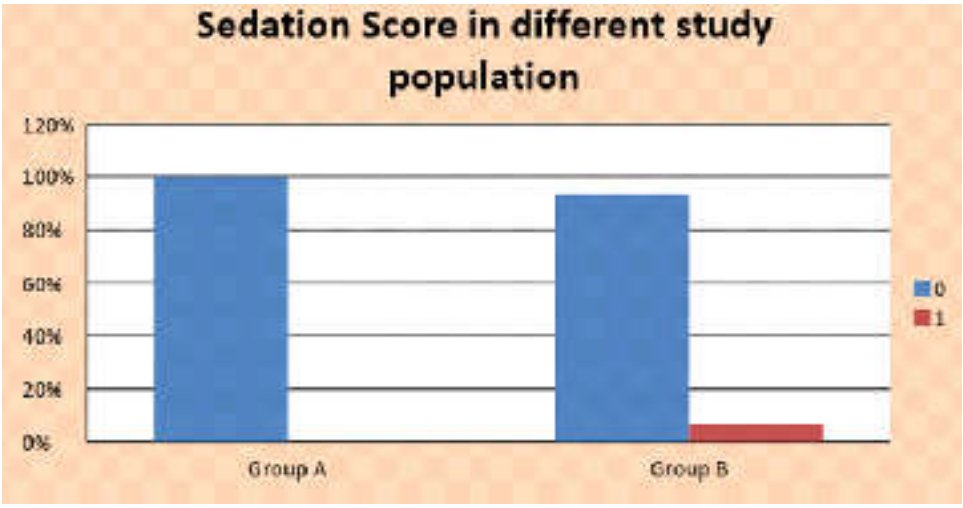
As seen in the above table 3, quality of analgesia



Graph 1: Duration of action amongst different study population



Graph 2: Quality of analgesia amongst different study population



Graph 3: Sedation Score amongst different study population

was better in Group B as compare to Group A. No motor blockade was noted in either of the groups. (Graph 2)

Table 4: Sedation Score amongst different study population (Graph 3)

Sedation Score	Group A	Group B	Total
0	30 (100%)	28 (93.3%)	53 (96.67%)
1	0 (0%)	2 (6.70%)	7 (3.3%)
Total	30 (100%)	30 (100%)	60 (100%)

Discussion

The benefits of adequate postoperative analgesia are many and include a reduction in the postoperative stress response, a reduction in postoperative morbidity and in certain types of surgeries postoperative analgesia leads to improvement in surgical outcome [10,11]. Other benefits of effective regional analgesic techniques include reduced pain intensity, decrease in the incidence of side effects from analgesics and improved patient comfort [12]. Orthopedic surgery associated with intraoperative and postoperative pain can stimulate the stress response and autonomic system. It may cause various complications such as myocardial ischemia, thromboembolic phenomena, impaired pulmonary function, ileus, fatigue and muscle catabolism.

Role of epidural analgesia is well known. It provides satisfactory analgesia and very minimal side effect. It is very effective in relieving intraoperative and postoperative pain after major upper abdominal, thoracic and orthopedic surgeries. Epidural analgesia technique has welcomed in labour analgesia because it reduces the pain and sympathetic response without any motor deficit. Epidural analgesia provides analgesia and helps in early mobilization in postoperative period

and allow to resume early routine activity. Epidural analgesia for postoperative analgesia will give specific advantages like reduced requirement for systemic opioids hence less side effect associated with it and leads to early return of bowel function. The side effects or complications associated with epidural analgesia might be related to procedure or drug like dural perforation, epidural hematoma, infection, urinary retention, hypotension, pruritus and respiratory depression. The benefit of adequate epidural analgesia includes improved respiratory function, decrease in postoperative cardiac complication, decreased chances of deep vein thrombosis. Most commonly used local anaesthetic for epidural analgesia in India are bupivacaine and Lignocaine. Drawback of lignocaine is its intermediate duration of action and bupivacaine is its cardiotoxicity. Though bupivacaine has fair safety profile, currently it is replaced by newer local anesthetics: levobupivacaine and ropivacaine. These newer local anesthetics have less risk for cardiac and central nervous system toxicity and less postoperative motor blockade [13,14]. Levobupivacaine is a long acting local anaesthetic and the pure S (-) enantiomer of racemic bupivacaine, is an effective and safer alternative local anaesthetic in epidural analgesia. Levobupivacaine has a lower risk of cardiovascular and CNS toxicity than bupivacaine [15]. Various studies have been done using different concentration of levobupivacaine like in study by De Negri et al., compared epidural bupivacaine, levobupivacaine and ropivacaine on postoperative analgesia and motor blockade in patient undergoing hypospadias surgery and found that there is no motor blockade associated with 0.125% levobupivacaine whereas bupivacaine associated with postoperative motor blockade in 20% of patient. Good quality of analgesia was observed in patient given 0.125% levobupivacaine [16].

S.J.V. Kameshwara Rao et al., in their study compared 0.5% bupivacaine with 0.75% ropivacaine and 0.5% levobupivacaine in sub umbilical surgeries under epidural anaesthesia and found high concentrations of these drugs were associated with significant hypotension, motor blockade and high incidence of side effects [17]. We chose levobupivacaine concentration of 0.125% because low concentration of local anaesthetic is not associated with unwanted postoperative motor blockade, provide satisfactory analgesia and less incidence of side effects. Use of combined local anaesthetic and an opioid in epidural analgesia may have advantages over local anaesthetic or opioid alone. It provides better postoperative analgesia, prolongs sensory block, decreases the dose of local anaesthetic and incidence of side effects are also reduced [18]. It is unclear whether the analgesic effect of local anaesthetic and opioid in the epidural analgesia is additive or synergistic. The choice of opioid also varies, although many clinicians choose to use a lipophilic opioid fentanyl 2 mcg/ml. Cooper DW, Turner G et al., in their study concluded that combination of epidural local anesthetic and fentanyl has better analgesic actions and reduces the requirements of each individual agent. Therefore we have combined local anaesthetic along with fentanyl [19]. Gaurav S. Tomar et al., in their study concluded that addition of fentanyl 2 mcg/ml to 0.125% bupivacaine decreases the time of onset of analgesia and prolonged duration of analgesia along with better level of maternal satisfaction during labour as compare to 1 mcg/ml fentanyl [20]. Hence in our study we chose to evaluate the effect of adding inj fentanyl 2mcg/ml to epidural 0.125% levobupivacaine will result in no motor blockade with adequate analgesia and lesser incidence of side effect. Thus the aim of this investigation was to compare the effect of a postoperative single epidural dose of these two local anaesthetic drugs on motor blockade and pain relief after lower limb orthopedic surgery. Duration of Post Operative Analgesia: All patients were given bolus dose of epidural after appearance of VAS score of 4 and the VAS score was again assessed after giving bolus dose of epidural. Following the dose, VAS score reduced to either 0,1 or 2 in most of the patients among both the groups. In the present study, duration of postoperative analgesia for group A was 236±34.99 min and for Group B 366±39.70 min. Hence, the mean duration of postoperative analgesia was significantly longer in Group B as compared to Group A. Our findings correlate well with the studies conducted by Gaurav S. Tomar et al., [20] and Danyalönal et al, [21] in which levobupivacaine with opioid group had longer duration of postoperative analgesia after surgery as compared to levobupivacaine group alone.

Quality of Analgesia: In our study, VAS score of 1 and 2 was observed in 96.7% and 3.3% patients in Group A respectively while in group B 86.7% patients had VAS score of 0 and 13.3% patient had VAS score 1 following epidural bolus. Thus the difference was statistically significant. Lee Wai- Keung et al. [22] and Bayazit EG et al. [23], concluded that pain relief was significantly better in the ropivacaine/fentanyl group after the first hour and this difference lasted for the remaining time. The quality of analgesia was significantly improved

by addition of fentanyl 1 µg/ml to local anaesthetic in their study. This findings is in agreement with the study conducted by Paraskevi Matsota et al. [24]. it was concluded that the combination of ropivacaine 0.15% with fentanyl 2 µg/ml appeared superior as it provided higher patient satisfaction. Sedation Score: In our study, in group A all patients were wide awake whereas In group B 76.7% patients were wide awake and 6.7% patients had grade 1 sedation score. This difference was statistically not significant. This result well correlates with study conducted by Kopacz et al. [25].

Motor Blockade: No motor block was observed in any patient in both the groups. De Negri P et al., concluded that significantly less unwanted motor blockade was associated with postoperative epidural analgesia of 0.125% levobupivacaine in children after hypospadias repair as compared with a similar infusion of bupivacaine [16].

Haemodynamic Changes: There was no significant difference amongs two group with respect to Systolic blood pressure, diastolic blood pressure, heart rate, respiratory rate and SpO_2 at any time interval. None of the patients showed systolic pressure decrease of more than 20% of the value after epidural bolus [26].

Side Effect: None of our patients experienced respiratory depression, headache, urinary retention. In our study, side effect like Pruritus and nausea was observed 6.7% and 10% in group B respectively and no patient in group A complained of prutritus or nausea. This difference was statistically not significant [27,28].

Conclusion

We conclude that addition of fentanyl 2 mcg/ml to epidural 0.125% levobupivacaine produces significantly both quality and longer duration of postoperative analgesia as compared to 0.125% levobupivacaine alone in patient undergoing for elective lower limb orthopedic surgeries.

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Evaluation of Postoperative Analgesic Requirement in Patients Undergoing Surgery with Buprenorphine Transdermal Patch

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Abstract

Introduction and Aims: Transdermal drug delivery is a simple non-invasive and compliant method. It provides a sustained drug release. The aims of this study was to assess the analgesic requirement of patients under General Anesthesia postoperatively after application of Buprenorphine Transdermal patch preoperatively, to assess added analgesic sparing effect, and to assess anxiety level and post extubation discomfort after surgery. *Methods and Materials:* In this prospective randomized controlled study sixty adult patients, undergoing elective open surgery under General Anesthesia were randomized into 2 groups: Group C (control group) receiving conventional intravenous analgesics, and Group B (study group) receiving transdermal Buprenorphine patch of 10 mcg/hr. All patients were monitored for vital parameters, VAS, MRSS, rescue analgesic requirement and adverse effects till fifth postoperative day. The data was analysed statistically using 't' test. *Results:* Number of patients requiring postoperative rescue analgesics was higher in group C. Total number of drug doses given in group C was also higher. Haemodynamic parameters were statistically insignificant in both groups at all time periods. VAS score was significantly less in group B till POD2, after which VAS was less in Group B, though not significant. MRSS scale was higher in Group B throughout postoperative period and at time of emergence. Number of patients having adverse effects was slightly high in group B but comparable in both groups. *Conclusion*: Transdermal buprenorphine patch is effective for postoperative analgesia for elective abdominal and head neck oral surgeries under General Anesthesia. It can reduce requirement of rescue post operative analgesics over atleast five days and maintain hemodynamic stability without serious complications.

Keywords: Buprenorphine; Transdermal patch; Rescue analgesia; Elective surgery.

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Introduction

Effective control of post operative pain is a necessary component of perioperative patient management, which calls for a multidimensional approach. Transdermal drug delivery is a simple non-invasive and compliant method. It provides a steady and sustained drug release. It overcomes

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the pharmacokinetic problems of oral and parentral methods [1].

Buprenorphine is a partial agonist opioid, acting at the mu receptors. It also has antagonistic activity at kappa opioid receptors, and a ceiling analgesic effect [2]. It has high lipid solubility, hence, highly effective through transdermal route.

Aims and Objectives

The aims of this study was to assess the analgesic requirement of patients postoperatively after application of Buprenorphine transdermal patch preoperatively in patients undergoing surgery under General Anesthesia, and to assess the analgesic sparing effect of the patch.

Methods and Materials

A prospective randomized controlled study was done in our institute between March 2015 to August 2016. After approval from Institutional Research Committee, a total of sixty ASA grade 1/2 physical status patients, of either sex, between ages of 18 to 60 years undergoing elective open surgery under General Anesthesia were included in the study. Informed written consent was obtained from all the patients. Patients exclusion criteria were ASA 3/4 physical status, opioid-dependent and sensitive patients, patients on antidepressants, or history of psychiatric illness, compromised cardiorespiratory function, pregnancy, skin allergy and refusal to consent.

Patients were randomized into 2 groups (1;1 randomization): Group C (control group), and Group B (study group), with thirty patients in each group.

Pre-anesthetic check up was done for all patients one day prior to surgery, during which they were explained about study and VAS (Visual Analogue Scale of 0 to 10, with 0 showing no pain and 10 showing extreme pain) score.

Buprenorphine transdermal patch of 10 mcg/h was applied 12 hours prior to surgery for every alternate patient, on hairless sites, most commonly upper outer arm, chest, upper back or side of chest.

On day of surgery, all baseline vital parameters (pulse rate, blood pressure, SpO_2) were recorded. VAS and MRSS (Modified Ramsay Sedation Score) scales were also noted. In OT, after securing intravenous line, and standard monitors, all patients were given anesthesia with uniform protocol. Inj. Fentanyl in dose of 0.5mcg/kg IV was supplemented when required. All group A patients were given Inj. Paracetamol 1 gm (in 100 ml NS) and Inj. Diclofenac 75 mg (in 100 ml NS) IV slowly as analgesics. At end of surgery, all patients were extubated after reversal of residual neuromuscular blockade with IV Inj Neostgmine 0.03-0.05 mg/kg and Inj. Glycopyrollate (0.4 mg), and after confirming adequate recovery of tone, power and consciousness. Patients were shifted to postoperative recovery area and monitored till shifted to ward.

Vital parameters and MRSS and VAS scores were recorded at time of emergence from anesthesia, then post-operatively at 1 hr, 4 hr, 8 hr, 12 hr, 24 hr, then on third, fourth and fifth day of surgery. In Control group, Inj. Paracetamol 1gm IV TDS was given till fifth day of surgery for routine analgesia. Rescue analgesic (inj Diclofenac 75 mgIV in 100 ml NS slowly) was administered when VAS>/=2 in both groups. Patients were also observed for any complication or side-effects due to drugs such as nausea, vomiting, application rash, constipation, headache, respiratory depression, till fifth day of surgery.

The analgesic efficacy of Buprenorphine transdermal patch (TDB) was evaluated by comparing total number of added analgesics in postoperative period till postoperative fifth day in both groups, apart from associated haemodynamic changes, and VAS. Safety of TDB was assessed by monitoring side effects such as nausea, vomiting, constipation, headache and serious complications such as respiratory depression. Level of sedation was assessed via MRSS (Modified Ramsay Sedation Scale, 1-awake, 2-lightly sedated, 3-moderately sedated, 4-deeply sedated, 5-responds only to painful stimuli, 6-unresponsive.). All the untoward side effects were managed accordingly.

The data was analysed statistically using 't' test.

Results

Total 60 patients were studied, (30 patients in each group), from the time of Preanesthetic Checkup and preoperative area till fifth postoperative day. In both groups, demographic characteristics such as age, sex, ASA status, duration of surgery were comparable.

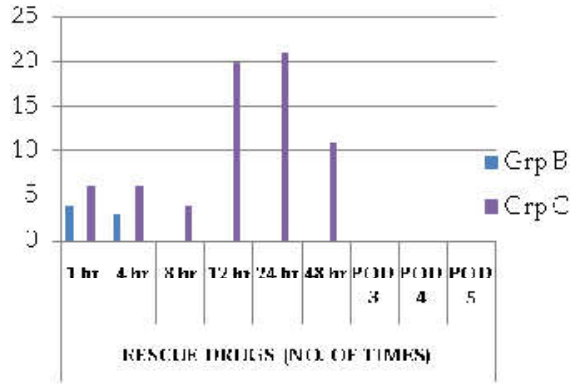
Table 1: Demographics

Demographics	Group B	Group C
No. of Males	11	12
No. of Females	19	18
Avg. Age (in years)	40.4	39.1
Avg. Duration of Surgery (Hours)	3	2.766

There was no significant difference in preoperative VAS score and vital parameters, that is, pulse rate, SBP, DBP and SpO_2, between the two groups ($p \leq 0.05$). Haemodynamic parameters were statistically insignificant in both groups at all time periods (emergence and postoperatively), though bit more stable in buprenorphine group. Number of patients requiring postoperative rescue analgesics was higher in group A (control) (n=27 vs n = 7 in group B). Total number of drug doses given in group C was also higher, as shown in Table 2 and Graph 1.

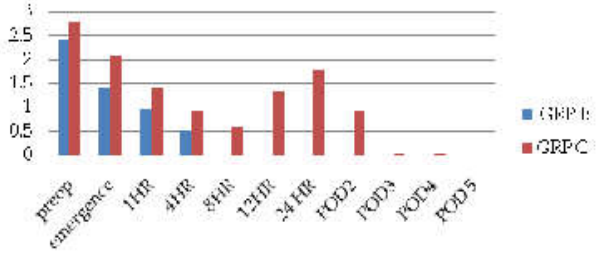
Table 2: Rescue Drugs (No. of Times).

Time	Group B	Group C
1 hr	4	6
4 hr	3	6
8 hr	0	4
12 hr	0	20
24 hr	0	21
48 hr	0	11
POD 3	0	0
POD 4	0	0
POD 5	0	0

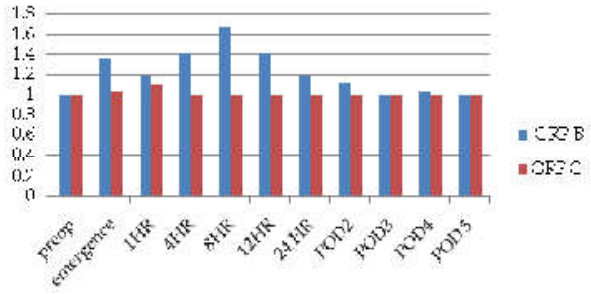


Graph 1:

VAS score was significantly less in group B at time of emergence and postoperatively after 4 hours till POD2, after which VAS was less in Group B, though not significant. (Graph 2).



Graph 2: VAS



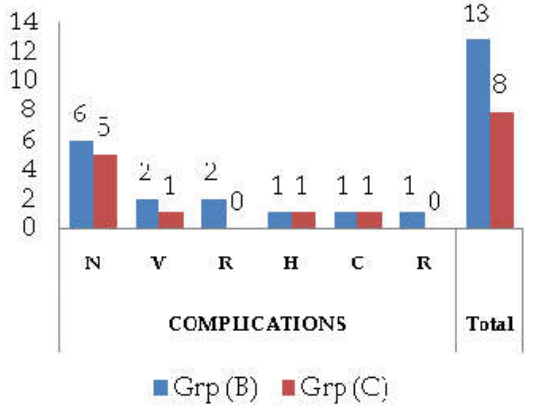
Graph 3: MRSS

MRSS scale was higher in Group B throughout postoperative period and at time of emergence (statistically significant), though it was always less than 3, not leading to excessive sedation. (Graph 3).

Number of patients having adverse effects was slightly high in group B, though comparable, most common effect being postoperative nausea. Two patients developed mild rash at site of patch application on POD3 and POD5. One patient had mild respiratory depression with fall in SpO_2 <95%, requiring oxygen through nasal prongs at 2L/ min on POD4 for a day, after which it was normal. (Table 3 and Graph 4)

Table 3: Complications.

Complications	Group B		Group C	
	No.	(%)	No.	(%)
Nausea	6	20	5	16.667
Vomiting	2	6.6667	1	3.3333
Rash	2	6.6667	0	0
Headache	1	3.3333	1	3.3333
Constipation	1	3.3333	1	3.3333
Resp Depr	1	3.3333	0	0
Total	13	43.33	8	26.66



Graph 4:

Discussion

Noxious stimuli like surgical incision produces

central sensitization and hyperexcitability, leading to amplification of the postoperative pain. It is postulated that if adequate analgesia is given intraoperatively, development of this sensitization is blocked, and hence, postoperative analgesia becomes more profound [2]. Transdermal Drug Delivery system provides safe, convenient and steady method of drug delivery as it bypass the first-pass metabolism and avoids peaks and troughs in plasma levels of the drug. It is more compliant as it is non-invasive and avoids multiple dosing. It also decreases incidence of drug related side effects [3] But some studies showed that gastrointestinal side effects associated with oral and transdermal opiods are comparable [2].

Buprenorphine is a partial agonist for mu-opioid receptors and has an antagonistic effect for kappa and delta receptors. It is 75 to 100 times more potent than morphine, and has good skin penetration [4]. But transdermal patches were not widely used for postoperative pain due to their slower onset (6-24 hrs), unpredictable absorption especially during hypothermia, interpatient variability, high cost, availability of limited number of drugs and physician's familiarity with injectable drugs [2].

In India, Buprenorphine patches are available in three different strength: 5, 10, 20 mcg/hr (over a period of 7 days). After removal of patch, buprenorphine concentration decline decreasing approximately 50% in 12 hrs (range 10-24 hrs).

In our study, we found that hemodynamic parameters were comparable in both groups, though slightly better controlled in group B. In a study by Niyogi et al. [3], intraoperative haemodynamic difference between transdermal buprenorphine and transdermal placebo groups was significant, with better controlled parameters inTDB group, for elective spinal instrumentation surgeries.

The efficacy of TDB has been established by many studies. Privitera, G. Gazzella et al. [5] used 35 mcg/hr of TDB for shoulder and upper femur surgeries and concluded that transdermal buprenorphine can be safely used for effective postoperative analgesia with high patient satisfaction rates. Similarly, Tang et al. [4] found that analgesic effect of transdermal buprenorphine was better compared with conventional analgesic regimen of paracoxib intravenous injections and oral celecoxib, with significantly higher degree of patient satisfaction in transdermal buprenorphine group, but VAS score was not significantly higher. In our study too, VAS score was significantly low in group B at time of emergence and postoperatively after 4 hours till POD2, after which VAS was less in group B but not statistically significant. In immediate postoperative period at 1 and 2 hours VAS was comparable in both groups, may be due to effect of intraoperative analgesics administration along with delayed effect of transdermal patch. Similarly, requirement of rescue analgesics was higher in control group.

In our study patients of group B were more comfortable, though not highly sedated as observed by MRSS score. But one patient got mild respiratory depression in group B, with SpO_2 decreasing to 92% requiring 1-2 litres of oxygen for few hours. In a study by Santosh Kumar et al. [1] for postoperative pain control in abdominal surgeries, mean RSS was lowest in group A (placebo patch), followed by group B (transdermal buprenorphine patch 10 mg) and highest for group C (transdermal buprenorphine patch 20 mg).

Two patients in our study developed skin rash at site of patch application. Local skin allergy and pruritis were also found by Tang et al [4] and by Privitera at al. [5] in their studies. PONV was found in various studies as minor side effect of drug or surgery, but statistically significant difference was not observed between study and control groups [1,3,4]. In our study nausea was most common side effect in both groups, though incidence was comparable. Few patients had other side effects too, like headache, constipation. High incidence of PONV in our study was may be due to type of surgeries (abdominal, oral, head neck) or duration of operations (average 2.5 - 3 hrs).

Conclusion

Transdermal buprenorphine patch is effective for postoperative analgesia for elective abdominal and head neck oral surgeries under General Anesthesia, in which patch can be applied atleast 12 hours prior to surgery. It can reduce requirement of rescue post operative analgesics over atleast five days and maintain hemodynamic stability without serious complications. But further studies with greater sample size may be required to support this.

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Comparison of Efficacy of Intravenous Paracetamol Versus Intravenous Tramadol for Postoperative Analgesia in Surgeries under General Anaesthesia

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Abstract

Introduction: The under treatment of postoperative pain is recognized as an important issue to the anesthesiologists and treating surgeons despite of improvement in mechanisms and introduction of acute pain services. *Aim:* To compare analgesic properties of Intravenous Paracetamol and Tramadol for postoperative analgesia in lower abdominal surgeries under general anesthesia. To study the adverse effects of Tramadol and Paracetamol. *Materials and methods:* It is a randomized study done in 100 patients ASA grade 1 and 2 of either sex, 20 to 60 years of age who underwent lower abdominal surgery under general anaesthesia. It was conducted to compare the efficacy of IV Paracetamol and IV Tramadol for postoperative analgesia. Group 1 received Intravenous Paracetamol and group 2 Intravenous Tramadol 15 min before the end of the surgery and the study drug was administered every 6th hourly for 24 hours. Patients were monitored for pain at 0, 2, 4, 6, 8, 10, 12 and 24 hours postoperatively. Also the time of first dose of rescue analgesia and number of doses of rescue analgesia given was noted. Side effects like nausea and vomiting was also observed. *Results:* Found that the pain scores were significant at 2 hours and 4 hours (except in the early postoperative period) and pain scores decreased over time in both the groups. About 60% of the patients in the Tramadol group had nausea and vomiting sensation at 0 hours, 12% at 2 hours, 14% at 4 hours, 48% at 6 hours, 26% at 8 hours respectively whereas in Paracetamol group about 4% of the patients had nausea at 2 hours, 4% at 4 hours and 2% at 6 hours. The rescue analgesia in the form of morphine was required in 22% of the patients of Paracetamol group at 0 hour, 32% at 2 hours and 2.0% at 10 hours after surgery. But Tramadol group required additional rescue analgesia in 10% of the patients. Total doses of rescue analgesic required by the Paracetamol group was 1.04 (± 0.2) and in group 2 (Tramadol) was 1.0 (± 0). There was no significant difference between Paracetamol and Tramadol groups. *Conclusion:* Paracetamol is as effective as Tramadol when used for postoperative pain relief in patients for lower abdominal surgeries except in the early postoperative period.

Keywords: Tramadol; Paracetamol; Postoperative analgesia.

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Introduction

Pain serves a biological function. It signals the presence of damage or disease within the body. Acute postoperative pain is a complex physiologic reaction to tissue injury, visceral distension or disease. Its manifestation of autonomic, psychological and behavioral responses results

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in unpleasant, unwanted sensory and emotional experience. Despite advances in knowledge of pathophysiology of pain, pharmacology of analgesics and development of effective techniques for postoperative pain control, many patients continue to experience considerable discomfort [1].

Postoperative pain is a result of surgery, specially involving the body cavities, large joint surfaces and deep tissues. The severity and frequency of postoperative pain depends upon the site affected, nature and extent of the surgery. The under treatment of postoperative pain is recognized as an important issue to the anesthesiologists and treating surgeons despite of improvement in mechanisms and introduction of acute pain services. The available literature shows that up to 75% of the patients after surgery have reported pain and 80% of the patients experienced the severe pain at some time during the hospital stay. Another survey also demonstrated that 70% of the approximately still complain of moderate or severe pain during the postoperative period [2].

Poorly controlled postoperative pain mainly results in increased catabolism, increased cardiorespiratory work, immunosuppression and coagulation disturbances [3]. Pain and postoperative nausea and vomiting prolong recovery and discharge times and contribute to unexpected admission after ambulatory surgery. Higher levels of postoperative pain can result in poor patient satisfaction, impair quality of recovery and increase in healthcare costs [9]. The goal of optimizing the postoperative pain is to relieve patients suffering early mobilization, shortened hospital stay, reduced costs and side effects and thereby reduces the burden on patients health and pocket.

The quality of postoperative patient care depends critically on effective pain management, which includes accurately assessing pain and monitoring the patient's response to treatment. Inadequate postoperative pain treatment can contribute to unnecessary discomfort, increased morbidity, delayed discharge, and unanticipated readmission to hospital.

The Paracetamol is an effective analgesic for mild to moderate pain with a favourable adverse effect profile [3]. It is an effective adjuvant to opioid analgesia and reduction in opioid requirement by 20–30% when combined with regular regimen of oral or rectal Paracetamol. Intravenous Paracetamol is a soluble diethyglycidyl ester of Paracetamol. It acts on both central and peripheral components of pain pathways. It is found to be a good drug in relieving the postoperative pain and has no side effects like nausea and vomiting and it is well tolerated by patients. However, except for oral Paracetamol, there is a marked discrepancy between the extent to which Paracetamol is used and available evidence for an analgesic effect in postoperative pain.

Intravenous Tramadol is also a potent analgesic which is a synthetic 4-Phenyl piperidine analog of codeine. It is a centrally acting atypical opioid with low affinity for μ receptors. It is also a weak inhibitor of reuptake of norepinephrine and serotonin and is a good analgesic in postoperative pain. It is reported adverse effects include nausea, dizziness, sleepiness, dry mouth, sweating and lowering of seizure threshold. Its advantages over other narcotic drugs are that it causes less respiratory depression than morphine and codeine and does not share the propensity of non-steroidal anti-inflammatory drugs (NSAIDs) to provoke asthma, gastrointestinal mucosal damage and renal impairment.

However, the studies comparing the efficacy between the Paracetamol and Tramadol are scant in India and across the world. Most of the studies available are western studies. Hence, it was decided to take up this study in the context of this part of country. This study mainly focuses on comparison of effects, efficacy and side effects of these two different drugs.

Materials and Methods

A randomized controlled study was undertaken in the Department of Anesthesia in order to study the analgesic efficacy of Tramadol and Paracetamol. An informed bilingual, written consent was obtained from the patients before they were enrolled in to the study. A total of 100 patients undergoing surgeries under general anaesthesia were included in the study as study subjects. The inclusion and exclusion criteria were as follows:

Inclusion Criteria: Patients of ASA grade I & II, Age group of 20 to 60 years Undergoing surgeries under general anesthesia.

Exclusion Criteria: Patients allergic to Tramadol or Paracetamol, Liver dysfunction, Advanced renal dysfunction, Drug abuse, Patients belonging to ASA III and IV, Patients less than 20 years and more than 60 years, Difficulty in communication.

The study subjects were divided two equal groups:

Group I: 50 patients received intravenous

Paracetamol (15-17 mg/kg).

Group II: 50 patients received intravenous Tramadol (1.5 – 2 mg/kg).

The patients enrolled were randomly assigned to groups by marking on the slips of papers. The slips picked randomly to group the patient. The patients thus selected were administered with their first dose of the drug 15 minutes before the end of the surgery and 6th hourly for 24 hours. If adequate pain relief is not achieved with the study drugs or VAS > 4 intravenous morphine (0.1 mg/kg) was administered as a rescue analgesic and the efficacy of the study drugs were compared respectively. Patients were also instructed to request pain medication from the nurse whenever they required pain relief and not to wait for their next schedule pain assessment. The patients were followed subsequently assessed for the level of pain by using the VAS scores at 0, 2, 4, 6, 8, 10, 12 and 24 hours. All the data so obtained was meticulously documented and statistically analyzed. VAS score was compared between two groups using Student T test of unequal variances. Chi-square test was used to study the association between different parameters measured.

Results

A randomized controlled trial was undertaken in 100 patients who have undergone lower abdominal surgeries were divided in to two equal groups. One group received Paracetamol and another group received Tramadol. In Group 1 (Paracetamol), 34% of the patients were males and 66% of the patients were females. Since the Tramadol group was sex matched, 34% were males and 66% were females.

Table 1: Distribution of the study groups according to age group

Age group	Group 1	Group 2
21 – 30 years	20 (40.0)	17(34.0)
31 – 40 years	11(22.0)	13(26.0)
41 – 50 years	9 (18.0)	16(32.0)
51 – 60 years	10 (20.0)	4 (8.0)
Mean ± SD	37.3 ± 11.4	36.7 ± 10.4
Z value	0.257	
p value, Sig	0.56, NS	
Weight		
Mean ± SD	57.6 ± 5.0	59.1 ± 4.8

The mean age of Paracetamol group was 37.3 years and Tramadol group was 36.7 years. There was no significant difference between the two groups and hence they were comparable in all respects. However, there was no statistically significant difference in weight between group 1 and group 2 patients (Table 1).

Table 2: Distribution of the study groups according to VAS scores

VAS scores	Group 1	Group 2	Z value	p value, Sig
0 hours	3.1 ± 1.1	2.8 ± 0.9	1.496	0.438, NS
2 hours	3.2 ± 1.4	2.6 ± 0.5	2.72	0.008, Sig
4 hours	2.0 ± 0.7	2.5 ± 0.5	4.454	0.000, Sig
6 hours	2.2 ± 0.6	2.5 ± 0.5	1.619	0.109, NS
8 hours	2.2 ± 0.6	2.2 ± 0.7	0.585	0.56, NS
10 hours	2.2 ± 0.6	2.4 ± 0.5	1.421	0.158, NS
12 hours	2.3 ± 0.6	2.1 ± 0.6	1.459	0.148, NS
24 hours	2.2 ± 0.6	2.1 ± 0.7	0.742	0.46, NS

The mean VAS scores at 0, 2, 4, 6, 8, 10, 12 and 24 hours in group 1 (Paracetamol) group were 3.1, 3.2, 2.0, 2.2, 2.2, 2.2, 2.3 and 2.2 respectively. The mean VAS scores for group 2 (Tramadol) were 2.8, 2.6, 2.5, 2.5, 2.2, 2.4, 2.1 and 2.1 respectively. There was a significant difference between the VAS scores of group 1 and group 2 at 2 hours and 4 hours (Table 2).

Table 3: Distribution of the study groups according to use of recue analgesia

Rescue analgesia	Group 1	Group 2
0 hours	11 (22.0)	5 (10.0)
2 hours	16 (32.0)	0
4 hours	0	0
6 hours	0	0
8 hours	0	0
10 hours	1 (2.0)	0
12 hours	0	0
24 hours	0	0

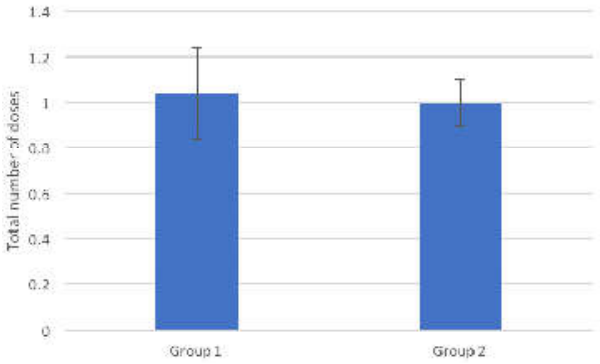
The rescue analgesia in the form of morphine was required in 22% of the patients of Paracetamol group at 0 hour, 32% at 2 hours and 2.0% at 10 hours after surgery. But Tramadol group required additional rescue analgesia in 10% of the patients (Table 3).

Table 4: Distribution of the study groups according to Nausea and vomiting in groups

Nausea and Vomiting	Group 1		Group 2	
	Frequency	Percent	Frequency	Percent
0 hours	0	0	30	60.0
2 hours	2	4	6	12.0
4 hours	2	4	7	14.0
6 hours	1	2	24	48.0
8 hours	0	0	13	26.0
10 hours	0	0	0	0
12 hours	0	0	0	0
24 hours	0	0	0	0

Tramadol is a drug known to result in nausea and vomiting. About 60% of the patients of Tramadol

group had nausea and vomiting sensation at 0 hour, 12% at 2 hours, 14% at 4 hours, 48% at 6 hours and 26% at 8 hours had nausea and vomiting sensation. In Paracetamol group about 10% of the patients had nausea at 4% at 2 hour, 4% at 4 hours and 2% at 6 hours (Table 4).



Graph 1: Total doses of rescue analgesia needed in the study group

Total doses of rescue analgesic required by the Paracetamol group was 1.04 (± 0.2) and in group 2 (Tramadol) was 1.0 (± 0). There was no significant difference between Paracetamol and Tramadol groups (Graph 1).

Discussion

Postoperative pain specially involves the body cavities, large joint surface and deep tissues as a result of surgery. The site of surgery, nature and extent of surgery decides the severity and frequency of pain. The postoperative pain is often under treated as emerged as an important issue for the anesthesiologists and treating surgeons even with improvement in the mechanism and introduction of acute pain services. The available literature shows that up to 75% of the patients after surgery have reported pain and 80% of the patients experienced the severe pain at some time during the hospital stay. Another survey also demonstrated that 70% of the approximately still complain of moderate or severe pain during the postoperative period.

Poorly controlled postoperative pain mainly results in increased catabolism, increased cardiorespiratory work, immunosuppression and coagulation disturbances. Pain and postoperative nausea and vomiting prolong recovery and discharge times and contribute to unexpected admission after ambulatory surgery. Higher levels of postoperative pain can results in poor patient satisfaction, impair quality of recovery and increase in healthcare costs.

Paracetamol has emerged as an effective analgesic for mild to moderate pain with adverse effect profile. The use of Paracetamol reduces the opioid requirements by 20-30% when combined with regular dose of oral or rectal Paracetamol. Intravenous Paracetamol mainly acts on both central and peripheral components of pain pathways. The available literature has shown that it relives postoperative pain with minimal adverse effects and also well tolerated by the patients. However, except for oral Paracetamol, there is a marked discrepancy between the extent to which Paracetamol is used and available evidence for an analgesic effect in postoperative pain.

Intravenous Tramadol has been emerged as an important and potent analgesic now-a-days. It mainly acts centrally and also a weak inhibitor of reuptake of norepinephrine and serotonin. But the reported adverse effects include nausea, dizziness, sleepiness, dry mouth, sweating and lowering of seizure threshold. Its advantages over other narcotic drugs are that it causes less respiratory depression than morphine and codeine and does not share the propensity of non-steroidal anti-inflammatory drugs (NSAIDs) to provoke asthma, gastrointestinal mucosal damage and renal impairment.

This study was mainly taken up to compare the efficacy of Paracetamol and Tramadol as postoperative analgesic. Hence, a randomized controlled study was undertaken in the Department of Anesthesia. About 100 patients who have undergone surgery for lower abdominal surgeries were divided in to two equal groups. One group received Paracetamol and another group received Tramadol.

Timing of Administration of First Dose of the Drug

In our study, the drug under the study was given 15min before the end of thesurgery and subsequently the drug was administered every 6th hourly for 24 hours, and the patient was assessed for the level of pain by using the VAS score at 0, 2, 4, 6, 8, 10, 12 and 24 hours.

In a similar study done by Mustafa Arslan et al. [5] the study drug was administered 10 min before the skin incision and the level of pain was assessed by using the VAS scores at 15, 30 min and 1, 2, 4, 6, 8, 12 and 24 hours after the end of the surgery. In a study done at Bomay by Manish Kela et al. [6] patients received the study drug at the end of the surgery, and the doses were repeated every 8th hourly till 48 hours postoperatively and pain was

assessed using the VAS scale. In a study done by Lahtinen P et al. [7], patient received the study drug at 6 hours intervals for 72 hours.

Dosage

In our study, we used the drugs IV Paracetamol and IV Tramadol. IV Paracetamol was given at 15-17 mg/kg and IV Tramadol 1.5-2 mg/kg body weight. The study drug was given 15 min before the end of the surgery and repeated at every 6 hours for 24 hours. In a comparative study done by Manish Kela et al. [6], the patients were divided into two groups of 30 each. One group received Inj. Paracetamol (20 mg/kg) and the other group received Inj. Tramadol (2 mg/kg). In a comparative study done by Uysal HY et al. [8] the patients were divided into two groups, Paracetamol group received 15 mg/kg of IV Paracetamol and Tramadol group received 1.0 mg/kg IV Tramadol.

Analgesia

In our study, the mean VAS scores for Paracetamol were between 2.2 to 3.1 from immediate postoperative time to 24 hours after operation. The VAS scores of Tramadol were significantly different at 2 hours and 4 hours. The pain scores decreased over time in both the groups. In a comparative study by Cattbriga et al. [9], done for over 72 hours, patients who received Paracetamol had significantly less pain at the time point of 12 hours, 1 (0-6) vs. 2 (1-10) p=0.0041,18 hour 1 (0-5) vs. 2 (0-8) p=0.0039, 24 hour 1 (0-5) vs 2 (0-8) p=0.0044. The pain scores progressively decreased in both the groups over the time, and there was no significant difference in pain 30-72 hours after operation. During a deep breath, the Paracetamol group had significantly less pain than placebo group only 12 hours after operation. A study done by Manish Kela et al. [6], observed that the mean score of VAS scale at rest and deep inspiration between the two groups was similar and the difference was not significant. At the end of 24 hours, mean VAS score had a significant reduction in both the groups and the difference was not significant.

Additional Analgesic Requirement

Paracetamol in this study needed additional analgesic especially immediately after surgery. Comparatively, less number of patients of Tramadol group needed additional analgesics. The rescue analgesic in the form of morphine was required in 22% of the patients of Paracetamol group at 0 hour, 32% at 2 hours and 2% at 10 hours after surgery. The total doses of rescue analgesic required by the Paracetamol group was 1.04 (± 0.2) and in Tramadol group was 1.0 (± 0). In a comparative study between IV Paracetamol and Tramadol done by Manish Kela et al. [6], 6.7% of Paracetamol group and 13.3% in the Tramadol group required rescue analgesic.

Adverse Effects

Tramadol is a drug known to result in nausea and vomiting. Majority of the patients in Tramadol group had sense of nausea and vomiting. About 60% of the patients in the Tramadol group had nausea and vomiting sensation at 0 hours, 12% at 2 hours, 14% at 4 hours, 48% at 6 hours, 26% at 8 hours respectively whereas in Paracetamol group about 4% of the patients had nausea at 2 hours, 4% at 4 hours and 2% at 6 hours. In a similar study by Manish Kela et al. [6] about 10% of the subjects in the Paracetamol group and 13.3% in the Tramadol group suffered nausea and vomiting. In a study done by Cattabriga et al. [9], it was observed that PONV was a very unusual adverse event, it was observed in three patients (6%) of Paracetamol group and in one patient (2.12%) in the placebo group.

Conclusion

Paracetamol is as effective as Tramadol when used for postoperative pain relief in patients for lower abdominal surgeries except in the early postoperative period. Incidence of postoperative nausea and vomiting is more with Tramadol when compared to Paracetamol.

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Original Research Article

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Evaluation of Pre Incision Infiltration of A Local Anesthetics Regimen Prior to Modified Radical Mastectomy: A Randomized Single Blinded Study

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Abstract

Introduction: Breast surgery can be emotionally distressing and physically painful. Although regional anesthesia and nerve block techniques are widely used in many situations, many anesthetists are still minded by the simplest way of wound infiltration. Preemptive analgesia is the concept of providing analgesia before surgical incision. Suggested advantages of this technique include a reduction in postoperative pain, analgesic consumption and an improvement in patient satisfaction. In addition adverse effect of opioids consumption such as postoperative nausea and vomiting, drowsiness and risk of respiratory depression can be minimized. *Aims & Objective:* To evaluate the efficacy of preincision mastectomy flap infiltration with a cocktail of bupivacaine 0.5% and lignocaine with adrenaline over intraoperative and postoperative analgesic requirement compared with patients receiving placebo. To investigate the efficacy of preincision local anesthetic regimen infiltration in postoperative pain score in modified radical mastectomy compared with patients receiving placebo. To study their effect on hemodynamic parameters, any side effects and complication. *Material and method:* In this randomized single blinded study, 60 patients of ASA grade I and II posted for modified radical mastectomy were randomized into group I and group II. Group I receive pre incision infiltration of mastectomy flap with cocktail of 10 ml bupivacaine (0.5%)+10 ml of lignocaine 2% with adrenaline, Group II receive pre incision infiltration with 20 ml normal saline. All patients undergo standardized general anaesthesia. We assessed intraoperative requirement of analgesic drugs,haemodynamic parameters, postoperative supplementary analgesia, VAS score and side effects. *Results:* There was no statistical difference between both groups regarding the demographic data. The mean blood pressure, pulse rate was less in group I which was statically significant. The mean supplementary analgesic requirement was significantly less in group I. The postoperative VAS score was significantly less in study group. *Conclusion:* Preemptive local anaesthetic infiltration at the incision site is safe and effective method for reducing postoperative pain and stress response with a significant reduction of analgesic requirement.

Keywords: preemptive analgesia; mastectomy; bupivacaine; lignocaine; preincision infiltration

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Introduction

Breast surgery can be emotionally distressing and physically painful. Most patients may further evolve into post mastectomy chronic pain syndrome [1,2]. Tissue damage resulting from surgery causes in the first phase, a nociceptive stimulation in the CNS and in the second phase, a transient inflammatory reaction [3,4].

Preemtive analgesia is one of the method of pain management used in the perioperative period. The preemptive analgesia strategy originated in early 1980 [5]. Preemtive analgesia has been shown to have a beneficial analgesic effect in a large number of surgical procedures including laparoscopy, hernia, amputation, spinal and orthopedics surgeries [6,7].

It is very important to mention that wound infiltration with long standing local anesthetics decreases the anesthetic and analgesic doses during surgery. The addition of adrenaline to the local anesthetic prolongs its duration of action. It decrease its systemic absorption thus decreasing its toxicity [8].

The aim of this study is evaluating the efficacy of preincision infiltration in the area of planned surgical incision in the patient undergoing modified radical mastectomy with a cocktail of bupivacaine 0.5% and lignocaine with adrenaline over intraoperative and postoperative analgesic requirement and pain score compared with patients receiving placebo.

Materials and Methods

The study was designed as a prospective, randomized, single blinded study. After taking approval from ethics committee 60 patients of age group 20 to 60 years with ASA grade I and II posted for modified radical mastectomy under general anesthesia were assigned with informed consent into two groups (n=30).

Group I (n=30) received preincision infilteration with mixture of 10 ml of bupivacaine (0.5%)+ 10 ml of lignocaine with adrenaline and group II (n=30) received 20 ml of normal saline. Patients with history of any associated systemic disease, patient refusal, local anesthetic sensitivity were excluded from this study. All patient underwent thorough pre anesthetic checkup and were explained about the visual analogue scale. (0-10) scoring system for pain. The multichannel monitor were applied to the patient on arrival to the operating room. A suitable peripheral vein was cannulated and IV ringer lactate solution was started to all patients before the procedure. Baseline blood pressure, pulse rate, oxygen saturation was recorded. A standard anesthetic technique was adopted. IV glycopyrolate 0.2 mg, IV midazolam 1mg, IV fentanyl 2 ug/kg were given for premedication. General anesthesia was induced with propofol 2 mg/kg and succinyl choline 2 mg/kg to facilitate tracheal intubation. After intubation the preparation of local anesthetic was infilterate along the intended incision line then 15 minute later the operation began. Loading dose of IV atracurium 0.5 mg/kg was given then further bolus doses of 0.1 mg/kg was used as during intermittent positive pressure ventilation. Anesthesia was maintained with oxygen, nitrous oxide and sevoflurane. Fentanyl was used for analgesia. Neuromuscular block reversed with 0.5 mg glycopyrolate and 2.5 mg neostigmine. Extubation was done and then patient was shifted to recovery room.

Hemodynamic monitoring, requirement of anesthetic drugs were recorded intraoperatively every 15 min till extubation. In postoperative period hemodynamic monitoring, VAS score for pain assessment, requiremet of supplementary analgesia and side effects were recorded every hr till 6 hr. Any patient expressing VAS score >4 was given iv diclopenac.

Results

Sixty patients were taken up for the study, thirty in group I (receive preincision infiltration of 20 ml 0.5% bupivacaine + lignocaine with adrenaline) and thirty in group II (pre incision infiltration of 20 ml normal saline). demographic data such as age, weight and duration of surgery did not vary significantly between two groups [Table 1]. Regarding hemodynamic parameters the mean SpO_2 (group I =98.28) (group II=98.14) (p value=0.188) the difference in mean (±SD) was found to be statistically insignificant (p>0.05) between two Groups [Figure 1].

The mean pulse rate (group I = 88.10) (group II=88.50) (p value=0.045) which was statistically significantly less in group I [Figure 2].

The mean systolic (group I=127.79) (group II=132.12) (p value=0.0039) and mean diastolic blood pressure (group I=81.09) (group II=84.04) (p value=0.001) were significantly less in group I [Figure 3].

Post operatively, the pain experienced was evaluated by visual analogue scale (0-10) at different time interval following surgery. Pain score were significantly less (p=0.002) in group I

when compared with Group II [Figure 4]. The need of supplementary analgesia intraoperatively and postoperatively was significantly less in group I [Figure 2].

Discussion

Pain is inevitably associated with any surgical procedure, having first the form of acute & later chronic disturbances. Pain sensation depends on the degree of surgical trauma, previous pain experience of the patient. The concept of preemptive analgesia is the application of local anaesthetic drugs by regional nerve blockade, infiltration of surgical wound or by topical instillation into the operative bed before tissue trauma. Thus, preventing the noxious stimuli that result from the tissue damage. Many studies reported that the preemptive analgesia is more effective than post operative infiltration [12] & preincision mastectomy flap infiltration with bupivacaine adrenaline solution is a safe and effective for reduction of post mastectomy pain, stress response with a significant reduction of the analgesic requirement [13].

Many trial demonstrate a significant reduction of the opioid requirement in mastectomy after local bupivacaine infiltration [14]. However the intra operative and postoperative assessment of the stress response in the form of pulse rate, blood pressure and respiratory rate is an important parameter to be assessed in any painful surgical maneuver. A significant reduction of the VAS score and opioids consumption was reported by several studies [15].

As per the present study postoperative VAS score was significantly reduced [Figure 4]. All parameters of the stress response were reduced in the study group with a significant p value. The same was noticed in the dose of intraoperative and postoperative analgesic consumption.

In our study we concluded that Preemptive analgesia application in the form of skin infiltration in the area of planned surgical incisions with 10 ml 0.5% Bupivacaine and 10 ml lignocaine + adrenaline in patients undergoing modified radical mastectomy decreases postoperative pain, limits the amount of fentanyl used during surgery, reduces the demand for supplementary analgesia in post operative period and provide hemodynamic stability.

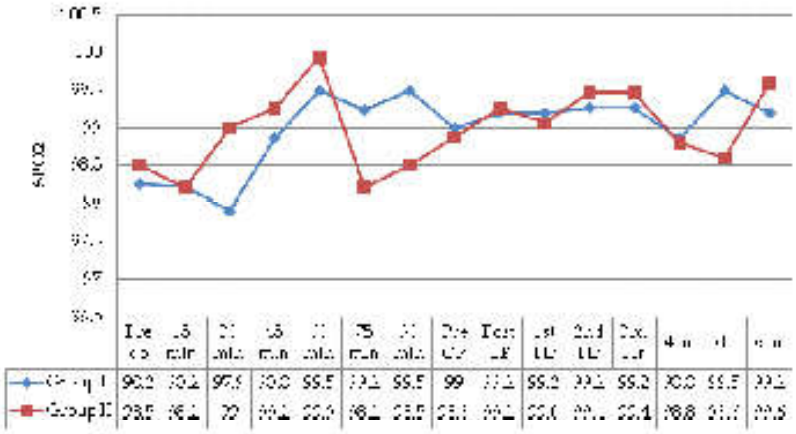

Fig. 1: Showing mean SpO_2 of patient in both the groups

Table 1: Requirement for supplemental analgesia in patients receiving pre emptive infiltration of local anesthetic regimen (group I) or saline (group II). Values are number (proportion). Group I require significantly less supplementary analgesia as compared to Group II

	Intraop	
Supplemental analgesia	Group I	Group II
None	24 (80%)	12 (40%)
1st Dose	4 (13%)	13 (43%)
2nd Dose	2 (7%)	5 (16%)
3rd Dose	0	0
	Post op	
None	22 (73%)	6 (20%)
1st Dose	5 (16%)	14 (46%)
2nd Dose	2 (7%)	7 (24%)
3rd Dose	1 (3%)	3 (10%)

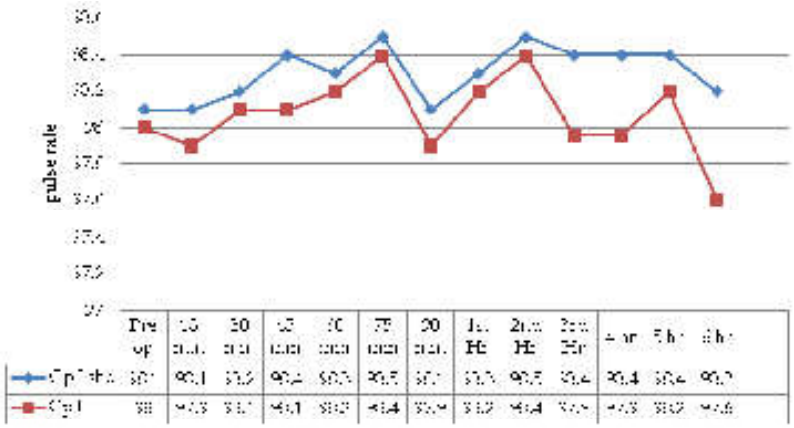

Fig. 2: Showing Comparision of heart rate (beat/min) of the two study group. There were no significant difference in the heart rate between group I and II

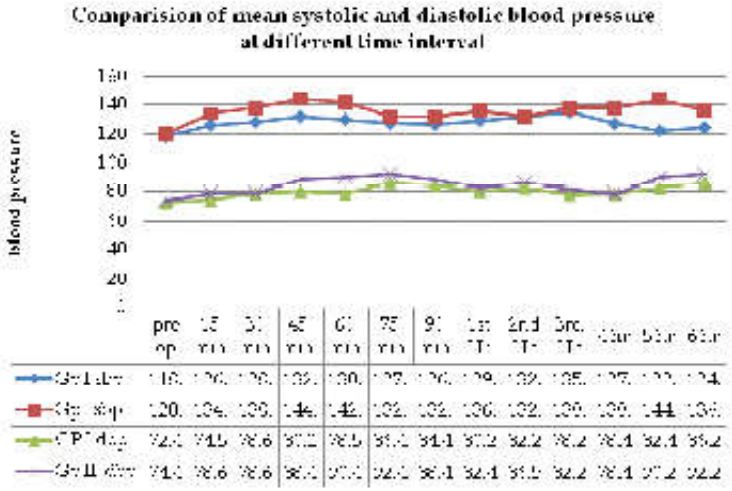

Fig. 3: Figure Showing Comparision of systolic and diastolic BP between two study groups

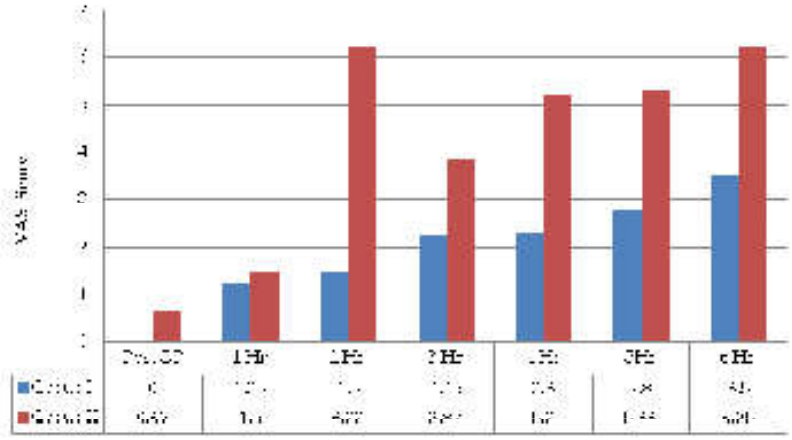

Fig. 4: The VAS score chart shows that group I (local anesthetic regimen) has lower VAS score than Group II (Placebo). This was statistically significant with p value of 0.042

Conclusion

In our study we concluded that Preemptive analgesia application in the form of skin infiltration in the area of planned surgical incisions with 10 ml 0.5% Bupivacaine and 10 ml lignocaine + adrenaline in patients undergoing modified radical mastectomy decreases postoperative pain, limits the amount of fentanyl used during surgery, reduces the demand for supplementary analgesia in post operative period and provide hemodynamic stability.

Key Messages

Preemptive local anesthetic infiltration at the incision site with 10 ml 0.5% bupivacaine and 10 ml lignacaine + adrenaline is safe and effective method for reducing postoperative pain and stress response, with a significant reduction of analgesic requirement during surgery and in the postoperative period.

Conflict of Interest: none

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Title	Frequency	Rate (Rs): India		Rate ($):ROW	
Community and Public Health Nursing	3	5500	5000	430	391
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Indian Journal of Agriculture Business	2	5500	5000	413	375
Indian Journal of Anatomy	4	8500	8000	664	625
Indian Journal of Ancient Medicine and Yoga	4	8000	7500	625	586
Indian Journal of Anesthesia and Analgesia	4	7500	7000	586	547
Indian Journal of Biology	2	5500	5000	430	391
Indian Journal of Cancer Education and Research	2	9000	8500	703	664
Indian Journal of Communicable Diseases	2	8500	8000	664	625
Indian Journal of Dental Education	4	5500	5000	430	391
Indian Journal of Forensic Medicine and Pathology	4	16000	15500	1250	1211
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Indian Journal of Forensic Odontology	2	5500	5000	430	391
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Indian Journal of Hospital Infection	2	12500	12000	938	901
Indian Journal of Law and Human Behavior	2	6000	5500	469	430
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Indian Journal of Maternal-Fetal & Neonatal Medicine	2	9500	9000	742	703
Indian Journal of Medical & Health Sciences	2	7000	6500	547	508
Indian Journal of Obstetrics and Gynecology	4	9500	9000	742	703
Indian Journal of Pathology: Research and Practice	4	12000	11500	938	898
Indian Journal of Plant and Soil	2	65500	65000	5117	5078
Indian Journal of Preventive Medicine	2	7000	6500	547	508
Indian Journal of Research in Anthropology	2	12500	12000	977	938
Indian Journal of Surgical Nursing	3	5500	5000	430	391
Indian Journal of Trauma & Emergency Pediatrics	4	9500	9000	742	703
Indian Journal of Waste Management	2	9500	8500	742	664
International Journal of Food, Nutrition & Dietetics	3	5500	5000	430	391
International Journal of Neurology and Neurosurgery	2	10500	10000	820	781
International Journal of Pediatric Nursing	3	5500	5000	430	391
International Journal of Political Science	2	6000	5500	450	413
International Journal of Practical Nursing	3	5500	5000	430	391
International Physiology	2	7500	7000	586	547
Journal of Animal Feed Science and Technology	2	78500	78000	6133	6094
Journal of Cardiovascular Medicine and Surgery	2	10000	9500	781	742
Journal of Forensic Chemistry and Toxicology	2	9500	9000	742	703
Journal of Geriatric Nursing	2	5500	5000	430	391
Journal of Microbiology and Related Research	2	8500	8000	664	625
Journal of Nurse Midwifery and Maternal Health	3	5500	5000	430	391
Journal of Organ Transplantation	2	26400	25900	2063	2023
Journal of Orthopaedic Education	2	5500	5000	430	391
Journal of Pharmaceutical and Medicinal Chemistry	2	16500	16000	1289	1250
Journal of Practical Biochemistry and Biophysics	2	7000	6500	547	508
Journal of Psychiatric Nursing	3	5500	5000	430	391
Journal of Social Welfare and Management	3	7500	7000	586	547
New Indian Journal of Surgery	4	8000	7500	625	586
Ophthalmology and Allied Sciences	2	6000	5500	469	430
Otolaryngology International	2	5500	5000	430	391
Pediatric Education and Research	3	7500	7000	586	547
Physiotherapy and Occupational Therapy Journal	4	9000	8500	703	664
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Original Research Article

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Comparison of the Efficacy of Palonosetron and Ondansetron in Prevention of Postoperative Nausea and Vomiting

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Abstract

Background and objectives: Post-operative nausea and vomiting (PONV) is commonly seen in female patients undergoing laparoscopic surgeries under general anaesthesia. Adverse consequences of PONV are patient dissatisfaction, unexpected hospital admission, and delayed recovery. In this randomized double blind prospective study, we compare the efficacy of ondansetron and palonosetron for prevention of PONV. *Material and methods:* After obtaining ethical clearance and informed consent, 130 female patients undergoing laparoscopic surgery were randomly divided into two groups by sealed envelope method. Group A 8mg ondansetron and group B received 8 mg ondansetron and 0.075 mg palonosetron iv respectively just before induction of general anaesthesia. During the postoperative period occurrence of nausea and vomiting, severity of nausea, rescue antiemetic use and adverse effects were monitored at 0-2 hrs, 2-6 hrs and 6-24 hrs. *Results:* Number of episodes of vomiting, risk for nausea and vomiting, severity of nausea and need for rescue medication was comparable between the 2 groups during the early post operative period (0- 2 hrs). During 2-6 hrs, the episode of vomiting and use of rescue antiemetic was not different between the two groups but severity of nausea and risk of nausea and vomiting was significantly lower in palonosetron group. During the late post operative period (6-24 hrs), the episodes of vomiting, risk for nausea and vomiting, severity of nausea and need for rescue antiemetics was significantly lower in palonosetron group. *Conclusion:* Intravenous palonosetron 0.075 mg has a better antiemetic profile when compared to ondansetron 8mg over 24hrs following laparoscopic surgeries under general anaesthesia.

Keywords: Laparoscopic surgery; anaesthesia; PONV; ondensetron; palanosetron.

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Introduction

Post operative nausea and vomiting (PONV) is a distressing side effect associated with general anaesthesia. Sir John Snow described the phenomenon of nausea and vomiting with chloroform anaesthesia [1]. The incidence of PONV was 75–80% when ether was used.

With the advent of modern and safer anaesthetic technique, incidence of PONV has decreased significantly. This is because ether is no longer used as anaesthetic, and use of prophylactic use of anti emetics in patients who are at risk of PONV.

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Aetiology of PONV is multi-factorial and several drugs have been used to treat this condition. At present the overall incidence ranges from 25-30% and intractable nausea and vomiting is seen in 0.18% of the patients under general anaesthesia.

PONV can lead to patient dissatisfaction, unexpected hospital admission for day care procedures, delayed recovery and return to work. It is difficult to ambulate patients with nausea and vomiting. Thus, PONV is one of the most undesirable post operative complications.

Causes of PONV are multi-factorial which include anaesthetic, surgical and patient factors. Apfel and his colleagues [2] have shown that it is possible to predict the individual patient's risk of PONV following balanced inhalational anaesthesia by considering a 4 factor risk score ; a) Female gender b) Non smoking status c) Previous h/o PONV and motion sickness d) Use of post operative opioids.

At present it is generally accepted that PONV can be controlled by blocking of all the receptors involved in vomiting. Various drugs have been used in the treatment of nausea and vomiting. 5-HT_3 receptor antagonist is one such antiemetic which has proven to be safe and effective in the treatment of PONV. 5-HT_3 receptor antagonists are also used in cancer chemotherapy. The drugs belonging to this group are Ondansetron, Granisetron, Ramosetron and Palonosetron, of which Ondensetron is most widely used. Palonosetron is a newly developed 5-HT_3 receptor antagonist. Its receptor-affinity is more potent than other antagonists. Its plasma half-life is very long ($t_{1/2}$ = 41 hrs). It is also known to be more effective than ondansetron against nausea and vomiting in patients using anticancer drugs. However, studies comparing the effects of preventing PONV between palonosetron and other 5-HT3 receptor antagonists are sparse.

The present randomized double blind study is designed to evaluate the efficacy of palonosetron compared with ondansetron for preventing PONV in female patients undergoing laparoscopic surgeries.

Materials and methods

After obtaining the approval from the institutional ethical committee, this prospective, randomized, comparative study was undertaken comparing the effects of ondansetron and palonosetron in preventing PONV in female patients undergoing laparoscopic surgeries.

Female patients belonging to American Society of Anaesthesiology Physical Status (ASA PS) I and II, aged between 18 and 60 years, undergoing elective laparoscopic surgery under general anaesthesia with endotracheal intubation were enrolled for the study. Patients who had received anti emetics, steroids or psychoactive medications within 24 hrs of the study initiation or received cancer chemotherapy within 4 weeks or emetogenic radiotherapy within 8 weeks before the study entry, pregnant or lactating patients and patients with vomiting or retching in the 24 hours preceding the surgery were not included in the study.

Based on study by S K park et al. [3], it was calculated that a sample size of 61 per group was required to compare PONV between the two groups with 5% level of significance and 80% power. We allocated 65 patients to each group in our study

Preoperative assessment: Preoperative evaluation of all the patients was performed including detailed history regarding motion sickness and PONV in the past. All the patients were kept nil per oral for 8 hours and were premedicated with Tab pantoprazole 40 mg and Tab alprazolam 0.5 mg on the night before the surgery.

Induction and maintenance: Patient were randomly allocated into either Group A (ondansetron) or group B (palonosetron) by sealed envelope method. In all selected patients baseline vital parameters were noted. In subjects of group A - ondansetron 8 mg as a bolus iv dose and in group B-palonosetron 0.075 mg diluted up to 4 ml with distilled water was administered before induction of anaesthesia. The person administering the study drug and assessing post operatively was different and both were blinded to study drug.

Anaesthesia was induced with intravenous (iv) Fentanyl 2 mcg/kg and Propofol 2 mg/kg and tracheal intubation facilitated with atracurium 0.5 mg/kg. Anaesthesia was maintained with N_2O in oxygen 60 : 40% mixture and a 1 - 1.5 mac of isoflurane. At the completion of surgery patients received Neostigmine 0.05 mg/kg and Glycopyrollate 0.008 mg/kg for reversal of neuro-muscular blockade.

Post operative monitoring: The occurrence of nausea and vomiting, severity of nausea according to verbal descriptive scale (VDS) (0 = no nausea, 1 = mild nausea, 2 = moderate nausea, 3 = severe nausea) and rescue antiemetic drug use was monitored at 0-2 hrs, 2-6 hrs and 6-24 hrs after surgery.

Nausea was defined as a subjective unpleasant sensation associated with awareness of urge to vomit. Vomiting was defined as forceful expulsion of gastric contents from the mouth. Retching was defined as laboured, rhythmic, spasmodic contractions of respiratory muscles without expulsion of gastric contents. Metoclopramide 10 mg iv was used as a rescue antiemetic when 2 episodes of vomiting had occurred or VDS more than 2 or if the patient requested for it. A detail of any adverse effects was recorded.

Data was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was used as test of significance. Continuous data was represented as mean and standard deviation. ANOVA test was the test of significance for mean difference between more than two groups. Paired t test was the test of significance for paired data (baseline versus at different interval comparison). p value <0.05 was considered as statistically significant. Poisson regression was used to compare the number of episodes of vomiting over time between the study groups. Generalized estimating equation was done to assess the effect of intervention on the presence of nausea or vomiting over time.

Results

The study was conducted on 130 female patients. Laparoscopic surgery was converted to open surgery in two patients who received palonosetron, and hence, they were excluded from the study. Patient characteristics such as age, ASA status, baseline vital parameters, weight and history of motion sickness or previous history of PONV and surgical factors like duration of anaesthesia and surgery were comparable between the two groups (Table 1).

The number of episodes of vomiting, risk for nausea and vomiting with respect to duration for intervention, severity of nausea and need for rescue medication was comparable between the 2 groups during 0- 2 hrs.

Table 1: Demographic details

Variables		Ondansetron (n=65)	Palonosetron (n=65)	p value
Age (years)		41.95 ± 12.21	38.52 ± 12.46	0.118
Blood pressure (mmHg)	systolic	136.65 ± 15.422	13.6 ± 16.193	0.818
	diastolic	82.02 ± 8.005	81.62 ± 8.713	0.789
SPO2 (%)		98.57 ± 1.015	98.59 ± 0.90	0.916
ASA PS	1	36(55.4%)	35(55.6%)	0.984
	2	29(44.6%)	28(4.4%)	
Body weight (kgs)		63.09 ± 7.875	61.90 ± 7.237	0.376
Motion sickness history	No	84.6%	82.5%	0.751
	Yes	15.4%	17.5%	
PONV in past	No	83.1%	82.5%	0.936
	Yes	16.9%	17.5%	
Duration (mins)	Surgery	102.54 ± 46.02	110.95 ± 49.79	0.323
	Anaesthesia	137 ± 50.996	145.95 ± 49.98	0.318

Table 2: Comparison of episodes of vomiting, severity of nausea vomiting according to VDS, use of rescue anti emetics and adverse effects between ondansetron and palonosetron at 0-2, 2-6 and 6-24 hrs

			Groups			P Value
			Ondensetron	Palonosetron	Total	0.05
0-2 hours	Episodes of vomiting	1 Episode	5	0	5	
		2 Episodes	0	1	1	
		No	60	62	122	
	Severity of nausea (VDS)	0	45	51	96	0.378
		1	14	8	22	
		2	5	4	9	
		3	1	0	1	
	Use of rescue antiemetics	No	59	60	119	0.323
		Yes	6	3	9	
	Adverse effects	Headache	0	2	2	0.148
		Absent	65	61	126	

2-6 hours	Episodes of vomiting	1 Episode	10	3	13	0.05
		2 Episodes	0	1	1	
		No	55	59	114	
	Severity of nausea (VDS)	0	26	47	73	<0.001
		1	26	11	37	
		2	5	2	7	
		3	8	3	11	
	Use of rescue antiemetics	No	54	58	112	0.181
		Yes	11	5	16	
	Adverse effects	Headache	3	6	9	0.210
		Headache + lightheadedness	0	1	1	
		Headache + dizziness	0	2	2	
		Absent	62	54	116	
6-24 hours	Episodes of vomiting	1 Episode	12	5	17	0.060
		2 Episodes	6	2	8	
		No	47	56	103	
	Severity of nausea (VDS)	0	20	41	61	<0.001
		1	27	16	43	
		2	12	5	17	
		3	6	1	7	
	Use of rescue antiemetics	No	45	57	102	0.003
		Yes	20	6	26	
	Adverse effects	Headache	4	12	16	0.027
		Absent	61	51	112	

During 2-6 hrs, severity of nausea and risk of nausea and vomiting was significantly lower in palonosetron group.

During 6-24 hrs, the episodes of vomiting, risk for nausea and vomiting, severity of nausea and need for rescue antiemetics was significantly lower in palonosetron group.

The side effect profile was comparable between the two groups in 0-2 and 2-6 hrs postoperatively but was significantly higher in palonosetron group during 6-24 hrs of post operative period (Table 2).

Table 3: Poisson Regression analysis: To find the relationship between type of intervention and number of episodes with respect to duration of intervention.

Time	Parameter	B	Std. Error	95% Wald Confidence Interval		Hypothesis Test			Exp (B)	95% Wald Confidence Interval for Exp (B)	
				Lower	Upper	Wald Chi-Square	df	Sig.		Lower	Upper
0-2 hrs	(Intercept)	-3.450	0.7071	-4.836	-2.064	23.805	1	0.000	0.032	0.008	0.127
	Ondansetron Group	.662	0.8660	-1.035	2.359	0.584	1	0.445	1.938	0.355	10.583
	Palonosetron Group	0[a]	.	.	.	.	.	.	1	.	.
2-6 hrs	(Intercept)	-2.534	0.4472	-3.410	-1.657	32.098	1	0.000	0.079	0.033	0.191
	Ondansetron Group	0.662	0.5477	-0.412	1.735	1.460	1	0.227	1.938	0.663	5.671
	Palonosetron Group	0[a]	.	.	.	.	.	.	1	.	.
6-24 hrs	(Intercept)	-1.946	0.3333	-2.599	-1.293	34.079	1	0.000	0.143	0.074	0.275
	Ondansetron Group	0.950	0.3909	0.183	1.716	5.902	1	0.015*	2.585	1.201	5.560
	Palonosetron Group	0[a]	.	.	.	.	.	.	1	.	.

Table 4: Generalized estimating equation: To assess the effect of intervention on the presence of nausea or vomiting over time – Linear regression model

Time	Parameter	Parameter Estimates									
		B	Std. Error	95% Wald Confidence Interval		Hypothesis Test			Exp(B)	95% Wald Confidence Interval for Exp(B)	
				Lower	Upper	Wald Chi-Square	df	Sig.		Lower	Upper
0-2 hrs	(Intercept)	0.190	0.192	-0.186	0.567	0.981	1	0.322	1.210	0.830	1.764
	Ondansetron Group	0.117	0.075	-0.031	0.265	2.401	1	0.121	1.124	0.969	1.304
	Palonosetron Group	0a	.	.	.	.	.	.	1	.	.
2-6 hrs	(Intercept)	0.254	0.233	-0.204	0.712	1.179	1	0.277	1.289	0.815	2.039
	Ondansetron Group	0.346	0.060	0.227	0.465	32.573	1	<0.0001*	1.413	1.255	1.592
	Palonosetron Group	0a	.	.		.	.	.	1	.	.
6-24 hrs	(Intercept)	0.349	0.285	-0.211	0.910	1.492	1	0.222	1.418	.810	2.483
	Ondansetron Group	0.343	0.044	0.256	0.430	60.058	1	<0.0001*	1.409	1.292	1.537
	Palonosetron Group	0a	.	.	.	.	.	.	1	.	.

Discussion

PONV continues to be an undesirable problem postoperatively, in spite of significant advances in general anaesthesia care. It results in significant patient distress and potentially affects post operative recovery, may result in delayed discharge from hospital and/or readmission. Morbidity associated with PONV includes dehydration, electrolyte imbalance, aspiration and surgical complications like bleeding and wound dehiscence.

Female gender, non-smoker status, history of PONV or motion sickness, use of perioperative opioids, use of volatile anaesthetics, duration of surgery, duration of anaesthesia, and type of surgery are all risk factors for PONV. In this study, these risk factors were similar in the two groups. Therefore, the difference in PONV incidence between the groups can be attributed to the study drug.

The newest class of antiemetics used for the prevention and treatment of PONV are the serotonin receptor antagonists (Ondansetron, Granisetron, Dolasetron, Palonosetron).

Ondansetron is a potent, highly selective 5-HT_3 receptor antagonist. The mechanisms of action of Ondansetron are both central and peripheral. It blocks the 5-HT_3 in the area postrema, nucleus tractus solitarius (NTS) and adjacent areas in the brain, which are related to nausea and vomiting. Also, it blocks 5-HT_3 receptors in the mucosal vagal afferents in the gastrointestinal tract.

Palonosetron is a "second generation" 5-HT_3 receptor binding agent newly approved by FDA for the prevention of PONV since March 2008. It has the highest binding affinity to the 5-HT_3 receptor and at approximately 40 hours, has the longest elimination half life. Unlike the representatives of the first generation with competitive inhibition of the 5-HT_3 receptor, Palonosetron seems to exhibit allosteric binding leading to effects persisting beyond the mere receptor binding time.

Paventi et al. [4] compared the efficacy of 4 mg versus 8 mg ondansetron for the prevention of PONV after laparoscopic cholecystectomy and concluded that 8 mg was more effective than 4 mg. A study by Candiotti and colleagues [5] comparing three different doses of palonosetron with placebo in elective laparoscopic abdominal and gynaecological surgery, a single 0.075 mg i.v. dose of palonosetron significantly increased the complete response rate (no emetic episodes and no rescue medication) compared with placebo during the 0–24 hr postoperative period, but not during the 24–72 hr postoperative interval. The doses of drugs used in the present study were based on the optimal dose for prophylaxis of PONV in these studies; thus, 0.075 mg palonosetron and 8 mg ondansetron were chosen. We did not include a control group receiving placebo in our study,

since placebo controlled trials may be considered unethical in view of the distressing implications of PONV.

It has been reported that patients receiving general anaesthesia with volatile agents, nitrous oxide and opioids were 11 times more likely to experience PONV than in other forms. In our study as our purpose was to compare the efficacy of two drugs under similar surgical and anaesthetic 0conditions, we did not avoid any of these agents.

In this study, 92.3% patients who received ondansetron didn't have any vomiting in the first 2 hrs postoperatively compared to 98.4% patients who received palonosetron. 84.6% patients and 72.3% patients in ondansetron group didn't have vomiting between 2-6 hrs and 6-24 hr period respectively compared to 93.7% and 88.9% in palonosetron group. This was statistically insignificant (p= 0.05 for 0-2 hrs, p = 0.087 for 2-6 hrs, p = 0.060 for 6-24 hrs).

In a study done by B. Laha et al. [6] comparing efficacy of ondansetron and palonosetron in preventing PONV following laparoscopic cholecystectomy, the incidence of vomiting between the two groups was also found to be statistically insignificant (p = 0.262 for 0-2 hrs, p = 0.176 for 2-6 hrs, p = 0.523 for 6-24 hrs). This was comparable to the results of our study.

Y.E. Moon et al. [7] in a study comparing ondansetron with palonosetron in prevention of PONV following thyroidectomy, used VDS to assess the severity of nausea and found it to be statistically insignificant in the first 2 hrs but significantly less in palonosetron group than ondansetron group during 2-24 hrs (p = 0.03). In our study, severity of nausea as assessed by VDS was found to be statistically insignificant between the two groups during the first 2 hours. However during the 2-6 hrs time period and 6-24 hr period, the severity of nausea was significantly higher in ondansetron group compared to palonosetron group (p = 0.001{2-6 hrs}, p<0.001 {6-24 hrs}) This was comparable to study by Y. E Moon et al.

In studies done by Taninder Singh et al. [8] and Nupur Chakravarthy et al. [9], the incidence of nausea was found to be significantly lower in palonosetron group compared to ondansetron group (p = 0.037 and p = 0.026 respectively). However the severity of nausea at different time intervals was not assessed in these studies.

Poisson's regression was used to find the relation between the type of intervention and number of episodes of vomiting with respect to duration of intervention and we found statistically significant higher risk of vomiting in ondansetron group compared to palonosetron group during 6-24 hrs post operatively (p = 0.015). This showed that with increase in duration of intervention, the number of episodes of vomiting was significantly higher in ondansetron group than palonosetron group.

Generalised estimating equation was used to assess the effect of intervention on the presence of nausea and vomiting over time and it showed that there was no significant difference in the risk of nausea and vomiting between the two groups during the first 2 hrs (p= 0.125). However, there was statistically significant higher risk for vomiting and nausea in the ondansetron group compared to the palonosetron group in 2-6 hrs and 6-24 hrs (p < 0.001).

Thus in our study, the number of episodes of vomiting, the severity of nausea and the risk for vomiting and nausea over time was significantly higher in ondansetron group than palonosetron group.

It has been recommended that in cases of breakthrough PONV, repeat antiemetic should be of a different class than the one used for prophylaxis. Metoclopramide was used as a rescue antiemetic for this very reason. In our study, there was no difference in the use of rescue antiemetics between the two groups in the first 6 hours post operatively. However from 6 to 24 hrs period, the use of rescue antiemetic was significantly higher in those who received ondansetron than those who received palonosetron (p = 0.003).

Sukhminderjit Singh Bajwa, et al. [10] in a prospective double blind study comparing the efficacy of 8 mg of Ondansetron with Palonosetron 0.075 mg iv in preventing PONV and also found similar results. This suggests that palonosetron has an antiemetic effect which lasts longer than ondansetron. The exact reason for the difference in effectiveness between the two drugs is believed to be related to the half lives (ondansetron 3-5 hrs versus palonosetron 40 hrs) and/or the binding affinities of 5-HT_3 receptor antagonists. Both the manner as well as the site of binding of palonosetron with 5-HT_3 receptors is different from that of ondansetron. The nature of this receptor binding may modify the functional responses to serotonin thus affecting the efficacy of drug.

The comparable PONV characteristics in both groups in the early post operative phase, followed by a significant difference in response in the later recovery period serve to accentuate the efficacy of palonosetron in long term prophylaxis.

The 5-HT_3 antagonists are safe with mild and transient side effects (e.g. headache, constipation, dizziness).

S K Park et al [3], in their study found comparable side effect profiles between palonosetron and ondansetron when used for prevention of PONV. However in our study, we found the incidence of sides effects namely headache and dizziness to be higher in palonosetron group compared to ondansetron at all time periods.

Conclusion

0.075 mg of palonosetron when administered before induction of general anaesthesia, the severity of nausea and risk for nausea and vomiting was significantly less compared to 8mg of ondansetron during 2 -6 hrs of post operative period.

The number of episodes of vomiting with respect to duration of intervention, severity of nausea and risk of nausea and vomiting was significantly lower in palonosetron group compared to ondansetron group during 6-24 hrs of post operative period.

The use of rescue antiemetics was also found to be significantly less in the palonosetron group compared to ondansetron group in 6-24 hrs of post operative period.

The side effects namely headache and dizziness was higher in palonosetron group than ondansetron group.

Thus we conclude that palonosetron is more effective antiemetic as compared to ondansetron for prevention of PONV in female patients undergoing laparoscopic surgeries under general anaesthesia.

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Effect of Oral Clonidine as a Premedication in Patients Receiving Spinal Anaesthesia with Hyperbaric Bupivacaine

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Abstract

Background: Spinal anaesthesia is the most commonly used technique for infraumbilical surgeries. Hyperbaric Bupivacaine has limited duration of action. Clonidine has been used to prolong the duration of local anaesthetic. Hence, we studied the effects of oral clonidine premedication on spinal anaesthesia with hyperbaric Bupivacaine vs placebo with reference to sedation, onset and duration of sensory and motor blockade including its effects on hemodynamic status and also on postoperative analgesic requirement. *Objectives:* To study the effect of oral clonidine premedication on spinal bupivacaine anaesthesia with respect to - The onset time, duration of sensory and motor blockade, Effect on haemodynamic status, Sedation, Duration of analgesia, Need for further analgesics in the first 24 hours postoperatively. *Materials & methods:* 60 adult (18-65 yrs) ASA physical status class I and II patients scheduled for lower abdominal, perineal and lower limb surgeries under spinal anaesthesia were recruited into the study. Patients were randomized to receive either 150 µg clonidine or placebo tablet using a random number table. Prespinal heart rate, blood pressure, oxygen saturation and sedation score recorded. Subarachnoid block performed with 3.0 ml of 0.5% hyperbaric Bupivacaine. Sensory & motor block assessed along with hemodynamic parameters and interventions required intraoperatively. Postoperatively heart rate, systolic and diastolic blood pressure, time of first request of analgesic and number of analgesics required in 24 hours were recorded and statistically analysed with p value < 0.05 considered as significant. *Results:* Clonidine group had higher incidence of sedation, faster onset of sensory block without any effect on the onset of motor block, prolonged duration of both sensory and motor block, reduction in blood pressure and heart rate with minimal requirement of haemodynamic interventions, reduced analgesic requirement in the early postoperative period compared to the Placebo group. *Conclusion:* Oral clonidine premedication in patients receiving hyperbaric bupivacaine spinal anaesthesia produces moderate sedation, hastens the onset of sensory block, prolongs the duration of sensory and motor block. Although causes reduction in blood pressure and heart rate, the haemodynamic interventions required is minimal. It also reduces analgesic requirement in early postoperative period.

Keywords: Clonidine; Bupivacaine; Spinal anaesthesia; Sedation; Sensory & motor block; haemodynamic interventions; postoperative rescue analgesics.

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Introduction

Regional anaesthesia has been known to be a better technique for lower limb and lower abdominal surgeries especially in patients with respiratory impairment [1]. It causes minimal intervention of airways, reduces the metabolic changes associated with surgery and at the same

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time provides residual postoperative analgesia [1]. Spinal anaesthesia is the most commonly performed regional anaesthetic technique, [1] due to its safety, reliability, rapid onset of neural blockade and the ease with which it is performed.

As expertise and time are required for epidural anaesthesia, it would be very useful to prolong the duration of spinal analgesia by alternative techniques or methods for prolonged surgeries. Several agents have been used to hasten the onset and prolong the duration of spinal anaesthesia. Vasoconstrictors like phenylephrine, opioids, dextran-40, carbonated local anaesthetics, proteins, potassium, clonidine etc. are some of the well-known agents [2].

Clonidine, an alpha 2 adrenoceptor agonist was introduced into clinical practice as an antihypertensive medication during early 1970. It has been shown to be an effective premedicant, providing preoperative sedation [3,4], perioperative haemodynamic stability [5,6], decrease in the dose of narcotics required to prevent reflex cardiovascular response to tracheal intubation or surgery [7] decrease in minimum alveolar concentration (MAC) of inhalational anaesthetics [8], and postoperative analgesia [9,10].

Regional anaesthesia too is benefited by using clonidine added to local anaesthetic for epidural, spinal, or peripheral block [11]. Clonidine has also been used in alleviating postoperative pain as an adjuvant to opioids [12].

In view of large number of literatures supporting the beneficial effect of clonidine in central neuraxial blockade, we aimed to study the effect of oral clonidine premedication (0.15 mg) during spinal anaesthesia (3 ml of 0.5% hyperbaric bupivacaine).

Materials and Methods

After institutional approval and informed written consent 60 adult ASA class I & II patients scheduled for lower abdominal, perineal and lower limb surgeries under spinal anaesthesia were recruited into the study. The study was conducted from October 2005 to September 2006. Exclusion criteria were Patients with spinal deformities, coagulopathies, local sepsis, Patients with known cardiovascular disease or on cardioactive drugs, Patient's refusal, Patients in whom lumbar puncture could not be performed at L_{3-4} level, Patients in whom supplementation of regional block was required.

Our study was a prospective, double blind, randomized, placebo-controlled study. Patients were randomized to receive either 150 μg clonidine or placebo tablet using a random number table. Blinding was achieved by pharmacy prepared sealed packets containing either study drug or placebo.

A routine pre-anaesthetic evaluation was conducted on the evening before surgery and relevant investigations done. Informed written consent was obtained after explaining the anaesthetic procedure. The patients were pre-medicated with tablet diazepam 10 mg at bed time on the previous night before surgery. They were kept nil orally for 6 hours prior to surgery for solid food and 2 hours for clear liquids.

On the day of surgery, before premedication, heart rate, systolic and diastolic blood pressure, and sedation were recorded. These were taken to be "baseline" readings. Sedation was assessed using the Ramsay scale [13]. Premedication consisted of either clonidine 0.15 mg or placebo, and was administered orally with sips of water 90 minutes before anaesthesia.

After the patient was shifted to the operation theatre, heart rate, systolic and diastolic blood pressure and SpO_2 were recorded using a 3 leads ECG, automated non-invasive blood pressure monitors and pulse oximeter. Sedation score was recorded. These were taken as "prespinal" values. Intravenous line was secured with an 18-gauge cannula and all patients were given 500 ml of ringer's lactate before performing spinal anaesthesia. Under strict aseptic precautions, with the patient in sitting posture, lumbar puncture was performed through a midline approach at L3-4 interspace using either a 23 or 25G Quincke's bevelled spinal needle. Once a free flow of cerebrospinal fluid was obtained, 3.0 ml of 0.5% hyperbaric Bupivacaine was injected. Patients were made to lie supine immediately after the completion of the injection and were retained in that position for at least 20 minutes before positioned for surgery. Sensory block was evaluated by pinprick every minute for first 20 minutes followed by every 10 minutes interval thereafter and the following parameters recorded - Time for the loss of pinprick sensation at T 10 dermatomal level, Highest level of sensory block achieved, Time to achieve highest sensory level, Time for 2 segment regression of sensory anaesthesia from highest level.

Motor block was assessed using Modified Bromage scale [14], and following parameters recorded - Time for onset of Bromage 3 motor block, Time taken for the recovery of motor block to Bromage 2.

Blood pressure and heart rate were recorded every 2 minutes for the first 20 minutes, every 10 minutes till the end of 1 hour, every 15 minutes for 2nd hour, followed by every 30 minutes until 360 minutes from the time of premedication (270 minutes from time of spinal anaesthesia). Time intervals at which hypotension and bradycardia occurred were noted. Hypotension (Systolic blood pressure < 90 mmHg) [15,16] was treated with injection Mephenteramine 6 mg increments intravenously. Bradycardia (Heart rate < 60 beats/ minute) was treated with injection Atropine 0.6 mg intravenously. Any desaturation (SpO_2< 90%) was treated with oxygen supplementation at 5 litres/ minute via face mask.

After surgery, patients were shifted to postoperative recovery room and following parameters recorded - Heart rate, systolic and diastolic blood pressure up to 360 minutes from the time of premedication, time of first request of analgesic, and number of analgesics required by the patient in 24 hours.

Data obtained are presented as mean±standard deviation. Age, sex distribution, ASA class, needle used for SAB and position of surgery were compared using Contingency coefficient (CC). Height, weight and sedation score were compared using Student's t-test. Intergroup comparison of onset and duration of sensory as well as motor block was done using Student's t-test. Haemodynamic parameters comparison between groups was done again by Student's t-test. Intergroup comparison of requirement of Atropine and Mephenteramine was done by Contingency coefficient. Intergroup comparison of time of 1st analgesic request and the number of analgesics needed in 24 hours postoperatively was done by Student's t-test.

Significant figures: p>0.05 is not significant, p<0.05 is significant, p<0.01 is highly significant.

Results

The demographic profile of the patients comparing age, sex, height, weight, ASA class, needle used for SAB and also position for surgery show no statistically significant difference and were comparable in both groups in our study.

The mean sedation score at the time of premedication in clonidine group 1.53±0.51 and placebo group 1.70±0.53 was not significant (p < 0.221). However, the mean sedation score just before spinal, in the clonidine group was 2.67±0.71 compared to placebo group of 1.50±0.57 was found to be statistically significant (p < 0.000) (Table 1).

The clonidine group showed faster onset of sensory block at T10 and also for maximum sensory height achieved (Table 2). Mean time for onset of sensory block at T10 in clonidine group was 2.43±0.73 min, in placebo group was 4.63±1.50 min. this was statistically significant (p < 0.001).Mean time required to achieve the maximum sensory height in clonidine group was 6.67±2.50 min, in placebo group was 11.67±3.13 min. Both the above were statistically significant with p < 0.001. The mean time for onset of maximum motor block in clonidine group was 10.47±2.66 min and in placebo group was 11.40±4.30 min, which had no statistical significant difference (p < 0.317), (Table 2).

The mean time for 2 segment sensory regression and motor block regression to Bromage 2 was longer in clonidine group (Table 2). Mean time for 2 segment sensory regression from the highest level in the clonidine and placebo group was 129.67±30.68 min and 77.33±13.88 min respectively, which was statistically significant (p < 0.0001), (Table 2). Mean time for recovery of motor block to Bromage 2 in clonidine group 198.50±29.36 min, in placebo group153.00±31.08 min was statistically significant (p < 0.0001).

Table 1: Sedation Score

	Clonidine (Mean±SD)	Placebo (Mean±SD)	t	p
Before Pre-med	1.53±0.51	1.70±0.53	-1.238	0.221
Before Spinal	2.67±0.71	1.50±0.57	7.0000	0.000

Table 2: Intergroup Comparison of Sensory and Motor Block

	Clonidine (Mean SD)	Placebo (Mean±SD)	T	P
Time for sensory onset at T 10 (min)	2.43±0.73	4.63±1.50	-7.240	0.0001
Time for max sensory height (min)	6.67±2.50	11.67±3.13	-6.837	0.0001
Time for max motor block (min)	10.47±2.66	11. 40±4.30	-1.010	0.317
Time for 2 seg sensory regression (min)	129.67±30.68	77.33±13. 88	8.512	0.0001
Time for motor block reg to bromage 2 (min)	198.50±29.36	153.00±31.08	5.827	0.0001

Baseline haemodynamic parameters like heart rate, systolic and diastolic blood pressure were comparable in both the groups and were not statistically significant (p>0.05) (Table 3, 4 and 5).

The haemodynamic parameters before spinal and at 360 min from the time of premedication were statistically significant (p < 0.05) (Table 3, 4 and 5). Mean heart rate, mean systolic and mean diastolic pressures in clonidine group were 76.73 +10.74 beats/min, 119.63±9.65 mmHg and 74.00 ±7.17 mmHg in clonidine group compared to 92.76±15.04 beats/min, 130.76±8.97 mmHg and 79.10±7.90 mmHg in the placebo group.

Following spinal anaesthesia, the lowest mean heart, lowest mean systolic and mean diastolic pressure were comparable in both groups without any statistical significance (p>0.05) (Table 3, 4 and 5).

Comparison of haemodynamic changes from baseline to Prespinal showed statistical significance (p < 0.0001), (Table 3, 4 and 5). The change in the mean heart rate in clonidine and placebo group was 7.06±10.66 beats/min and -10.86±12.96 *beats/min* respectively. The changes in the mean systolic and mean diastolic pressure in clonidine group were 7.70±10.32 mmHg and 7.53±7.01 mmHg respectively, whereas in placebo group it was - 4.10 ±9.72 mmHg and 0.03±8.29 mmHg respectively.

Comparison of haemodynamic changes from baseline to 360 min showed statistical significance (Table 3, 4 and 5). The change in the mean heart rate in clonidine and placebo group was 6.06±9.13 beats/min and -1.13±7.37 *beats/min* respectively. The changes in the mean systolic and mean diastolic pressure in clonidine group were 8.60± 11.47 mmHg mmHg and 3.73±7.32 mmHgmmHg respectively, whereas in placebo group it was -0.20 ±8.40 mmHg and -2.20±6.56 mmHg respectively.

Intergroup comparison of number of atropine doses required to treat bradycardia (heart rate <60 beats/min) was compared between the two groups using contingency coefficient. One dose of atropine was required in 7 patients in clonidine group and 4 patients in placebo group. Second and third doses of atropine were required by 3 and 2 patients only in clonidine group. Intergroup comparison was found statistically nonsignificant (p < 0.064), (Table 6).

Intergroup comparison of number of vasopressor doses (Mephenteramine 6 mg) required to treat hypotension (SBP <90 mmHg) was compared between the two groups using contingency coefficient scores. One dose of mephentermine was required in 3 patients in clonidine group and 4 patients in placebo group. Second dose of

Table 3: Intergroup Comparison of Heart rate (BPM)

	Clonidine (Mean±SD)	Placebo (Mean±SD)	t	P
Baseline	83.80±5.01	81.90±6.90	1.220	0.228
Pre-spinal	76.73±10.74	92.76±15.04	-4.749	0.0001
Lowest	63.90±7.98	67.40±8.91	-1.601	0.115
At 360 Mins	77.73±7.91	83.13±7.47	-2.67	0.01
Change (Baseline-Pre-spinal)	7.06±10.66	-10.86±12.96	5.852	0.0001
Change (Baseline to 360 Mins)	6.06 ±9.13	-1.13 ±17.37	3.359	0.001

Table 4: Intergroup Comparison of Systolic Blood pressure (mmHg)

	Clonidine (Mean±SD)	Placebo (Mean±SD)	T	P
Baseline	127.33±10.63	126.66±11.57	0.232	0.817
Pre-spinal	119.63±9.65	130.76±8.97	-4.625	0.0001
Lowest	100.00±9.11	101.80±9.79	-0.737	0.464
At 360 Mins	118.73±9.01	126.87±10.58	-3.205	0.002
Change (Baseline-Pre-spinal)	7.70±10.32	-4.10±9.72	4.556	0.0001
Change (Baseline to 360 Mins)	8.60±11.47	-0.20±8.40	3.388	0.001

Table 5: Intergroup Comparison of Diastolic Blood pressure (mmHg)

	Clonidine (Mean±SD)	Placebo (Mean±SD)	T	P
Baseline	81.53±7.53	79.13±6.67	1.306	0.197
Pre-spinal	74.00±7.17	79.10±7.90	-2.616	0.011
Lowest	56.93±7.14	56.90±6.89	0.018	0.985
At 360 Mins	77.80± 5.54	81.33±6.52	-2.261	0.028
Change (Baseline-Pre-spinal)	7.53±7.01	0.03±8.29	3.780	0.0001
Change (Baseline to 360 Mins)	3.73±7.32	-2.20±6.56	3.302	0.002

Table 6: Number of Atropine and Mephentermine doses required

	Atropine doses				Mephentermine doses		
	0	**1**	**2**	**3**	**0**	**1**	**2**
Clonidine	18	7	3	2	25	3	2
Placebo	26	4	0	0	26	4	0
CC		0.329				0.187	
p-Value		0.064				0.339	

Table 7: Post-operative Analgesic requirement

	Clonidine (Mean±SD)	**Placebo (Mean±SD)**	**t**	**P**
1st Analgesic Request	336.63±155.22	245.17±77.70	2.886	0.005
Rescue Analgesics Needed In 24 Hours	2.07±0.74	2.70±0.65	-3.520	0.001

mephentermine was required by 2 patients in clonidine group only. Intergroup comparison was found statistically nonsignificant ($p < 0.339$), (Table 6).

Intergroup comparison of the mean time for the first analgesic request and the mean number of rescue analgesics needed in first 24 hours done using student t-test was statistically significant. (Table 7). The mean time for the first analgesic request was 336.63±155.22 min and 245.17±77.70 min for clonidine and placebo groups respectively. The mean number of rescue analgesics needed in first 24 hours in clonidine and placebo group was 2.07±0.74 and 2.70±0.65 respectively.

Discussion

Spinal anaesthesia is the most commonly performed regional anaesthetic technique [1], for infraumbilical surgeries and several agents have been used to hasten the onset and prolong the duration of spinal anaesthesia. Vasoconstrictors like phenylephrine, opioids, dextran - 40, carbonated local anaesthetics, proteins, potassium, clonidine etc are some of the well-known agents [2]. Clonidine was introduced into clinical practice as an antihypertensive medication during early 1970. It has shown to be an effective premedicant, providing preoperative sedation, [3,4] perioperative haemodynamic stability, [5,6] and postoperative analgesia [9,10]. Clonidine, added to local anaesthetic for epidural, spinal, or peripheral block, prolongs and intensifies anaesthesia for surgery [11]. Orally or intrathecally administered clonidine in a dose ranging from 75 µg to 300 µg has shown to prolong duration of spinal anaesthesia. The purpose of our study was to investigate the effect of 150 µg oral clonidine premedication on bupivacaine spinal anaesthesia.

In our study, patients were more sedated in the clonidine group compared to placebo. Similar results were found in studies done by Liu et al. [17] and Niemi [18]. Sedative effect of clonidine may be mediated by postsynaptic α2A subtype adrenoceptors located in the locus coeruleus, causing a decrease in noradrenergic activity [19].

We found in our study that the time taken for onset of sensory block at T 10 and the attainment of highest level of sensory block was significantly shorter in the clonidine group compared to placebo. The time for 2-segment regression was prolonged in clonidine group compared to placebo. The results of this study match well with the studies done by Ota et al. [15,16,20]. However our study was in contrast with study done by Bonnett et al. [21] who showed that subarachnoid clonidine but not oral clonidine prolonged the duration of sensory block. In our study we found no difference in the time of onset of complete motor block between the two groups and the duration of motor block was prolonged in clonidine group, in accordance with the studies by Singh et al. [22,23]. Thus, we confirm that oral clonidine (0.15 µg) premedication prolongs the sensory and motor blockade during bupivacaine spinal anaesthesia. Studies using intrathecal clonidine have demonstrated prolongation of sensory and motor block indicating antinociceptive action of clonidine in the dorsal horn of the spinal cord [18]. 150 µg oral clonidine used in our study seems too small to increase the concentration of clonidine in cerebrospinal fluid. Clonidine is highly lipid soluble and crosses tissue barriers rapidly and therefore may interact with a- adrenergic receptors at spinal and supraspinal sites within the central nervous system [17].

In our study, the mean systolic pressures were comparable before premedication. However, prespinal mean systolic blood pressure showed

significant difference between the two groups. The lowest mean systolic pressure recorded after spinal anaesthesia were comparable in both groups. The number of patients requiring intravenous Mephentermine to treat hypotension were 5/30 in clonidine group and 4/30 in placebo group ($p < 0.339$). Our study coincided with the study done by Ota et al. [15] showing no significant difference in SBP before premedication and also the lowest SBP after spinal anaesthesia. However, it differed from Ota et al. [15] by being statistically significant between the two groups. Thus, we conclude that oral clonidine (150 μg) premedication though lowers the mean SBP for prolonged period, the incidence of intervention to treat hypotension is minimal and comparable to that of placebo.

In our study, the heart rates were comparable at baseline between the groups. Even the lowest heart rate recorded following spinal anaesthesia were comparable. However, prespinal heart rates were significantly lower in the clonidine group compared to placebo. The results of this study match well with the studies done by Ota et al. [15]. The number of patients requiring intravenous Atropine to treat bradycardia were 12/30 in clonidine group and 4/30 in placebo group. The heart rates recorded at 360 min from the time of premedication was significantly lower in clonidine group compared to placebo.

Singh et al. [23] used 200 μg oral clonidine 90 minutes before spinal anaesthesia. They found that incidence of bradycardia (HR <50 beats/min) was higher in clonidine group (40%) compared to placebo (10%). Ota et al. [20] in their study of dose related prolongation of tetracaine spinal anaesthesia used 75 μg, 150 μg and 300 μg oral clonidine 60 minutes before anaesthesia. They found that frequency of bradycardia (HR<45 beats/min) was significantly greater with 300 μg than with 150 μg of oral clonidine. Though the incidence of bradycardia was higher in the above studies, the dose of clonidine used by them was more than 150 ug. In our study there was a higher incidence of bradycardia in clonidine group (12/30) as compared to placebo (4/30). The definition of bradycardia in our study was a heart rate < 60 beats/min, whereas in other studies bradycardia was defined as either heart rate < 50 beats/min [29] or < 45 beats/min [15,20]. This might explain the higher incidence of bradycardia for 150 μg clonidine in our study. However, the lowest heart rate seen in our study was 52 beats/min. Thus, we confirm that 150 μg oral clonidine, though lowers the heart rate, the requirement of intervention is minimal and comparable to that of placebo, and this dosage may be safely used as a premedicant.

In our study, we found a significant difference in the time of 1st analgesic request and the number of rescue analgesics needed in first 24 hours between the two groups. The analgesic effect of clonidine has been demonstrated by many studies. Our study results were in accordance with the results by Niemi, [18] Bernard et al. [11] and Bonnet et al. [24] in which clonidine group showed delayed onset of pain and decreased opioid dose requirement during the 24-hour postoperative period. The analgesic property of clonidine administered intrathecally or epidurally has been attributed to its action on an adrenoceptor of the dorsal horn of the spinal cord [18]. Oral clonidine used in the present study also showed reduction in the analgesic requirement in the early postoperative period. The mechanism of action of oral clonidine may be same as that of systemically administered clonidine and needs further evaluation.

Several limitations of our study need to be discussed, though they may not have significant influence in our study. Lack of dose-response or time-response design. We used a standard dose of 150 μg oral clonidine irrespective of the weight of the patients, volume of distribution, gastric emptying, metabolism etc which may affect the plasma levels of clonidine and we did not measure the plasma level of clonidine in each patient during the study. Higher incidence of sedation after clonidine premedication may have resulted in unblinding of the subjects and biased our results. The type of surgery might have influence on recorded lowest blood pressures and heart rate values.

Conclusion

we conclude that oral clonidine at a dose of 0.15 mg given 90 min before bupivacaine anaesthesia produces higher incidence of sedation, hastens the onset of sensory block without any effect on the onset of motor block, prolongs the duration of both sensory and motor block. Although produces a reduction in blood pressure and heart rate, the haemodynamic interventions required is minimal. It also reduces the analgesic requirement in the early postoperative period.

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A Comparative Study of Plain and Hyperbaric Solutions of Bupivacaine HCl During Spinal Anaesthesia

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Abstract

Background: Spinal anesthesia is often used for both elective and emergency surgeries. Anesthesia-related mortality is decreased when general anesthesia is avoided. *Aim:* To compare the anaesthetic behaviour and haemodynamic consequences produced by the intrathecal injections of plain and hyperbaric solutions of Bupivacaine with the patients in supine horizontal position. *Materials and methods:* Sixty patients of ASA I – II were divided into 2 groups of 30 each. Group-A was given 3 ml. of -0.5% plain Bupivacaine sub arachnoidally whereas Group-B was given 3 ml. of 0.5% hyperbaric Bupivacaine. *Results:* It was found that extent of sensory blockade was much higher in Group-B as compared to Group-A. The degree of motor blockade was also much more intense in Group-B as compared to Group-A. The duration of analgesia was more in Group-A as compared to Group-B, but the time onset of analgesia was faster in Group-B (hyperbaric). Haemodynamically patients in Group-A were stable due to lesser extent of sympathetic blockade when compared to patients in Group-B. *Conclusion:* Plain Bupivacaine gives a lesser cephalad spread and can be effectively used for lower limb surgeries, it has to be used with caution for lower abdominal surgery as the spread is relatively unpredictable.

Keywords: Bupivacaine; Lower abdominal surgery; Haemodynamic consequences.

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Introduction

Pain is the most common and distressing effect of disease and surgery. It is an unmeasurable entity and has been a challenge and concern for researchers. For good and prolonged analgesia, systemic analgesics are required to be given in high doses and with higher doses the side effects could be disastrous. General anaesthesia mostly necessitates tracheal intubation, administering volatile anaesthetics and muscle relaxants that are potentially dangerous and require a certain degree of expertise in their usage. Centro-neuraxial blocks – spinal & epidural (including caudal) eliminate these problems associated with general anaesthesia and also minimise post-operative complications like vomiting [1,2].

Centro-neuraxial block results in sympathetic blockade, sensory analgesia and motor blockade in that order depending on the dose, concentration and/or volume of local anaesthetic administered. Bupivacaine has emerged as an important local

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anaesthetic drug used for spinal anaesthesia in view of its relatively longer duration of action as compared to Lignocaine and also due to its ability to produce adequate sensory and motor blockade.

In view of substantiating the above studies a study was undertaken with plain 0.5% Bupivacaine and hyperbaric 0.5%, Bupivacaine (with 8% glucose) administered intrathecally in a fixed volume of 3 ml, with the patient in supine horizontal position. Our aim is to evaluate the level of sensory block, the quality of motor block and haemodynamic changes separately with each preparation of Bupivacaine.

Materials and Methods

A clinical study was undertaken using spinal analgesia as an anaesthetic technique and Bupivacaine hydrochloride of 0.5% strength as the local anaesthetic drug of two types of baricity namely plain and hyperbaric.

The baricity of plain solution used was 0.99266 and that of hyperbaric solution was 1.02346. Sixty patients belonging to age groups between 20-50 years of either sex and belonging to ASA I were selected who were undergoing lower abdominal and lower limb surgeries. They had a mean age of 31 years and a mean weight of 54 kg. These patients were divided into 2 groups A & B, consisting of 30 patients each. Patients in group A were given plain Bupivacaine and patients in group B received hyperbaric Bupivacaine. The demographic and pre-anaesthetic haemodynamic data were comparable in both groups.

Detailed history and a complete pre-operative examination were made so as to exclude patients with any systemic disorder, especially neurological disease and bleeding diathesis. All patients were submitted to routine investigations such as urine analysis, complete blood picture, blood sugar, blood urea and blood grouping and tying and informed consent was obtained.

Technical Aspects

Pre-medication, especially with analgesics was avoided as this might influence and modify the haemodynamic changes produced. Pre-operatively the heart rate and blood pressure of the patient was recorded and an intravenous line established with a large bore i.v. cannula in a large peripheral vein and a crystalloid solution such as Ringers lactate infused. Intra-operatively, the heart rate and blood pressure and respirations of the patient were monitored at frequent intervals. Sterility is of vital importance. Since infection introduced from without is a dangerous but completely avoidable complication.

The anaesthesiologist should scrub up as for a surgical operation and wear a sterile gown and gloves. As much as possible of the necessary equipment should be contained in a sterile pack. This includes sterile towels for covering the trolley top and one for the patient, cotton swabs, swab holding forceps, a gallipot for skin cleansing solutions and glass syringes. The patients back should be cleaned widely using spirit and sterile towels draped appropriately.

The patient was placed in the lateral decubitus position with the shoulders and anterior superior iliac spine in straight line, with back parallel to edge of operating table nearest the anaesthesiologist, with thighs flexed on the abdomen and neck flexed. The operating table was adjusted to a horizontal position.

Lumbar puncture was done using midline approach at L 3-4 space using a 24 gauge disposable needle which tends to split or spread the dural fibres rather than cut it, when introduced with the bevel parallel to dural fibres. This was done to decrease the incidence of post-spinal headache.After lumbar puncture was performed and subarachnoid space entered a free flow of CSF was obtained and the drug, either plain or hyperbaric Bupivacaine, 3 ml of 0.5% strength was instilled and the time recorded. The patient was immediately placed in supine position for the rest of the study.

Pre-loading with I.V. fluids consisted of 15 ml/Kg of a crystalloid solution infused over 20-30 minutes. After the injection of local anaesthetic another 8 ml/Kg was given over 30 minutes. Thereafter fluids were administered on the basis of changes in arterial pressure. Blood loss was replaced with a crystalloid solution on a 3:1 basis.

The following variables were measured every 5 minutes during the first 30 minutes after the intrathecal injection.

- Progression and upper level of sensory blockade, evaluate by pinprick after 30 minutes of injection.
- The time taken by drug to produce motor paralysis and the quality of motor blockade according to modified BROMAGE scale, ranging from 0 indicating no motor block to 3 indicating complete motor blockade.
- Duration of sensory blockade, defined by re-appearance of pain at the operative site.

- Duration of motor blockade, defined by return to normal lower limb movement.
- Changes in heart rate, blood pressure, Incidence and amount of vasopressors and/ or anticholinergics used.
- Other complications.

A decrease in systolic arterial pressure of 30% or more below preoperative levels as well as decrease in heart rate of more than 20% were considered significant and treated with 3 mg of mephentermine and 0.6 mg atropine sulphate respectively.

Modified Bromage Scale:

0 - No paralysis (full flexion of knee and feet)

1 - inability to raise extended leg (just able to move knees)

2 - inability to flex knees (able to move feet only)

3 - inability to flex ankle joint (unable to move feet or knees)

All the patients were clinically assessed during their stay in hospital until discharge. Incidence of post-spinal headache was recorded.The results were expressed as the arithmetic mean and standard deviation.

Results

There were 30 patients in each group.

Table 1: Demographic and pre-anaesthetic haemodynamic data in the two groups.

Patient characteristics	Group- A	Group- B
Age (yr.)	32.7±10.3	30±9.8
Weight (Kg)	53.2±7.23	54.7±6.0
Height (Cm)	66.8±2.63	66.5±3.1
ASA±	1	1
Systolic (mm Hg) B.P.	119.3±9.6	117.6±9.2
Heart Rate (bpm)	83.1±5.05	81±4.8

Surgery lasted 134±23 minutes in group A and 124±26 min in group B with no significant difference

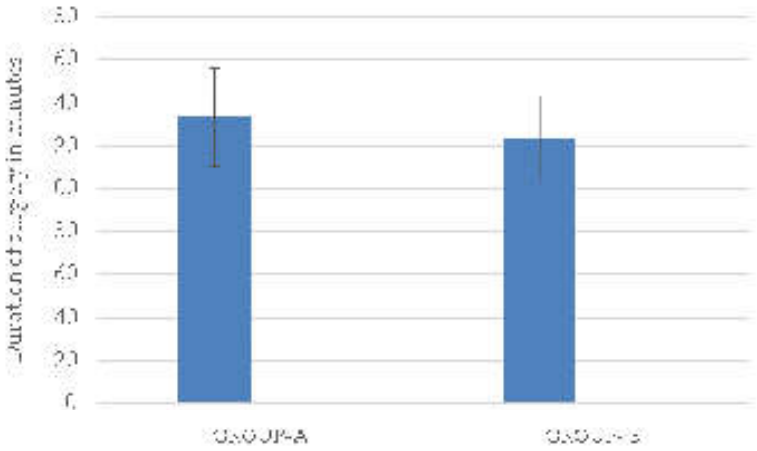

Fig. 1: Duration of surgery in both groups

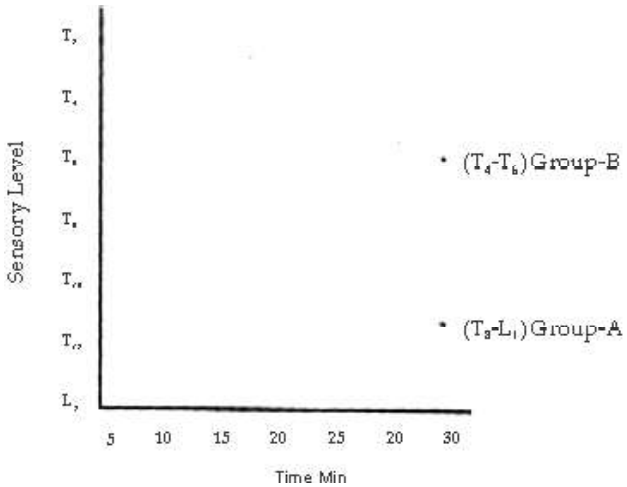

Fig. 2: Comparison between two groups of the spread of sensory level in first 30 minutes, after administration of 3 ml. of 0.5% Bupivacaine.

between groups (Table 1 and Figure 1).

Cephalad spread of sensory blockade, assessed by pinprick was significantly higher at all times with the hyperbaric solution than with plain group. The spread of sensory block was assessed every 5 minutes upto 30 minutes (Figure 2).

Table 2: Degrees of motor blockade assessed on the basis of modified BROMAGE Scale:

Degree of Blockade	Group - A	Group - B
Grade I	0	0
Grade II	17 (58%)	0
Grade III	13 (42%)	30 (100%)

In Group-B (hyperbaric group) all the patients achieved grade 3 blockade (100%) whereas in the Group-A (plain group) 58% had grade 2 blockade and (42%) had Grade 3 (Table 2).

There was a significant difference between the two groups (Figure 3).

Table 3: Haemodynamic Changes

Changes from pre-anaesthetic values in	Group-A	Group-B
Systolic pressure (mean +/- SD)	-15.4 ±5.57	-25.6 ± 7.2
Heart rate (mean SD)	-8 ± 4.56	-11.9 ± 4.7
No. of patients receiving		
a. Me phentermine	5	0
b. Atropine Sulphate	11	0

Significantly greater decrease in systolic arterial pressures and heart rate was observed in Group-B

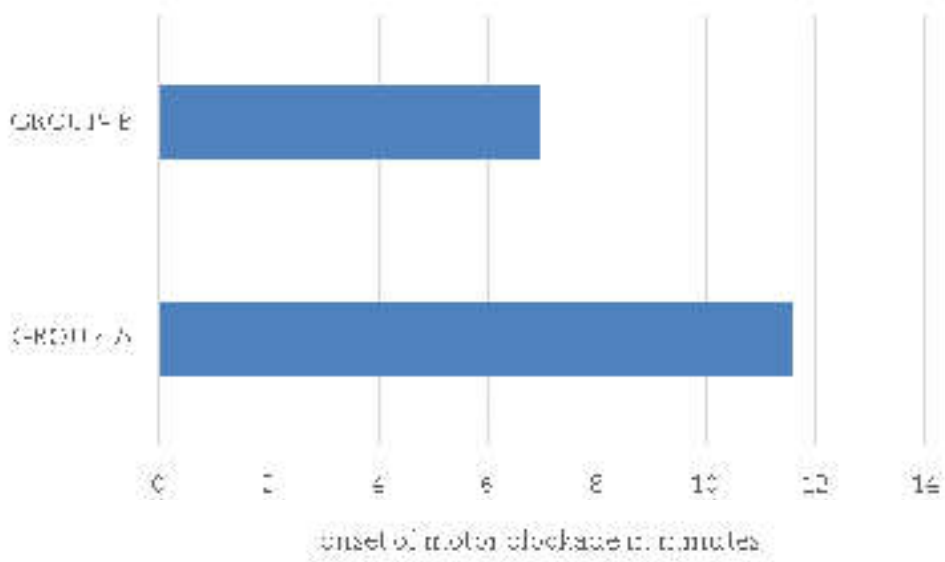

Fig. 3: Time taken for onset of motor blockade from time of intrathecal injection in groups

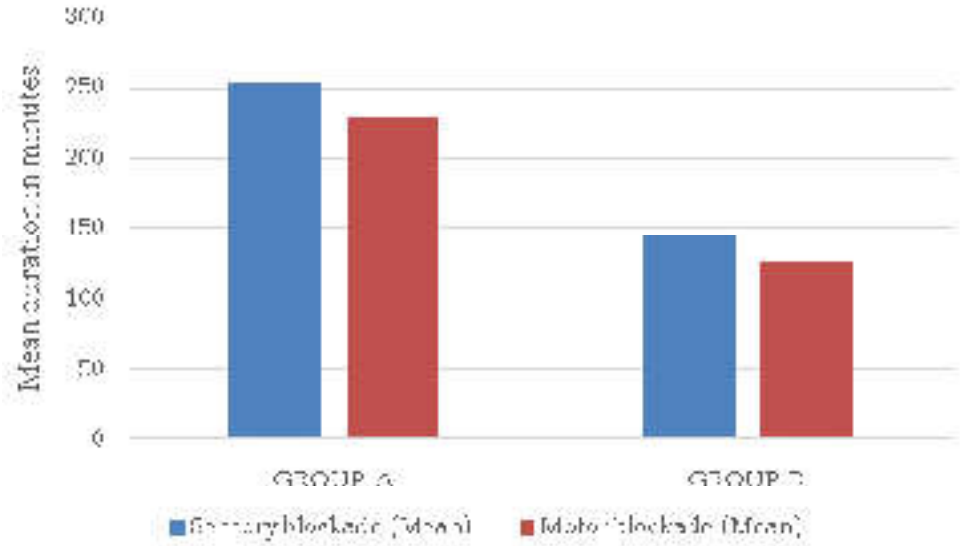

Fig. 4: Duration Sensory blockade and of motor blockade

and consequently more number of patients receiving vasopressors (16%) and anticholinergics (33%) respectively (Table 3).

In the hyperbaric group (i.e. Group-B) the sensory block averaged around 144 Minutes and motor block was around 126 minutes (Figure 4).

In contrast, the sensory blockade in Group-A was around 253 minutes and motor block averaged 228 minutes showing significant difference between the groups. It confirms the feature of Bupivacaine that it can provide significant separation of sensory anaesthesia and motor blockade. The amount of crystalloids administered throughout the study was 2000 ml. in Group-B and 1600 ml. in Group-A indicating significant differences.

No post-spinal headache was observed in any of the sixty patients.

Discussion

Spinal anaesthesia is one of the commonly used anaesthetic technique for lower abdominal and lower limb surgeries. More so in the developing and 3rd world countries where the facilities for general anaesthesia are scarce. Different drugs are being used for spinal anaesthesia of which Lignocaine and Bupivacaine are commonest. Of late Bupivacaine in its different forms as far as its baricity is concerned has been used for spinal anaesthesia.

In our study plain Bupivacaine compared with hyperbaric Bupivacaine was given sub arachnoidallyfor lower abdominal and lower limb surgery. The drug was instilled at the L 3-4 space with the patient in lateral position and then turned supine.

Previous studies (Van Gesseletal) [3] have shown that hyperbaric Bupivacaine results in a higher cephalad spread as compared with plain solution in horizontal supine position. In our study the median height of sensory analgesia in Group-A was T 11(Range T 8 – L 1) as compared to Group –B in which it was T 6 (Range T 4 –T 12). Thus showing the higher spread of hyperbaric solution. Since in the supine position highest patient of spinal column is L 3 an d subarachnoid space is inclined downwards in a cephalad direction it can be understood why there was a lesser cranial spread of the plain solution. The factors which determine intrathecal spread of local anaesthetic agents have been investigated in numerous clinical studies, the results of which have been the subject of a recent review [4]. Many of the factors have a relatively minor influence and manipulation of these is largely beyond the clinician's control. However, the two main factors, the baricity of the injected solution and the patient's position immediately after intrathecal injection, are amenable to alteration by the clinician.

Moller et al. [5] have shown in their study that the onset time of motor blockade was very much dependent on the baricity of solution (that is the percentage of glucose added). In our study the mean onset time of motor blockade in Group-A was 11.6 min. as compared to 7 min. in Group-B. We also compared the degree of motor blockade using the modified Bromage scale and found that in Group-A grade 3 blockade was present in 60% and Grade-2 in 40% whereas in Group-B all the patients (100%) had Grade-3 block thus highlighting the importance of baricity on the degree of motor blockade.

In our study the mean duration of motor blockade in Group- A was 228 min as compared to 126 min. in Group-B which is a very significant finding. This finding is also in accordance with Moller et al [5].

We found that the mean time onset of sensory analgesia as assessed by pinprick method was 8 min. in Group-A when compared to 6 min. in Group-B. Another important finding is that there was a lower blockade with hyperbaric solutions, which is consistent with previous studies [6,7,8,9], while other studies also proposed that hyperbaric solutions may be more suitable to reach the higher thoracic dermatomes as opposed to their plain (i.e., isobaric) [7,10].

Chambers et al. [11] reported in their study that duration of analgesia with 3 ml of 0.5% hyperbaric Bupivacaine was about 2 hrs. And 2.5 – 3 hrs. with plain Bupivacaine. In our study the mean duration of sensory analgesia in Group-A was 253 min. and Group-B 144 min. As previous studies have shown that duration varies with extent of block, we found that in our study, as already mentioned the extent of block was much higher with hyperbaric (Group-B) than plain (Group-A) Bupivacaine.

In our study we also tried to compare the haemodynamic changes in the two groups in the form of heart rate and blood pressure. We found that incidence of hypotension i.e., a fall of systolic presence more than 30% of pre-anaesthetic value, was more in Group-B (16%) as compared to Group-A where there was no significant fall of blood pressure

This is due to the extensive sympathetic block in Group-B patients because of higher spread of hyperbaric solution. In our study 11 patients in Group-B required injection of Atropine sulphate for

the correction of bradycardia whereas bradycardia was not observed in Group-A.

Thus patients in Group-A were more stable haemodynamically than Group-B. The main reason being, a lesser spread of sympathetic block as compared to Group-B this spread was not consistent in all patients in Group-A as reported by Logan Mr, Mc. Clure et al. [12].

Post operatively our patients were followed till time of discharge. None of them complained of any headache nor were there any neurological complaints or sequelae.

Conclusion

Sixty patients of ASA I – II were divided into 2 groups of 30 each. Group-A was given 3 ml. of -0.5% plain Bupivacaine sub arachnoidallywhereas Group-B was given 3 ml. of 0.5% hyperbaric Bupivacaine.

It was found that extent of sensory blockade was much higher in Group-B as compared to Group-A. The degree of motor blockade was also much more intense in Group-B as compared to Group-A. The duration of analgesia was more in Group-A as compared to Group-B, but the time onset of analgesia was faster in Group-B (hyperbaric).

Haemodynamically patients in Group-A were stable due to lesser extent of sympathetic blockade when compared to patients in Group-B. Thus concluding that though plain Bupivacaine gives a lesser cephalad spread and can be effectively used for lower limb surgeries, it has to be used with caution for lower abdominal surgery as the spread is relatively unpredictable. Post- operative complications do not vary with either drug and if they do occur they may be attributed to faulty techniques.

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Effect of Dexmedetomidine on Haemodynamic Response to Pneumoperitoneum in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Background: As laparoscopic cholecystectomy is a routinely performed surgery, it is desirable to have a stable intraoperative haemodynamic status. This study is designed to evaluate the efficacy of single intravenous bolus dose of dexmedetomidine, given 10 minutes before induction of anesthesia to provide hemodynamic stability in patients undergoing laparoscopic cholecystectomy. *Materials & Methods:* A Double blind randomized controlled study was conducted in the department of Anaesthesiology, Manipal Hospital Bangalore, Patients undergoing elective laparoscopic cholecystectomy, under general anaesthesia for a period of one year from June 2013 to May 2014. Total 60 patients belonging to ASA physical status I and II, in the age group of 18 to 65 years scheduled for elective laparoscopic cholecystectomy surgery were selected for this study. The two groups, Dexmedetomidine and control, were comparable with respect to age, sex, weight and ASA physical status. *Results:* We observed lesser magnitude of variation in HR, SBP, DBP, MAP atinsufflation of pneumoperitoneum until 30 minutes post pneumoperitoneum in dexmedetomidine group compared to control group ($p<0.05$). During pneumoperitoneum the maximum SBP and MAP attained in dexmedetomidine group was lesser compared to control group ($p<0.001$). Dexmedetomidine group also had less number of episodes of increase in SBP and MAP of more than 20% of baseline. We also found that the requirement for more than 1% of isoflurane in control group was higher (73%) compared to dexmedetomidine group. The recovery time was found to be similar in both groups. *Conclusion:* In conclusion, dexmedetomidine at a dose of 1 µgkg-1 bolus given at induction of anesthesia over 10 minutes resulted in statistically significant hemodynamic stability during pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy surgeries.

Keywords: Dexmedetomidine; Haemodynamic response; Laparoscopic Cholecystectomy; Pneumoperitoneum.

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Introduction

Laparoscopic surgeries require creation of pneumoperitoneum (PNP) which is produced by insufflation of Carbon Dioxide (CO_2) in the abdominal cavity by using an automated flow controlled Carbon Dioxide insufflator which supplies gas till the required intra-abdominal pressure is reached. Inflation pressure can vary from 0–30 mmHg whereas the total gas flow volume can be set from 0–9.9 L/min.

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The multiple benefits reported after laparoscopy explains its increasing use [1]. consequently, laparoscopy have now become the standard technique for cholecystectomy. However, the pneumoperitoneum (PNO) required for laparoscopy results in pathophysiologic changes. More importantly, changes in cardiovascular function occur during laparoscopy. These are characterized by an increase in arterial pressure and systemic and pulmonary vascular resistances (SVR and PVR) soon after the beginning of intra abdominal insufflation, with significant changes in heart rate (HR). A 10% to 30% decrease in cardiac output has also been reported in most studies [2-3] both mechanical and neuro-humoral factors contribute to these changes [2-4]. Several mediators have been proposed: catecholamines, prostaglandins, renin and vasopressin [5].

Joris et al. [5] studied the haemodynamic changes induced by laparoscopy. They observed that laparoscopy resulted in progressive and significant increase in plasma concentrations of cortisol, epinephrine, norepinephrine and renin. Vasopressin plasma concentrations markedly increased immediately after the beginning of pneumoperitoneum. The profile of vasopressin release paralleled the time course of changes in systemic vascular resistance. Prostaglandin and endothelin did not change significantly.

Also in addition, laparoscopic cholecystectomy is performed in reverse trendelenberg potion. This position leads to diminished venous return, further reducing the cardiac output [6].

Till date, many different techniques and pharmacological agents have been used to reduce the detrimental hemodynamic effects of pneumoperitoneum. Techniques like reduction in intra abdominal pressure during pneumoperitoneum and gasless laparoscopy using abdominal elevators have been employed [7]. Pharmacological agents like beta blockers, opioids, increasing concentrations of inhalational anesthetic agents, nitroglycerine and alpha 2 adrenergic agents have also been tested [1,8,9]. Again combined general anaesthesia with epidural anaesthesia [10] is yet another strategy employed by anaesthesiologists to control perioperative haemodynamic instability, with limited success. Interestingly, alpha- 2 adrenergic agonists have been shown to improve haemodynamic stability during gynecolologic laparoscopy [11].

Alpha 2 agonists produce diverse responses, including analgesia, anxiolysis, sedation, and sympatholysis, each of which has been reported to contribute to the treatment of surgical and chronic pain patients and in panic disorders as well. Recently, the Food and Drug Administration registered two novel alpha 2-adrenergic agonists clonidine and dexmedetomidine [12].

Dexmedetomidine is a imidazole derivative, a highly selective and potent alpha 2 adrenoreceptor agonist. It is a dextroenantiomer and the pharmologically active component of the medetomidine [13,14]. Dexmedetomidine with a elimination half life of two to three hours is a highly potent and specific alpha 2 agonist (1620: 1, alpha 2: alpha 1), compared to clonidine [(220:1) (alpha 2: alpha 1)] [14] and has a shorter duration of action Dexmedtomidine is considered a full agonist at alpha 2 receptors as compared to Clonidine which is considered as a partial agonist. Dexmedetomidine has sedative, analgesic and anesthetic sparing effects, and the ability to blunt the sympathetic response to surgery, resulting in intraoperative hemodynamic stability. Similar to clonidine, dexmedetomidine also attenuates the haemodynamic response to tracheal intubation, decreases plasma catecholamine concentration during anaesthesia and decreases perioperative requirements of inhaled anaesthetics [15].

Aims and Objectives

1. To study the effect of dexmedetomidine 1 μgkg^{-1}, given as a bolus prior to anesthetic induction in providing hemodynamic stability during pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy surgery.
2. To study the anesthetic sparing effect of dexmedetomidine in terms of isoflurane requirement during anesthesia.
3. To study the effect of dexmedetomidine on recovery time.

Materials and Methods

A Double blind randomized controlled study was conducted in the department of Anaesthesiology, Manipal Hospital Bangalore, Patients undergoing elective laparoscopic cholecystectomy, under general anaesthesia for a period of one year from June 2013 to May 2014. Total sample size of 60 patients, randomly allocated to two groups, each group comprising of 30 patients, using computer generated randomization table (Microsoft excel 2010).

Sample Size Estimation

Sample size was calculated on the basis of earlier study reference, Hemodynamic changes during laparoscopic cholecystectomy, by Jean L Joris et al [4] where there was a 28±7 mm Hg increase in the MAP (mean arterial pressure). We hypothesized that 20% attenuation in the magnitude of change in the MAP would be clinically significant.

Group size was determined by using the sample size estimation "for two group mean method" [mean 1±SD 1 = 28 ±7, mean 2±SD 2 = 23±7, common SD = 7] with a 95% power and 5% significance. With these assumptions we are required to study 25 patients in each group. Adding 20% to compensate for loss to follow up we would require to studying 30 patients in each group.

Sampling Technique

The study population consisted of 60 patients aged between 18 - 65 years belonging to class ASA I and class ASA II scheduled for elective laparoscopic cholecystectomy. The patients were divided in to two groups of 30 patients each.

Group A (dexmedetomidine group) [n=30]; received dexmedetomidine 1 μgkg^{-1} body weight infusion for 10 minutes before induction.

Group B (control group) [n=30]; received normal saline infusion for 10 minutes before induction.

Inclusion Criteria

- Patients undergoing elective laparoscopic cholecystectomy patients within age group of 18 to 65 years
- Patients with ASA grade I or II.

Exclusion Criteria

- Obese patients with BMI > 26
- Patients with hypertension, cardiac disease and patients on antihypertensive drugs.
- Patients with ASA grade III and above
- Patients with preoperative heart rate <45 bpm.
- Patients with hepatic and renal disease.

Methodology

The ethical clearance for the study was obtained from institutional ethics committee, Manipal Hospital, Bangalore.

Patients undergoing elective laparoscopic cholecystectomy, under general anesthesia were screened for the eligibility. Patients fulfilling selection criteria were selected for the study and briefed about the nature of study and explained about the anesthetic procedure. A written informed consent was obtained from the patient.

Statistical Methods: Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Student t test (two tailed, dependent) has been used to find the significance of study parameters on continuous scale within each group. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups.

Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc.

Observations and Results

60 patients were, recruited and randomly divided into two groups with 30 patients in each group receiving either Dexmedetomedine (group A) or Normal Saline (group B) 10 mins prior to induction. The data collected was analyzed and results are as mentioned below.

Table 1: Demographics Data Mean±SD

	Group A (Dexme)	Group B (NS)	P value
Age (years)	37±11	41±10	0.17
Gender Male:Female (%)	10:20 (33.3:66.7)	7:23 (23.3:76.7)	0.39
Weight (Kgs)	70±9	71±10	0.59
ASA Grade I: II (%)	23:7 (76.7:23.3)	23:7 (76.7:23.3)	1
Mean duration of surgery (minutes)	57±12	53±9	0.27

Values expressed as Mean±SD or Number (percentage). Dexme= Dexmedetomedine, NS= Normal saline. p value ≤ 0.05 considered significant.

Age: The average age of patients in group A was 37±11 years and 41±10 years in group B. The patients in both groups were well matched with respect to age (p=0.174). {Table 1}

Sex: In both the groups the number of female patients exceeded male patients. Group A had 20 (67.7%) female patients and 10 (33.3%) male patients compared to group B which had 23 (76.7%) female patients and 7 (23.3%) male patients. This gender distribution was comparable between two groups. (p=0.390) {Table 1}

Weight: The average weight of patients in group A was 70±9 kg and 71±10 kg in group B which was comparable. (p=0.590). {Table 1}.

ASA Grade: The number of ASA grade I patients in group A as well as group B were 23 (76.7%) and ASA grade II patients were 7 (23.3%)in both groups. (p= 1.00). {Table 1}

Mean duration of surgery: Mean duration of surgery in group A was 57±12 minutes and in group B was 53±9 minutes which was comparable with in two groups. p=0.27. {Table 1}

Haemodynamics

Base line: Base line in our study was defined as the hemodynamic variable measured prior to infusion of drug. This pre - infusion hemodynamic variable taken as baseline value against which all the subsequent hemodynamic variables are compared. Hemodynamic variable include HR, SBP, DBP, MAP.

A. Heart Rate

Table 2: Heart Rate (Hr) in Two Groups of Patients Studied

Sl.	Heart rate (Bpm)	Group A (Dexem)	Group B (NS)	P value
1	Baseline	80±11	83±14	0.271
2	After infusion of drug	77±15	81±12	0.175
3	1 minute after induction	72±13 #	82±12 #	0.004
4	1 minute after intubation	84±17	97±15	0.004
5	At pneumoperitoneum	75±14	83±15	0.049
6	Head up	81±12	88±12	0.042
7	5mins after pneumoperitoneum	80±14	85±16	0.335
8	10 mins after pneumoperitoneum	76±11	84±14	0.025
9	20 mins after pneumoperitoneum	76±12	83±14	0.042
10	30 mins after pneumoperitoneum	76±12	82±13	0.45
11	60 mins after pneumoperitoneum	81±16	87±13	0.67
12	End of pneumoperitoneum	75±12 #	80±14	0.113
13	End of extubation	88±14	96±17 #	0.036

Heart rate values are expressed as mean±SD $p < 0.05$ is statistically significant. For within groupanalysis after application of Bonferroni's correction, $p<0.004$ is considered statistically significant (#). Bpm= beats per minute, Dexem= Dexmedetomidine. NS= Normal saline (Table 2).

B. Systolic Blood Pressure

Table 3: SBP (mm Hg) in two Groups of Patients Studied

Sl.	SBP (mm Hg)	Group A (Dexem)	Group B (NS)	p value
1.	Baseline	133±20	134±21	0.79
2.	After infusion of drug	130±15	131±23	0.803
3.	1 minute after induction	108±16 #	102±17 #	0.156
4.	1 minute after intubation	119±23 #	137±29	0.008
5.	At pneumoperitoneum	105±17 #	116±27 #	0.065
6.	Head up	97±14 #	110±19 #	0.003
7.	5 mins after pneumoperitoneum	110±18 #	129.±26	0.001
8.	10 mins after pneumoperitoneum	113±16 #	135±22	<0.001
9.	20 mins after pneumoperitoneum	113±14 #	128±19	0.001
10.	30 mins after pneumoperitoneum	113±13 #	127±16	0.001
11.	60 mins after neumoperitoneum	121±20	135±16	0.26
12.	End of pneumoperitoneum	114±13 #	124±19	0.024
13.	End of extubation	133±15	152±18 #	<0.001

SBP values expressed as Mean±SD $p<0.05$ is statistically significant. For within group analysis after application of Bonferroni's correction, $p<0.004$ is statistically significant (#) (Table 3).

C. Diastolic Blood Pressure

Table 4: DBP (mm Hg) in two Groups of Patients Studied

Sl.	DBP (mm Hg)	Group A (Dexem)	Group B (NS)	P value
1	Baseline	80±13	81±10	0.859
2	After infusion of drug	80±12	78±12	0.661
3	1 minute after induction	69±12 #	64±13 #	0.189
4	1 minute after intubation	74±17	84±22	0.053
5	At pneumoperitoneum	65±12 #	69±22 #	0.31
6	Head up	57±9 #	66±16 #	0.009
7	5 mins after pneumoperitoneum	69±14 #	83±21	0.003
8	10 mins after pneumoperitoneum	74±12	82±14	0.017
9	20 mins after pneumoperitoneum	72±12 #	79±14	0.046
10	30 mins after pneumoperitoneum	73±11 #	77±14	0.176
11	60 mins after neumoperitoneum	77±17	86±9	0.312
12	End of pneumoperitoneum	72±11 #	77±13	0.188
13	At extubation	82±11	90±11 #	0.002

DBP values expressed as Mean±SD p<0.05 is statistically significant. For within group analysis after application of Bonferroni's correction, p<0.004 is considered statistically significant (#) (Table 4).

D. Mean Arterial Pressure

Table 5: MAP (mmHg) in two Groups of Patients Studied

Sl.	MAP (mmHg)	Group A (Dexme)	Group B (NS)	p value
1	Baseline	100±16	102±14	0.668
2	After infusion of drug	98±13	98±15	0.993
3	1 minute after induction	82±13	79±14#	0.437
4	1 minute after intubation	91±18 #	104±24	0.017
5	At pneumoperitoneum	80±12 #	88±21	0.07
6	Head up	70±9 #	81±16 #	0.002
7	5 mins after pneumoperitoneum	85±14 #	101±21	0.001
8	10 mins after pneumoperitoneum	89±12 #	102±16	0.001
9	20 mins after pneumoperitoneum	87±12 #	98±15	0.005
10	30 mins after pneumoperitoneum	87±11 #	96±14	0.011
11	60 mins after pneumoperitoneum	93±16	107±10	0.142
12	End of pneumoperitoneum	88±11 #	96±14.17	0.028
13	At extubation	101±11	114±12.27 #	<0.001

MAP values expressed as Mean±SD p<0.05 is statistically significant. For within group analysis after application of Bonferroni's correction, p<0.04 is considered statistically significant (#) (Table 5).

Isoflurane Requirement

Table 6: End Tidal Isoflurane Concentration in Percentages

End Tidal Isoflurane Concentration	Group A (Dexme) Number (%)	Group B(NS) Number (%)
<1%	23(76%)	8(26%)
>1%	7(24%)	22(73%)

Values expressed in number or percentages p=0.003

More [23 (76%)] patients in group A had end tidal isoflurane concentration <1% compared to [8 (26%)] in group B. More number of patients in group B had end tidal isoflurane concentration >1% compared to group A indicating higher Isoflurane requirements in group B (Table 6).

Recovery Time

Time at which patients were able to maintain spontaneous eye opening following reversal.

Table 7: Recovery time in Minutes

Recovery time (minutes)		
Group A (Dexme)	**Group B (NS)**	**P value**
8.26±1.57	7.73±1.47	0.16

Recovery time in group A was 8.26±1.57 minutes compared to 7.73±1.47 minutes in group B which was comparable. (p=0.16). (Table 7).

Discussion

Over recent years, laparoscopic cholecystectomy has become the treatment of choice for calculous cholecystitis, as this procedure is associated with less postoperative pain, rapid mobilization, shorter hospital stay as well as quicker resumption of normal activities [1].

Laparoscopic cholecystectomy using carbon dioxide insufflation is the current gold standard for the treatment of cholelithiasis.

Despite its many benefits over open cholecystectomy, laparoscopic cholecystectomy is known to cause significant hemodynamic changes especially when carbon dioxide pneumoperitoneum is used. These changes include increased peripheral vascular resistance, elevated serum catecholamine level and decreased cardiac output in laparoscopic cholecystectomy [5]. Hemodynamic changes may be due to increased intra abdominal pressure, neuro- hormonal response and absorbed carbon dioxide. Hemodynamic perturbations during pneumoperitoneum are usually well tolerated by normal patients but could be harmful especially in elderly and hemodynamically unstable patients [16]. Increases in mean arterial pressures (MAP) and systemic vascular resistance (SVR) were noted in patients with poor cardiac reserve which could be attributed to raised intra abdominal pressure and changes in positioning. In these patients, the right atrial pressure (RAP) and pulmonary artery occlusion pressure (PAOP) were greatly [17,18] or moderately [19] increased during pneumoperitoneum and cardiac index (CI) was either unchanged [18] or moderately decreased. These studies indicate that hemodynamic alterations are potentially deleterious in elderly patients and in those with limited cardiac reserve.

Intra operative opioids are associated with hemodynamic stability during laparoscopic surgeries but side effects such as postoperative nausea and vomiting [20] may delay discharge from PACU. Nervige Salman et al. [21] have

compared dexmedetomidine and remifentanyl in ambulatory gynaecological laparoscopic surgeries and have demonstrated that dexmedetomidine infusion cause reduced postoperative nausea, vomiting and analgesic requirements and at the same time provides hemodynamic stability compared to remifentanyl. Alpha 2 agonists like clonidine and dexmedetomidine are known to reduce sympathetic nervous system activity and plasma catecholamine concentrations under various stressful circumstances. S Kumar et al. [22] have compared the effects of dexmedetomidine and clonidine premedication on perioperative hemodynamic stability and postoperative analgesia in laparoscopic cholecystectomy and found that both clonidine and dexmedetomidine are effective in attenuating the hemodynamic response to pneumoperitoneum with equal efficacy and without any side effects. The two drugs were also found to provide reliable post operative analgesia. However, though dexmedetomidine is a shorter acting drug compared to clonidine, it was found to have longer duration of analgesia than clonidine. Based on this finding the authors have opined that dexmedetomidine can be used as an effective premedication for attenuating hemodynamic response due to pneumoperitoneum. Similarly Rajdip Hazra et al. [23] have compared the effects of intravenously administered dexmedetomidine with clonidine on hemodynamic response during laparoscopic cholecystectomy and observed that the patients in dexmedetomidine group had better control of blood pressure during pneumoperitoeum.

Choice of Dosage

Different doses of dexmedetomidine for attnenuating hemodynamic stress response have been studied by various authors. Jaakola et al. [24] found decreased blood pressure and heart rate during intubation following administration of 0.6 $\mu g kg^{-1}$ bolus dexmedetomidine preoperatively. Lawrence et al. [25] found decreased hemodynamic response to tracheal intubation and extubation following a single high dose of dexmedetomidine (2 $\mu g kg^{-1}$), but bradycardia was observed in first and fifteen minutes after administration of dexmedetomidine. Ghodki et al used [26] dexmedetomidine 1 $\mu g kg^{-1}$ intravenously over 15 minutes before induction followed by maintenance infusion of 0.2 $\mu g kg^{-1} hr^{-1}$ and observed minimal changes in blood pressure during laryngoscopy and pneumoperitoneum.

Since high dose (>1μkg^{-1}) of dexmedetomidine is associated with increased incidence of bradycardia and hypotension, we chose to conduct our study using 1 μkg^{-1} bolus dose of dexmedetomidine given over 10 minutes just prior to anesthetic induction. Since the elimination half-life of single intravenous bolus dose of dexmedetomidine is about 2 to 3 hrs and average duration of laparoscopic cholecystectomy surgery is between 60 to 90 minutes, we avoided maintenance infusion of dexmedetomidine in order to prevent prolonged duration of action of drug resulting in increase in the recovery time.

Intra Abdominal Pressure (IAP)

At IAP of 15 mm Hg Joris et al. [5] found 35% increase in MAP, a 65% increase in SVR, a 90% increase in PVR, while there was a 20% decrease in cardiac output. Ischizack et al. [27] tried to determine the safe range of IAP during laparoscopic surgery. At 16 mm Hg of IAP, significant fall in cardiac output was observed. However at 12 mm Hg of intra abdominal pressure hemodynamic alterations were not observed. During laparoscopy the current recommendation is to monitor IAP and to maintain it at just tolerable levels, not above 14 mm Hg. In our study IAP was maintained at 14 mm Hg throughout the surgery.

Haemodynamics

Preoperative hemodynamic parameters like heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressures were comparable between the two groups.

Heart Rate (Table 2)

We found significant difference in HR variations in dexmedetomidine group at intubation, at insufflation of pneumoperitoneum, up to 30 minutes after pneumoperitoneum and at extubation ($p<0.05$) compared to control group. Similar responses in HR were observed in studies where in same dose of dexmedetomidine (Rajdip Hajra et al. [23] and S kumar et al. [21]) was used as a premedication prior to induction. DP Bhattacharjee et al. [28] also have found similar results in heart rate response by using 0.2 $\mu g kg^{-1}$ of dexmedetomidine maintenance infusion during laparoscopic cholecystectomy. In our study, we also found a decrease in HR, at different time points after insufflations of pneumoperitoneum till the end of pneumoperitoneum when compared to baseline. The incidence of HR varying above 20% of the baseline were also lesser in the dexmedetomidine group. However, this lesser magnitude of variation noted in HR response was not statistically

significant when compared to control group.

Systolic Blood Pressure (Table 3)

There was a significant difference in SBP variation in dexmedetomidine group compared to control group at intubation, at insufflation of pneumoperitoneum until 30 minutes post pneumoperitoneum ($p<0.05$). SBP was lower in dexmedetomidine group compared to its baseline value whereas there was not much change noticed in SBP response in control group, when compared to the baseline, during pneumoperitoneum, thus indicating a muted stress response to carbon dioxide pneumoperitoneum. Similar results have been found in studies by S Kumar et al. [21] and Rajdip Hajra et al. [23] when $1\mu gkg^{-1}$ of dexmedetomidine was compared with clonidine and normal saline.

In our study, during pneumoperitoneum the maximum SBP attained in dexmedetomidine group was 133±13 mm Hg compared to 152±19 mm Hg in control group, which was statistically significant ($p<0.001$). Dexmedetomidine group also had less number of episodes of increase in SBP of more than 20% of baseline. The magnitude of variation of SBP around baseline in dexmedetomidine group during pneumoperitoneum was more in control group which was a statistically significant finding ($p=0.004$) SBP around baseline in dexmedetomidine group during pneumoperitoneum was more in control group which was a statistically significant finding ($p=0.004$).

Diastolic Blood Pressure (DBP) (Table 4)

There was a statistically significant ($p<0.05$) difference in DBP variation in dexmedetomidine group from beginning of pneumoperitoneum until 20 minutes post pneumoperitoneum when compared to control group, thus indicating a decreased response to carbon dioxide pneumoperitoneum. Similar kind of response was seen in studies by S Kumar et al. [22] and Rajdip et al. [23] where in dexmedetomidine was compared to control group. The magnitude of variation in DBP around baseline was lesser compared to the control group which was found to be statistically significant ($p=0.05$).

Mean Arterial Blood Pressure (MAP) (Table 5)

The decreased stress response was also reflected in mean arterial pressure which was significantly less in dexmedetomidine group compared to control group from beginning to end of pneumoperitonem ($p<0.001$), this difference between the two groups was statistically significant. S Kumar et al. [22], Rajdip et al. [23] and DP Bhattacharjee et al. [28] have found similar decreases in MAP in dexmedetomidine group during pneumoperitoneum when compared to control group.

During pneumoperitoneum, the maximum increase in MAP wasless in dexmedetomidine group (100±16 mmHg) compared to control group (111±14 mmHg)($p=0.001$). The incidence of increase in MAP of more than 20% of their baseline values was significantly low in dexmedetomidine group ($p=0.005$). The magnitude of variation of MAP from baseline was significantly lower in dexmedetmidine group compared to control group ($p=0.02$).

Pneumoperitoneumisknowntocausefluctuations in hemodynamics as measured by increases in MAP, SVR, pulmonary vascular resistance and decrease in cardiac output [5] In our study, we found that $1\mu gkg^{-1}$ bolus dose of dexmedetomidine, given 10 minutes prior to induction, resulted in lesser magnitude of variation in HR, SBP, DBP and MAP during pneumoperitoneum giving the much desirable hemodynamic stability.

Recovery Time

Dexmedetomidine is associated with 'arousable sedation' or 'conscious sedation'. Turan et al. [29] in their study on patients undergoing craniotomy found that dexmedetomidine improved extubation conditions without prolonging recovery. Norimasa et al. [30] studied the recovery profile when dexmedetomidine was used as a general anaesthetic adjuvant in patients undergoing lower abdominal surgery and concluded that postoperative recovery was not affected by dexmedetomidine administration. Studies have reported prolonged recovery time with dexmedetomidine especially when large infusion doses were used during anesthesia or when used as an adjuvant along with propofol infusion as a part of TIVA (Total intravenous anesthesia) [31].

In our study, recovery time is defined as spontaneous eye opening following reversal of muscle relaxant. We found no difference in recovery time between the two groups. We used only single bolus dose 1 μgkg^{-1} of dexmedetomidine given 10 minutes prior to induction of anesthesia. Maintenance infusion of dexmedetomidine was avoided and adequate anesthetic depth was maintained using entropy monitoring in all patients.

Conclusion

In conclusion, dexmedetomidine at a dose of 1 μgkg^{-1} bolus given at induction of anesthesia over 10 minutes resulted in statistically significant hemodynamic stability during pneumoperitoneum in patients undergoing elective laparoscopic cholecystectomy surgeries. It also resulted in reduced Isoflurane requirements without prolonging recovery.

We have done this study on ASA1 and 2 physical status patients. Further studies may be required to be conducted on similar lines in patients with lesser cardiopulmonary reserve, to find out if dexmedetomidine can result in better tolerance of hemodynamic variations associated with pneumoperitoneum during laparoscopic surgeries.

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Original Research Article

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Effect of Low Dose Magnesium Sulphate on Succinylcholine Induced Fasciculations & Postoperative Myalgia

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Abstract

Objectives: To investigate the effect of Magnesium Sulphate on Succinylcholine induced fasciculations during General Anaesthesia & postoperative myalgia. *Methods:* Double blind randomised clinical trial on patients who were candidates for surgery under general anaesthesia. Patients were selected & divided into two equal groups of Study & controls using block randomisation. Study group received Magnesium Sulphate while Controls received Normal Saline. SPSS 18 was used for statistical analysis. *Results:* Out of the 100 subjects in the study 49 (49%) were men & 51 (51%) were women ($p<0.072$). The mean age of the two groups were 37.5±12.2 year & 37.7±12 year ($p<0.9$). There was significant difference between the two groups in terms of the degree of fasciculations & post operative myalgia ($p<0.001$). *Conclusion:* Even low dose of magnesium sulphate can prevent & reduce the degree of succinylcholine induced fasciculation & postoperative myalgia.

Keywords: Magnesium sulphate; muscle fasciculation; succinylcholine; Postoperative Myalgia (POM).

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Introduction

Succinylcholine is a depolarising muscle relaxant used to facilitate endotracheal intubation. One of its adverse effect is fasciculation & post operative myalgia (POM) along with other minor adverse effect.

Mechanism of fasciculation is attributed to prejunctional deploarising action of Sch resulting in repetitive firing of motor nerve terminals and antidromic discharges that manifests as uncoordinated muscle contractions [18]. $MgSO_4$ reduces this by acting prejunctionaliy. Phenytoin & d-tubocurarine have same action.

Mechanism of Post Operative Myalgia (POM): Fasciculations involves vigorous contraction by muscle bundles with no shortening & without synchronous activity in adjacent bundles. This leads to fibre rupture or damage, release of phosphokinase, increased myoplasmic calcium, changes in membrane phospholipids, releasing free fatty acids & the involvement of free radicals [4,6] causing pain. Postoperative myalgia is attributed to muscle damage produced by the sheering forces associated with fasciculations at onset of phase-I block.

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There have been suggestions that fasciculations and muscle pains are related. Therefore, various methods & drugs have been suggested for the prevention of these complications. Magnesium sulphate is one of the drugs that has been recently investigated largely.

Magnesium acts as an adrenergic antagonist and inhibits the release of catecholamine & controls the undesirable effects of laryngoscopy for tracheal intubation such as tachycardia, hypertension, raised intraocular pressure, reduces the potassium concentration by reducing fasciculations. It is also very effective in reducing postoperative myalgia following Sch. It is wonderful drug to reduce undesirable effects of Sch but only few studies are there investigating this drug.

Therefore this study was planned to assess the effect of magnesium sulphate on muscle fasciculation & postoperative myalgesia following succinylcholine administration.

Material & Methods

Double blind randomised clinical trial was conducted on patients undergoing elective surgery under general anaesthesia

ASA Grade I and II between the age group of 18 to 60 years.

Exclusion criteria - pregnancy, extremes of age, emergency surgery, history of muscular disease, malignant hyperthermia, patients on calcium channel blockers or beta blockers, hypotension, hypoparathyroid & hypocalcaemia, contraindication to suxamethonium.

Sample size was 100 with two equal group of Study & control. Written informed consent was taken from patients.

Study group received 20 mg/kg of magnesium sulphate in 100 ml of normal saline infused in 5 minutes, started 6.5 min before anaesthesia. The controls received 100 ml of normal saline without magnesium sulphate in 5 minutes, started 6.5 min before anaesthesia.

Fasciculation was observed & graded by scoring system.

		Score
Nil	No visible fasciculations	0
Mild	Very fine fingertip or facial muscle movements	1
Moderate	Minimal fasciculations on trunk or extremities	2
Severe	Vigorous faciculations on trunk or extremities	3

Postoperative myalgia was observed at the 1 hour, 12 hour, 24 hour & 48 hours after surgery & grading done.

Grading & scoring system of Postoperative Myalgia.

Grade		Score
Nil	No muscle pain or stiffness	0
Mild	Muscle stiffness or pain at one site but not causing disability or limitations of activity	1
Moderate	Muscle pain or stiffness noticed by patient spontaneously & requiring analgesic therapy	2
Severe	Generalised severe or incapacitating discomfort	3

Data were entered into SPSS 18 & was analysed using Mann-whitney U test and chi-square test.

Results

Mean age of the study & control groups were 37.5±12.2yr and 37.7±12yr (p<0.9). There were 49 (49%) men & 51 (51%) women in the study (p<0.072)

- Faciculations were nil among study group while 100% among the controls (p<0.001) with various grades.
- Postoperative myalgia was nil in study group while in control group patients had various degrees of myalgia.

Table 1:

Variables	Study Group	Control Group	P-Value
Male	20 (40%)	29 (58%)	0.072
Female	30 (60%)	21 (42%)	
ASA I	41 (82%)	37 (74%)	0.334
ASA II	9 (18%)	13 (26%)	
Fasciculations Grade			
0	50 (100%)	0 (0%)	<0.001 (Significant)
1	0 (0%)	10 (20%)	<0.001 (Significant)
2	0 (0%)	25 (50%)	<0.001 (Significant)
3	0 (0%)	15 (30%)	<0.001 (Significant)
Postoperative Myalgia			
0	48 (96%)	0 (0%)	<0.001 (Significant)
1	2 (04%)	10 (20%)	<0.001 (Significant)
2	0 (0%)	25 (50%)	<0.001 (Significant)
3	0 (0%)	15 (30%)	<0.001 (Significant)

Discussion

In this study both study group & control group have similar baseline characteristics. Therefore, the findings are the results of the interventions. Based on the results, magnesium sulphate can greatly reduce the muscle fasciculation & post operative myalgia caused by succinylcholine.

Various drugs & methods are used to reduce succinylcholine induced fasciculations but magnesium sulphate is excellent drug, cheap, easily available and can be effective in low doses without any side effects.

In our study no patients had fasciculations, while all patients in control group had mild to severe fasciculations which is stastically significant.

Two patients in study group experienced mild postoperative myalgia and 48 (98%) patients had no postoperative myalgia. While in control group all pts experienced postoperative myalgia with mild to severe grades.

In a study done by Aldrete, et al [14] after Magnesium Sulphate and thiopentone, no patients had fasciculation.

In a study done by Kararmaza, et al. [12] on the effects of propofol on succinylcholine induced fasciculation reported that 20% of people in propofol group did not experience any type & faciculations. In a meta analysis by Schreiberju, et al [7] fasciculations were observed in 95% in placebo group & 50% in the intervention group. Another study by Sakurabas, et al. [2] also showed that Magnesium sulphate is useful both for reducing fasciculations, blood pressure and heart rate changes during anaesthesia. In their study 33% of the magnesium sulphate group did not experience fasciculations at all.

In a study done by Kumar M, et al. [10] investigated the effect of magnesium sulphate on succinylcholine induced fasciculation & found very minimal degree of fasciculations in study group compared to control group.

In study by done by sakuraba, et al. [2] found reduced fasculations and attenuated pressor response to laryngoscopy & tracheal intubation.

Various studies done by Shin YH, et al. [9], MC Bin et al. [17], Tauzin-fin et al[18], showed intra operative & postoperative analgesic action of magnesium sulphate and reduced requirement of analgesics.

Most of the studies had used high doses of Magnesium Sulphate ranging 40 mg/kg to 60 mg/kg. Here we took efforts to use low dose of magnesium sulphate i.e. 20 mg/kg to get the desirable effects & reduce Magnesium Sulphate associated complications.

Conclusion

Magnesium sulphate is a wonderful drug even in low doses to reduce fasciculations & postoperative myalgia after succinylcholine. Even though a number of drugs have been used to reduce fasciculations but Magnesium Sulphate is economical, easily available, free of side effects. So we can use this method routinely in our day to day practice to make our patients comfortable with best outcome.

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Original Research Article

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Evaluation of Ultrasound Guided Transversus Abdominis Plane Block for Post Operative Analgesia after Lower Segment Caeseraen Section

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Abstract

Background: transversus abdominis plane (TAP) block as an effective chunk of post operative multi modal analgesia for lower abdominal surgeries. *Objective:* to evaluate the effectiveness of TAP block as a post-operative analgesia technique and usefulness in decreasing requirement of opioids as well as other pain killer medicines. *Materials and Methods:* This was a prospective study conducted from June 2018 to October 2018. Using convenient sampling technique, a total of 60 patients of American Society of Anaesthesiologists (ASA) physical status grade I or II, randomly divided into two groups: CONT group and TAP group by the sealed envelope technique. The 'control' group acted as control and was given spinal anesthesia (SA) with hyperbaric bupivacaine with a 27G BD spinal needle in lateral position. 'TAP' group' received the same spinal anesthesia and TAP block under ultrasound guidance with 23G 100-mm needle with 0.25% bupivacaine 20 ml along with dexamethasone 4 mg on each side. *Results:* Mean time to rescue analgesia in TAP & Control group was 612.8 min and 84.4 min respectively ($p<0.05$) and Mean time to rescue analgesia was 612.8 min and 84.4 min respectively ($p<0.05$). Average VAS score was higher in control group in compare to TAP group participants. Mean tramadol requirement for Group TAP was 55 mg and for the control group was 150 mg ($p<0.05$). *Conclusion:* TAP block reduces pain, prolongs the time to first analgesic request and decreases supplemental opioid analgesic requirement when used as a component of multimodal analgesic regimen for pain relief after caesarean section.

Keywords: Bupivacaine; Lower Segment Caesarean Section; Transversus Abdominis Plane Block; Ultrasound-Guided Regional Anaesthesia.

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Introduction

Analgesic regional blocks are sometimes dangerous when given blindly [1]. Pain is very much critical and most frequent issues in which patient required medical help and decreasing pain is the main function of Anaesthesiologist as perioperative physician [2]. Surgical complications like venous thromboembolism, respiratory complications and prolonged hospital stay can be avoid by post-operative analgesia. Post-operative analgesia must be effective and safe to consequential pain and discomfort are occurring mostly after lower section caesarean delivery (LSCS) [3,4].

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Discussion was continuing from last many years on transversus abdominis plane (TAP) block as an effective chunk of post-operative multi-modal analgesia for lower abdominal surgeries. TAP cater the analgesia to the parietal peritoneum and anterior abdominal wall by blocking the nerves traversing between the transversus abdominis and internal oblique muscle [5,6]. Nowadays, ultrasound to guide injection of the local anaesthetic become more effective method as TAP block [7,8]. Efficacy of TAP block depends on concentration and the higher volume of the injected local anaesthetic is favour to dissemination more toward paravertebral spaces and block more nerves [9,10,11]. This study was undertaken to evaluate the effectiveness of TAP block as a post operative analgesia technique and usefulness in decreasing requirement of opioids as well as other pain killer medicines.

Material and Methods:

Study setting and duration

This study was conducted in department of Anesthesiology within the premises of civil hospital Palanpur, BMCRI from June 2018 to October 2018.

Study design and study population

This was a prospective study designed to compare the effect of post-operative analgesia of TAP block with other pain killer medicines. A total of 60 adult patients of American Society of Anaesthesiologists (ASA) physical status grade I or II, randomly divided into two groups: CONT group and TAP group by the sealed envelope technique. The 'control' group acted as control and was given spinal anesthesia (SA) with hyperbaric bupivacaine with a 27G BD spinal needle in lateral position. They were immediately turned in supine position. Patients in 'TAP' group received the same spinal anesthesia, but after completion of surgery and before applying dressing on the wound, were also given TAP block under ultrasound guidance with 23G 100-mm needle with 0.25% bupivacaine 20 ml along with dexamethasone 4 mg on each side after informed consent. Pain score was monitored in the postoperative period, every hour for 4 h and 2 hourly for next 4 h and then at 12, 18, 24, 36, and 48 h with visual analog scale (VAS) from 0 to 10 with 0 being no pain and 10 being maximum pain they could imagine. When the pain score came above 4, the patient was given injection diclofenac sodium 75 mg and time to rescue analgesia was noted. Vital parameters were monitored every 10 min during intraoperative period and half-hourly for 24 h in the postoperative period. All the patients in ASA-III or above, who were unwilling, allergic to LA, on anticoagulants, and those with local infection in the thigh were excluded from the study. All the patients were randomly allocated into one of the two groups using computer generated random number table. Hence each group contained a total of 30 patients.

Transversus abdominis plane block

After local cleaning and draping, high frequency linear probe was kept horizontally on the flank at the level of umbilicus in anterior axillary line. All the three layers of abdominal muscles were identified and a 23 g 100 mm needle attached with local anesthetic mixture with a 50 mm extension line was introduced by in-plane technique. When the tip of the needle reached the fascia between IO and TA, after careful aspiration to rule out intravascular placement, a test injection of 0.5 ml was made, opening up of TAP plane was looked for and needle adjusted if required accordingly and test injection repeated, when the TAP plane is seen opening up, the whole amount of drug was injected. The same procedure was repeated on the other side.

Data analysis

Qualitative data were expressed as percentages and proportions. Quantitative data were expressed as mean and standard deviation. The differences between two groups with respect to continuous variables were analysed using unpaired t-test while categorical variables were analysed using chi-square test. All the statistical tests were performed in Epi Info 3.5.1 software by CDC, USA [6]. P value $<0.05$was considered as statistically significant while P value<0.01 was considered as statistically highly significant.

Ethical consent

Before proceeding with study, appropriate ethical clearance was obtained from Hospital Ethics Committee. Each patient was included in the study only after informed consent.

Result

Table 1: Demographic variables of study participants (N=60)

Variables	TAP Group (n=30) (Mean±SD)	Control Group (n=30) (Mean±SD)	P value
Age (in years)	28.4±5.1	29.4±4.8	0.32
Weight (in kg)	59.5±8.8	59.4±6.1	0.8
Height (in cm)	152.4±4.8	151.9±3.9	0.35
BMI (kg/m2)	26.8±3.3	26.1±4.1	0.62

Table 1 shows that mean age of TAP and Control group was 28.4 years with 5.1 SD and 29.4 years with 4.8 SD respectively. Mean weight of TAP and Control group was 59.5 kg years with 8.8 SD and 59.4 kg with 6.1 SD respectively. Mean height of TAP and Control group was 152.4 cm with 4.8 SD and 151.9 cm with 3.9 SD respectively. Mean BMI of TAP and Control group was 26.8 kg/m^2 with 3.3 SD and 26.1 kg/m^2 with 4.1 SD respectively. But difference between TAP & Control group regarding age, weight, height and BMI was statistically not significant (p>0.05).

Table 2: Clinical variables of study participants (N=60)

Variables	TAP Group	Control Group	P value
ASA Grade			
I	3 (10.0%)	4 (13.3%)	0.56
II	27 (90.0%)	26 (86.7%)	
Dose of Bupivacaine H (mg) (mean±SD)	13.6±0.8	12.4±0.6	0.85
Duration of anaesthesia (min) (mean±SD)	71.3±12.4	74.1±15.7	0.4
Duration of surgery (min) (mean±SD)	50.0±7.3	54.7±9.0	0.03
Mean time to rescue analgesia	612.8±48.0	84.4±6.7	0.0001

Table 2 shows that most of participants (90.0% & 86.7%) of TAP and control group was belonged to ASA grade II and difference was statistically not significant (p>0.05). Mean dose of hyperbaric bupivacaine consumed in TAP & Control group was 13.6 mg and 12.4 mg respectively and difference was statistically not significant (p>0.05). Mean duration of anesthesia in TAP & Control group was 71.3 min and 74.1 min respectively and difference

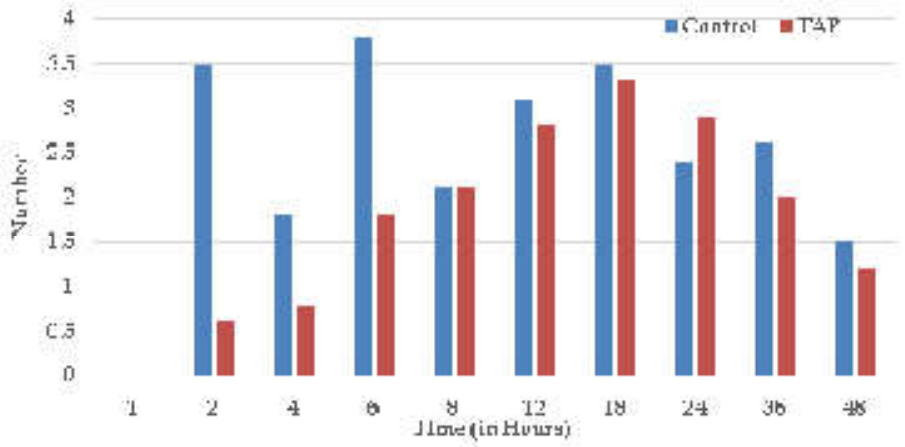

Fig. 1: Average post-operative Visual Analog Scale (VAS) among study groups (N=60)

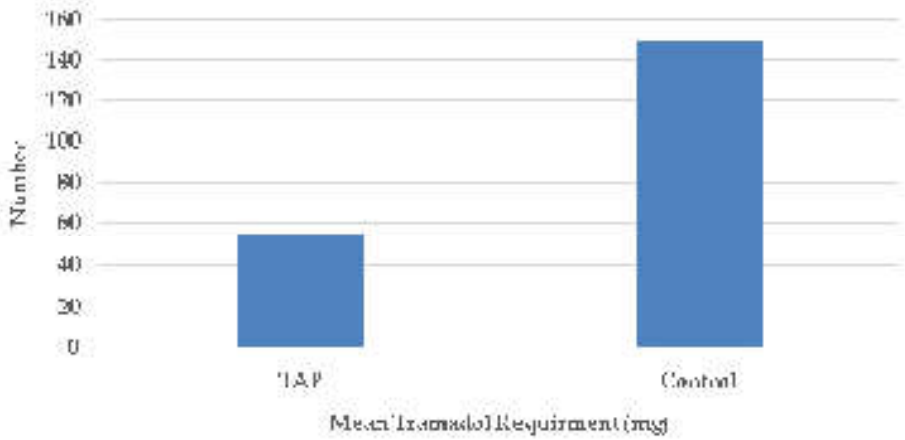

Fig. 2: Mean tramadol requirement in milligrams in the first 24 h after caesarean delivery

was statistically not significant (p>0.05). Mean duration of surgery in TAP & Control group was 48.5 min and 54.7 min respectively and difference was statistically significant (p<0.05). Mean time to rescue analgesia in TAP & Control group was 612.8 min and 84.4 min respectively and difference was statistically significant (p<0.05).

Figure 1 shows the post-operative mean VAS score of TAP and control groups. Average VAS score was higher in control group in compare to TAP group participants.

Figure 2 shows mean post-operative requirement of tramadol (in mg) in 24 hours after surgery. Mean tramadol requirement for Group TAP was 55 mg and for the control group was 150 mg, which was statistically significant (t value = 8.5, p<0.001).

Discussion

Following LSCS surgery, Post-operative analgesia is helpful for maternal satisfaction and also prevent the harmful effect of other pain killers on the new born. Many times observed that neuraxial opioids have many side effects like nausea and pruritus which resulted in patient dissatisfaction in spite of it provides excellent analgesia [12]. TAP block caters superior analgesia, decrease supplemental opioid analgesic requirement and decreases the incidence of opioid induced side effects [13-16].

Present study observed the demographic indicators were almost similar in both the groups and difference was statistically not significant. Similar findings were also observed in study done by Jadon A et al. [17], Naveen S et al. [2] and Adeel S et al. [11] but not comparable with the study findings done by Dwivedi D et al. [1].

Present study observed that out of enrolled cases, most of patients belonged to ASA grade II which Is not correlate with the study findings done by Jadon A et al. [17]. Study found the less duration of surgery and higher time to rescue analgesia in TAP group compare to control group and this difference was statistically significant. These findings are comparable with the study done by Jadon A et al. [17], Dwivedi D et al. [1] but not comparable with the study done by Naveen S et al. [2] & Adeel A et al. [11]. Our study did not find statistically significant relation between TAP and control group regarding Dose of hyperbaric Bupivacaine & Duration of anaesthesia.

Present study observed lower VAS score among TAP group participants compare to control group participants even after 48 hours after surgery. This finding is also supported by other similar study done by Naveen S et al. [2], Adeel S et al. [11], Jadon A et al. [17], Sivapurapu V et al. [18], Manikikar MA et al. [4], Mcdonnell JG et al. [13], Cansiz KH et al [19], Chansoria S et al. [20], Srivastava V et al. [21], Eslamian L et al. [22] and Abdullah FW et al. [23].

TAP block is also useful in different abdominal procedures other than LSCS such as large bowel resection, open/laparoscopic appendectomy, total abdominal hysterectomy, laparoscopic cholecystectomy, open prostatectomy, abdominoplasty with or without flank liposuction, inguinal hernia and iliac crest bone graft. Due to poor vascularity of the TAP block, its action is prolonged and less incidence of any major complications [24,25].

Conclusion

Our study conclude that TAP block reduces pain, prolongs the time to first analgesic requirement and decreases supplemental opioid analgesic requirement when used as a component of multimodal analgesic regimen for pain relief after caesarean section. TAP block is a very good technique for postoperative analgesia after LSCS. The patients remain more pain free and likely to be more alert, leading to better mother and child bonding and likely to keep the mother more capable of doing her child-caring chores and lactation.

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Original Research Article

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Pre-Emptive Oral Gabapentin for Postoperative Laproscopic Shoulder Pain Relief in Patients Undergoing Elective Abdominal Laproscopic Surgeries

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Abstract

Background: In laparoscopic surgery acute postoperative shoulder tip pain is common entity despite of the use of new drugs and novel drug delivery modalities, studies have shown that acute post-operative pain continues to be under managed. We tried to evaluate efficacy of oral gabapentin for the relief of postoperative pain after laparoscopic surgery. *Objective:* To evaluate the effect of oral Gabapentin on post operative shoulder pain after abdominal laparoscopy. *Method:* a prospective, randomized, clinical controlled study was conducted on 60 ASA grade I & grade II patients of either sex, aged between 18 to 65 years, planned for laparoscopic abdominal surgery under general anaesthesia. Group G: 30 patients would receive 600 mg oral gabapentin 1 hour prior to surgery. Group M: 30 patients would receive tab multivitamin 1 hour prior to surgery. After that presence of post operative shoulder pain and its severity was assessed by Visual Analog Scale (VAS) in the beginning of surgery and 0, 2, 4, 8, 12,18,24 hours after the surgery. *Results:* VAS score was lower in Group G when compared to Group M throughout the different time interval during first 24 hours. The incidence of post operative laproscopic shoulder pain in group M was 21 compared to group G where it was 12 in first 24 hours post operatively.

Keywords: Postoperative Laproscopic Shoulder Pain; Gabapentin; VAS Score; Analgesic.

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Introduction

Pain is subjective unpleasant experience with psychosomatic problems. In spite of the use of new drugs and novel drug delivery modalities, studies have shown that acute post-operative pain continues to be undermanaged. Shoulder pain is a frequent problem following laparoscopic procedure [1,2]. Many patients may feel much more discomfort from their shoulder pain than incision pain [3]. Gabapentin is a structural analogue of γ-amino-butyric acid and is safe and effective for the treatment of neuropathic pain syndrome, as well as for the prevention of postoperative pain [4]. Gabapentin inhibits C-fibre responses to noxious stimuli by modulating both central and peripheral nociceptive responses [5,6].

Aim of Study

To evaluate the effect of oral Gabapentin on post operative laproscopic shoulder pain.

Objectives of Study observe: 1. Postoperative analgesic requirement in first 24 hours. 2. Intra and

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post operative hemodynamic changes. 3. Adverse effects and complications, if any.

Materials and Methods

Inclusion criteria: Patients with the informed written consent. Age group of 18 to 55 years. ASA grades I and grade II. Patients with no known history of allergy, sensitivity or other form of reaction to the drugs to be used.

Exclusion criteria Patient refusal. History of drug allergy to gabapentin. Pregnant and lactating mothers. Patient with neurological, renal, hepatic, chronic respiratory diseases. Patient with endocrinologic disease (e.g. obesity, diabetes mellitus). After obtaining informed written consent, patients were randomly allocated into 2 groups *Group G:* Gabapentin group (30 patients) *Group M:* Placebo group (30 patients). Pre anaesthetic checkup: Detailed history, Airway examination, Systemic examination, Routine investigations were done, Nil by mouth for at least 8 hours prior to surgery. Tab. Alprazolam 0.25 mg was given the night before the surgery. On the day of surgery 1 hour prior to induction of anaesthesia Oral tablet gabapentin in dose of 600 mg was given with sips of water and in other group tab multivitamin (supradyn) with sips of water was given. In operation theatre, following Multipara monitor attached Base line vital parameters were recorded (HR, BP, SPO2, ECG, 20G vein flow secured and Inj. RL started.)

Premedication: Patients were premeditated with: Inj. Glycopyyrolate 0.04 mg/kg i/v, Inj Ondansetron 0.1 mg/kg i/v, Inj. Midazolam 1 mg i/v, Inj. Tramadol 1 mg/kg i/v.

Induction & Intubaton - Pre-oxygenation with 100% oxygen for 3 minutes.

Induced by Inj. Propofol 1.5-2.5 mg/kg/I.V. Endotracheal intubation was facilitated by Inj. Succinylcholine 1-2 mg/kg I/V by using appropriate sized cuffed endotracheal tube following direct laryngoscopy.

Maintenance O_2 50% + N2O50% + Isoflurane dial flow concentration of (0.2% to 2%) + Inj. Atracurium. Intravenous fluid was calculated according to body weight and intra operative needs.

Reversal: Inj Neostigmine (0.05 mg/kg/I.V) + Inj Glycopyrrolate (0.008mg/kg/I.V)

Extubation: After fulfilling extubation criteria. Post Operatively Following Parameters were observed:-

1. Hemodynamic parameter and SpO_2.

2. Pain was assessed by VAS score at 0, 2, 4, 8, 12, 18 and 24 hours. If VAS >3 then in Inj. Diclofenac 75 mg was given. (Vas scale - No Pain – 0 to 3 Moderate Pain - 4 to 8, worst pain 9 to 10) Sedation was assessed by Modified Ramsay Sedation Score.

Results

Statistical tools: Data were entered and analysed with the Graph Pad.com. Statistical tests used for comparison is Student's t-test. Results are presented as mean (SD) and number (%) of cases as appropriate. The level of significance was set at $p < 0.05$, and 95% confidence intervals were calculated for the main outcome measures.

Table 1: Demographic Data

Serial no.	Variable		Group M	Group G
			Mean+SD	Mean+SD
1	Age		32±11 years	31±8.5 years
2	Weight		56.7±9.93 Kgs	54.9±6.87 Kgs
3	Gender	Male	16	14
		Female	14	16
4	ASA	Grade 1	21	20
		Grade 2	9	10

In study both groups were similar & comparable in respect to demographic data. Group G age is mean±SD 31±8.5 years, weight 54.9±6.87 kgs, Group M age mean±SD 32±11 years, weight 56.7± 9.93 Kgs.

Table 2: Incidence of Post-operative Laproscopic Shoulder Pain (PLSP)

Groups	Group G	Group M	p value
Incidence of PLSP	12	21	<0.001

In Table 2 the incidence of post operative laproscopic shoulder pain in group M was 21 compared to Group G it was 12 in first 24 hours post operative (p value = 0.001)

Table 3: Analgesic Requirement

Groups	Group G	Group M	P value
Diclofenac Requirement (mean ± SD)	190±27.54	128.33±31.30	<0.001

In the study it was observed that the mean post operative Diclofenac requirement in group P was 190±27.54 mg compared to group G where it was 128.33±31.30 mg in first 24 hours post operatively. This analysis was found to be statistically significant (p- value =0.001).

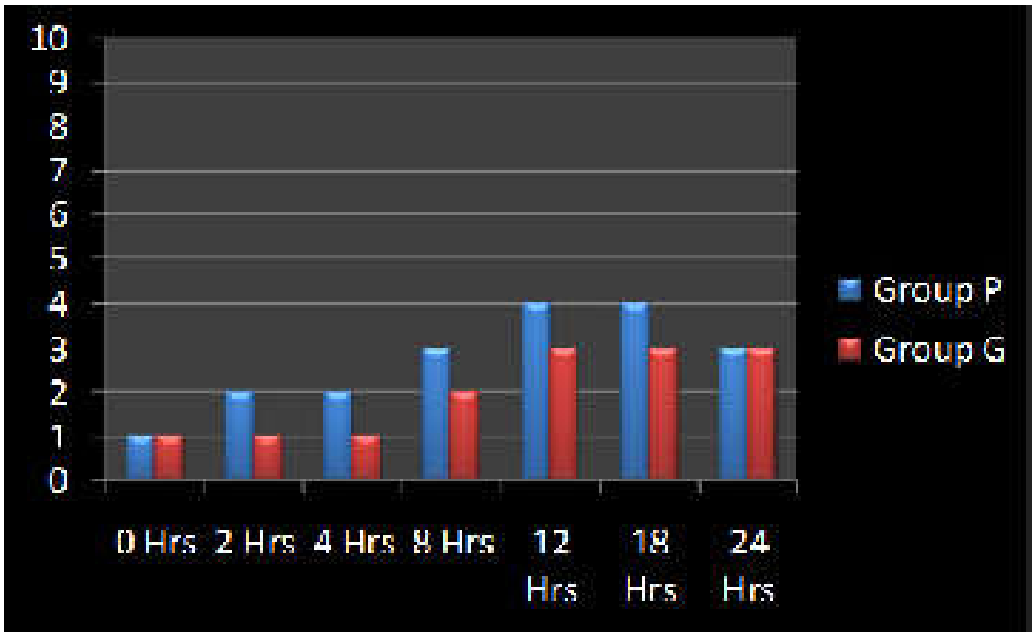

Fig. 1: Showing that VAS Score lower in Group G as compared to Group Placebo (Group P or M) throughout the different time interval during first 24 hrs.

Discussion

Shoulder pain is a frequent problem following laparoscopic procedure with overall incidence of 75%-80% [1,2]. Many patients may feel much more discomfort from their shoulder pain than incision pain [3]. PLSP is caused by irritation and/ or injury of the diaphragm and phrenic nerve by local acidosis and irritative effect of CO_2 during pneumoperitoneum or distention forces on the diaphragm [7,8,9,10].

In the study it was observed that the mean post operative Diclofenac requirement in group P was 190±27.54 mg compared to group G where it was 128.33±31.30 mg in first 24 hours post operatively. Use of Gabapentin resulted in 33% reduction in consumption of postoperative Inj. Diclofenac.

The choice to give gabapentin 2 hour before the induction appears rational in order to attain maximal plasma concentration at the time of surgical stimuli. Gabapentin also possesses antihyperalgesic and antiallodynic properties, which is beneficial in acute postoperative pain [11,12].

It may also reduce hypersensitivity induced by nerve injury, inflammation and postoperative pain [12]. The incidence of nausea and vomiting was less in gabapentin group with lesser number of patients requiring ondansetron.

Conclusion

Pre-emptive administration of 600 mg of gabapentin results in statistically significant reduction in incidence and severity of postoperative laparoscopic pain in immediate post operative period (p value = 0.001).

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Effect of Clonidine and Dexmedetomidine on Haemodynamic and Recovery Responses During Tracheal Extubation: A Randomised Double-Blind Comparative Study

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Abstract

Background and Aims: Emergence from anaesthesia and tracheal extubation are associated with transient surge in catecholamines due to sympathetic stimulation causing hypertension, tachycardia, myocardial ischaemia etc. Various drugs are being studied to attenuate the haemodynamic response to tracheal extubation. This study aimed to compare the effect of a bolus dose of different drugs of alpha 2 adrenergic agonists (clonidine and dexmedetomidine) on haemodynamic, airway reflexes and recovery responses during tracheal extubation. *Materials and methods:* ninety patients aged 20 to 45 Y of either sex of ASA gr I/II scheduled for elective surgical and gynaecological surgeries studied after randomisation into three groups. Technique of anaesthesia was standardised for all three groups. just 5 minutes before anticipated end of surgery Group A, Cand D received inj. Placebo (normal saline), Clonidine 0.75 µg/kg and Dexmedetomidine 0.5 µg/kg respectively intravenously over 2 min. Monitoring of heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MAP) were recorded at the time of bolus drug injection and there after 1,2 and 3 min after injection, during extubation, at 1, 3, 5, 10 and 15 min after extubation. Quality of extubation was evaluated immediately after extubation based on cough using five point rating score, postoperative sedation was evaluated on a six point scale. Side effects like laryngospasm, bronchospasm respiratory depression, desaturation, vomiting, hypotension, bradycardia and undue sedation were noted. *Results:* Haemodynamic parameters (HR, SBP, DBP and MAP) were significantly lower in study groups from 3 min of drug injection till the study period as compared to the placebo group. In majority of the cases the extubation quality score was 1 and 2 in study groups and score 3 in placebo group. Sedation scale was 2 and 3 group C and group D where as 2 in placebo group. *Conclusion:* Our study observes that alpha 2 adrenergic agonist are good and safe adjuvants to attenuate the stress response to emergence from anaesthesia and tracheal extubation. Dexmedetomidine behaved slightly better than clonidine to supress the haemodynamic response.

Keywords: Airway reflexes; Clonidine; Dexmedetomidine; Extubation; Haemodynamic responses.

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Introduction

Tracheal extubation is an important event in the course of general anaesthesia, which causes modest (10% to 30%) and transient (lasting 5 to 15 minutes) increase in heart rate and blood pressure [1]. Extubation is associated with reflex sympathetic discharge caused by epipharyngeal

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and laryngopharyngeal stimulation. These changes are transient and probably of no consequences in healthy individual going for surgery but has a major concern for patients with CAD, cerebrovascular disease and in hypertensive patients [2-4]. Different drugs and techniques has been used to attenuate the pressor response such as narcotic analgesics, local anaesthetics, calcium channel blockers and adrenoceptor blockers but none has been found completely successful [5,6].

Clonidine and dexmedetomidine are highly selective alpha-2 adrenergic receptor agonists without effect on respiration. They inhibit the release of catecholamines and vasopressin and thus helps to modulate the haemodynamic changes andalso has analgesic, sedative and anaesthetic sparing properties.

The present study was aimed to evaluate and compare the efficacy of clonidine and dexmedetomidine as compared to placebo on haemodynamic, airway reflexes and recovery responses during tracheal extubation.

Materials and Methods

This study was carried out from June 2016 to May 2018 after obtaining approval from the hospital ethics committee. Ninety patients of either sex (30 in each group) between 20 to 45 yr. of age belonging to ASA physical status I/II scheduled for elective general surgical and gynaecological cases under general anaesthesia. Patients suffering from cardiovascular, respiratory disorders, diabetes, hypertension, obesity, difficult airway, history of sleep apnoea, pregnancy, breast feeding women and medications that affect heart rate or blood pressure and emergency procedures were excluded from the study.

Preanesthetic check-up was conducted and a detailed history and a complete physical examination recorded. Routine investigations like complete blood picture, blood grouping and typing, blood urea, serum creatinine, bleeding time, clotting time, blood sugar, ECG and chest radiography were done. Written informed consent was taken from each patient.

Randomisation procedure

The patients were randomly divided into three groups of thirty each using computer generated sequential number placed in sealed envelopes and opened only before the commencement of the study. The study was double blinded so that the patients and the assessor were unaware of the group. Only the attending consultant administering the drugs knew the group allocation.

Group A: Placebo group

Group C: Clonidine group

Group D: Dexmedetomidine group

Anaesthesia technique was standardized for all the three groups with glycopyrrolate, midazolam, propofol, fentanyl, vecuronium, nitrous oxide-oxygen, isoflurane and IPPV with closed circuit. Standard monitoring consisted of ECG, pulse oximetry (SpO_2), $EtCO_2$ and non-invasive blood pressure. Inhalational agent was cut-off 5 minutes before the estimated time of end of surgery and patients in each group received the specified solution intravenously over 2 minutes. Patients in group A received 10 ml of normal saline, group C received clonidine 0.75 µg/kg IV in 10 mL saline and group D received dexmedetomidine 0.5 µg/kg IV in 10 mL saline over 1-2 minutes.

Heart rate, systolic, diastolic and mean arterial blood pressures were recorded at the time of bolus drug injection and there after 1,2 and 3 min after injection, during extubation, at 1, 3, 5, 10 and 15 min after extubation. Residual neuromuscular blockade was reversed with neostigmine and glycopyrrolate. When spontaneous respirations were sufficient and able to obey simple commands, suction of the throat was done, and trachea was extubated.

The anaesthesiologist performing the extubation was blinded to the study drugs. Heart rate, systolic, diastolic and mean arterial blood pressure were recorded at the time of extubation and thereafter 1, 3, 5, 10 and at 15 minutes after extubation. Any side effects like laryngospasm, bronchospasm, respiratory depression, desaturation, vomiting, hypotension, bradycardia and undue sedation were noted. Hypotension was defined as a decrease in systolic blood pressure of more than 20% decrease from baseline or systolic blood pressure less than 80 mmHg. Bradycardia was defined as heart rate of less than 60/min.

Quality of extubation was evaluated based on cough immediately after extubation, using a 5-point rating scale [7].

1. No coughing.
2. Smooth extubation with minimal coughing (1 or 2 times).
3. Moderate coughing (3 or 4 times).
4. Severe coughing (5 to 10 times) and straining.
5. Poor extubation, very uncomfortable (Laryngospasm and coughing >10 times).

Post-operative sedation was evaluated 5 minutes after extubation on a 6-point scale (Ramsay sedation scale) [8].

1-Anxious or agitated and restless or both; 2-Cooperative, oriented and tranquil; 3-Drowsy, but responds to commands; 4- Asleep, brisk response to glabellar tap or loud auditory stimulus; 5-Asleep and slow response to stimulation and 6-Asleep and unarousable, no response to stimulation.

Statistical analysis

The normality distribution of the data was confirmed by Kolmogorov-Smirnov test. The continuous data was displayed by mean and standard deviation and discrete data as Median and interquartile range (IQR).

As all the assumptions of ANOVA were accomplished. The ANOVA and ANOVA (repeated measures) was performed for haemodynamic parameters, followed by Tukey-Kramer multiple comparison analysis. The discrete data were analysed using Mann-Whitney U test. The chi-square test was performed for categorical data. The p value of < 0.05 was considered as significant.

Results

The patients in all the three groups were comparable for age, weight, male: female ratio, ASA physical status and Mallampati class. The difference between these groups were insignificant (Table 1).

Base line values of haemodynamic parameters were comparable in all the three groups. We observed statistically significant difference in HR from 3 minutes post drug administration till the study period (Table 2). When the study groups

Table 1: Demographic Variables

Variable	Group A	Group C	Group D
Mean Age±SD (Yr)	34.93±7-21	35,32±2.43	33±6.95
Male : Female	11:21	13:17	18:12
ASA Gr I/II	20/10	22/8	21/9
Mean Weight±SD(Kg)	63.43±7.95	63.94±7.14	62.43±6.84
Mean Height±SD(Cm)	154.9±6.65	156.8±12.43	155.73±8.61

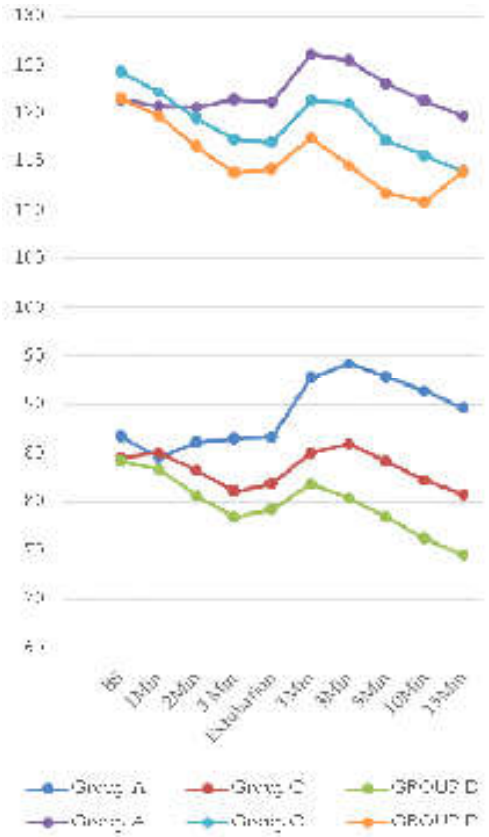

Fig 1: Changes in HR and MAP in all three groups

were compared to the placebo group significant difference was found from 2-3 minutes of drug administration till 15 min. whereas the two study groups comparison showed difference ($p<0.05$) from 3 min post extubation.

Even the SBP, DBP and MAP (table 3) showed significant difference from 3 min of drug injection till the end of the study period. Analysis between the placebo group and group C and group D was also statistically significant (Fig. 1) from 3 min onwards. The comparison between the study groups showed difference (Fig. 2) only after 1 min post extubation for SBP but no difference for DBP and MAP.

We observed statistically significant difference in the quality of extubation in the control group when compared to group C and group D. 67% of patients in the control group showed moderate coughing at the time of extubation and only 33% of the patients could be extubated smoothly with minimal coughing (Table 4). Where as in group D 60% of the patients could be extubated smoothly without any cough and 40% of the patients showed minimal coughing at the time of extubation. The Group C had smooth extubation without cough in 77% of patients and the remaining 23% with minimal cough.

Table 2: HR Variations

Heart Rate	Group A		Group C		Group D		F	P Value
	Mean	SD	Mean	SD	Mean	SD		
BS	84	8.99	84.56	7.08	84.13	9.13	0.998	0.373
1 Min	84.6	8.07	85.07	6.86	83.4	8.72	0.354	0.704
2 Min	86.07	8.23	83.27	6.96	80.67	8.49	3.487	0.035
3 Min	86.47	7.98	81	7.12	78.47	8.35	8.175	0.001
Extubation	86.6	7.6	81.8	6.98	79.2	7.67	7.675	0.001
1 Min	92.7	8.46	85.07	6.62	81.87	7.52	16.115	0.000
3 Min	94.2	7.42	86	7.52	80.4	8.15	24.378	0.000
5 Min	92.87	6.51	84.2	7.2	78.47	7.43	31.653	0.000
10 Min	91.47	6.64	82.2	7.17	76.2	7.6	34.735	0.000
15 Min	89.6	6.61	80.77	7.4	74.6	7.76	32.226	0.000

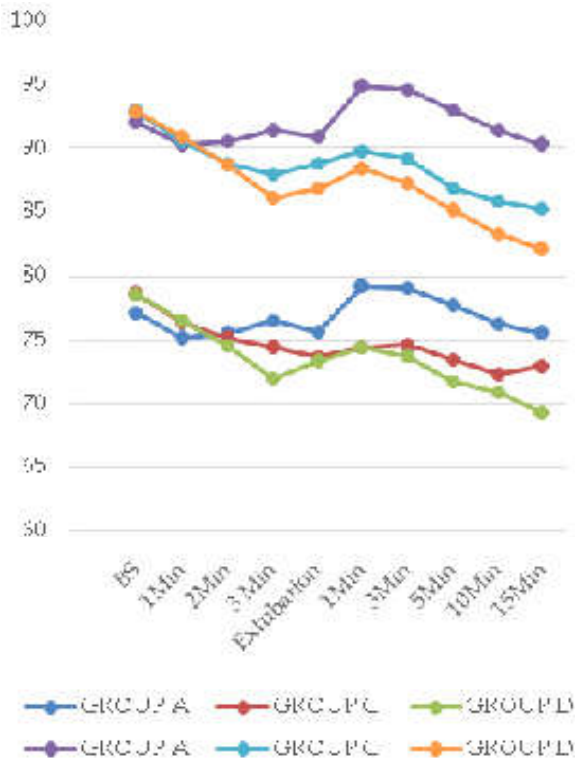

Fig 2: Changes in SBP and DBP in all three groups

Table 3: MAP Variations

MAP	Group A		Group C		Group D		F	P Value
	Mean	SD	Mean	SD	Mean	SD		
BS	91.97	3.73	92.83	4.15	92.9	4.9	4.575	0.013
1 Min	90.3	3.43	90.57	4.29	90.93	4.72	0.173	0.841
2 Min	90.53	3.48	88.83	4.35	88.7	4.39	1.845	0.164
3 Min	91.43	2.96	88	3.71	86.1	4.39	15.761	0.000
Extubation	90.93	3.23	88.87	3.58	86.9	4.12	11.573	0.000
1 Min	94.77	3.32	89.8	4.54	88.47	3.76	17.323	0.000
3 Min	94.57	2.86	89.2	4.38	87.23	3.88	30.535	0.000
5 Min	93	3.43	86.86	4.83	85.07	3.4	33.363	0.000
10 Min	91.37	3.13	85.87	4.53	83.3	2.86	35.733	0.000
15 Min	90.23	3.04	85.27	4.67	82.03	3.86	33.474	0.000

Table 4: Distribution of Extubation and Sedation Score in all threegroups

Extubation quality score				Ramsay sedation scale			
Score	Group A	Group C	Group D	Scale	Group A	Group C	Group D
1	18	0	0	1	0	0	2
2	12	30	10	2	7	14	28
3	0	0	20	3	23	16	0
4	0	0	0	4	0	0	0
5	0	0	0	5	0	0	0
				6	0	0	0

A significant difference in the level of post-operative sedation was observed between control and both the study groups ($p<0.05$) (Table 4). In group A 93% of cases were co-operative, oriented and tranquil with sedation score of 2 on Ramsay scale, 57% of patients in group C had score of 3 and the rest with score of 2 on the Ramsay sedation scale. While Dexmedetomidine group had sedation score of 3 in 77% of patients and the remaining (23%) with score of 2 on Ramsay scale.

Bradycardia was observed in one patient and hypotension in 2 patients in the Dexmedetomidine group. But none in the other two groups. The incidence of nausea and vomiting was more in group A. Other side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation was not observed in any of the three groups. No significant difference in all the three groups in SpO_2 values.

Discussion

Similar totracheal intubation, extubation is also associated with haemodynamic changes due to reflex sympathetic discharge caused by epipharyngeal and laryngopharyngeal stimulation. The airway irritation during tracheal extubation may cause cough or difficulty in breathing and may contribute to an increase in BP [1]. These changes are transient but probably of risk concern for patients with CAD, [2] Cerebrovascular disease [3] and in hypertensive patients [4] as against negligible consequences in healthy individual going for surgery under general anaesthesia. Smooth tracheal extubation is therefore essential requiring the absence of straining, coughing, movements, breath holding or laryngospasm.

Very few studies are there in the literature where clonidine and dexmedetomidine are used for extubation to reduce the stress response. Our study aimed to evaluate and compare the effect of two different alpha-2 adrenergic receptor agonists with the placebo group. Normal saline, clonidine (0.75 µg/kg) and dexmedetomidine (0.5 µg/kg) was used in 10 ml dilution as a single bolus dose over 2 min and observed the haemodynamic response to tracheal extubation, the quality of extubation, the level of post-op sedation and incidence of complications.

Alpha-2 receptors are physiologically located presynaptic, post synaptic and extra synaptically [9] Pre synaptical receptors clinically produce more impact due to regulation of noradrenaline and ATP release through negative feedback mechanism [10]. Pharmacological studies show dexmedetomidine is 8 times more specific alpha-2 adrenoceptor than clonidine; so dexmedetomidine has more efficacy compared with clonidine [11].

The present study observed that with endotracheal extubation there was significant rise

in HR during and after extubation (from second minute onwards after drug administration, at extubation and all times post extubation) in the placebo group. Alpha-2 agonists (clonidine and dexmedetomidine) did not show significant rise in HR from the basal value. Our results are in concurrence with the Shrirang Rao et al. [12] and Anita Kholi et al. [13].

There was significant rise in the mean values of SBP, DBP and MAP values in group A at all times till post extubation as compared to base line values. Where as both group C and group D always showed stable haemodynamic till the end of study period, this is in conjunction with the study done by Bindu et al. [14] and Manisha Kapdi et al. [15]. Similarly, Kumar S et al. [11] also observed stable MAP with dexmedetomidine and clonidine during extubation.

The incidence of bradycardia and hypotension was observed in group D but not in other two groups. Bradycardia was observed in one (3.3%) patient and hypotension in two (7%) patients, but none of them required treatment. These results are like the results of Anita Kholi et al. [13] and Guler et al. [16].

Anita Kholi et al. [13] in their study concluded that dexmedetomidine caused better attenuation of pressor response, airway reflexes during emergence from anaesthesia and better sedation than clonidine. This co-relates with our study results.

Alpha-2 adrenergic receptor agonists (clonidine and dexmedetomidine) by their analgesic and sedative properties blunt airway response and thereby prevents bronchoconstriction. We observed a smooth extubation without any cough in study groups (group C and group D) while moderate cough was seen in Group A. These results are in accordance with the study of Sharma VB et al [17] and Guler et al.[16] who used dexmedetomidine in their study. Similarly, the results of Manisha Kapdi et al. [15] and Aksu R et al. [18] supports our results for study groups.

There was a significant difference in the level of postoperative sedation observed between group A and study groups (group C and group D). We observed significant number of patients had sedation score of 3 in group C and group D, while in group A most of the patients had sedation score of 2 and few had sedation score of 1. Central stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the locus coeruleus in the brainstem plays an important role in the sedation and anxiolysis produced by dexmedetomidine and clonidine. Our findings are in conjunction with the other studies [13,14,18].

The incidence of nausea and vomiting was observed in group A. Other side effects like respiratory depression, laryngospasm, bronchospasm, undue sedation was noted in any of the three groups. SpO_2 values were comparable in all three groups with insignificant difference in our study. These observations are consistent with the study of Anita Kholi et al. [13] and Guler et al. [16].

Conclusion

A single bolus dose of clonidine or dexmedetomidine given 5 minutes before extubation attenuates the haemodynamic and airway reflexes during emergence from anaesthesia. Smooth tracheal extubation and adequate sedation with negligible side effects were also observed in this study. However, dexmedetomidine causes better attenuation of haemodynamic and airway reflexes with undue sedation than clonidine.

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Conflict Of Interest: Nil

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Comparative Evaluation of Different Local Anaesthetics in Supraclavicular Brachial Plexus Block in Pediatric Patients

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Abstract

Introduction: Peripheral neural blockade remains a well-accepted component of comprehensive anaesthetic care in adults, but nowadays it is gaining popularity for children also. This study aims toevaluate the onset, duration of action, hemodynamic changes and side effects if any of lignocaine 2% plain at 5 mg/kg, lignocaine 2% with epinephrine at 7 mg/kg and bupivacaine 0.5% at 2 mg/kg in children of age group 5-10 years. *Materials and Methods:* This was a prospective, randomized and double-blinded clinical trial study. 75 pediatric patients of ASA I/ II age group of 5-10 years of either sex, undergoing upper limb surgeries were distributed equally into three groups and given supraclavicular nerve block. Group L patients received lignocaine 2% plain at 5 mg/ kg, Group LE received lignocaine 2% with epinephrine (1:200000) at 7 mg/kg, and Group Breceived Bupivacaine 0.5% plain at 2 mg/kg body weight. *Results:* 0.5% plain Bupivacaine prolongs the duration of analgesia more than lignocaine 2% plain and lignocaine 2% with epinephrine 1:200000. There was no statistically significant difference in onset of sensory and motor blockade with lignocaine 2% or lignocaine 2% with epinephrine but it is prolonged with 0.5% bupivacaine. There was no significant occurrence of complication in all 3 groups. *Conclusion:* Lignocaine with or without epinephrine having the quick onset of action than bupivacaine 0.5% plain 2 mg/ kg is good for supraclavicular brachial plexus block in children but for the longer duration of surgery(>2 hr), bupivacaine remains the best option.

Keywords: Brachial block; bupivacaine; lignocaine; supraclavicular block.

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Introduction

Regional anaesthesia use in pediatric anaesthesia practice has increased the popularity of peripheral nerve blocks in children [1]. This expansion was in part due to the recognition of the need for better modalities of pain management in children as well as the demonstration of the safety of peripheral regional anaesthesia in children [1,2].

For upper limb surgeries, supraclavicular brachial plexus block is a known anaesthetic option. Among anesthetists there is an increased concern about local anaesthetic toxicity secondary to a narrow therapeutic window and the possibility of an iatrogenic injury related to the awake child's inability to cooperate with the procedure adds to the difficulty in children [3]. Prolonged reduction of pain and nausea and increased possibility of faster discharge from hospital when compared with GA are some of the clinical advantages of this option. The most common local anaesthetic drugs used for a brachial block are lignocaine and bupivacaine.

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Many additives were tried and used to prolong the efficacy of these drugs, to speed up the onset of action and to limit their toxicity [4]. These additives are epinephrine, opioids, ketamine, neostigmine, tramadol, butorphenol etc. [5,6]. The present study was done to evaluate the onset, duration of anaesthesia, analgesia, sensory and motor blockade following various different local anaesthetics in supraclavicular brachial plexus blocks in children. The study was mainly focused on patient and surgeon comfort and avoidance of complication of general anaesthesia in the pediatric age group.

Materials and Methods

The present study was approved by the Institutional Review Board of our hospital and written informed consent of patients was taken. 75 ASA Grade I-II patients of either sex, aged 5-10 years undergoing routine or emergency upper limb surgeries were selected for the study at Gandhi Medical College, Bhopal. All patients under went a pre-anaesthetic checkup and particular emphasis was put on a history of present and past illness and sensitivity to the drugs particularly local anaesthetics. Proper history taking and thorough general and systemic examinations were carried out.

Inclusion criteria was ASA (American Society of Anaesthesiologists) grade I/II patients with age between 5-10 years. Exclusion criteria were patients who refused to participate in the study, infection at the proposed site of block, coagulopathies, allergy to local anaesthetics, severe pulmonary, cardiac, hepatic, renal or CNS disorder. In the present study, a block was not given for short procedures like close reduction or casting (requires only 5-15 min). After sedation with intranasal (0.05-0.25 mg/kg) Midazolam hydrochloride, the patient was transferred to the block room. A secure intravenous line was introduced, and through a face mask supplemental oxygen (4-6 l/min) was applied, followed by 0.5 mg/kg of intravenous propofol (Propofol 1% MCT/LCT Fresenius; Austria). Povidone-iodine 10% solution was used to prepare and drape the neck and supraclavicular region of the patient [7].

In present study, three groups (n=25) were investigated:Group L (lignocaine plain 2%) received 5 mg/kg body weight, Group LE (lignocaine 2% with epinephrine 1:200000) received 7 mg/kg body weight, and Group B (Bupivacaine 0.5% plain) 2 mg/kg body weight. For assigning the anaesthetic solution, a random-number table was generated through a computer-generated randomization list by an anaesthetist not otherwise involved in present study. Anaesthetist performing the procedure and observations were blinded to the treatment group.

Brachial plexus block was performed by the supraclavicular technique. The injection site was disinfected and infiltrated s.c. with 1 ml 2% lidocaine. A nerve stimulator (Stimuplex Dig RC; Germany) for localization of brachial plexus was used. The location end point was finger flexion or extension as the distal motor response with an output lower than 0.5 mA [8].

Monitoring of pulse rate, respiratory rate, oxygen saturation, blood pressure (systolic), sensory and motor blockade wasdone till 30 minutes at every 5 minutes, then till one hour at every 15 minutes and then upto 6 hours at hourly intervals and then every 2 hourly till effect remains. Sensory block onset was assessed as the time from injection to onset of analgesia in each of the major peripheral nerve distributions (ulnar, radial, medial and musculocutaneous).

Onset of Motor block was assessed by the time from injection to the inability of the patient to move fingers or raise the hand. If surgical manipulation could be performed without pain than the motor block was considered satisfactory. When the patient did not allow manipulation and general anaesthesia had to be given that was considered unsatisfactory [9,10]. Postoperative analgesia was assessed by Wong-Baker FACES pain rating scaleand defined as a time from onset of sensory block to a time when a patient has a pain rating scale ≥ 2. Any possible complications such as bradycardia, hypotension, convulsions, respiratory insufficiency, hematomas, headache, nausea, vomiting pneumothorax, pruritus and diaphragmatic paralysis were noted. In the circumstance of an inadequate or patchy block, the block was supplemented with general anaesthesia [11].

Assuming that the establishment of sensory and motor block occurred in 30 min and a standard deviation (SD) of 7 min with an α of 0.05, and a power of 80%, it was calculated that a sample size of 25 patients per group would be required to show a difference of 5 min for establishment of successful surgical block [12]. This sample size could also detect a 30% reduction in block success assuming a control block success of 70%. Statistical tests used for data was SPSS statistical software (version 18) [IBM Corp. NY, USA] presented in mean and SD and the groups were compared by one-way ANOVA. $p < 0.05$ was taken as statistically significant.

Result

The patients' age ranged from 5-10 years of age, the maximum number of cases being in 9-10 years age group in all 3 groups (Group L, LE and B) with the mean age of 8.32, 10 and 9.41 respectively. There was no significant difference among the three groups with respect to demographic parameters such as height, weight, and gender. Out of 75 patients, 51 were males and 24 were females. Group L, LE and B had 80%, 64% and 60% males respectively. For mean time of onset of sensory blockade, difference was statistically insignificant for group L ($p > 0.1$) and group LE ($p > 0.1$) but significant for group B ($p < 0.05$).

The mean duration of the sensory blockade in group L was 108.28±20.14, in group LE was 160.80±22.08 minutes and in the group B was 278.84±32.28 minutes. The mean onset time and duration of the motor blockade in three groups are discussed in [Table 1]. Duration of sensory as well as the motor block was significantly longer in group B than group L and group LE. The side-effect incidence of nausea was 4% in group L and incidence of vomiting was 4% in group B. No statistically significant change in mean pulse rate, mean systolic blood pressure, mean respiratory rate and mean oxygen saturation between all 3 groups at different time intervals during the study period ($p > 0.1$).

Discussion

Comprehensive anaesthesia care with a better patient outcome is the focus of all pre, peri and post-operative care. Peripheral nerve blocks allow patients to remain conscious, preserve their protective airway reflexes and are advocated in high-risk patients to reduce morbidity and mortality associated with general anaesthesia and polypharmacy.

All patients selected in the present study were between 5-10 years of age with majority group belonging to 8-10 years of age. As per our knowledge, no study has been done before for lignocaine 2% plain, lignocaine 2% with epinephrine and bupivacaine 0.5% in supraclavicular brachial plexus block in children of age group 5-10 years. No significant difference in mean time of onset of sensory blockade as well as mean time of onset of motor blockade in group L and group LE but was greater in group B. Bromageet al have shown that Bupivacaine had a longer onset of sensory and motor blockade than lignocaine plain which is similar to our study [9,13]. While Bernards et al have found that epinephrine added to lignocaine didn't affect the onset of sensory and motor blockade [14].

Duration of sensory as well as the motor block was significantly longer in group LE and longest in group B. One study [15], concluded a significant increase in time occurred with bupivacaine as compared to lignocaine, mepivacaine and prilocaine following brachial plexus block which is similar to this study. Mean duration of analgesia was statistically highly significant in group B, compared to group Las Ware et al found that degree of analgesia was significantly better in bupivacaine group when compared with lignocaine similar to the present study [11,16]. Athelail and colleagues found bupivacaine had a longer duration of analgesia than lignocaine with adrenaline used for digital nerve blocks [17].

Epinephrine was used with lignocaine for local anaesthesia to retard absorption, reduce toxicity and prolong analgesic activity. Addition of epinephrine to lignocaine decreases the rate of vascular absorption thereby allowing more anaesthetics molecules to reach the nerve membrane and thus improving the depth and duration of anaesthesia, as well as providing a marker for inadvertent intravascular injections [18,19,20].

In present study, we could not find the statistically significant change in mean pulse rate, mean systolic blood pressure, mean respiratory rate and mean oxygen saturation between all three groups at different time intervals during the study period ($p > 0.05$). Klein et al didn't observe any

Table 1: Onset and time to peak of sensory-motor blockade in three study groups

Block characteristics	Group L	Group LE	Group B
Onset time of sensory block (min)	13.12±3.78	12.6±3.04	18.28±3.02
Onset time of motor block (min)	6.4±2.69	6.64±2.78	15.92±3.30
Total duration of sensory block (score 0)(min)	108.28±20.14	160.80±22.08	278.84±32.28

Values are expressed as Mean±Standard Deviation (SD).

Group L = lignocaine plain 2% at 5 mg/kg, Group LE= lignocaine 2% with epinephrine 1:200000 at 7 mg/kg, Group B= Bupivacaine 0.5% plain at 2 mg/kg.

significant change in the hemodynamic parameter, respiratory rate or oxygen saturation [21].

Only one patient in group L develops nausea whileone patient in group B develops vomiting as side-effect which was mild and reversible. There was no statistically significant difference in the occurrence of complications among the three groups. Lignocaine with or without epinephrine having a quick onset of action than bupivacaine 0.5% plain is good for supraclavicular brachial plexus block in children but for a longer duration of surgery(>2 hr), bupivacaine remains the best option.

Conclusion

Lignocaine with or without epinephrine having the quick onset of action than bupivacaine 0.5% plain 2 mg/kg is good for supraclavicular brachial plexus block in children but for the longer duration of surgery (>2 hr), bupivacaine remains the best option.

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Ebola Virus Disease in the year 2014-2015: Retrospective Study of Suspected Cases of Ebola Virus Disease at Intensive Care Unit of Tertiary Care Center

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Abstract

Aim: Containment of a dangerous and fatal disease outbreak and measures to control in present and future. *Design*: Retrospective observational Study. *Material and Methods*: A team of researchers studied the demographic characteristics of international passengers, to India during Public health emergency of International concern declared on 8 August 2014 for Ebola Virus disease. A person with history of fever, bleeding from any site, stomach pain, diarrhea, vomiting, headache, joint pain, muscular pain, bleeding from any site and rashes should report to tertiary care center. In our study, we observed person under investigation for Ebola virus disease under integrated disease surveillance program for forty-two days. If the contacts had any clinical symptoms, they were supposed to inform immediately [1]. The tertiary care facility was responsible for treatment and management of suspected patients suffering from Ebola virus disease. Sample collection for confirmation of Ebola disease was responsibility of Airport Authority of India. One passenger was quarantined for 165 days at the airport authority of India, as he was Ebola treated patient. His semen sample tested positive for Ebola virus [2]. *Statistical Analysis:* Collected data was analyzed and the categorical variables were presented in number and percentage. Qualitative variable was compared using Chi-Square test. *Results*: Satisfactory containment of Ebola virus disease during Public health emergency of International concern. *Conclusion and Recommendation*: To design intensive care facilities for future control and spread of Ebola Virus disease.

Keywords: Ebola Virus disease; Personal prophylaxis equipment; N-95 mask; sharp needle container; quarantine; PIUs; infection control.

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Introduction

Public Health emergency of International concern declared on 8 August 2014 for the outbreak of Ebola virus disease in west Africa [3]. 28,616 were confirmed cases worldwide of Ebola virus disease and 11,316 deaths as found on 10 June 2016. There are 10000 survivors of Ebola Virus disease at that time. As there was no vaccine or definitive treatment robust step taken to control spread of infection. The Public health emergency of International concern lifted on 24th march 2016 [3].

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India has a staggering population of 1.35 billion based on the most recent UN data and faced challenges to control the spread of Ebola disease [4]. A 24-hour emergency help line was set up. Thermal scanners and a "virus tracking equipment" was installed at 18 airports, seaports and roadway and steps were taken to track and isolate passengers suspected to be carrying the virus. All health care workers dealing with the suspected patients asked to wear personal prophylaxis equipment. Health care workers instructed about donning and doffing of personal prophylaxis equipment. All health care workers were advised to wear personal prophylaxis equipment while carrying samples The Indian missions had contacted resident Indians in the affected countries and they were supplied all instructive materials so that they can take preventive measures [5,6].

Material and Method

A team of researchers studied the demographic characteristics of international travelers to India during Public health emergency of International concern declared on 8 August 2014 for Ebola Virus disease.

Provisions to quarantine passengers with Ebola-like symptoms at Airport Authority of India. and arrangement made to keep them under observation was made at the tertiary center. The tertiary center was set up to manage Ebola virus disease suspects and infected patients. The suspected patients were passengers from countries Guinea, Sierra Leone, Liberia, Nigeria and Congo who were having signs and symptoms of disease or who traveled as medical tourists to India from these Nations. The tertiary center also deployed a team of doctors and nurses, round the clock for identifying high-risk suspects at the Airport. Patients having symptoms such as fever, headache, joint pain, vomiting, diarrhea, bleeding from any site transferred to the designated tertiary care center by the airport authority of India. Highly suspicious patients got transfer to nodal center for further management. The airport authority of India collected samples of suspected patient's. Report for Ebola virus disease was dispatched within 24 hours. Data collected and the variables described in descriptive analysis. Advisory issued to State Surveillance Officers of all the states/Union territories, Airlines, travelers visiting from/to affected countries and families staying in the affected countries [7,8].

The total samples tested for Ebola virus disease were 106 at NCDC. The passengers with clinical symptoms transferred to tertiary center. Fourteen patients managed as A person under investigation for Ebola virus disease at the tertiary Center. Two patients out of fourteen patients tested positive for malaria disease, three patients were medical tourists with symptoms, and four patients were Indian Nationals who had visited area of disease outbreak. The most common symptom was febrile illness and the most common age group was between 30-50 years age. Two patients were of extreme age group (4 years and 70 years). Eighty percent Person under investigations for Ebola Virus disease belonged to Nigeria and rest from other West African countries.

Eighty percent patients had febrile illness and 20 percent had headache and muscle pain and close contact with Person under investigations for Ebola Virus disease.

All the patients received supportive treatment

Maintaining fluids and electrolytes in the patient's body

Maintaining oxygen level of the body

Maintaining blood pressure

Treatment for pain relief

Treatment of fever

Medicines used for infections according to the culture and sensitivity report.

Superadded infections of A person under investigation for Ebola virus disease were treated with appropriate medicines. The average duration of stay in the hospital ranged from one to three days.

All the samples tested at NCDC* Delhi for ELISA and R T-P C R were negative for Ebola virus disease. Some samples were sent for confirmation to NIV Pune. Ebola virus not detected by commercial ELISA test and No evidence of Ebola virus- Specific gene found on RT-PCR in any of the patients tested for EVD* at the Nodal center.

India, had diagnosed an Indian resident's semen sample showing traces of Ebola virus in virus isolation by cell culture at NIV Pune. The man, a 26-year old Indian, working in Liberia, was earlier treated and cured of the deadly virus, was kept in isolation at Delhi's Airport Health Authority Quarantine Center for 165 days. The passenger discharged from Airport authority of India when his sample tested negative.

Case Definition EVD

*Suspected (clinical) case**: Any person ill or deceased who has or had fever with acute clinical symptoms and signs of hemorrhage, such as bleeding of the gums, nose-bleeds, conjunctiva injection, red spots on the body, bloody stools and/ or Melena (black liquid stools), or vomiting blood (haematemesis) with the history of travel to the affected area. Documented prior contact with an EVD case is not required.

Probable case (with or without bleeding): Any person (living or dead) having had contact with a clinical case of EHF and with a history of acute fever. OR Any person (living or dead) with a history of acute fever and three or more of the following Symptoms: headache/vomiting/nausea/loss of appetite/ diarrhea/intense fatigue/abdominal pain/ general muscular or articular pain/difficulty in swallowing/difficulty in breathing/hiccoughs OR Any unexplained death. The distinction between a suspected case and a probable case in practice relatively unimportant as far as outbreak control is concerned.

Contact: A person with no clinical symptoms of EVD* but had Physical contact with EVD* case or Physical contact with the body fluids of EVD* case within three weeks of exposure. The notion of physical contact may be proven or highly suspected such as having shared the same room/bed, cared for patient, touched body fluids, or closely participated in a burial (e.g. physical contact with the corpse).

Confirmed Case: A suspected or probable case with laboratory confirmation (positive I g M antibody, positive PCR or Viral isolation).

APUI: A person under investigation for Ebola Virus Disease:

Defined as person having signs and symptoms of EVD*, Temperature ≥100.4 or subjective fever, headache, fatigue, pain in muscle, abdominal pain, vomiting, diarrhea, or unexplained hemorrhage, and epidemiological risk for EVD, with history of travel to a country with widespread transmission, within 21 days before onset of symptoms. Because of the known possibility of falsely negative results early in the disease, the decision to perform specific Ebola testing based on the degree of exposure and clinical assessment.

Sample Collection

Samples collected at AAI* and Nodal center for Ebola virus disease North India for confirmation of EVD*.

Blood collected by venipuncture into a special vacutainer in which the serum separates out. The tube packaged very carefully into a 3-bag container. A triple packaging for bio-safety provided protection from spillage. Then, shipping took place according to the CDC/WHO guidelines.

As soon as the sample arrived at NCDC in BSL-3/4 Containment Lab and opened in the contained environment. The sample processed as per CDC guidelines and infections confirmed using a real-time RT-PCR assay. Results of tests obtained within 24-48 hours. The NCDC, further sent the sample to NIV Pune* bio safety lab for confirmation if deemed necessary [5,6,9,10].

Ebola virus infections diagnosed definitively in a laboratory through several types of tests: antibody-capture enzyme-linked immunosorbent assay (ELISA), antigen detection tests, serum neutralization test, reverse transcriptase polymerase chain reaction (RT-PCR) assay, electron microscopy. Virus isolation by cell culture samples from patients are an extreme biohazard risk; testing conducted under maximum biological containment conditions [9,10].

Table 1:

No. of passengers screened

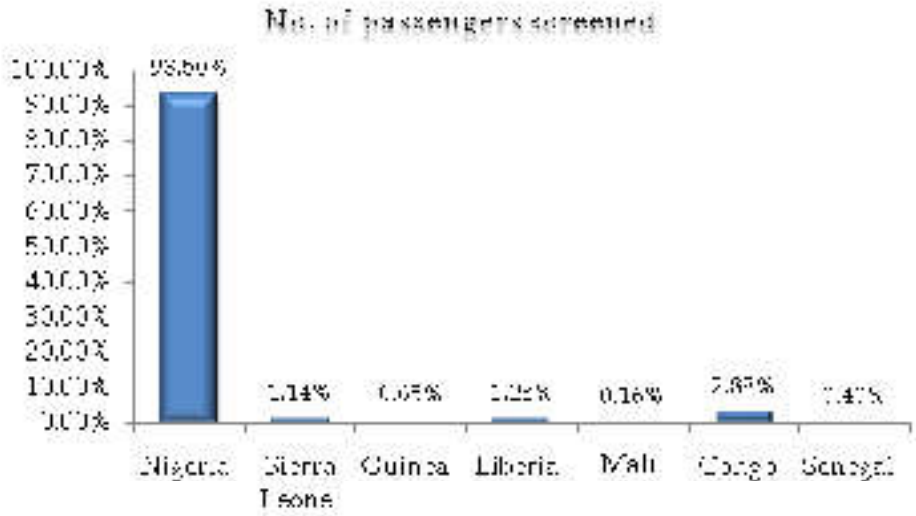
	Percentage
Nigeria	93.50%
Sierra Leone	1.14%
Guinea	0.65%
Liberia	1.28%
Mali	0.16%
Congo	2.88%
Senegal	0.40%
Total	100.00%

Suspected/non suspected

	Percentage
Non suspected	99.53%
Suspects	0.47%
Total	100.00%

Suspected patients

	Percentage
Taken to hospital	16.87%
Not taken to hospital	83.13%
Total	100.00%



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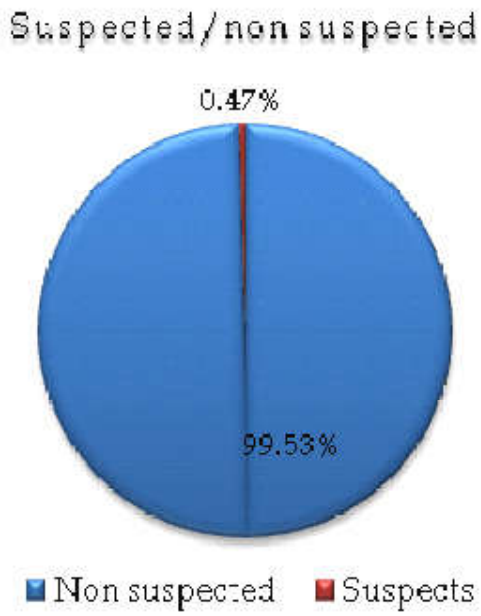

Chart 1:

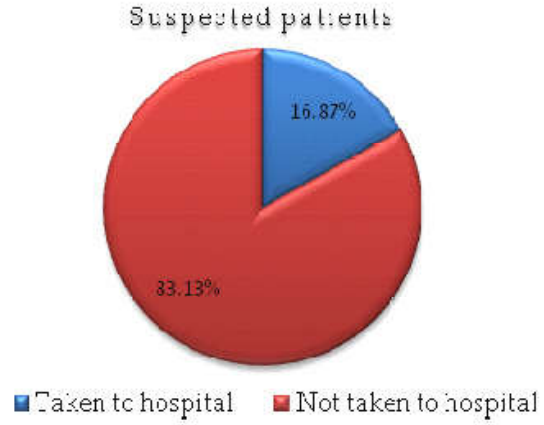

Chart 2:

Discussion

Nearly 45,000 Indian nationals lived and worked in Guinea, Liberia, Sierra Leone and Nigeria, the worst Ebola virus affected places. In case of further deterioration of the Ebola outbreak situation in the affected countries, Indian nationals would have certainly travelled back to India. Therefore, India was at a high risk of EVD as even a single case could have meant disaster for human security and seriously affected the environment. The risk was even higher since the patients were likely to travel back by air to one of India's megacities like Delhi, Mumbai or Chennai [11].

Since neither vaccine nor definitive treatment was available, prevention was the only option available to control the spread of disease. Therefore, robust surveillance measures were taken to control the spread of the disease.

(i) The study focuses on Screening of passengers travelling from countries having Ebola outbreak, namely Nigeria, Sierra Leone, Guinea, Liberia, Mali, Congo and Senegal from August 2014 to august 2015.

The number of passengers screened was 774683. The table shows that majority 93.50 percent of passengers screened were from Nigeria and rest only 7 percent from the remaining Ebola hit countries.

Medical Tourism in India is the largest service industry, with a contribution of 6.23% to the National GDP and 8.78% of the total employment in India [12] It focuses on medical treatment and utilization of Health care services. India is the choicest destination for people from Low socioeconomic countries because of its high standards of health care and affordability in terms of health care and visa services. In this study, we found that three PUIs were medical tourist with febrile illness. The Nodal center for EVD managed all PUIs. Before international travel, the medical tourist should undergo necessary investigations to avoid quarantine and discomfort in a foreign country. A protocol and specific travel guidelines should be in place for medical tourist during public health emergencies of International concern. Out of the total number of passengers screened only 83 passengers were suspects, which is a statistically significant lower value as shown in the Pie charts. Even the value of suspects or PUIs was statistically insignificant. Although statistically insignificant, the values are clinically of notable significance, as even a single undiagnosed case could have spread into uncontrolled outbreak of EVD. The challenges to India were a high population density, middle lower income status, poor adult literacy rate 13 and greater than 70 percent population lived in rural India. Apart from this, India had highest number of people living below poverty line.

(ii) Our study indicates that during alert or Pre-epidemic our surveillance system was robust to identify the suspected cases at the earliest possible time. A public health Surveillance system and active monitoring was in place to immediately report cases of Ebola virus disease like symptoms [14,15].

In our study, we found that surveillance for 42 days which was double the incubation period. This was done as a doubly safety measure. If the contacts had any fever, intense weakness, muscle pain, headache, sore throat, vomiting, diarrhea, rash, impaired kidney and liver function, and In some cases, both internal and external bleeding then they had to inform Immediately.

(iii). Out of these 83 suspected patients, one 26-year-old passenger was Ebola treated patient from Liberia and 14 patients were with clinical symptoms. He was the first confirmed patient diagnosed with the virus to have landed in India, according to Health Ministry officials. Though his blood samples tested negative for three different tests, his semen samples, tested positive for the virus. Despite the efforts of Indian missions abroad giving advice to the Indian residents abroad, one patient who was Ebola virus cured patient tested positive as his semen samples showed traces of Ebola virus. The patients sample was tested in NIV Pune* and NCDC Delhi. Ebola virus persists in immune-privileged sites in some people who have recovered from Ebola virus disease. These sites include the testicles, the inside of the eye, and the central nervous system. In women infected while pregnant, the virus persists in the placenta, amniotic fluid and fetus. In women who have been infected while breastfeeding, the virus may persist in breast milk. The most common mode is human-to-human transmission.

Studies of viral persistence indicate that in a small percentage of survivors, some body fluids may test positive on reverse transcriptase polymerase chain reaction (RT-PCR) for Ebola virus for longer than 9 months.

Relapse-symptomatic illness in someone who has recovered from EVD due to increased replication of the virus in a specific site is a rare event. In our study, we found that patients treated of EBV recently could transmit; disease via body fluid should avoid travel. As long as blood and secretions contain virus, the person can spread infection [16]. Such patient need to follow protocol while travelling to prevent further spread of infection. The most common mode of human-to-human transmission is direct contact through broken skin or unprotected mucous membranes e.g., the eyes, nose, or mouth, with the blood or body fluids (urine, feces, saliva, semen, and other secretions) of a person who is sick or has died of EVD.

This patient was travelling by air and the he travelled according to the Ministry of Health and Family Welfare guidelines issued to the Airlines. The airline advised to keep first aid kits, triple layer masks, hand sanitizers, disposable bags, isolation management of the patient on board and aircraft disinfection as per the international civil aviation organization (ICAO) guidelines. The ill passenger assisted by dedicated crewmembers. The crewmembers followed all universal precautions and biomedical waste guidelines while handling this passenger. In addition, the crew assisted the Airport Health officer (APHO) and health personnel's in contact tracing. Universal precaution kits as per the International Civil.

Aviation Organization (ICAO) guidelines and a stock of triple layer masks, disposable hand gloves, hand sanitizer and disposal bags were available on board. The NCDC issued guidelines for isolation and management of the cured patient on-board and subsequent aircraft disinfection to the airline. On arrival, aircraft crew helped the Airport Health Officer (APHO) and health personnel's in contact

tracing. Health alerts displayed on airports and at strategic locations. A health declaration card and point of screening of all passengers was at airport.

(iv) According to this study, 14 passenger with clinical symptoms transferred to the Nodal center, as they were APUIs* [17]. In our study, we found that most of the patients admitted in the tertiary care center were due to febrile illness. Two patients turned out to be malaria positive. The initial symptoms of suspected patients of Ebola virus disease were similar to other endemic illnesses like malaria, dengue and it was difficult to diagnose Ebola virus disease based on initial clinical symptoms. Thus, clinical symptoms led to suspicion of EVD and not confirmation. Laboratory tests were the only means to confirm the illness. Suspected patients of EVD* triaged with positive clinical symptoms and travel to country with widespread transmission is direct contact through broken skin or unprotected mucous membranes e.g., the eyes, nose, or mouth, with the blood or body fluids (urine, feces, saliva, semen, and other secretions) of a person who is sick or has died of EVD.

(v) Researchers in this study found that a mother had to accompany a 3.5-year-old child who had febrile illness. Since mother was close contact of PUIs*, and developed fever subsequently she was kept under investigation for EVD*. A contact is any person who has been exposed to a suspect, probable, or confirmed case of EVD in at least one of the following ways: - has slept in the same household as a case - has had direct physical contact with the case (alive or dead) during the illness - has had direct physical contact with the (deceased) case at a funeral or during burial preparation rituals - has touched the blood or body fluids of a case during their illness - has touched the clothes or linens of a case - a baby who has been breastfed by the patient Family, friends, co-workers, and medical staff are the most at risk (WHO)

(vi) Our study showed that the passengers suspected for Ebola virus disease was statistically insignificant. India is a low middle-income country with high density of population. Even a single positive case of EVD* could have become source of uncontrolled spread of the disease. Prevention was the best way of controlling spread of the disease [18].

(vii) Our study showed that all International guidelines for infection control and waste disposal followed meticulously.

(viii) Our study showed the initial symptoms of suspected patients of Ebola virus disease were similar to other endemic illnesses like malaria, dengue and it was difficult to deferentially diagnose EVD* solely on clinical symptoms. A laboratory test was the only means to confirm the illness. Positive clinical symptoms and travel to country with widespread transmission identified suspected patients of EVD*. Other diseases ruled out before a diagnosis of EVD: malaria, typhoid fever, shigellosis, cholera, leptospirosis, plague, rickettsiosis, relapsing fever, meningitis, hepatitis and other viral hemorrhagic fevers, while dealing with Ebola virus disease suspected passengers [19].

(ix) Guidelines for Ministry of Health and Family welfare for Management of Ebola Virus disease patients are single room with attached toilet or patient bed separated at least 3 meters apart, the intensive care facility of EVD* to be designed outside the hospital for isolation.

We faced many challenges in managing Ebola virus disease suspected patients in our tertiary care facility. The facility is a seven-bedded ICU with a common washroom. It is an open ICU where patient beds are kept 3 meter apart.

Since we received international patients, we had to arrange special diet for them, as they were not comfortable with the native diet. The quarantined travelers also brought luggage with them unlike routine ICU patients. Because all the patients were conscious and stable patients, they demanded permission to use mobile phones and laptops inside the ICU. The EVD* suspect patients were from Nigeria and west Africa and had difficulty in communication because of language problem.

Ideally, a biological toilet and treatment of sewerage is essential while dealing with such patients. In our study, we did not have this facility.

Our study indicates that health care workers, doctors and nurses had apprehensions for working with Ebola virus disease patients and counseling was necessary.

Our study shows that the ICU staff was trained in dealing with EVD* patients and also donning and doffing of PPE Kit. Trexler negative pressure isolator system was not available.

Our research indicates that the PPE Kit and N95 mask were used while handling EVD* suspect patients.

Statistical Analysis

Categorical variables were presented in number and percentage (%). Qualitative variable was compared using Chi-Square test. A p value of <0.05 was considered statistically significant. The data collected and entered in MS EXCEL spreadsheet

and analysis done using Statistical Package for Social Sciences (SPSS) version 21.0.

Results

Satisfactory containment of Ebola virus disease during Public health emergency of International concern.

Conclusion and Recommendation

(A) To interrupt all remaining chains of Ebola transmission

(B) To respond to the consequences of residual risks

(C) To work on health systems recovery

(D) To design ICU facility for future use.

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Abbreviation

PUIs* Person Under Investigation for Ebola Virus Disease

EVD* Ebola Virus disease

WHO* World Health Organization

PHEIC* Public Health Emergency of International Concern

NCDC* National Center for Disease Control, New Delhi

NIV* National Institute of Virology Pune.

AAI* Airport Authority of India

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Original Research Article

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A Study on Combined Spinal Epidural Labour Analgesia a Comparison between 0.125% Bupivacaine with Fentanyl Versus 0.1% Ropivacaine with Fentanyl

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Abstract

Introduction: The responsibility of the Anaesthesiologist in obstetrics is arguably greater than in any other fields of anaesthesia. *Aim:* To compare the quality of epidural analgesia of 0.125% bupivacaine with 0.1% ropivacaine after intrathecal administration of fentanyl 25 µg in combined spinal epidural labour analgesia. *Methodology:* After obtaining ethical committee approval and written consent 60 term healthy primi gravida with cephalic singleton pregnancy were selected. Intrathecal fentanyl 25 µg initiated in all parturients. Group B receives epidural 0.125% bupivacaine 10 ml with 2 µg of fentanyl/mL agroup R receives epidural 0.1% ropivacaine 10 ml with 2 µg of fentanyl/mL two groups were compared in terms of quality of analgesia, vitals & fetal outcome. *Results:* Quality of analgesia was excellent in both the groups. Maximum motor blockade (grade 1 Bromage) has occurred during the first stage of labour and doesn't affect the progression of labour or fetal outcome. *Conclusion:* We had concluded that both epidural bupivacaine 0.125% and ropivacaine 0.1% provides equal

Keywords: Combined spinal epidural labour analgesia; Intrathecal fentanyl; Bupivacaine; Ropivacaine.

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Introduction

Labour is defined as events that occur serially in female genital tract in order to expel the products of conception out of the womb into outer world through the vagina [1].

History of obstetric anaesthesia began with James Young Simpson, who administered Ether to a woman with deformed rachitic pelvis in 1847. She survived the complicated delivery absolutely free of pain [2]. John Snow administered chloroform to Queen Victoria during hereighth child birth, Prince Leopold In 1950 [3]. Labour pain leads to cortisol, epinephrine and nor epinephrine release into maternal circulation which may affect the uterine blood flow Neuraxial techniques especially combined spinal epidural technique provides rapid onset of analgesia and better maternal satisfaction [4].

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In this study, we compared the quality of labour analgesia of epidural 0.125% bupivacaine with fentanyl µg/mL and 0.1% ropivacaine with fentanyl 2 µg/mL following intrathecal fentanyl 25 mcg.

Aim of the study

The aim of the study is to compare the quality of epidural analgesia of 0.125% bupivacaine with fentanyl µg/mL and 0.1% ropivacaine with fentanyl 2 µg/mL after intrathecal administration of fentanyl 25 mcg in combined spinal epidural labour analgesia.

Objectives

Primary Objective

To compare the quality of analgesia during the labour in both the groups.

Secondary Objective

To compare duration and progression of of labour.

To compare newborn evaluation with APGAR score.

To study the side effects of the drugs and procedure.

Methodology

This comparative clinical study of combined spinal epidural labour analgesia for vaginal delivery with intrathecal fentanyl 25 µg +epidural 0.125% bupivacaine 10 mL with 2 µg of fentanyl/ mL versus intra thecal fentanyl 25 µg+ epidural 0.1% ropivacaine 10 mL with 2 µg of fentanyl/mL was conducted in 60 parturients, who consented for painless labour in Kilpauk Medical College and Hospital, Chennai after obtaining permission from the Institutional Ethical committee. After taking a written informed consent, only those who fulfilled the selection criteria were included in this study.

Inclusion criteria

1) Pregnant women with singleton pregnancy, term gestation, cephalic presentation, in active first stage of labour, the mothers who are booked and all antenatal investigations are within normal limits.

2) Cervical dilation >3 cm and <5 cm.

3) Age 18-35 years, Height >150 cm.

4) BMI 18-25

5) Primi gravida

Exclusion criteria

1) Mothers with co-existing diseases like diabetes, hypertension, PIH, bronchial asthma, epilepsy, thyroid disorders, IHD, valvular heart disease, previous LSCS

2) Spine abnormalities and local skin infections.

3) Coagulopathies.

4) Cephalo pelvic disproportion.

5) Preterm gestation.

6) Fetal distress.

Antenatal mothers in antenatal wards and those who attended outpatient department were counselled about labour analgesia. Thorough assessment of mothers including investigation, systemic examination was done. Those mothers who fulfilled inclusion criteria when enters the active stage of labour was enrolled in our study.

The study population consisted of 60 parturients allocated into two groups, 30 in each group. The parturients satisfying the selection criterianwere randomized by computer generated randomization table into two groups of thirty each - Group B and Group R. The randomization sequence was prepared in double-blinded manner. The study blinding was broken after the statistical analysis.

(1) Group B (Bupivacaine): received intrathecal fentanyl 25 µg + epidural 0.125% Bupivacaine 10 mL with 2 µg of fentanyl/mL.

(2) Group R (Ropivacaine): received intrathecal fentanyl 25 µg + epidural 0.1% Ropivacaine 10 mL with 2 µg of fentanyl/mL.

Preparation of the Parturient

She was prepared as per the routine preparation done for delivery, in addition to preparation of back to perform epidural block.

The onset of active labour, degree of cervical dilatation and the adequacy of pelvis for vaginal delivery were assessed by attending obstetrician, before performing the block.

Monitors (NIBP, pulse oximeter, ECG and CTG) connected and base line vitals were recorded.

An IV line was started on the non dominant and with an 18 G cannula.

The parturient was preloaded with 500- 1000 mL 0f Ringer lactate solution.

Anti aspiration prophylaxis (Inj. Ranitidine 50 mg and Ondansetron 4 mg IV) was given.

All equipments needed for airway management and resuscitation of the mother and baby was kept ready before performing the block.

Preparation of epidural bupivacaine and ropivacaine

The epidural drug preparation (including top up doses) was done by the duty assistant professor who prepared it according to the group allocation. 2 mL of 100 mcg fentanyl (50 µg/mL) diluted with 3 mL of normal salinewhich gives 20 mcg /mL fentanyl. For group B-2.5 mL of 0.5% bupivacaine mixed with 20 mcg of prepared inj. fentanyl (1 mL) and 6.5 mL of normal saline which gives 0.125% bupivacaine with fentanyl 2 mcg/mL. For group R- 5 mL of 0.2% ropivacaine mixed with 20 mcg of prepared inj. fentanyl (1 mL) and 4 mL of normal saline which gives 0.1% ropivacaine with fentanyl 2 mcg/mL.

Performing the Block

Block was performed after shifting patient to operation theatre. We used separate needle CSE technique for this study. Subartachnoid block was performed under aspesis and local analgesia at L 4-5 AND 25 µg Fentanyl given after confirming free flow of CSF. Epidural space was located at L3-4 L2-3 using loss of resiistance technique using 18G Tuohy needle with bevel directed upwards Catheter was placed 3-5 cm in the epidural space. After negative aspiration for blood and CSF, the epidural catheter was secured. Two mL of prepared solution was given as epidural test dose. Each increment of the therapeutic dose was considered the test dose. These precautions were followed in all bolus injections of local anaesthetic through an epidural catheter. With patient in supine position, left uterine displacement was done by placing a wedge under the right buttock. Remaining 8 mL of 0.125% bupivacaine with 2 µg/mL fentanyl for group B or 8 mL of 0.1% ropivacaine with 2µg/ mL fentanyl for group R was given epidurally and patient was shifted back to labour room. After 60 minutes or when pain recurred or after two segments was regressed whichever was earlier, 5 mL (0.125% bupivacaine or 0.1% ropivacaine with fentanyl µg/mL) was given epidurally in presence of duty assistant professor. Left uterine displacement was maintained throughout the labour. Intermittent bladder catheterisation was done. At the time of onset of second stage of labour; she may feel pain over perineum, inner thigh, anus or vagina.

Full dose of 10 mL of (bupivacaine 0.125%/ ropivacaine 0.1%) was administered regardless of previous dose at second stage, relieves the pain without affecting course of labour and this avoids further analgesia for episiotomy also. Obstetric management was decided by obstetricians.

Continuous maternal and fetal monitoring was done and epidural catheter was removed six hours after delivery.

Monitoring

1) Time of onset of analgesia (Time taken for achieving visual analogue scale to become less than 3).

2) Assessment of sensory blockade (every 15 minutes using spirit cotton for loss of cold sensation in the midclavicular line bilaterally from the nipple to the pubic symphysis).

3) Assessment of motor blockade (Modified Bromage Scale)

4) Assessment of sedation (5- point scale).

5) Duration of analgesia (Time interval from the onset of analgesia till the return of painful contraction (VAS more than 3) or till regression of sensory level to below T12)

6) Hemodynamics.

7) Complications or side-effects if any.

8) Obstetric progress by partograph.

9) Fetus monitoring by fetoscope, cardio tocograph.

At birth, the APGAR score of the neonate at 1 and the 5th minute was used to assess the neonatal well being. Any neonate with an APGAR score of less than 7 was resuscitated with suctioning, mask ventilation and intubation if needed and ventilated with 100% oxygen.

Patient Satisfaction Score

1-excellent

2-good

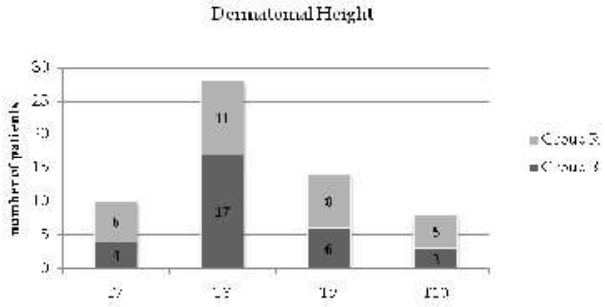
3-poor

Statistical Analysis

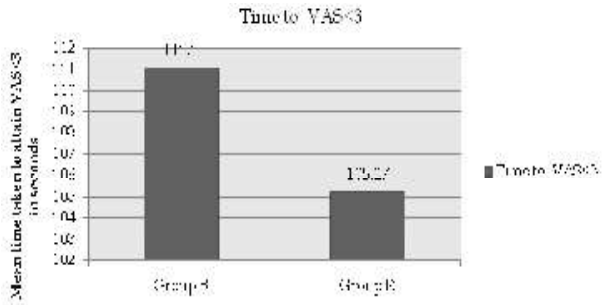
The statistical analysis were done using SPSS

(Statistical package for social sciences) version 17 for windows. Descriptive statistics are presented as mean±SD. Two sided independent student's t tests to analyze continuous data and Chi-square test for association was used to compare categorical variables between treatment allocations. $p<0.05$ was considered as statistically significant

Result



Graph 1: Dermatomal Height



Graph 2: Time to VAS<3

Table 1: Demoography

	Group B	Group B	P value
Age	21.97 ± 2.356	22.63 ± 2.484	0.291
Weight (mean±S.D)(kg)	71.30 ± 5.484	71.53 ± 5.941	0.875
Height (mean±S.D)(cm)	160.23 ± 4.400	158.77 ± 5.117	0.239

	Group B	Group B	P value
Cervical dilatation(cm)	4.23±0.430	4.23±0.430	1.0
Active phase of first stage of labour	171.97±19.089	172.03±25.926	0.991
Second stage of Labour	31.30±5.240	31.10±5.762	0.889
Total duration	203.77±19.856	203.13±22.793	0.909

	Group B	Group B	P value
Total number of epidural bolus	4.33±0.547	4.00±0.947	0.1
Total Volume of Epidural Drug(mL)	33.33±4.011	32.17±4.676	0.991
Total Dose of Fentanyl(µg)	66.67±8.023	64.33±9.353	0.304

Table 2: Dermatomal Height (Chi-square test)

	T7	T8	T9	T10	P Value
Group B	4(13.3%)	17(56.7%)	6(20.0%)	3(10.0%)	0.48
Group R	6(20.0%)	11(36.7%)	8(26.7%)	5(16.7%)	

	Group B	Group B	P value
Baseline VAS(student's t test)	9.70±0.466	9.53±0.507	0.19
Time to VAS<3 (in seconds)	111.10±17.197	105.27±8.828	0.104
Total Dose of Fentanyl(µg)	66.67±8.023	64.33±9.353	0.304

Table 3: Motor blockade

Motor blockade	0	1	2	3
Group B	20(66.7%)	10(33.3%)	0	0
Group R	26(86.7%)	4(13.3%)	0	0
P value	0.67			

Table 4: Outcome

Outcome	Group B	Group B	P value
Vaginal delivery	29(96.7%)	29(96.7%)	
Forceps	1(3.3%)	1(3.3%)	1.0
Emergency LSCS	0	0	

Table 5: APGAR Score

APGAR Score	Group B	Group B	P value
1 Min	7.57±0.504	7.57±.0504	1.000
5 Min	8.57±0.504	8.87±0.346	.009

Table 6: Complications

Complications	Group B	Group B	P value
Pruritus	22(73.3%)	20(66.7%)	0.5
None	8(44.4%)	10(55.6%)	

Table 7: Patient satisfaction

Patient satisfaction score	Group B	Group B
1	30(100%)	30(100%)
2	0	0
3	0	0

Discussion

Neuraxial method provides excellent and satisfactory analgesia without compromising maternal and fetal safety hence it is considered till now as a gold standard technique for providing labour analgesia [5].

Many studies showed that ropivacaine is 60% as potent as that of bupivacaine. There have been many studies compared equal concentration of drugs [14,17], (0.125% bupivacaine vs 0.125% ropivacaine) and equi-potent concentration [18,19]

of both drugs (0.1% bupivacaine vs. 0.15% ropivacaine).

In our study, there were no difference between two groups with respect to age, height and weight.

Mean baseline VAS in group B was 9.7 with S.D of 0.466 and in group R mean baseline VAS was 9.53 with S.D of 0.507. p value of 0.19 and it was statistically insignificant.

Labour analgesia was initiated in both groups between 4-5 cms of cervical dilatation. Mean cervical dilatation in both groups was 4.23 cm with S.D of 0.430. P value of 1.0 which was statistically insignificant.

CSE analgesia often initiated with intrathecal opioid (fentanyl 25 μg or sufentanyl 5 μg) in early latent phase with cervical dilatation less 4-5 cm followed by epidural catheter placement in healthy nulliparous women. Addition of local anesthetics to opioid intrathecally is unnecessary for achieving complete spinal analgesia especially in early stage will result in hypotension and profound motor blockade particularly if it is followed by an epidural injection of local anesthetics [12,13].

In our study, we initiated labour analgesia with intrathecal fentanyl 25 μg followed by epidural catheter placement in L3-L4/L2-L3 space and catheter tip fixed at T12/L1. Ten min after spinal analgesia group B received ten mL of 0.125% bupivacaine with fentanyl 2 μg/mL and group R received ten mL of 0.1% ropivacaine with fentanyl 2 μg/mL.

Mean onset of analgesia (time to VAS <3) was 111.10 sec with S. D of 17.197 in group B and mean onset of analgesia was 105.27 sec with S.D of 8.828. P value of 0.104 was statistically insignificant. There is no significan difference between two groups with respect to onset of analgesia.

Maximum dermatomal level of sensory blockade achieved in both groups was T7. 13.3% in group B and 20.0% in group R had T7 level. 56.7% in group B and 36.7% in group R had T8 level.10.0% in group B and 16.7% in group R achieved T10 level .20% in group B and 26.7% in group R achieved T9 level. P value was 0.48 and statistically insignificant.

This was comparable to the level achieved by Owen et al. [14] and Guisasola [18] et al. Incidence of motor block was less in many studies and it was statistically significant in many studies (Gautier et al, Fischer et al, Meister et al, Campbell et al., Fine gold et al.) [14,17]. In our study, 20(66.7%) of patients in group B and 26(86.7%) of patients in group R had no motor blockade. 10 patients (33.3%) in group B and 4 (13.3%) patients in Group R had grade 1 Bromage (minimal) motor blockade. No patient in any groups was developed grade 2 or 3 motor blockade P value of 0.67, which is statistically insignificant. Maximum motor blockade (grade 1 Bromage) has occurred during first stage of labour and was seen immediately following bolus dose. There were no statistically significant differences in blood pressure, pulse rate, saturation in both the groups.

No statistically significant differences in Sedation score of both groups. Some patients showed mild drowsiness (score 1) mainly due to effective pain relief. Fetal heart rate changes in both groups were within normal limits. Pvalue of both the groups shows no statistically significant changes.

In both the groups VAS was maintained with less than 3. In most cases VAS 3 usually coincide with the onset of 2nd stage of labour. Repeating the 10 mL of bupivacaine maintained the analgesia.

Mean duration of active phase of 1st stage of labour in group B was 171.9±19.089 minutes and 172.03 ± 25.926 minutes in group R. Mean duration of 2nd stage of labour in group B was 31.30±5.240 minutes and i n group R it was 31.10 ±5.762 minutes. Mean total duration of labour in group B was 203.77 ±19.856 minutes and in group R it was 203.13± 22.793 minutes. All durations were statistically insignificant

Our results were correlated well with many studies (Feranandez 2001, Owen 20024, Boselli 2003, Halpern 2003) [18,14]. In contrast Lee et al. 2002, found that the bupivacaine group had longer first stage of labour than ropivacaine group. However they concluded that the difference may be of limited clinical significance.

In our study CSE is associated with more rapid cervical dilatation and shorter duration of labour. This result was consistent with studies conducted by Amit. G. Bhagwat et al. [9] and Lawrence C Tsen et al. [8].

Mean of total number of epidural bolus doses used in group B was 4.33 with SD of 0.547. In group R Mean of total number of epidural bolus doses used was 4.00 with SD of 0.947. P value of0.100 and was statistically insignificant.

Mean of total volume used for epidural analgesia in group B was 33.33 mL with SD of 4.011. In group R mean of total volume used for epidural analgesia used was 32.17 mL and SD of 4.676. p value of 0.102 and was statistically insignificant. There was no difference between two groups in volume

requirements.

During second stage, all parturients in our study required ten mL of local anaesthetic bolus for effective pain relief during episiotomy. This was not influenced by position of patient and mainly depends on volume Merry AF et al., Park WY et al., Erdemir HA et al studies showed that inconsistent results with position of patient during drug administration but by increasing the volume of drug [22,23,24] during second stage of labour.

Mean of total dosage of fentanyl used in group B was 66.67 µg with SD of 8.023. In group R mean of total dosage of fentanyl used was 64.33 µg with SD of 9.353. p value of 0.304 and was statistically insignificant.

Most studies showed that incidence of emergency caesarean delivery were less with CSE technique when compared to conventional epidural [9,10] Risk of caesarean delivery does not increased by neuraxial techniques and also by time of initiation of labour analgesia in latent phase (cervical dilatation 4 cm).

In both groups all babies delivered by normal vaginal delivery except two babies were delivered by forceps delivery. Both of them were secondary to poor maternal efforts. No other case underwent caesarean section.

The recent Cochrane review [20] which compared epidural analgesia with inhalational and intravenous analgesia (mainly opioid) and observed that there was less fetal acidosis and less nalaxone administration in babies born to mothers having labour epidural analgesia.

Beilin and Halpern in 2010 [16,21] did a focused review with various studies that compared bupivacaine and ropivacaine and concluded that there was no evidence that neonatal outcome is adversely affected when ropivacaine or bupivacaine is used for labour analgesia. In our study, at 1 minute in group B mean of APGAR score was 7.57 and SD was 0.504. In group R mean was APGAR score 7.57 and SD was 0.504. P value of 1.0 and was statistically insignificant.

At 5 minutes in group B mean of APGAR score was 8.57 and SD was 0504. In group R mean was APGAR score 8.87 and SD 0.346. p value of 0.009 and was statistically insignificant.

In our study, Pruritus was seen in both the group B (73.3%) and group R (66.7%). In most of womens it was self limiting and got settled within hour of fentanyl administration. Some responded well to Ondansetron 4 mg IV. No other complications were seen during labour analgesia RE Collis, DWL Davies concluded that overall satisfaction was greater in CSE group than conventional epidural because of CSE produces rapid onset of analgesia [4,7]. In our study, all parturients in both the group experience and gave satisfaction score of (=1) excellent analgesia during labour till delivery.

Conclusion

The observation of this study shows that both bupivacaine 0.125% and ropivacaine 0.1% administered epidurally as a part of combined spinal epidural technique following intrathecal 25 µg provides equal and effective analgesia. Duration of labour was not prolonged rather combined spinal epidural analgesia decreases the duration of labour. Patient satisfaction, level of sensory blockade, mode of delivery, duration of labour, neonatal outcome and complications are comparable between both the groups. Bupivacaine group had relatively more motor blockade which was grade 1 Bromage when compared to ropivacaine group but that was not statistically significant. Maximum motor blockade of grade 1 Bromage was seen during first stage of labour especially immediately after first epidural bolus dose which doesn't affect the progress of labour. But the observation of this study with respect to motor blockade was not statistically significant which needs further future studies in large scale.

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Original Research Article

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Complications of Dexmedetomidine in Patients Undergoing Laparoscopic Surgery: A Descriptive Study

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Abstract

Background: Stress response is common in any of the operative or laparoscopic procedure. Anesthetic agents like Dexmedetomidine are roped into, to attenuate these hemodynamic responses and to smoothen the operative and postoperative period. This study evaluates the side effects or complications encountered in patients receiving Dexmedetomidine infusion. *Methods:* This was a descriptive study done in patients with age group 18-65 years age of either sex undergoing laparoscopic surgery and receiving the Dexmedetomidine infusion. *Result:* Total of 30 patients were included in the study. The mean + SD age of the patients were 31+13.2 years. Bradycardia and hypotension was present in 10% of patients receiving Dexmedetomidine infusion. *Conclusion:* Bradycardia and hypotension were most common side effects seen with Dexmedetomidine infusion though were self resolving. Thus it is effective in attenuating haemodynamic response to laryngoscopy, intubation, surgery and pneumoperitoneum without significant complications.

Keywords: Complications; Dexmedetomidine; Laparoscopic; Surgery.

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Introduction

Stress response usually gets exaggerated during any of the surgical procedure including the perioperative or the postoperative period. Anesthetic agents are roped in, to attenuate these stress responses and to maintain the physiological and hemodynamic stability. Dexmedetomidine has almost 8 times more affinity for α-2 adreno-receptors as compared to Clonidine [1].

Dexmedetomidine is a novel α2 agonist with sedative, sympatholytic and analgesic properties and hence, it can be a very useful adjuvant in anaesthesia as stress response buster, sedative and analgesic [2]. It also reduces the catecholamine levels and its release in response to surgical stress or any nociceptive stimuli [3,4,5]. Though the Opioids are also effective in attenuating the stress response; however, the dose required is very high for similar results [1]. The pneumo-peritoneum created during the laparoscopic surgeries poses an extra risk for haemodynamic instability [6,7]. Hence, the study was proposed to assess the side effects related with the use of dexmedetomidine infusion in patients undergoing laparoscopic surgery.

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Methods

This was a descriptive study conducted at a tertiary care teaching institute in western India. Institute ethical Committee approval was taken before the initiation of the study. Part of the study describing the hemodynamic changes with the use of Dexmedetomidine compared with controls has already been accepted and under process for publication. [8] All patients receiving Dexmedetomidine during laparoscopic surgery were included in the study after informed consent. A total of thirty patient of ASA Grade I & II, aged 18–65 years of either sex scheduled for elective laparoscopic surgeries i.e Lap. Choleycystectomy, Lap. Appendicectomy, Lap assisted VH, Diagnostic Laparoscopic procedure under general anaesthesia were included in the study. ASA Grade III & IV patients with decreased autonomic control such as the elderly, diabetic patients, patients with chronic hypertension or severe cardio - pulmonary disease, patients on drugs like β blockers or calcium channel blockers, pregnant or lactating women, patients with history of egg protein allergy and to drugs particularly α 2 agonists were excluded from the study.

Study subjects received injection Dexmedetomidine with loading dose 1 mcg/kg before induction over a period of 10 minutes followed by maintenance dose of 0.2 mcg/kg/hr throughout the pneumoperitoneum till extubation. The study drug was prepared in a similar 50 ml syringe by anaesthesiologist. Dexmedetomidine 200 mcg/kg (2 ml) was added to 0.9% normal saline (48 ml) making a total volume of 50 ml (with concentration of 4 mcg/ml).

Patient on arrival to operation room were secured with two 18 G (iv) cannula, one for loading and infusion of study drug and other for induction and maintenance of general anaesthesia.

Routine vital monitor, ECG (Electrocardiography), Pulse Oximetry, Non Invasive Blood Pressure (NIBP) monitors were attached and baseline parameters like Heart Rate (HR), SpO_2. Blood Pressure were recorded at pre decided interval. Loading dose of Dexmedetomidine infusion at 1 mcg/kg was started and infused over a period of 10 minutes, thereafter maintenance infusion was given at a rate of 0.2 mcg/kg/hr.

Premedication was done for all subjects with inj. Glycopyrolate 4 mcg/kg, inj.midazolam 0.03 mg/kg and inj. ondansetron 4 mg, inj. Fentanyl 2 mcg/kg i.v. Patients were preoxygenated with 100% oxygen, induced 5 minutes after infusion of loading dose with inj.Thiopentone 5 mg/kg i.v, inj.succynylcholine 1.5 mg/kg. All the patients were intubated with appropriate size endotracheal tube and correct position of tube was confirmed by auscultation and $EtCO_2$ measurements. Anaesthesia was maintained with nitrous oxide and oxygen gas mixture (60:40) and Isoflurane on a closed circuit. Injection Vecuronium was administered for neuromuscular blockade. Carbon di oxide was insufflated in to the peritoneum (at a rate of 2 litre/min) to create pneumoperitoneum. Intraabdominal pressure was maintained upto 12-14 mmHg throughout the procedure. All the patients were observed for vital parameters like pulse rate, mean arterial pressure and SpO_2 levels at regular intervals at baseline, during laryngoscopy, intubation, 1,3,5 minutes after intubation, before pneumoperitoneum, 15 and 30 minutes after pneumoperitoneum and after extubation.

Dexmedetomidine infusion was continued till extubation of patient. Residual neuromuscular blockade was reversed by appropriate dose of Neostigmine and Glycopyrolate and tracheal extubation performed. Any adverse effects like hypotension, hypertension, bradycardia, respiratory depression were recorded. Patients were observed in recovery room for 2 hrs and thereby shifted to ward.

Throughout the study, patients were observed for any adverse events like bradycardia, tachycardia (pulse rate less than or more than 20% of pre-operative level respectively on two consecutive readings), hypotension and hypertension (MAP less than or more than 20% of pre-operative level respectively on two consecutive readings), sedation score more than RSS(Ramsay sedation score) 4, respiratory depression (SaO_2 < 90%) and dryness of mouth and were managed conservatively.

Hypotension was managed with fluid bolus of normal saline. If it didn't responded to fluid administration then injection Mephentermine 5mg i.v was administered. Any incidence of bradycardia was treated with inj. Atropine 0.6 mg i.v. Any hypertension (MAP >20% Preoperative value) was treated by increasing Isoflurane concentration to maintain SBP within 20% of preoperative value.

Statistical Analysis

All the data which was expressed as mean±SD or as n (%) was filled in the predesigned proforma and then entered in the computer using Excel sheet. The analysis of data was done using SPSS software version 17.0.

Results

Total of 30 patients were enrolled in the study. Demographic profile of the patients is described in Table 1. The mean age ± SD of patient was 31+13.2. Side effects of the Dexmedetomidine infusion are described in Table 2. The common side effects which were seen in the present study were bradycardia, hypotension. The other minor side effects were dry mouth, nausea, fever, chills, vomiting and agitation.

Table 1: Demographic variables of study population

Variables	Study population (n=30)
Age(Years) Mean±SD	31±13.2
Weight(Kg) Mean±SD	50.5±9.7
Sex (M:F)	8:22
ASA Grading (I/II)	5:25

Legend; SD- Standard Deviation, ASA- American Society of Anaesthesiologists.

Table 2: Side effects seen in the study population with use of Dexmedetomidine infusion

Variables	n(N = 30)	% ages
Bradycardia	3	10%
Tachycardia	2	6.7%
Hypotension	3	10%
Hypertension	1	3.3%
Nausea	3	10%
Dry mouth	3	10%
Fever	1	3.3%
Vomiting	1	3.3%
Agitation	1	3.3%
Chills	1	3.3%
Hyperglycemia	-	-
Hypothermia	-	-
Hyperthermia	-	-
Desaturation (Spo2<90%)	-	-
Post Procedure bleeding	-	-
Oliguria	-	-
Bronchospasm	-	-
Metabolic acidosis	-	-
RSS *score >4	2	6.7%

*RSS: Ramsay sedation score

Discussion

Anaesthetic manoeuvres like direct laryngoscopy, tracheal intubation and extubation involve severe sympathetic stimulation. Moreover, the pneumoperitoneum and carbon dioxide insufflations required in laparoscopic surgeries, lead to increase in plasma nor-epinephrine, epinephrine levels and plasma renin activity [7]. All these changes lead to tachycardia, hypertension and increased systemic and pulmonary vascular resistance, and reduced cardiac output.

Modern day anaesthesia practices, therefore, plan to prevent sympathetic discharge and provide haemodynamic stability perioperatively. [2] Various agents in the form of opioid analgesics, benzodiazepines, beta blockers, calcium channel blockers and vasodilators have been used to achieve this goal with variable success. Recently, a great enthusiasm has been shown toward the use of α2 agonists in anaesthesia practice because of their anxiolytic, sedative, sympatholytic and analgesic sparing properties [9].

Dexmedetomidine is a highly selective novel α 2 adrenergic agonist. It acts through three types of α 2 receptors- namely α 2 A, α 2 B and α 2 C situated in brain and spinal cord. The resultant action is sedation, anxiolysis, analgesia and sympatholysis, the latter leading to decrease in the blood pressure and heart rate [2]. Activation of α 2 A receptors in brain stem vasomotor centre results in suppression of norepinephrine release, hypotension and bradycardia. Stimulation of α 2 A adreno receptors and α 2 C adreno receptors in locus ceruleus causes sedation. In the spinal cord, activation of both α 2 A and α 2 C receptors directly reduce pain transmission by reducing substance P release [2].

Therefore, the Dexmedetomidine has proven analgesic, sedative, anxiolytic and sympatholytic activity [10-13]. The added advantage of dexmedetomidine is that it provides conscious sedation and analgesia without causing much respiratory depression leading to a cooperative patient [14]. Dexmedetomidine infusion in the perioperative period decreases serum catecholamine levels by 90%, [13] blunt the haemodynamic response to laryngoscopy, tracheal intubation, pneumoperitoneum and extubation, [15] provides sedation without respiratory depression [16] and decreases post-operative analgesic requirements also [17].

The Dexmedetomidine has been used in IV infusion form with or without bolus dose. Infusion rates range from from 0.1 to 10 mcg/kg/h [10,18,19] However, with higher dose infusion, higher incidence of adverse cardiac effects have been observed [13]. A biphasic response on blood pressure occurs with a bolus dose [7]. Initially, there occurs hypertension followed by fall in blood pressure. This response is seen often more in young and healthy patients [14]. Stimulation of α 2 B adreno-receptors in vascular smooth muscles is responsible for this biphasic response. Low dose infusion of 0.25–0.5 mcg/kg/h results in a monophasic response of 10–15%

fall in mean arterial blood pressure and pulse rate. [13] Furthermore, in low dose, dexmedetomidine exhibits linear kinetics, meaning that a constant amount of drug is eliminated per hour rather than a constant fraction of drug.

Dexmedetomidine was found to have sympatholytic effect while preserving the baro-reflex mechanisms [20]. It is associated with hypotension and bradycardia [21] which was seen in the present study too. Both of these problems usually resolve without intervention [22] as was seen in the present study too. Significant bradycardia was noted in 3 (10%) patients receiving Dexmedetomidine. Bradycardia appeared mostly in the first 30 minutes of Dexmedetomidine infusion especially during loading dose administration as was seen in study by Bhagat N et al. [1] Current study also observed hypotension in 10% of the patients. Other minor side effects were nausea, vomiting, fever, chills, vomiting and sedation seen in the present study.

Conclusion

Dexmedetomidine infusion is effective in attenuating haemodynamic response to laryngoscopy, intubation, surgery and pneumoperitoneum. without significant complications. Though bradycardia and hypotension are common adverse event but most of the time they are self resolving.

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Original Research Article

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Comparative Study between Intravenous Clonidine and Intravenous Fentanyl to Attenuate Hemodynamic Response to Laryngoscopy and Tracheal Intubation

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Abstract

Background: Laryngoscopy and intubation are associated with acute hemodynamic responses. In susceptible patients even this short period (2-7 minutes) of hypertension and tachycardia can result in myocardial ischemia or increased intracranial pressure. *Aims and objectives:* To evaluate and compare the effect of intravenous (I.V.) Fentanyl and intravenous (I.V.) Clonidine in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation. *Settings and design:* This study was designed to compare the effect of I.V. Fentanyl and I.V. Clonidine in attenuating the hemodynamic response to laryngoscopy and endotracheal intubation in adult patients undergoing elective surgeries under general anaesthesia. *Methods and material:* A prospective, randomized, double-blind, comparative study was conducted on 60 patients, randomly allocated into two groups of 30 each i.e. group C and group F receiving 2mcg/kg Clonidine and 2mcg/kg Fentanyl, respectively, 5 minutes prior to induction. Hemodynamic parameters and postoperative sedation scores were recorded. *Statistical analysis:* Mean ± standard deviation for quantitative continuous data and compared by unpaired t-test. *Result:* The hemodynamic variables in Fentanyl group were significantly lower than Clonidine group for the first five minutes after laryngoscopy and intubation. *Conclusion:* Both fentanyl and clonidine were able to attenuate the hemodynamic response to laryngoscopy and intubation, however, fentanyl 2 mcg/kg I.V. given 5 min prior to intubation kept the hemodynamic variables significantly lower than those seen in clonidine 2 mcg/kg I.V. given 5 min prior to intubation. However, after 5 min of intubation the effects of both the drugs were comparable.

Keywords: Clonidine; Endotracheal Intubation; Fentanyl; Hemodynamic Response; Laryngoscopy.

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Introduction

Direct laryngoscopy and endotracheal intubation are known to cause sympathoadrenal stimulation which manifests as hypertension and tachycardia [1]. This response occurs 30 seconds (sec) after starting laryngoscopy and intubation and lasts for less than 10 minutes (min) [2]. If no specific measures are taken to attenuate these hemodynamic responses, the pulse rate can increase from 26% to 66% depending on the method of induction, and arterial systolic blood pressure can increase from 36% to 45% [3,4]. Also, it is previously reported that 10%–18% of the patients develop ischemic ST-segment changes during the procedure, making it important to blunt this response [5].

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Complications resulting from these hemodynamic events include left ventricular dysfunction, [6,7] hypertensive crisis, [8] pulmonary oedema,[8] cardiac dysrhythmias, [3,9] myocardial ischemia, [10,11] and myocardial necrosis [11].

Over the years, various pharmacological and non – pharmacological methods have been used to attenuate this hemodynamic response [12]. These include shorter duration of laryngoscopy, smooth and gentle intubation, McCoy laryngoscope, use of intravenous opioids, [13] vasodilators, [14] calcium channel blockers, [15] intravenous and topical lignocaine and adrenoceptor blocking drugs alone or in combination with other drugs. However, none of the above approaches or agents have proved to be ideal. Hence, the search for an ideal agent to attenuate the hemodynamic responses is still continuing.

Clonidine, an imidazoline derivative, is a centrally acting selective partial alpha-2 adrenergic receptor agonist (220:1 - alpha-2 to alpha1 receptor preference) [16]. It has sedative, analgesic and antihypertensive actions [17]. It binds to the alpha 2A receptors and mediates these effects. It stimulates alpha 2A inhibitory neurons in the medullary vasomotor centre. As a result, there is decrease in sympathetic nervous system outflow from central nervous system (CNS) to peripheral tissues. This is manifested as peripheral vasodilatation and decreases in systemic blood pressure, heart rate and cardiac output. The alpha-2 receptors are present in high density in the pontine locus coeruleus, inhibition of which is responsible for the sedative effects of clonidine. It blunts reflex tachycardia associated with direct laryngoscopy, decreases intraoperative lability of blood pressure and heart rate, decreases plasma catecholamine concentrations, and dramatically decreases anaesthetic requirements for inhaled (Minimum Alveolar Concentration, MAC) and injected drugs [16]. Therefore, clonidine seems well suited as premedication for attenuating hemodynamic response associated with laryngoscopy and intubation.

Fentanyl is a phenylpiperidine-derivative synthetic opioid agonist structurally related to meperidine. As an analgesic, it is 75-125 times more potent than morphine. It produces analgesia by binding to specific G protein-coupled receptors located in the brain and spinal cord regions involved in transmission and modulation of pain and also acts on opioid receptors on peripheral sensory nerve endings [18]. High concentrations of opioid receptors are present in the solitary nuclei and the nuclei of the 9th and 10th cranial nerves, associated with the visceral afferent fibres of these nerves which originate in the pharynx and larynx. These receptors provide a possible mechanism for blunting of the response to laryngeal stimulation [19,20]. Fentanyl reduces heart rate and decreases blood pressure and cardiac output. It reduces the dosing requirement for the volatile agents. Peak analgesic effect is achieved after 5 min of I.V. administration.

This randomized prospective study has been designed to compare the effects of I.V. fentanyl with I.V. clonidine on the changes in heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO_2) observed during laryngoscopy and tracheal intubation.

Materials and Methods

This prospective, randomized, double-blind, comparative study was conducted on 60 adult patients undergoing elective surgeries under general anaesthesia with endotracheal intubation.

Patients belonging to ASA (American Society of Anaesthesiologists) physical status I and II, aged between 20 to 50 years of either sex and hemodynamically stable patients with all routine investigations within normal limits were included in the study. Patients belonging to ASA physical status III or more, posted for emergency surgery, those who refused to participate, patients with anticipated difficult intubation, patients on antihypertensive medication, patients on any opioid or any sedative medication in the week prior to the surgery, patients who were known to be allergic to any of the test drugs, pregnant patients, patients with cardiovascular, respiratory, renal, hepatic or endocrine diseases were excluded from the study.

Data Collection

Sample Size

Sample size was calculated using Winpepi statistical package at significance level of 5% with power of 80% using the inputs given below –

According to study "Comparison of Fentanyl and Clonidine for Attenuation of the Haemodynamic Response to Laryngoscopy and Endotracheal Intubation", conducted by Sameenakousar et al. [21] we took the following inputs –

Heart Rate (beats per minute)	Fentanyl (Mean±SD)	Clonidine (Mean±SD)
Immediately after laryngoscopy and intubation	101.14±15.01	86.88±10.00

Standard Deviation (SD) of heart rate immediately after laryngoscopy for fentanyl was 15.01, Standard Deviation of heart rate immediately after laryngoscopy for clonidine was 10.0, and difference in mean heart rate between two groups immediately after laryngoscopy was 14.26, hence we arrived at a minimal sample size of 26 patients.

Hence, we enrolled a total of 60 patients (30 in each group) to account for potential dropouts or protocol violation.

Selection Method

Randomization was done. Patients were divided into two groups using computer generated random number table, where -

Group C received I.V. Clonidine 2 mcg/kg and Group F received I.V. Fentanyl 2 mcg/kg.

Method of Blinding

The patients were unaware of which study drug group they belonged to. The study drug syringes were prepared by a separate anaesthesiologist who was not involved in the study procedures. Therefore, the anaesthesiologist who administered the drugs and assessed the parameters was blinded to the study drugs. Also, the syringes were identical and the colours of the drugs were the same.

Methods

Institute Ethical Committee approval was obtained. After obtaining written informed consent from every case selected for the study, pre-anaesthetic evaluation of the patient was done and necessary investigations were sent and reviewed, a day prior to surgery. The patients were enrolled for the study according to the inclusion and exclusion criteria. These were then randomly allocated to one of the two study groups according to the drug to be used:-

Group C - received intravenous clonidine 2 mcg/kg diluted in 10 ml normal saline, given slowly I.V., 5 minutes prior to induction of anaesthesia.

Group F - received intravenous fentanyl 2 mcg/kg diluted in 10 ml normal saline, given slowly I.V., 5 minutes prior to induction of anaesthesia.

Patients were kept fasting as per standard NPO (nil per oral) guidelines. On arrival in the operative room, Ringer lactate infusion was started through 20 G I.V. cannula. Electrocardiograph (ECG), peripheral oxygen saturation and non-invasive blood pressure monitors were attached to the patient and the patient's heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO_2) were noted (baseline values).

All patients were premedicated with injection (inj.) glycopyrrolate 0.004 mg/kg I.V. and inj. ondansetron 0.1 mg/kg I.V. Thirty patients were given inj. fentanyl 2 mcg/kg slowly I.V. diluted in 10 ml normal saline. Thirty patients were given inj. clonidine 2 mcg/kg slowly I.V. diluted in 10 ml normal saline, both 5 min prior to induction. After 3 minutes of preoxygenation with 100% oxygen, anaesthesia was induced with inj. propofol 2 mg/kg I.V. and inj. succinylcholine 2 mg/kg I.V. The duration of laryngoscopy and intubation was limited to 30 seconds in all the patients. After confirmation of proper placement of endotracheal tube, inj. vecuronium 0.1 mg/kg I.V. was given as a long acting muscle relaxant. Thereafter mechanical ventilation was continued throughout the procedure and anaesthesia maintained with 33% oxygen, 66% nitrous oxide, 0.5-1% isoflurane and intermittent boluses of vecuronium as a relaxant. No other procedure was performed or medication was administered during the first 15 minutes of data collection period after tracheal intubation. Intraoperative analgesia was provided with inj. paracetamol 15 mg/kg I.V. At the end of the surgery, neuromuscular blockade was reversed with inj. neostigmine 0.05 mg/kg I.V. and inj. glycopyrrolate 0.008 mg/kg I.V. followed by extubation.

In case of severe hemodynamic fluctuations, medical intervention other than adjustment of isoflurane was done. Hypotension was defined as a decrease in systolic BP (blood pressure) of more than 30 mmHg from baseline or a mean arterial pressure of less than 60 mmHg and was corrected with I.V. fluids and if required, with small doses of inj. mephentermine 3 mg I.V. Bradycardia was defined as a HR of less than 60/minute and was corrected, if associated with hemodynamic instability, with inj. atropine 0.6 mg I.V. Replacement of fluid loss was done with crystalloids or colloids and if blood loss was more than 20% of the blood volume it was replaced with appropriate quantity of cross matched blood.

Following parameters i.e. heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP) and oxygen saturation (SpO_2) were recorded at baseline, 5 min after administration of study drugs, after induction, at laryngoscopy and intubation (T0), 1 min after

intubation (T1), 3 min after intubation (T3), 5 min after intubation (T5), 10 min after intubation (T10), 15 min after intubation (T15). ECG was continuously monitored.

Ramsay Sedation Score was used to assess postoperative sedation:

1 = agitated, restless

2 = cooperative, tranquil

3 = responds to verbal commands while sleeping

4 = brisk response to glabellar tap or loud noise while sleeping

5 = sluggish response to glabellar tap or loud noise while sleeping

6 = no response to glabellar tap or loud noise while sleeping

Patients were monitored for side effects of both the drugs preoperatively, intraoperatively and postoperatively.

Statistical Analysis

Data were tabulated using Microsoft Excel 2010 software. Results were statistically analysed.

Categorical variables of gender, ASA physical status were analysed using Chi Square test. Continuous variables like age, weight, heart rate, blood pressure were analysed using unpaired t – test. p value < 0.05 was considered significant.

Results

The patients in both the groups did not show any statistically significant differences in their age, gender and weight distribution [Tables 1,2,3]. Also they were similar in terms of ASA grading [Table 4].

Baseline values (before administering any drug) of HR, SBP, DBP, MAP were comparable (p=0.30, p=0.29, p=0.74, p=0.36 respectively) in both the groups C and F [Table 5].

Demographic Profile of the two Groups:

Table 1: Comparison of Age Between the two Groups (Mean±SD)

Demographic Profile	Group C	Group F	p Value	Significance
Age (Years)	29.5±7.56	28.96±9.16	0.806	Not Significant

Table 2: Comparison of Gender Distribution Between the two Groups

Demographic Profile	Group C (%)	Group F (%)	p Value	Significance
Male	16 (53.33)	12 (40)	0.300	Not Significant
Female	14 (46.66)	18 (60)		

Table 3: Comparison of Mean Weight Between the two Groups (Mean±SD)

Demographic Profile	Group C	Group F	p Value	Significance
Weight (Kg)	52.23±6.15	51.86±5.91	0.814	Not Significant

Table 4: ASA Physical Status Distribution Between the two Groups

ASA Grade	Group C (%)	Group F (%)	p Value	Significance
I	19 (63.33)	16 (53.33)	0.432	Not Significant
II	11 (36.66)	14 (46.66)		

Hemodynamic Parameters

Table 5: Baseline Vital Parameters (Mean±SD)

Vital Parameters	Group C	Group F	p Value	Significance
Heart Rate (beats per minute)	91.67±4.26	92.9±4.90	0.30	Not Significant
SBP (mmHg)	123.53±7.83	121.4±7.72	0.29	Not Significant
DBP (mmHg)	75.26±6.31	74.73±6.57	0.74	Not Significant
MAP (mmHg)	91.35±4.17	90.28±4.82	0.36	Not Significant

Heart Rate [Table 6, Figure 1]

There was significant difference in heart rate values 5 min after administration of study drugs and after induction when the values were lower in group C and the difference was statistically significant (p <0.05). However, at intubation (T0), 1 min and 3 min after intubation, the heart rate values were lower in group F and the difference was found to be statistically significant (p <0.05). At 5 min, 10 min and 15 min after intubation, there was no statistically significant difference between the heart rate values of both the groups (p >0.05).

Systolic Blood Pressure [Table 7, Figure 2]

There was significant difference in systolic blood pressure at intubation, 1 min and 3 min after intubation between the two groups. Values were relatively higher in group C and the difference was found to be statistically significant (p <0.05). However, there was no statistically significant difference between group C and group F with respect to systolic blood pressure values at baseline, 5 min after administration of study drug and after induction and 5 min, 10 min and 15 min after intubation (p >0.05).

Table 6: Changes in Heart Rates in two Groups (Mean ± SD)

Heart Rate	Group C	Group F	p Value	Significance
Baseline	91.67 ± 4.26	92.9 ± 4.90	0.30	Not Significant
5 min After Study Drug Administration	76.16 ± 4.23	84.23 ± 12.9	0.0025	Significant
After Induction	77.16 ± 4.57	81.63 ±10.58	0.04	Significant
At Intubation (T0)	86.26 ± 5.9	81.3 ± 10.07	0.02	Significant
1 min After Intubation (T1)	86 ± 3.98	81.16 ± 9.08	0.01	Significant
3 min After Intubation (T3)	84.73 ± 3.75	80.63 ± 7.81	0.01	Significant
5 min After Intubation (T5)	80.96 ± 6.03	78.33 ± 7.68	0.14	Not Significant
10 min After Intubation (T10)	79.8 ± 5.49	77.86 ± 7.27	0.25	Not Significant
15 min After Intubation (T15)	78.86 ± 5.33	77.93 ± 6.89	0.56	Not Significant

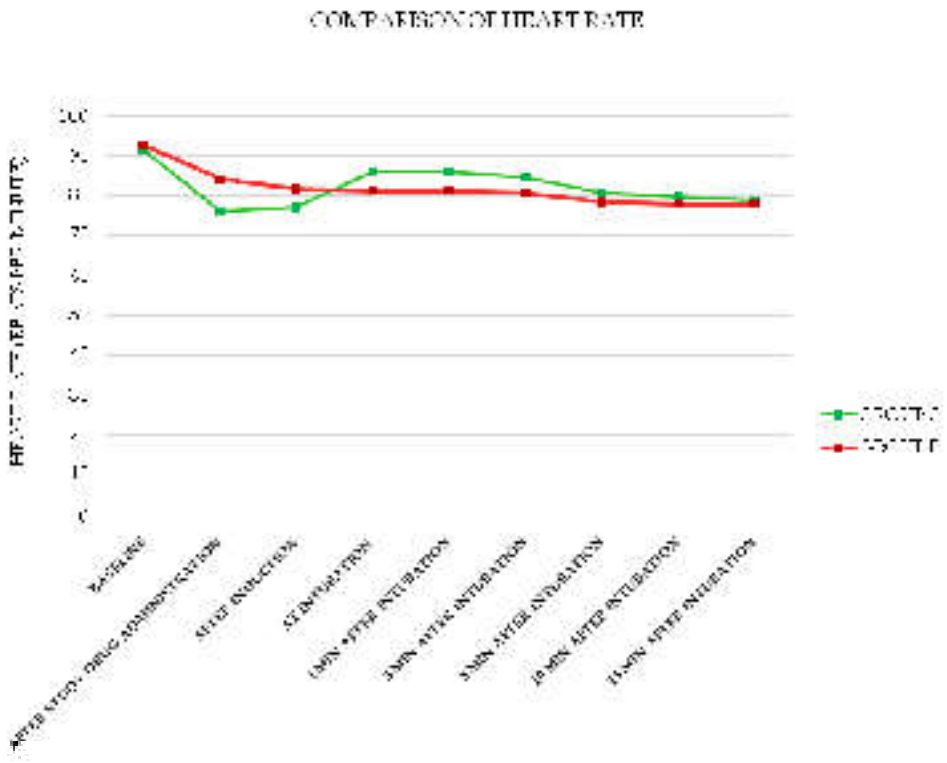

Fig. 1: Line diagram showing comparison of Heart rate between two groups

Diastolic Blood Pressure [Table 8, Figure 3]

Diastolic blood pressure values were relatively higher in group C at intubation, 1 min and 3 min after intubation and the difference was statistically significant ($p < 0.05$). All the other diastolic blood pressure readings did not show statistically significant difference ($p > 0.05$).

Table 7: Changes in Systolic Blood Pressure in two Groups (Mean±SD)

Systolic Blood Pressure	Group C	Group F	p Value	Significance
Baseline	123.53±7.83	121.4±7.72	0.29	Not Significant
5 min After Study Drug Administration	115.4±6.89	112.93±6.86	0.17	Not Significant
After Induction	107.06±5.57	104.8±5.13	0.10	Not Significant
At Intubation (T0)	113.66±5.46	109.53±6.98	0.01	Significant
1 min After Intubation (T1)	114.6±6.26	111.13±3.84	0.01	Significant
3 min After Intubation (T3)	114.66±4.40	111.46±5.96	0.02	Significant
5 min After Intubation (T5)	110.46±3.66	109.66±5.99	0.53	Not Significant
10 min After Intubation (T10)	108.06±4.77	106.26±3.99	0.11	Not Significant
15 min After Intubation (T15)	107.13±3.88	105.46±3.67	0.09	Not Significant

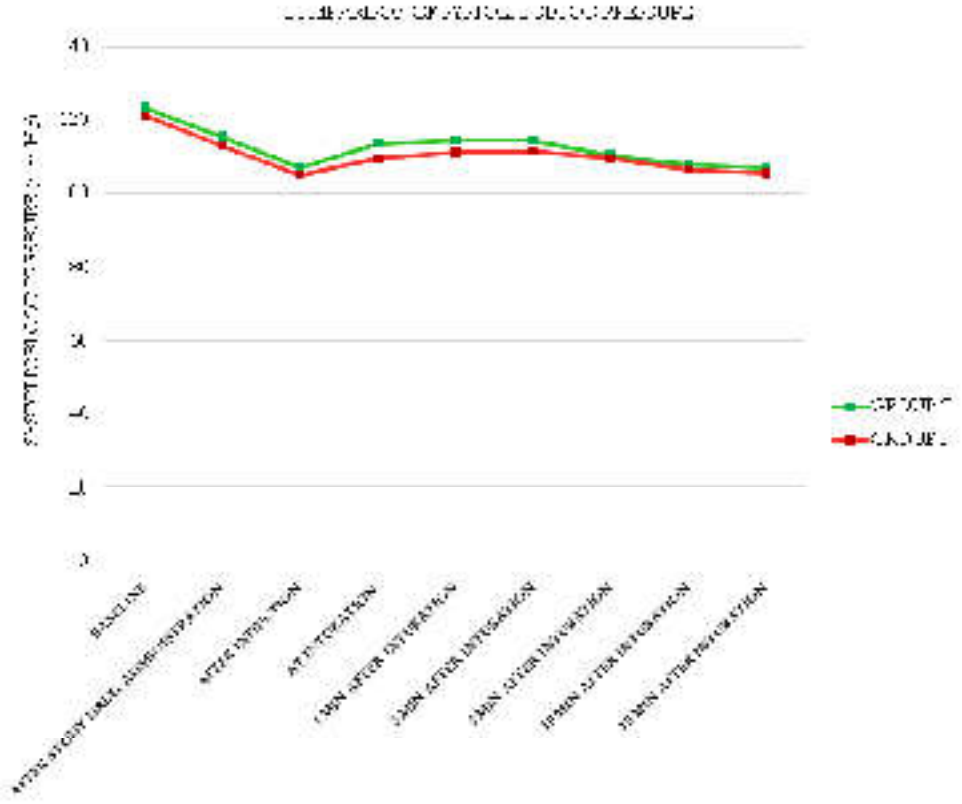

Fig. 2: Line diagram showing comparison of SBP between two groups

Table 8: Changes in Diastolic Blood Pressure in two Groups (Mean±SD)

Diastolic Blood Pressure	Group C	Group F	p Value	Significance
Baseline	75.26±6.31	74.73±6.57	0.74	Not Significant
5 min After Study Drug Administration	73.93± 3.76	72.66±6.06	0.33	Not Significant
After Induction	68.2±5.76	69.26±3.38	0.38	Not Significant
At Intubation (T0)	75±6.59	71±5.08	0.01	Significant
1 min After Intubation (T1)	73.2±6.29	69.73±3.88	0.01	Significant
3 min After Intubation (T3)	73.13±5.88	69.8±3.87	0.01	Significant
5 min After Intubation (T5)	73.13±5.42	71.4±3.86	0.15	Not Significant
10 min After Intubation (T10)	71.2±4.22	71.13±3.81	0.94	Not Significant
15 min After Intubation (T15)	69.73±3.81	70.33±3.24	0.51	Not Significant

Mean Arterial Pressure [Table 9, Figure 4]

A significant difference was noticed in the mean arterial pressure values between both the groups at intubation, 1 min and 3 min after intubation ($p < 0.05$). Values were relatively higher in group C. At all other times, both groups were not significantly different in terms of mean arterial

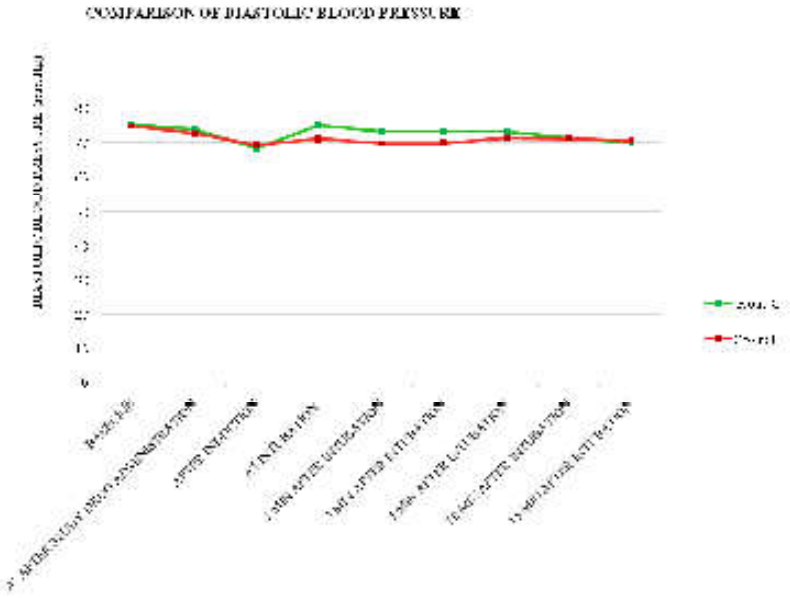

Fig. 3: Line diagram showing comparison of DBP between two groups

Table 9: Changes in Mean Arterial Pressure in two Groups (Mean ± SD)

Mean Arterial Blood Pressure	Group C	Group F	P Value	Significance
Baseline	91.35±4.17	90.28±4.82	0.36	Not Significant
5 min After Study Drug Administration	87.7±3.35	86.08±3.94	0.08	Not Significant
After Induction	81.15±3.70	81.11±2.52	0.95	Not Significant
At Intubation (T0)	87.88±4.48	83.84±4.37	0.00	Significant
1 min After Intubation (T1)	87±4.30	83.53±2.77	0.00	Significant
3 min After Intubation (T3)	86.97±4.28	83.68±3.55	0.00	Significant
5 min After Intubation (T5)	85.57±3.80	84.15±2.93	0.11	Not Significant
10 min After Intubation (T10)	83.48±3.04	82.84±2.87	0.40	Not Significant
15 min After Intubation (T15)	82.2±2.74	82.04±2.50	0.81	Not Significant

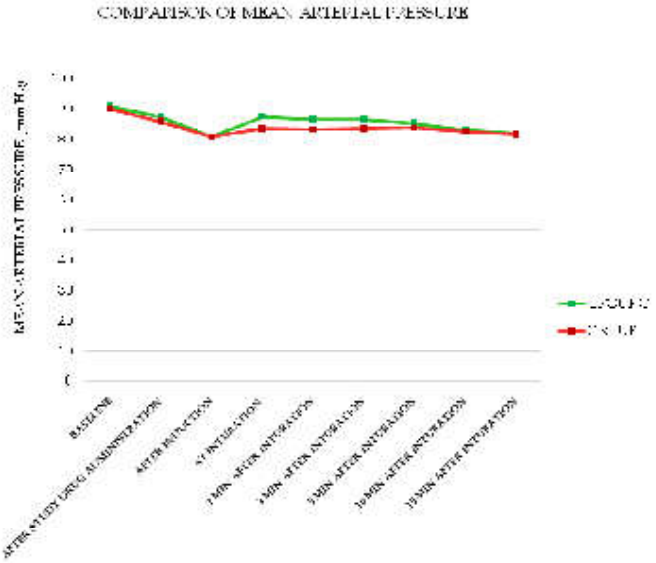

Fig. 4: Line diagram showing comparison of MAP between two groups

pressures (p >0.05).

Oxygen Saturation

There was no statistically significant difference between group C and group F with respect to SpO_2 values.

ECG

ECG was monitored continuously in all cases for both the groups. ECG was within normal limits throughout the procedures in all the patients.

Ramsay Sedation Scores [Table 10, Figure 5]

The values of Ramsay sedation score were recorded at fixed intervals in both the groups as shown in the table. There was significant difference

Table 10: Comparison of Ramsay Sedation Score Values of Patients in Both Groups (Mean ± SD)

Ramsay Sedation Score	Group C	Group F	p Value	Significance
Immediately After Surgery	3.06 ± 0.52	2.5 ± 0.57	0.00	Significant
15 Min After Surgery	2.9 ± 0.54	2.36 ± 0.61	0.00	Significant
30 Min After Surgery	2.7 ± 0.46	2.23 ± 0.50	0.00	Significant
45 Min After Surgery	2.6 ± 0.49	2.13 ± 0.57	0.00	Significant
60 Min After Surgery	1.86 ± 0.50	1.76 ± 0.43	0.41	Not Significant

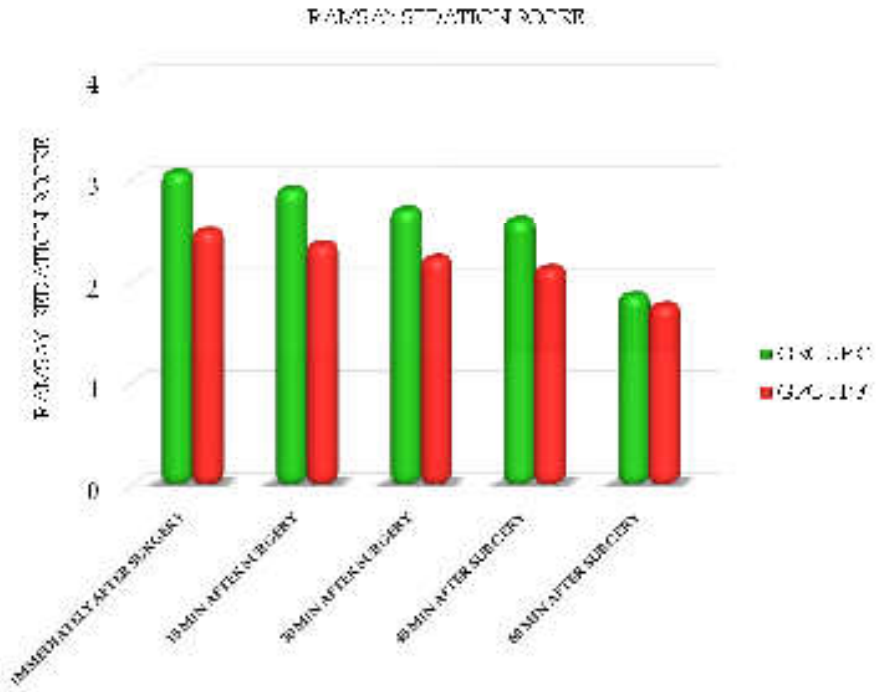

Fig. 5: Bar diagram showing comparison of Ramsay sedation score between two groups

Table 11: Side Effects in Group C

Side Effects	Group C (n=30)
Hypotension	2
Bradycardia	3
Sedation	2

Table 12: Side Effects in Group F

Side Effects	Group F (n=30)
Postoperative Nausea and Vomiting	2
Hypotension	1
Chest Rigidity	1

between the two groups with respect to sedation score values immediately after surgery, 15 minutes, 30 minutes and 45 minutes postoperatively. Values were higher in group C and the difference was found to be statistically significant ($p < 0.05$). 60 minutes post operatively, there was no statistically significant difference between the sedation scores of the two groups ($p > 0.05$).

Incidence of side effects as illustrated in tables 11,12 was minimum in both the groups.

Discussion

Laryngoscopy and tracheal intubation are potent stimuli that increase heart rate and blood pressure as has been recognised since 1951 by King and Harris [22]. These are produced due to sympathetic reflex provoked by stimulation of epipharynx and laryngopharynx. Reid and Brace in 1940 first described the effect of endotracheal intubation on electrocardiograph which were in the form of premature ventricular beat, nodal rhythm and sinus bradycardia [23]. The sensitive receptor area of epiglottis when mechanically stimulated by instrumentation evokes reflex response [22,23]. Measurements of the plasma catecholamines have demonstrated an increase in noradrenaline following laryngoscopy and thus confirmed sympathetic mediation to this response.

These above mentioned effects may have serious repercussions on the high risk patients like those with cardiovascular disease, increased intracranial pressure or anomalies of the cerebral vessels. Attenuation of such responses is of great importance in the prevention of the perioperative morbidity and mortality [24].

A diversity of results exists about the protective measures against the hemodynamic and the catecholamine responses to laryngoscopy and intubation, but no single anaesthetic technique has become generally accepted as being effective in preventing or attenuating these responses.

Selection of Drugs and Doses

In any study which is conducted, the criteria for the selection of the appropriate drug to prevent a sympathetic response must include the following:

1. The drug must prevent impairment of the cerebral blood flow.
2. It must avoid arousal of the patient.
3. The administration of the drug should neither be time consuming nor should the drug affect the duration or the modality of the ensuing anaesthesia.

Intravenous fentanyl and clonidine appear to best fulfil the above criteria [25].

Laryngoscopy and intubation are among the most painful processes carried out on the human body which are associated with acute hemodynamic responses.

Fentanyl is advocated for the attenuation of the sympathetic response to laryngoscopy and intubation. Narcotics may block afferent nerve impulses resulting from stimulation of the pharynx and larynx during intubation. Atweh and Kuhar used autoradiographic techniques in the rat, and found high concentrations of opiate receptors in the solitary nuclei and the nuclei of the 9th and 10th cranial nerves, associated with the visceral afferent fibers of these nerves which originate in the pharynx and larynx. Also, vagal motor nuclei involved in monosynaptic pharyngeal and laryngeal motor reflexes also have a high concentration of opiate receptors. These receptors provide a possible mechanism for the blunting of the response to laryngeal stimulation [19,20]. The blunting of the sympathetic response is dose dependent. Fentanyl at 6 mcg/kg, completely abolishes, while at 2 mcg/kg, it significantly attenuates the arterial pressure and the heart rate increase during laryngoscopy and intubation. The administration of fentanyl at the optimal time reduces the dose which is required. The optimal injection time of fentanyl is 5 minutes before an intubation, at a dose of 2 mcg/kg [26].

Clonidine is a potent antihypertensive drug. It produces a fall in the heart rate and blood pressure associated with decreased systemic vascular resistance and cardiac output. It has many properties of an ideal premedicant and it also has beneficial effects on the hemodynamics during stressful conditions like laryngoscopy and endotracheal intubation. It was shown by Zalunardo MP et al. [27] in 1997, that intravenous clonidine was better than oral clonidine in attenuating the pressor response. Hence, in our study, intravenous clonidine was used. The effects of clonidine on the hemodynamic variables are dose related but when the dose is increased to more than 4 mcg/kg, no further enhancement of the efficacy was seen. Hence, in our study, we used 2 mcg/kg.

This study was undertaken to compare the effects of I.V. fentanyl and I.V. clonidine on the attenuation of the hemodynamic response to laryngoscopy and

endotracheal intubation.

We enrolled 60 patients of ASA physical status I and II, of either sex, in the age group of 20-50 years undergoing elective surgeries under general anaesthesia. Patients were randomly divided into two groups of 30 each.

Group C- received intravenous clonidine 2 mcg/kg diluted in 10 ml normal saline, given slowly I.V., 5 minutes prior to induction of anaesthesia.

Group F- received intravenous fentanyl 2 mcg/kg diluted in 10 ml normal saline, given slowly I.V., 5 minutes prior to induction of anaesthesia.

We selected the optimal age range of 20 to 50 years. This is because, the variability of the heart rate changes decreases with increasing age and younger patients show more extreme changes. The anaesthetic technique was chosen such that the drugs which were administered did not have any significant effects on the heart rate or the blood pressure.

In our study, baseline values (before administering any drug) of HR, SBP, DBP, MAP were comparable (p=0.30, p=0.29, p=0.74, p=0.36 respectively) in both the groups C and F.

All the groups were similarly premedicated regarding anxiolysis.

There was clinically and statistically significant difference in heart rate values 5 min after administration of study drugs and after induction (p=0.002, p=0.04, respectively). The heart rate was lower in group C compared to group F at both these times. Clonidine stimulates the central alpha 2 adrenergic inhibitory neurons in the medullary vasomotor centre. As a result, there is a decrease in sympathetic nervous system outflow from central nervous system to peripheral tissues. Decreased sympathetic nervous system activity is manifested as peripheral vasodilatation and decrease in systemic blood pressure, HR, and cardiac output [16,28].

At intubation, 1 min and 3 min after intubation (p=0.02, p=0.01, p=0.01, respectively), the heart rate was maintained lower than baseline in both the groups, however, the values were lower in group F as compared to group C and this was statistically significant (p <0.05). Malde AD et al. [29] in a 2007 study, compared lignocaine and fentanyl efficacy on hemodynamic stability and revealed that lignocaine and fentanyl both attenuated the rise in heart rate, however, fentanyl produced better results. A single I.V. dose of fentanyl has a rapid onset of action because of greater lipid solubility which facilitates its passage across the blood brain barrier. The effect-site equilibration time between blood and the brain for fentanyl is 6.4 minutes [30].

In our study, the maximum rise in heart rate values was seen at 0 min after intubation (group C - 86.26±6, group F - 81.3±10.07). However, in the study by Sameenakousar et al [21] the first heart rate values were recorded only after 5 min of intubation where they found lower values in clonidine group.

Laryngoscopy and endotracheal intubation is often associated with hypertension and tachycardia because of sympathoadrenal stimulation which is usually transient and lasts for up to 5-10 minutes [31]. The above contradictory finding could be because clonidine was administered 5 min prior to induction in our study as per the study by Sameenakousar et al. [21] in contrast to all other studies done for observing the hemodynamic response to intubation after clonidine administration, where it was administered atleast 15 min prior to induction.

From the pharmacokinetic profile, it is seen that the distribution half-life of intravenous clonidine is approximately 11 minutes [31,32]. It has also been found that the maximum effect of intravenous clonidine occurs approximately 15 minutes after its administration [33-35]. In view of this, patients in the study by Harshavardhana HS et al. [31] in 2013, received injection clonidine 3 mcg/kg, diluted to 10 ml normal saline intravenously over 120 seconds, 15 minutes prior to laryngoscopy and intubation. Whereas, in case of fentanyl, 80% of the injected dose of fentanyl leaves the plasma to enter the highly vascular tissues (brain, lungs, heart) in less than 5 minutes (distribution half-life is about 5 minutes) [30].

At 5 min, 10 min and 15 min after intubation, the heart rate values continued to be lower than baseline in both the groups but after 5 min following intubation, there was no statistically significant difference between the two groups (p >0.05).

The maximum rise in systolic blood pressure values was seen at 1 min after intubation in our study (group C - 114.6±6.2, group F - 111.13±3.8). However, this value was lower in fentanyl group and was statistically significant (p <0.05). Malde AD et al. [29] in 2007, studied the efficacy of fentanyl and fentanyl plus lignocaine in attenuating the hemodynamic responses to laryngoscopy and endotracheal intubation in 37 hypertensive patients. The fentanyl group received 2 mcg/kg and the fentanyl plus lignocaine group received 1.5 mg/kg lignocaine and 2 mcg/kg fentanyl. They observed that lignocaine attenuated the rise

in blood pressure with intubation while fentanyl inhibited it totally.

Hoda A et al. [36] in 2011, concluded that addition of 2 mcg/kg fentanyl bolus to 1 MAC sevoflurane anaesthesia at induction attenuated the hemodynamic response to a maximum of 15% above baseline values.

The maximum rise in diastolic blood pressure values was seen at 0 min after intubation in our study (group C - 73.2±6.2, group F – 70± 3.8). However, this value was lower in fentanyl group and was statistically significant ($p < 0.05$). Splinter WM et al. [37] in 1989, conducted a study comparing hemodynamic responses to laryngoscopy and tracheal intubation in geriatric patients after administration of fentanyl, lignocaine and thiopentone and observed that fentanyl 1.5 or 3 mcg/kg reduced the rise in systolic, diastolic and mean arterial pressures and also decreased the incidence of marked fluctuations in hemodynamic variables, often seen in geriatric patients.

The maximum rise in mean arterial pressure values was seen at 0 min after intubation in our study (group C - 87.88±4.4, group F - 83.84±4.3). However, this value was lower in fentanyl group and was statistically significant ($p < 0.05$).

In our study, at 5 min, 10 min and 15 min after intubation, the mean arterial pressure values continued to be lower than baseline in both the groups but after 5 min following intubation there was no statistically significant difference between the two groups ($p > 0.05$).

Both clonidine and fentanyl were able to blunt the rise in mean arterial pressure occurring during laryngoscopy and intubation. However, fentanyl had a better efficacy in blunting the response which was statistically significant.

Thus, we see that fentanyl did not allow marked fluctuations in the systolic, diastolic and mean arterial pressures and these were well maintained near the baseline values. This property can have a positive significance in high risk patients.

Further, after 5 min of intubation, clonidine group also showed stable hemodynamics. This indicates that at the time of intubation, there was incomplete sympathetic blockade. Therefore, one can speculate that a higher dose or an earlier administration of clonidine before laryngoscopy would result in complete sympathetic outflow blockade which would keep the hemodynamic variables closer to the baseline.

The SpO_2 was maintained between 99 to 100% in both the groups. No fall in saturation was observed in any patient ($p > 0.05$).

The patients who received clonidine were sedated but arousable (i.e. showed a brisk response to glabellar tap or loud noise while sleeping) for 45-60 min postoperatively. However, in the fentanyl group, the patients responded to verbal commands and they were calm and co-operative.

Study done to evaluate the effect of clonidine as pre-anaesthetic medication by Wright et al [38] found that clonidine produced a significant reduction in anxiety ($p < 0.05$) and caused sedation.

In the clonidine group, three patients had bradycardia and responded to atropine, two patients had hypotension which was treated by reducing concentration of inhalational agents and giving bolus I.V. fluids. Two patients were sedated postoperatively for more than an hour. Side effects were found to be statistically insignificant ($p > 0.05$).

In the fentanyl group, chest rigidity was observed in one patient during bag and mask ventilation during induction. One patient had hypotension intraoperatively, which was managed by bolus of I.V. fluids. Two patients complained of nausea in the immediate postoperative period. None of them had an episode of vomiting. Side effects were found to be statistically insignificant ($p > 0.05$). Postoperative respiratory depression was not seen in any of the patients.

Limitations

Our study was conducted on patients with ASA physical status I and II. So, further studies on elderly patients and those with compromised cardiac function are required to recommend its use in such high risk patients. Also we did not measure the plasma catecholamine levels.

Conclusion

1. Both I.V. fentanyl and I.V. clonidine were able to attenuate the hemodynamic response to laryngoscopy and intubation, however, I.V. fentanyl 2 mcg/kg given 5 min prior to intubation was better than I.V. clonidine 2 mcg/kg given 5 min prior to intubation as fentanyl did not allow marked fluctuations in SBP, DBP and MAP and they were well maintained near baseline.
2. After 5 min of intubation both the drugs

were comparable in terms of hemodynamic stability.

3. Ramsay sedation score was higher with clonidine as compared to fentanyl for 45 min after extubation.
4. Incidences of side effects were less in both groups and those present, were not statistically significant.

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Original Research Article

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The Efficacy of Dexmedetomidine as Adjuvant in Caudal Block for Postoperative Pain Relief in Children

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Abstract

Introduction: In paediatric patients, optimum pain relief is a big challenge. An effective therapy to block or modify the physiological responses to painful stimulus is an essential. Hence, here is an attempt to study addition of dexmedetomidine, an alpha-2 adrenergic receptor agonist to bupivacaine with regards to analgesic potency and side effects. *Material and Methods:* After approval from institution ethics committee, the study was conducted to compare the effect of addition of dexmedetomidine to bupivacaine in caudal block for postoperative analgesia in paediatric infraumbilicalsurgeries. Written informed parental or guardian consent was obtained.30 cases in the age group of 1 to 6 years were studied. They were randomly divided into two groups, Group N and Group D. • Group N (n=30) – 0.25% Bupivacaine 1 ml/kg+ 0.5 ml normal saline • Group D (n=30) – 0.25% Bupivacaine 1 ml/kg+Dexmedetomidine 1 µg/kg, making the volume to 0.5 ml. Total volume for caudal block being 1 ml/kg in both groups. • after giving general anaesthesia child was placed in left lateral position and caudal block was performed under sterile conditions. The postoperative pain reliefwas evaluated using FLACC score hourly for first 6 hours, 2 hourly upto 12 hours and then 4 hourly upto 24 hours. Sedation is evaluated by Ramsay sedation score. *Results and Conclusion*: Addition of dexmedetomidine in the dose of 1µg/kg to 0.25% bupivacaine for caudal blockade showedduration of analgesia for Group N was 5.86±1.21 hrs and Group D was 15.5±3.02 hrs, without any significant haemodynamic changes, safe for use in paediatric patients without any adverse effects.

Keywords: Caudal Block; Bupivacaine; Dexmedetomidine.

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Introduction

The International Association for the Study of Pain has defined pain as 'an unpleasant sensory and emotional experience, associated with actual or potential tissue damage' [1].

Children have been undertreated for pain because of the wrong notion that they neither feel pain nor remember the painful experiences to the same degree that adult did. Pain experienced by infants and children often goes unrecognised, even neglected because they cannot express it [2]. An effective therapy to block or modify the physiological responses to painful stimulus is an essential component of paediatric anaesthesia practice [3]. Now, postoperative pain management is an integral part of paediatric anaesthesia.

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A caudal epidural analgesia has become one of the most popular and commonly performed regional blocks in paediatric anaesthesia after its first description by Campbell in 1933 [4]. It is relatively simple technique with good success rate [5]. Different additives have been used in order to improve the duration of action as well as the quality of analgesia of the local anaesthetic used in the single shot caudal block technique such as opioids, epinephrine, alpha 2 agonist, ketamine and neostigmine [6]. Dexmedetomidine is a potent as well as highly selective alpha 2 adrenergic agonist having a sedative, sympatholytic and analgesic effect and have been described as a safe and effective additive in many anaesthetic applications and analgesic techniques. Their stimulation decreases calcium entry in the nerve terminals resulting in an inhibitory effect on the neurotransmitter release thus facilitating analgesia [7]. It has an alpha2/alpha1 selectivity ratio of 1600:1, which is eight times more potent than clonidine (200:1) [8].

Hence here is an attempt to study addition of dexmedetomidine, an alpha-2 adrenergic receptor agonist to bupivacaine with regards to analgesic potency and side effects.

Material and Methods

Plan of study:

After approval from institution ethics committee, the present study was conducted to compare the effect of addition of dexmedetomidine to bupivacaine in caudal block for postoperative analgesia in paediatric infraumbilical surgeries. A written informed parental or guardian consent was obtained in vernacular language in each case.

Sample size:

Taking a significance level of 5%, power of 80% sample size was calculated using Winpepi Statistical Package. As per this the minimum sample size needed for study was 52.Considering dropouts, exclusions and loss for followup, we took a sample size of 60. They were randomly divided into two groups, Group N and Group D.

- Group N (n=30) – 0.25% Bupivacaine 1ml/ kg + 0.5 ml normal saline
- Group D (n=30) – 0.25% Bupivacaine 1 ml/ kg + Dexmedetomidine 1 µg/kg, making the volume to 0.5 ml. Total volume for caudal block being 1 ml/kg in both groups, with maximum of drug volume 20ml was used [9].

Inclusion Criteria:

- Children (age 1 to 6 years, ASA 1 and ASA 2) scheduled to undergo infraumblical surgeries were included in this prospective, randomized, double blinded study.

Exclusion Criteria:

- Infection at the site of block, bleeding diathesis, pre-existing neurological, spinal disease or abnormalities of the sacrum, those with a history of allergic reactions to local anaesthetics and test drug. Children with history of developmental delay or mental retardation.

Procedure and Conduct of the Study:

The cases were selected after thorough preanaesthetic evaluation. Patients were randomly assigned to Group N and Group D using computer generated random number table. All children kept Nil by mouth for 6 hours. Patients were premedicated with inj Odansetron 0.1 mg/kg, inj Glycopyrrolate 0.004 mg/kg, inj midazolam 0.02 mg/kg and preoxygenated with 100% oxygen. Induction was done with inj Propofol 2 mg/kg and inj Atracurium 0.5 mg/kg. Patient were intubated with appropriate size of plain endotracheal tube and anaesthesia was maintained with oxygen, nitrous oxide and sevoflurane (1.5-2%). Child placed in left lateral position and caudal block was performed under sterile conditions using 22G hypodermic needle. Heart rate (HR), non-invasive BP(NIBP), ECG and peripheral oxygen saturation was recorded before anaesthesia, after intubation and immediate after caudal block and at 10 min interval till the end of surgery. Skin incision was performed after 15mins of caudal block. After surgery, patients were reversed using inj. Neostigmine 0.05 mg/kg + inj. Glycopyrrolate 0.008 mg/kg. After reaching extubation criteria patients were extubated. Patients were then shifted to recovery room and monitored for 6 hours. Later they were shifted to ward and monitored upto 24 hours. The postoperative pain relief was evaluated using FLACC score [10] [face, legs, activity, cry, consolability] with its 0-10 score range hourly for first 6 hours, 2 hourly upto 12 hours and then 4 hourly upto 24 hours. Sedation is evaluated by Ramsay sedation score [11] at same interval. If FLACC pain score ≥ 4, syrup Paracetamol was

given 15 ml/kg as rescue analgesia. (If needed Paracetamol was repeated after 4 hours). Duration of analgesia (time from caudal block to FLACC≥ 4) was noted and total number of doses of Paracetamol required in 24 hours was noted.

Following clinical parameters were monitored:

Intraoperative:

- Haemodynamic monitoring(HR, MAP)
- SpO2
- ECG
- Duration of surgery

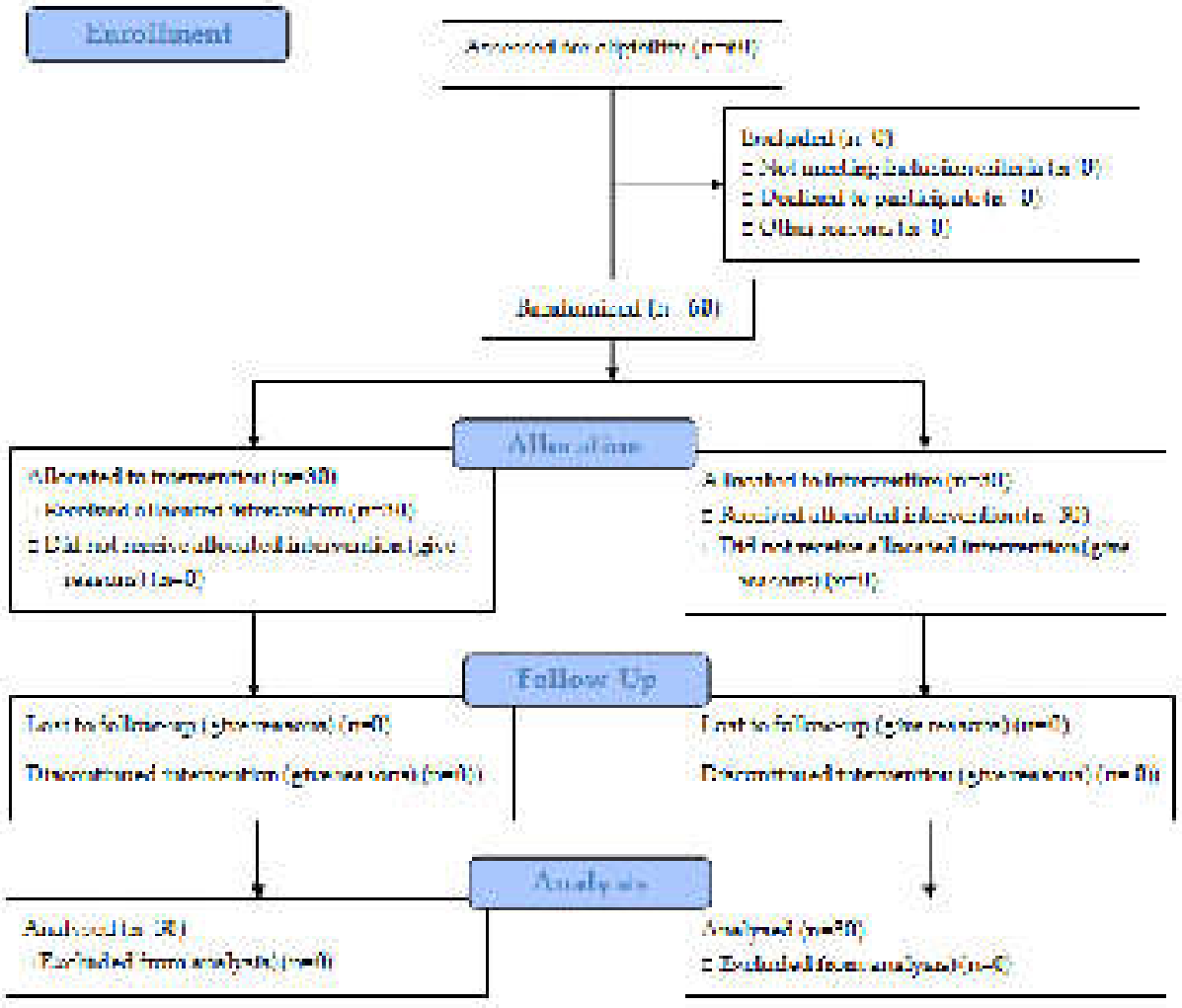
Postoperative:

- Duration of analgesia (FLACC score).
- Analgesia requirement in 24 hours (number of doses of paracetamol).
- Side effects-
  - Hypotension
  - Bradycardia (HR<60).
  - Sedation (Ramsay sedation score).
  - Postoperative nausea vomiting.
  - Urinary retention at 24 hours
  - Respiratory depression (SpO2 <95%)

Statistical analysis:

data analysis was done using the SPSS (Statistical Package for the Social Science) Version 17 for window. The t test, Mann Whitney test(MW), proportion test was used to find significant difference in age, weight, onset of analgesia, duration of analgesia, vital parameters, sedation score and side effects in study groups. A probability value of 0.05 or less was accepted as the level of statistical significance.

Consort 2010 Flow Diagram



Observation and Results

Table 1: Demographic Distribution

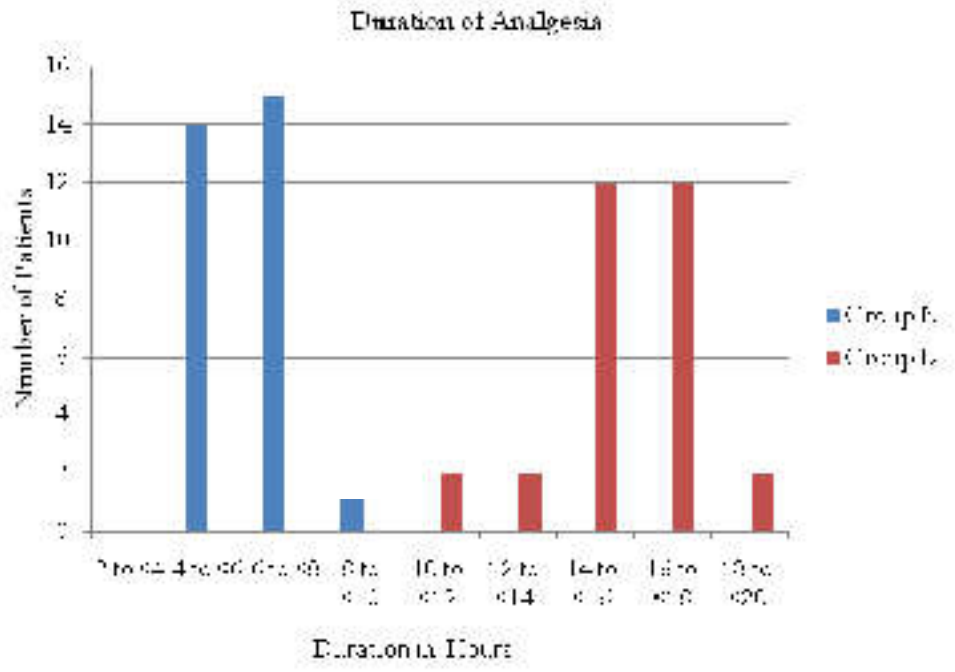
Parameters	Group N	Group D	p value	Significance
Age	3.8 ±1.46	3.2 ±1.37	0.10	NS
Male: Female Ratio	14:1	9:1	0.99	NS
Weight	12 ± 2.91	11.5 ± 2.78	0.50	NS
Duration of surgery (minutes)	58.12 ±7.20	58.12 ± 6.58	0.94	NS

Both the groups were comparable as there was no statistical significant difference between two groups with respect to age, sex, weight and duration of surgery (Table 1).

Table 2: Distribution of surgeries

Name of surgery	Group N	Group D
Herniotomy	18	15
Circumcision	5	12
Orchidopexy	4	1
Hypospadiasis	3	2

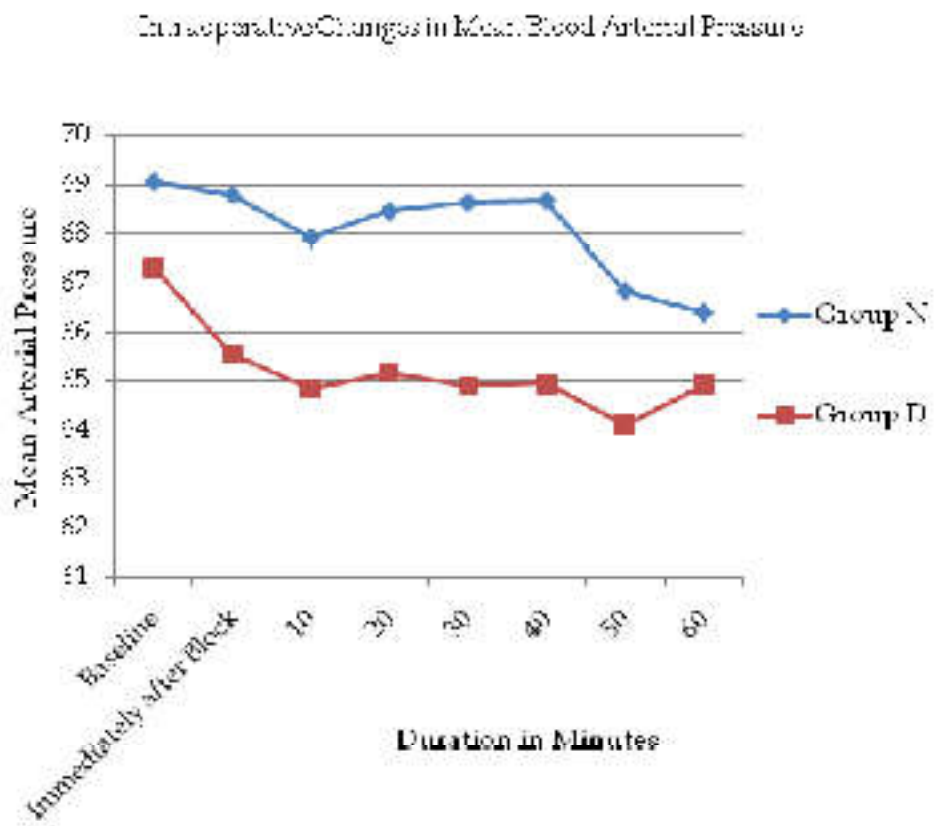
Above table 2 shows the different types of surgeries done in patients of both the groups.



Graph 1: Duration of Analgesia

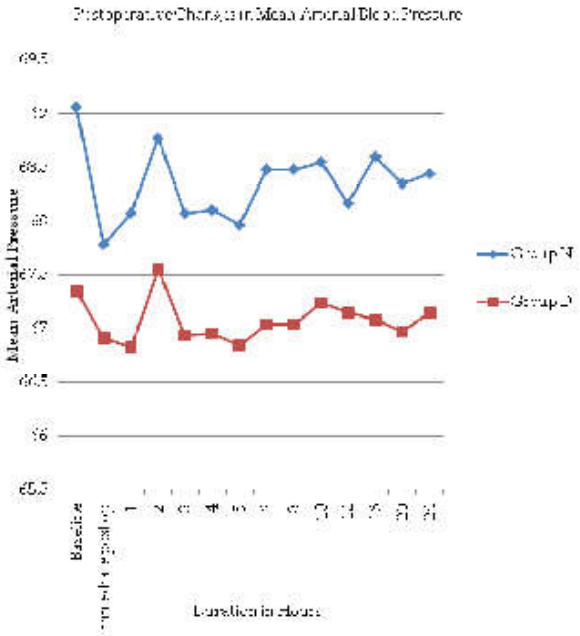
The above graph shows the total duration of analgesia from the time of caudal block to FLACC ≥ 4. The average duration of analgesia for Group N was 5.86 ±1.21 hours. The average duration of analgesia for Group D was 15.5± 3.02 hours.

Statistically the difference between two groups is highly significant ($p < 0.001$), indicating that duration of analgesia was more in Group D than Group N. (Graph 1).



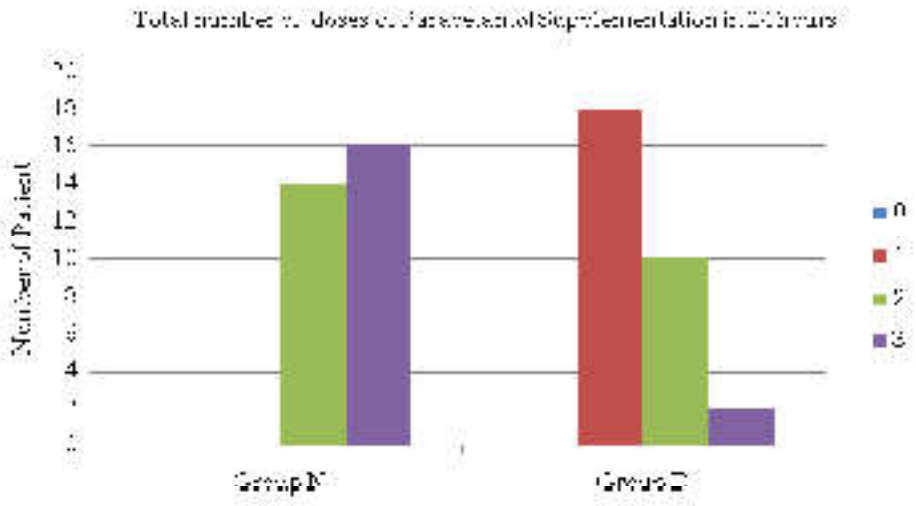
Graph 2: Intraoperative Changes in Mean Arterial Blood Pressure

There was fall in Mean Arterial Blood Pressure in both the groups. Fall in Mean Arterial Blood Pressure was more in Group D than Group N. The difference between both the groups is statistically significant. However, none of the patients required ionotropic support for hypotension from any of the groups (Graph 2).



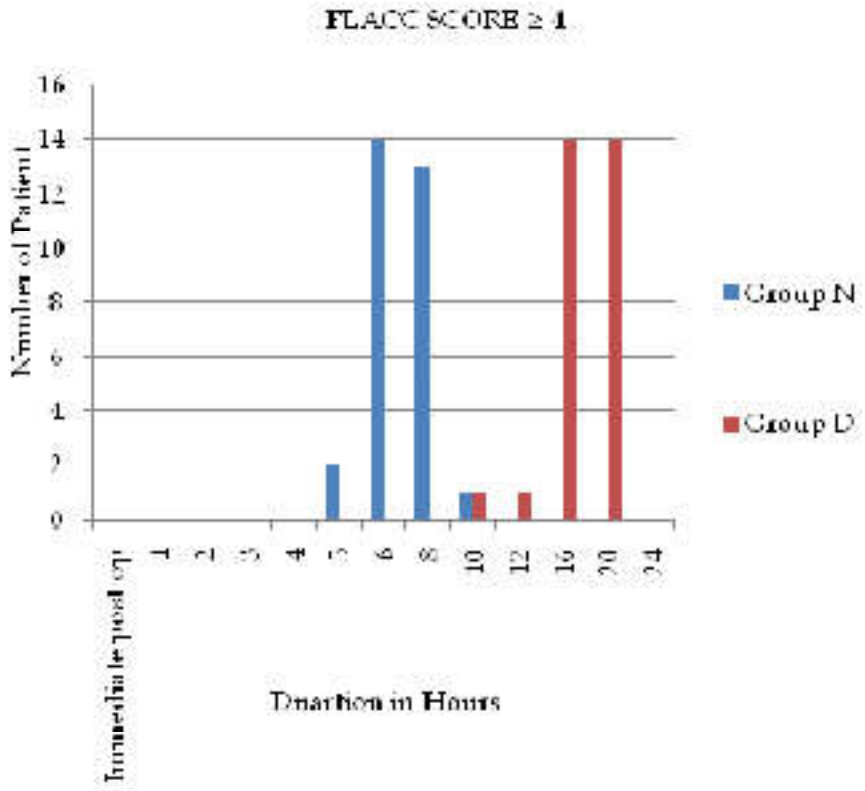
Graph 3: Postoperative changes in Mean Arterial Blood Pressure

Above graph shows the changes in Mean Arterial Blood Pressure in the recovery room in both the groups. There is no statistical difference between both the groups (Graph 3).



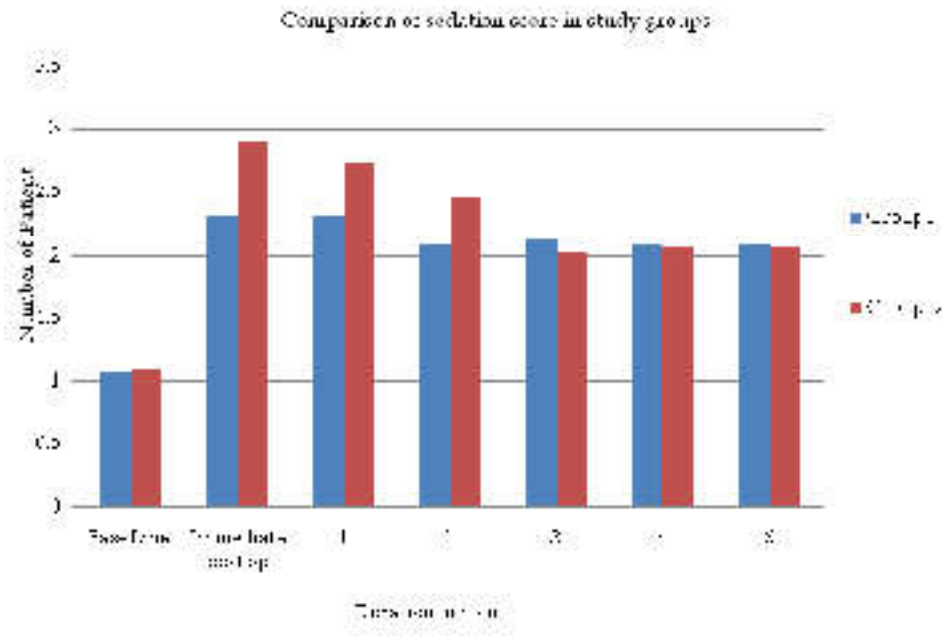
Graph 4: Total number of doses of Paracetamol Supplementation in 24 hours

Above graph 4 shows the supplementation of doses required in both the groups. The difference between both the groups is statistically significant (Graph 4).



Graph 5: FLACC Score≥ 4

Above graph 5 shows the distribution of patients in the two groups according to FLACC Score ≥ 4 at various time intervals postoperatively (Graph 5).



Graph 6: Comparison of sedation score in study groups

Above graph 6 shows ramsay sedation score. Group D had a better sedation score in immediate postoperative period, at 1 hour and 2 hour as compared to Group N. The p value was statistically significant ($p<0.05$). After 6 hours there was no sedation in both the groups. The patients were calm and easily arousable (Graph 6).

Discussion

Postoperative pain is an acute pain and should be treated adequately to decrease morbidity and hospital stay. Postoperative analgesia provides not only pain relief but also inhibits trauma induced nociceptive impulses so as to blunt autonomic reflexes. In the present study 0.25% bupivacaine in the dose of 1 ml/kg alone and in combination with dexmedetomidine 1µg/kg was used caudally and compared for the duration of analgesia and any adverse effects. Dexmedetomidine 1 µg/kg was selected based on studies by Fares KM [14].

Clinical Parameters noted were haemodynamic variations in operation room and recovery room, assessment of pain by FLACC Score, sedation score, number of doses of Paracetamol supplementations required, duration of analgesia and postoperative complications if any.

Demographic profile

Both the groups were comparable in respect to age, weight, sex, duration of surgery and distribution of surgeries.

Duration of analgesia

The average duration of analgesia for Group N and Group D was 5.86 ±1.21 and 15.5± 3.02 Hours respectively. Statistically the difference between two groups is highly significant ($p<0.001$), indicating that duration of analgesia was more in Group D than Group N. Similar prolongation of postoperative analgesia was seen in different studies. Saadawy et al [12] showed that the duration of analgesia was significantly longer with dexmedetomidine administration 1 µg/kg with bupivacaine 0.25% 1 ml/kg (18.5 hr) than plain bupivacaine 0.25% 1 ml/kg (6.2 hr) ($p<0.001$) and the incidence of agitation following sevoflurane anaesthesia was significantly lower with dexmedetomidine ($p<0.05$).

Hemodynamic parameters

There was no significant change in pulse rate in any of the groups intraoperatively and postoperatively. The difference between both the groups is statistically insignificant.

There was fall in Mean Arterial Blood Pressure in both the groups intraoperatively. Fall was more in Group D than in Group N. The difference between

both the groups is statistically significant. Similar findings were obtained in a study conducted by Schnaider et al. [13]. However, none of the patients required ionotropic support for hypotension from any of the groups.

Total number of doses of Paracetamol Supplementation in 24 hours

Number of patients requiring single dose of Paracetamol supplementation was significantly higher in Group D ($p< 0.001$) where as those requiring two and three doses was higher in Group N.

Fares KM et al. [14] concluded addition of dexmedetomidine (1 µg/kg) to caudal bupivacaine 0.25% (1 mL/kg) in paediatric major abdominal cancer surgeries achieved significant postoperative pain relief for up to 19 hours with less use of postoperative analgesics and prolonged duration of arousable sedation.

Flacc Score ≥ 4

Difference in FLACC score between two groups were statistically significant at 6^{th}, 8^{th}, 16^{th} and 20^{th} hour ($p<0.01$). Anand V G et al (2011) randomly assigned 60 patients to two groups. Group R received ropivacaine 0.25% 1 ml/kg caudally and group RD received ropivacaine 0.25% 1 ml/kg with dexmedetomidine 2 µg/kg. They concluded that Group R patients achieved a statistically significant higher FLACC score compared with Group RD. The difference was statistically significant ($p< 0.001$) [15].

Sedation score

Sedation was higher with group D. Patients were calm,q uite but easily aurosable. This was supported by studies from Koroglu et al [16].

Koroglu et al(2005) evaluated dexmedetomidine (1 µg/kg) in 80 children undergoing magnetic resonance imaging concluded dexmedetomidine provided adequate sedation in most of the children aged 1-7 years without haemodynamic or respiratory side effects [16].

Adverse effects

The adverse effects were noted in both the groups. Two patients from Group N had vomiting and retention of urine where as one patient from Group D had vomiting and two patients had urinary retention which was statistically insignificant. This was supported by studies conducted by El-Hennawy et al. They concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children ungergoing lower abdominal surgeries without increase in side effect [17].

Conclusion

Hence, we conclude that addition of dexmedetomidine in the dose of 1 µg/kg to 0.25% bupivacaine for caudal blockade-

- Significantly prolongs the duration of analgesia
- Without any significant haemodynamic changes
- Safe for use in paediatric patients without any adverse effects.

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Original Research Article

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The Evaluation of Proseal Laryngeal Mask Airway as an Alternative to Endotracheal Intubation in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract

Context: Proseal laryngeal mask airway is a supraglottic airway device with an additional drainage tube and a dorsal cuff which provides better seal and prevents aspiration. *Aims:* 1) tocompare the efficacy of PLMA with standard intubation in patients undergoing laparoscopic cholecystectomy. *Methods and Material:* After approval from institutional ethical committee a prospective randomized controlled study was conducted in sixty ASA class 1 and 2 patients. After induction Proseal LMA was introduced in group P and endotracheal tube was introduced in group E. Details of insertion, haemodynamic parameters, ventilatory performance were recorded. During surgery, oxygenation and ventilation variables were adjusted to maintain SpO_2 > 95% and $EtCO_2$< 45 mmHg. *Statistical analysis used:* Data was analysed using computer statistical software system openepi (open source epidemiological statistics for public health). The two tailed students t test was for unequal variance was used for intergroup comparisons except where specified. Probability values $p < 0.05$ were considered significant and $p < 0.001$ were considered highly significant. *Results:* There was no failed insertion of devices. The mean time of insertion of Proseal (80+43.56 seconds) was greater than conventional intubation (23+17.71 seconds). The difference was statistically highly significant ($p<0.01$). There were no statistically significant differences in oxygen saturation (SpO2) or end-tidal carbon dioxide ($EtCO_2$) between the two groups before or during peritoneal insufflation. There was no case of inadequate ventilation, regurgitation, or aspiration recorded. *Conclusions:* Proseal provides a safe alternative to endotracheal intubation for airway management in patients undergoing laparoscopic cholecystectomy.

Keywords: Proseal LMA; supraglottic airway device; alternative to endotracheal intubation.

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Introduction

Proseal LMA is a modification of classic LMA. It has a drain tube lateral to the ventilatory tube which helps in drainage of the regurgitated gastric secretions. When properly placed the drain tube separates the alimentary and the respiratory tracts completely [1]. In addition to the peripheral cuff PLMA has a dorsal cuff, which improves the seal around the glottic aperture and permits high airway pressures without leak [7]. Endotracheal intubation is considered the gold standard for laparoscopic surgeries. This study was designed to compare PLMA with endotracheal intubation in terms of efficacy and safety.

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Materials and Methods

After approval from institutional ethical committee of this study was conducted in government medical college, New Civil Hospital Surat. Sixty ASA physical status 1 and 2 patients aged between 18 to 60 years posted for laparoscopic cholecystectomy were included in the study. Patients were divided into two groups of 30 patients each using a computer generated table of random numbers. The patients with anticipated difficult airway, obesity, oropharyngeal pathology, trismus, cardiopulmonary disease, cervical spine fracture, gastro oesophageal reflux disease and risk of aspiration were excluded from the study.

After obtaining informed consent all patients were premedicated with injection glycopyrolate 0.04 mg/kg IV, injection ranitidne 50 mg IV and inj metaclopramide 10 mg IV thirty minutes before shifting the patient to the operating room. On arrival to the operating room routine monitors were attached and baseline values for heart rate, blood pressure were recorded. All patients were preoxygenated with 100% oxygen for 3-5 minutes [7]. Inj midazolam 0.02 mg/kg IV and fentanyl 2mcg/kg IV was given 3 minutes before induction of anaesthesia. All patients were induced with inj lignocaine 20 mg+ inj propofol 2-3 mg/kg IV and succinylcholine 2 mg/kg IV. No intermittent positive pressure (IPPV) was applied before securing the airway.

In group P PLMA size 3 or 4 were chosen depending on the weight of the patient. The cuff was fully deflated and the posterior aspect was lubricated using clear water based jelly. With the patients head on the pillow, the PLMA was introduced using the introducer tool pushing it slowly against the posterior pharyngeal wall. After insertion up to the integral bite block, cuff of PLMA was inserted with 25 or 30 ml of air (size 3 and 4 respectively). In case of group E patients endotracheal intubation was done with endotracheal tube size 7.5 or 8.5 by performing conventional laryngoscopy using Macintosh blade. All patients were ventilated the with same parameters VT-8 ml/kg, Fio2-0.33%, RR- 12/min, I: E ratio 1:2.

Correct placement of the device was confirmed by the following methods: 1) adequate chest rise, 2) square ETCO2 waveform, 3) expired tidal volume of 7-8 ml/kg 4) Silent epigastrium on auscultation 5) No audible leak from drain tube 6) gel displacement test- a drop of gel is placed on the drain tube of PLMA and if the drop moved out with ventilation the device position was considered improper. (5 and 6 were performed in case of PLMA) [5].

The time between picking up of airway device and establishment of adequate airway was recorded in both the groups. The number of attempts and ease of insertion were recorded as 1) easy: at first attempt with no resistance, 2) at second attempt or insertion with resistance, 3) failed: insertion not possible or three or more attempts required. The following parameters were recorded 1) haemodynamic variables: pulse, mean arterial blood pressure 2) ventilation variables - oxygen saturation, end tidal carbon dioxide $ETCO_2$ and peak airway pressure. All haemodynamic variables, $ETCO_2$ and oxygen saturation were recorded before induction, and 5 minutes after induction, before and after achieving carboperitoneum, after desufflation of carboperitoneum and at extubation. Peak airway pressure was recorded before and after achieving carboperitoneum.

Oxygenation and ventilation was aimed to maintained SPO_2 > 95% and $ETCO_2$< 45 mm of hg, by adjusting Fio 2, respiratory rate and tidal volume. If SpO_2 falls below 97% FIO2 was increased to 50 per cent, when saturation failed to improve tidal volume was increased to 10 ml /kg, then to 12 ml/kg. Oxygen saturation between 90-94 per cent was considered suboptimal and saturation <90% was considered failed. An increase in $ETCO_2$ above 45% was managed by increase in RR to 14 and then to 16 per minute.

A lubricated nasogastric tube was inserted in both groups, in group P nasogastric tube size 12 and 14 were used in PLMA size 3 and 4 respectively, in Group E size 14 or 16 nasogastric tubes were used. Ease of insertion was noted in both groups. Adequacy of ventilation and oropharyngeal seal provided by both devices was assessed by grading of stomach size from0 to 10, where grade 0 is deflated and grade 10 is fully distended. This was assessed by the surgeon by laparoscopy.

Anaesthesia was maintained with sevoflurane or isoflurane as maintenance agent along with long acting muscle relaxant.

Complication of aspiration and regurgitation was detected by litmus test, where a litmus paper was applied to the secretions on the dorsal aspect of PLMA and on the cuff of endotracheal tube in group E. If blue litmus turns red then the reaction is acidic indicating a regurgitation of acidic stomach contents. Any other complications like hypoxia, hypercarbia, laryngospasm, emphysema were noted.

After completion of the surgery, residual neuromuscular block was reversed with adequate dose of neostigmine and glycopyrolate. After regain of consciousness and return of protective airway refluxes, airway device was removed after gentle suction of the oral cavity. After transferring the patient to recovery room, heart rate and blood pressure was monitored at regular intervals. Patients were asked about soreness of throat after 24 hours.

Data was analysed using computer statistical software system openepi (open source epidemiological statistics for public health). All data was presented as mean and standard deviation (SD), except where specified. The two tailed students t test was for unequal variance was used for intergroup comparisons except where specified. Probability values $p < 0.05$ were considered significant and $p < 0.001$ were considered highly significant.

Results

There was no significant difference in age, sex, weight, between the two groups (Table 1). It was observed that the mean time of insertion of the airway device was greater in group P (80±43.56) seconds compared to group E (23±17.71 seconds. The difference was statistically highly significant ($p<0.01$). The baseline heart rate was comparable in both groups (Figure 1). The mean heart rate after 1 minute of insertion of the airway device was 96.67±12.00 in group P and 105.76±13.29 in group E and the difference was statistically significant ($p<0.05$). The mean heart rate was comparable in both the groups during the rest of the study (Table 2). The baseline mean arterial blood pressure was comparable in both the groups (Figure 2). The mean arterial blood pressure was 75.87±5.41mm of

Table 1: Demographic Profile

	Group P	Group E	p Value
Age (years)	35.33+11.13	38.53+9.46	p>0.05
Sex (M/F)	3/26	5/25	
Weight (KGS)	51.58+3.48	51.33+3.56	p>0.05

Table 2: Heart rate

	Heart Rate		
Time Interval	Group P	Group E	p value
Baseline	102.34+13.33	95.56+15.66	p>0.05
I minute after insertion	96.67+12.00	107.76+13.29	p<0.05
5 min after insertion	93.72+13.24	97.73+13.29	p>0.05
Before carboperitoneum	89.41+16.26	89.83+111.82	p>0.05
After carboperitoneum	90.82+16.17	86.53+11.82	p>0.05
Before desufflation	85.17+12.99	83.36+11.94	p>0.05
After extubation	91.86+11.69	91.60+11.57	p>0.05

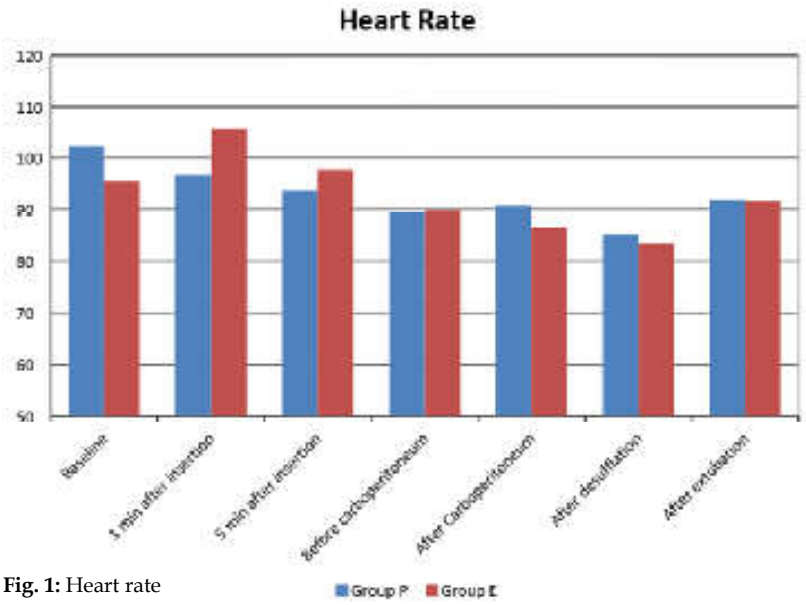

Fig. 1: Heart rate

Hg and 74.20±5.83 mm of Hg in group P at 1 and 5 minutes respectively after insertion of PALMA, 89.34±8.53 mm of Hg and 82.33±7.72 mm of Hg at 1 and 5 minutes respectively after insertion. The differences were statistically highly significant (Table 3). It was observed that the mean SpO_2 was comparable in both groups and it was never below 97% in both groups. The baseline $ETCO_2$ was comparable in both the groups at all times except for 5 minutes after insertion of the airway

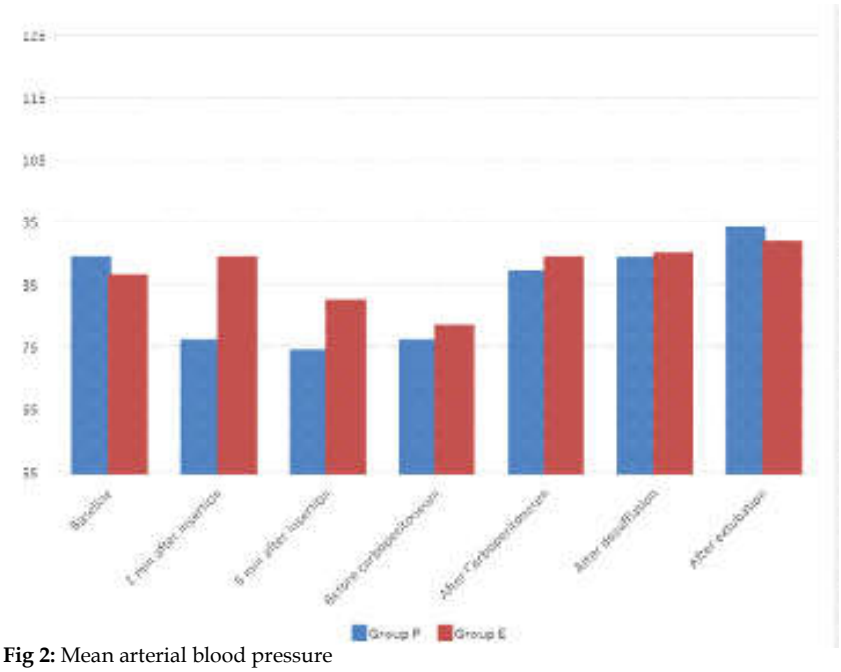

Fig 2: Mean arterial blood pressure

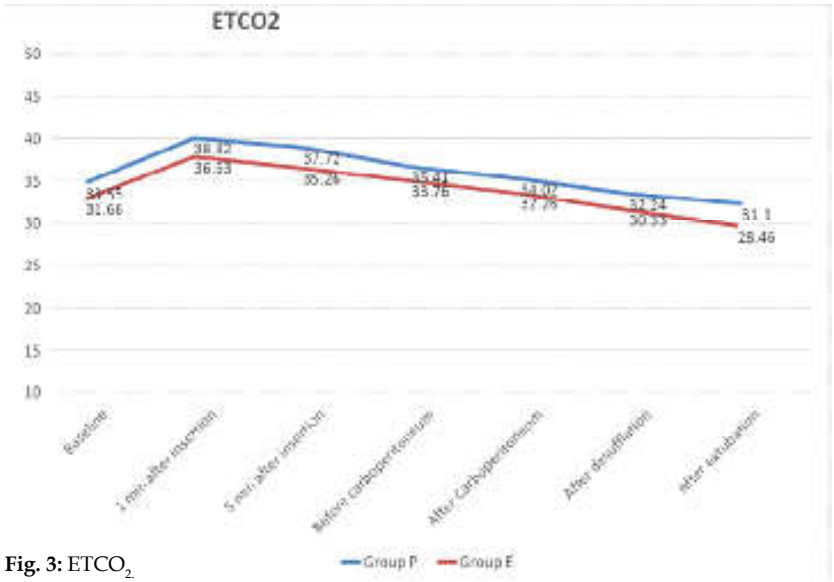

Fig. 3: $ETCO_2$

Table 3: Mean arterial blood pressure

Mean Arterial Blood Pressure			
Time Interval	**Group P**	**Group E**	**P value**
Baseline	89.33+5.99	86.34+8.29	P>0.05
I minute after insertion	75.87+5.41	89.34+8.53	P<0.01
5 min after insertion	74.20+5.83	82.33+7.72	P<0.01
Before carboperitoneum	75.89+5.95	78.17+6.96	P>0.05
After carboperitoneum	86.90+0.66	89.33+7.94	P>0.05
Before desufflation	89.05+5.80	89.92+5.29	P>0.05
After extubation	94.02+3.97	91.75+5.23	P>0.05

device where it was significantly higher (p<0.05) in group P (Table 4) (Figure 3). The mean peak airway pressure was comparable throughout the study except for after carboperitoneum (Table 5). After carboperitoneum there was significant rise in peak airway pressure in group E (Figure 4). Ease of Ryles tube insertion was comparable in both the groups (Table 6). The gastric insufflation was graded by the surgeon on a scale of 0 to 10, where 0 stands for fully deflated stomach and 10 for a stomach inflated to obstruct laparoscopic view. The mean value of stomach size grading was higher in group P (6.24±3.22) compared to group E (3.96±3.10) and the difference was statistically significant (p<0.05).

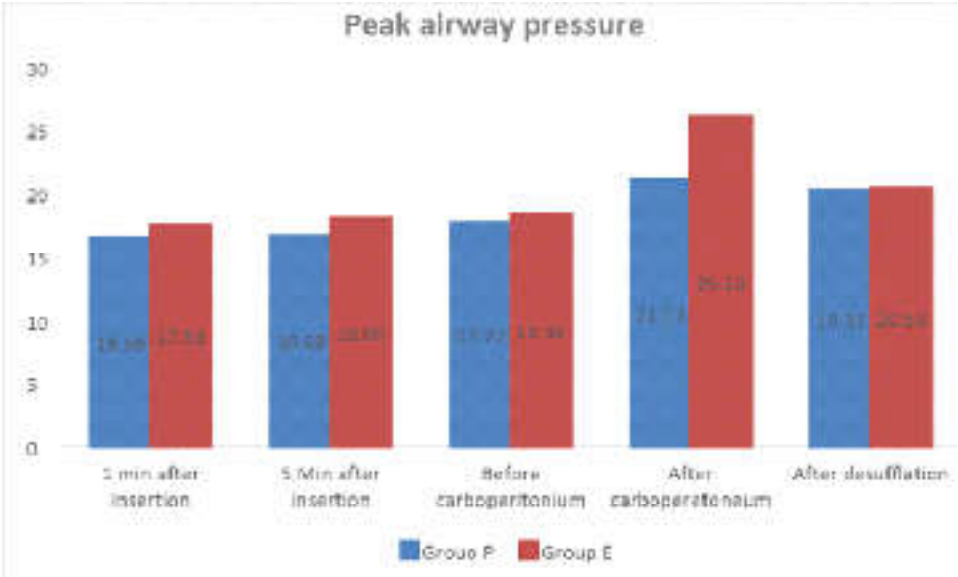

Fig. 4: Peak Airway Pressure

Table 4: $ETCO_2$

	$ETCO_2$		
Time Interval	**Group P**	**Group E**	**p>0.05**
Baseline	33.55	31.66	p>0.05
1 min after insertion	38.82	36.63	p>0.05
5 min after insertion	37.72	35.26	p<0.05
Before carboperitoneum	35.41	33.76	p>0.05
After Carboperitoneum	34.02	32.26	p>0.05
After desufflation	32.24	30.33	p>0.05
After extubation	31.1	28.46	p>0.05

Table 5: Peak Airway Pressure

	Peak Airway Pressure		
	Group P	**Group E**	
1 min after insertion	16.56	17.53	p>0.05
5 Min after insertion	16.69	18.06	p>0.05
Before carboperitoneum	17.72	18.36	p>0.05
After carboperitoneum	21.13	26.13	p>0.05
After desufflation	**20.31**	**20.53**	**p>0.05**

Table 6: Ease of Ryles tube insertion.

	Ease of Ryles tube insertion		
	Group P	**Group E**	**p value**
Easy	27(90%)	28(93.33%)	>0.05
Difficult	2(6.66%)	2(6.66%)	>0.05
Failed	1(3.33%)	0	

Blood staining of the device was noticed in 1 patient in group P (3.44%) and 6 patients in group E (20%). Trauma to the oropharyngeal structures were seen in 1 patient (3.44%) in group P and 2 patients (6.8%) in group E. The differences were not statistically significant. None of the patients developed aspiration or regurgitation. After 24 hours 2 patients (6.8%) in group P and 13 patients in group E (43.33%) complained of sore throat. The difference was statistically significant.

Discussion

Proseal LMA is a supraglottic airway device with drain tube, integral bite block and different cuff design, increased depth of the bowl to improve the seal with the larynx and helps to deliver positive pressure ventilation. When inserted properly it separates the alimentary tract from the respiratory tract, provides adequate seal around the glottic aperture. Endotracheal intubation is considered the gold standard for airway management in laparoscopic surgeries. However it is not devoid of complications like presser response to laryngoscopy and intubation, damage to the oropharyngeal structures during rigid laryngoscopy and sore throat. The use of Proseal LMA instead of conventional laryngoscopy and intubation may overcome these problems [8]. A Ryle's tube can also be passed through the drain tube for aspiration of the gastric secretions. In this study we compared Proseal LMA with endotracheal intubation in terms of ease of insertion, haemodynamic response to insertion, efficiency in delivering positive airway pressure and incidence of complications like aspiration, regurgitation and post-operative sore throat.

In our study there was no failed insertion, however the time taken for insertion of PLMA was greater than endotracheal intubation and the difference was highly significant. This can be attributed to the fact that our anaesthesiologists had lesser exposure to PLMA. Previous studies conducted by anaesthesiologists who had more experience with LMA, concluded that time of insertion of LMA was greater that time required for endotracheal intubation however the difference was not statistically significant [3,7].

The haemodynamic response to PLMA was minimal compared to endotracheal intubation. This can be attributed to the fact that PLMA insertion was relatively easy and does not involve rigid laryngoscopy therefore does not invoke a sympathetic response.

The Proseal drain tube allows the passage of a gastric tube which helps in drainage which helps in emptying gas or gastric secretions from the stomach [1,2]. A lubricated nasogastric tube was inserted in both groups, in group P nasogastric tube size 12 and 14 were used in PLMA size 3 and 4 respectively, in Group E size 14 or 16 nasogastric tubes were used. Ease of insertion of Ryles tube was comparable in both the groups.

Both groups maintained oxygen saturation above 97 per cent throughout the surgery. Following peritoneal insufflation, CO_2 is absorbed transperitoneally and the rate at which it occurs depends on gas solubility, perfusion of peritoneum and duration of pneumoperitoneum [7]. $ETCO_2$ levels were within normal limits in both the groups.

Adequacy of ventilation and oropharyngeal seal provided by both devices was assessed by grading of stomach size from 0 to 10, where grade 0 is deflated and grade 10 is fully distended in our study the stomach was more deflated in group E.

There was no intraoperative displacement of the device. There was no aspiration on regurgitation in any patients.

After 24 hours nine of the patients in group E had sore throat, and 1 patient in group P developed sore throat. The absence of sore throat could be because LMA is a supraglottic airway device and mucosal pressures achieved are usually below pharyngeal perfusion pressures [7].

Conclusion

Proseal LMA can be used as an effective alternative to endotracheal intubation, without increasing the incidence of complications in patients undergoing laparoscopic surgeries.

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Conflict of Interest: Nil

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Original Research Article

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Therapeutic Efficacies of Dexmedetomidine and Tramadol on Post Subarachnoid Block Shivering: A Prospective Study

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Abstract

Background and Aim: Shivering is a physiological response to core hypothermia in an attempt to raise the metabolic heat production. Non-pharmacological methods using equipment to maintain normal temperature of the body are effective but expensive and lack practicality, while the pharmacological methods are simple, cost-effective and easy to implement. Present study aimed to compare therapeutic efficacy of Dexmedetomidine and Tramadol on post subarachnoid block shivering. *Material and Methods:* This prospective study was conducted in the department of Anaesthesiology at Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat for the period of one year. Seventy ASA Grades-I & II patients of either gender, aged 17 to 61 years scheduled for elective surgeries under subarachnoid block were randomly allocated to two groups (A and B) after obtaining written informed consent. *Results:* Time interval from injecting the study drug to cessation of shivering was quite less with Dexmedetomidine (39.90±5.98) than with Tramadol (209.14±25.78 seconds). Insignificant difference was noted between the two groups in relation to dizziness. Incidence of sedation (Grade 2) was 17/30 in group D while it was 4/30 in group T and the difference was highly significant (p= 0.0012). *Conclusion:* Both Dexmedetomidine and Tramadol can be used for treating post sub-arachnoid block shivering but Dexmedetomidine is more efficacious than Tramadol but should be used cautiously in hemodynamically unstable patient.

Keywords: Dexmedetomidine; Kutch; Shivering; Tramadol.

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Introduction

Shivering, a common post-anaesthesia occurrence is defined as an involuntary, repetitive activity of skeletal muscles. The incidence of shivering has been found to be quite high, approximately 40-50% in different studies [1]. Shivering is a potentially serious complication, resulting in increased metabolic rate; oxygen consumption (up to 100-600%); carbon dioxide (CO_2) production; ventilation and cardiac output; adverse postoperative outcomes, such as increased surgicalbleeding; and morbid cardiac events. Therefore, shivering may cause problems in patients with low cardiopulmonary reserves [2].

Shivering is a physiological response to core hypothermia in an attempt to raise the metabolic heat production. Main causes of intra/ postoperative shivering are temperature loss,

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increased sympathetic tone, pain, and systemic release of pyrogens [3,4,5]. Spinal anaesthesia significantly impairs thermoregulation by inhibiting tonic vasoconstriction. It also causes redistribution of core heat from trunk (below the block level) to peripheral tissues. Postoperative shivering can be controlled both pharmacologically and non-pharmacologically.

Non-pharmacological methods using equipment to maintain normal temperature of the body are effective but expensive and lack practicality, while the pharmacological methods using drugs like pethedine, tramadol, clonidine, doxapram, katenserin, nefopam,etc., are simple, cost-effective and easy to implement. During the last decade, Tramadol has become favored and commonly used drug for post-spinal anaesthesia shivering. However, it has many adverse effects like nausea, vomiting, dizziness etc. which cause further discomfort to the patient [6,7].

Dexmedetomidine is a highly selective α2-adrenoceptor agonist with potent effects on the central nervous system [8,9]. The stable haemodynamics and the decreased oxygen demand make it a very useful pharmacologic agent [10,11,12]. However, adverse effects such as bradycardia and hypotension limits its use.

Few studies have compared the antishivering effect of above mentioned drugs. Hence, this study aimed to compare therapeutic efficacy of Dexmedetomidine and Tramadol on post subarachnoid block shivering.

Material and Methods

This prospective study was conducted in the department of Anaesthesiology at Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat for the period of one year. Seventy ASA Grade-I & II patients of either gender, aged 17 to 61 years scheduled for elective surgeries under subarachnoid block were randomly allocated to two groups (A and B) after obtaining written informed consent.

Group A (n=35) received Dexmedetomidine 0.5 µg/kg IV

Group B (n=35) received Tramadol 0.5 mg/kg IV

Patients with known hypersensitivity to Dexmedetomidine or Tramadol, ASA > 2 class were excluded from the study. The patients were randomly allotted to one of the two groups using a random list. Baseline pulse rate, non-invasive blood pressure (NIBP), oxygen saturation (SpO_2) and body temperature (axillary) were recorded 2 before the commencement of surgery and thereafter at every 5 minutes from the spinal block (SAB), for 1st hour; and every 15 minutes, for the rest of the observation period.

Subarachnoid block was given with inj. Bupivacaine 0.5% (10-15 mg) at L3-4 or L4-5 interspace using 26 gauge spinal needle and sensory block up to T6-7 dermatome was achieved. All operation theatres in which the operations were performed maintained an ambient temperature of 21-24°C. No means of active re-warming were used. Intravenous fluids and anaesthetic drugs were administered at room temperature. Grade of shivering was determined by Wrench classification 13 as:

Grade 0: No shivering

Grade 1: One or more of the following: Piloerection, Peripheral vasoconstriction, peripheral cyanosis with, but without visible muscle activity

Grade 2: Visible muscle activity confined to one muscle group

Grade 3: Visible muscle activity in more than one muscle group

Grade 4: Gross muscle activity involving the whole body

Patients who developed either grade 3 or grade 4 shivering were included in the study. Either of the two drugs was given as slow IV bolus injection. Time at which shivering started after spinal anaesthesia, severity of the shivering, time to disappearance of shivering and response rate were recorded. If shivering did not subside by 15 minutes, the treatment was considered to be ineffective. Recurrence of shivering was also noticed until the patient left the operation theatre. Patients who did not respond or in whom recurrence of shivering occurred were treated with additional dose of study drug. Side effects like nausea, vomiting, bradycardia (<50/min), hypotension (>20% fall from baseline), dizziness; and sedation score were recorded. Sedation score was assessed with a four-point scale as per Filos [14].

1: Awake and alert

2: Drowsy, responsive to verbal stimuli

3: Drowsy, arousable to physical stimuli

4: Unarousable

Bradycardia, hypotension and vomiting were treated with atropine, mephentermine and ondensetrone respectively, in titrated doses when required.

Statistical Analysis

Qualitative data will be expressed as percentages and proportions. Quantitative data will be expressed as mean and standard deviation. The differences between two groups with respect to continuous variables will be analysed using t-test while categorical variables will be analysed using chi-square test. All the statistical tests will be performed in SPSS version 15 software. p value <0.05 will be considered as statistically significant while p value <0.01 will be considered as statistically highly significant.

Results

Dexmedetomidine is as effective as Tramadol in treating post subarachnoid block shivering. Time interval from injecting the study drug to cessation of shivering was quite less with Dexmedetomidine (39.90±5.98) than with Tramadol (209.14±25.78 seconds) [Table 1]. The response rate was 100% in both groups. Incidence of recurrence of shivering post-operatively was 4/30 in group T while 1/30 in group D. Side effects hypotension and bradycardia in group D while nausea and vomiting in group T were significantly high.

Insignificant difference was noted between the two groups in relation to dizziness. Incidence of sedation (Grade 2) was 17/30 in group D while it was 4/30 in group T and the difference was highly significant (p= 0.0012).

Table 1: Time duration for recovery from shivering in A and B Group

Groups	Mean±SD Time Duration (Seconds)	P value
Group A (n=35)	39.90±5.98	0.01*
Group B (n=35)	209.14±25.78	

* indicates statistically significance at p≤0.05, test applied student t test

Discussion

Postoperative shivering is an unpleasant experience for the patient affecting the quality of recovery. Various researchers have compared many drugs with each other to find an ideal agent to prevent intra and postoperative shivering. Tsai YC, Chi KS et al. [15] did a comparison of tramadol, amitriptyline, and meperidine for postepidural anesthetic shivering in parturients. Bilotta F et al. [16] studied Nefopam and Tramadol for the prevention of shivering during neuraxial anesthesia.

We chose Dexmedetomidine and Tramadol in our study because of their anti-shivering property and compared their efficacy in treating post sub-arachnoid block shivering as well as side effects. The same anti-shivering property was studied in various researches done by Kim YS et al. [17], Bajwa SJ et al. [18], and Blaine Easley R, Brady KM et al. [19] Kim YS et al. [17] searched for an optimal dose of prophylactic dexmedetomidine for preventing postoperative shivering. Bajwa SJ et al. [11,18] found reduction in the incidence of shivering with peri-operative dexmedetomidine. Elvan EG, Oc B, Uzun S et al. [9] used dexmedetomidine in postoperative shivering in patients undergoing elective abdominal hysterectomy. Blaine Easley R, Brady KM et al. [19] studied dexmedetomidine for the treatment of post-anesthesia shivering in children. Tramadol is an opioid analgesic. The anti-shivering action of tramadol is probably mediated via its opioid or serotonergic and noradrenergic activity or both. In the present study, factors that influence the occurrence of shivering, like temperature of IV fluids etc, were not tightly controlled, but this should not affect the validity of our study because the present study is focused on response to treatment used rather than incidence of shivering; and by randomization, both groups were subjected to similar degrees of influence of these factors.

In present study, we found that Dexmedetomidine is as effective as Tramadol in treating post-spinal anaesthesia shivering. In addition, the time interval from the commencement of treatment to cessation of shivering is quite less with dexmedetomidine than with tramadol. Result of our study is coinciding with another similar comparative study of Dexmedetomidine and Tramadol for post-spinal anaesthesia shivering done by Geeta Mittal et al. [10].

Conclusion

Both Dexmedetomidine and Tramadol can be used for treating post sub-arachnoid block shivering but Dexmedetomidine is more efficacious than Tramadol but should be used cautiously in hemodynamically unstable patient.

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Original Research Article

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I Gel Versus Endotracheal Tube for Pediatric day Care Surgeries

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Abstract

Background: The I-gel TM (Intersurgical, Wokingham, UK) is a novel second generation supraglottic airway device with a non inflatable cuff, made up of a unique soft gel like material (Styrene Ethylene Butadiene Styrene). The device is transparent and latex free. It is easy to insert and has minimal tissue compression. An integrated gastricchannel is provided for passage of gastric drainage tube to empty the stomach. *Objectives:* The aim of the present study wasto compare the efficacy of I-gel with Endotracheal tube in airway management in children. *Materials and methods:* This study was conducted at tertiary referral centre for new born and children with Children of age 2 to 6 years, weighing 10 to 18 kg, ASA Grade I-II posted for elective day care procedures. *Results:* Males were predominant in both the groups. Insertion and ease of placement was successful in first attempt in 86.66% of patients in Group I as compared to 80% in Group II (ET). 13.33% of patients in Group I (3 out of 30) required adjustment like jaw thrust, neck extension or reinsertion because of forward displacement. One patient had been recorded in Group I (I- gel) as failure because of inadequate ventilation and required endotracheal intubation. 20% in Group II required second attempt for ET tube placement because of early learning curve of anaesthesia trainees in the teaching institute. There was a significant rise in HR & BP in Group II during laryngoscopy and intubation and at the time of extubation. Airway related adverse events (coughing, breathholding, laryngospasm) were more in Group II when compared to Group I. *Conclusion:* The I-gel is ease of insertion, success rates, minimal hemodynamic perturbations and minimum perioperative adverse effects.

Keywords: Pediatric Airway Management; I-gel; Endotracheal Intubation; Supraglottic Airway Devices (SAD).

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Introduction

The boundaries of day-care surgery are redefined exponentially with time. The rapidly changing financial situation in the world has led to the increase in the incidence of ambulatory surgery. The advances in surgery, anaesthesia and pain management have allowed huge expansion of this modality of care with a consequent reduction in the need for hospitalization. Though data are not available for India, there is huge potential in view of a massive population of 1.2 billion and recent huge expansion in the private sector has created an opportunity for expansion in day care surgery in India.

Advances in drugs, techniques and devices is transforming the quality and efficacy of daycare

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anaesthesia by reducing perioperative adverse events and facilitating efficient pediatric airway management for disposition or discharge of the patient on the same day of surgery [1].

The endotracheal tube remains the gold standard for the secured airway but supraglottic airway devices (SAD) are an evolving future and may cause less laryngeal irritation than endotracheal tubes and has advantage of placing without visualisation of the airway (Brimacombe, 1995) [2].

I gel device which was first demonstrated in 2007 in UK, provides a good anatomical seal of the pharyngeal, laryngeal and perilaryngeal structures. This device is easy to use and has low pharyngolaryngeal morbidity.

Materials and Methods

This study was conducted at Niloufer hospital, a tertiary referral centre for new born and children with over 3000 pediatric surgeries per annum. Children of age 2 to 6 years, weighing 10 to 18 kg, ASA Grade I-II posted for elective day care procedures such as herniotomy, hydrocoele & hypospadias repairs, Orchiopexy etc., with surgery duration less than one hour were included in the study done over a period of three months. They were randomly divided into two groups of 30 each. Airway management included I-gel in Group I patients and Endotracheal tube in Group II. The airway management was done in all patients by the postgraduate trainees with two years experience under the supervision of senior faculty.

Patients with anticipated difficult airway, upper respiratory tractinfection, emergency surgeries, ASA Grade III/IV, oropharyngeal pathology and full stomach patients were excluded from the study. Informed and written consent was obtained from parents.

All patients were premedicated with midazolam inj. 0.05 mg/kg intravenously. Anaesthesia was induced with intravenous fentanyl 2 µg/kg and propofol 3 mg/kg with atracurium 0.5 mg/kg. Muscle relaxant was used in all surgical procedures as part of a balanced anaesthesia technique and controlled ventilation for uniformity and also to decrease airway traumatism related to device insertion. However muscle relaxation is not routinely recommended when using I-gel. Standard monitoring for all patients included ECG, pulse oximetry, capnometry and non invasive blood pressure measurement.

Correct placement of the device was assessed by visible chest expansion on manual ventilation, absence of audible leak and good tidal volume ventilation, bilateral air entry and square shaped capnograph.

Anaesthesia was maintained with O_2 and N_2O (50:50) and sevoflurane 1%-2% using Jackson Ree's modified circuit and controlled ventilation. At the end of surgery stomach was aspirated with the help of gastric tube and neuromuscular block was reversed. Extubation was done when the patient was fully awake.

During the insertion of I-gel and ETT the following parameters were noted. Ease of insertion and number of attempts required for placement of the device.

The ease of device insertion was recorded as

1. Very Easy : No resistance to insertion in the pharynx in a single manoeuvre

2. Easy : When insertion into the pharynx required manoeuvre like jaw thrust

3. Difficult : When more than two manoeuvres were needed like device rotation and jaw thrust.

Failure of device was considered when inadequate ventilation with two attempts needing an alternate SAD device or endotracheal intubation.

Hemodynamic variations such as heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as oxygen saturation (SpO_2) and $EtCO_2$, were recorded before and during induction and later every 5, 10, 15, 20, 30 minutes of surgery, during removal and in the postoperative period for 30 min. Airway related complications like coughing, breath holding, hypoxemia, laryngospasm and bronchospasm were noted.

The stastical software of Microsoft word and excel have been used to generate graphs, tables, etc. Results on continuous measurements are presented as Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. p value <0.05 was considered significant

Results

Table 1: Demographic data

Variables		Group-I	Group-II	P value
Age (years)		2.54+1.26	2.68+1.30	>0.05
Weight (kg)		10.2+2.30	9.82+2.52	>0.05
Sex	Male	23	24	>0.05
	Female	7	6	>0.05
		ASA grade		
I		28	27	>0.05
II		2	3	>0.05

Table 2: Insertion Characteristics

		Group-I	Percentage	Group-II	Percentage
No of attempts for insertion	First attempt	26	86.66%	24	80%
	Second attempt	3	13.33%	6	20%
	Failure	1	3.33%	0	-
Ease of Insertion	Very easy	26	86.66%	23	76.66%
	Easy	3	10%	5	16.66%
	Difficult	1	3.33%	2	6.66%

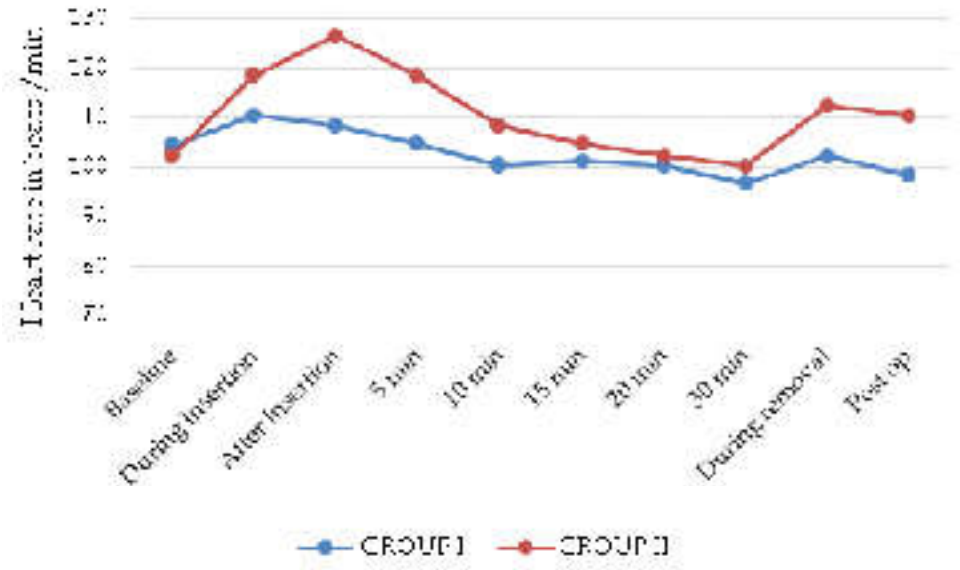

Fig. 1: Heart rate in comparison in both groups

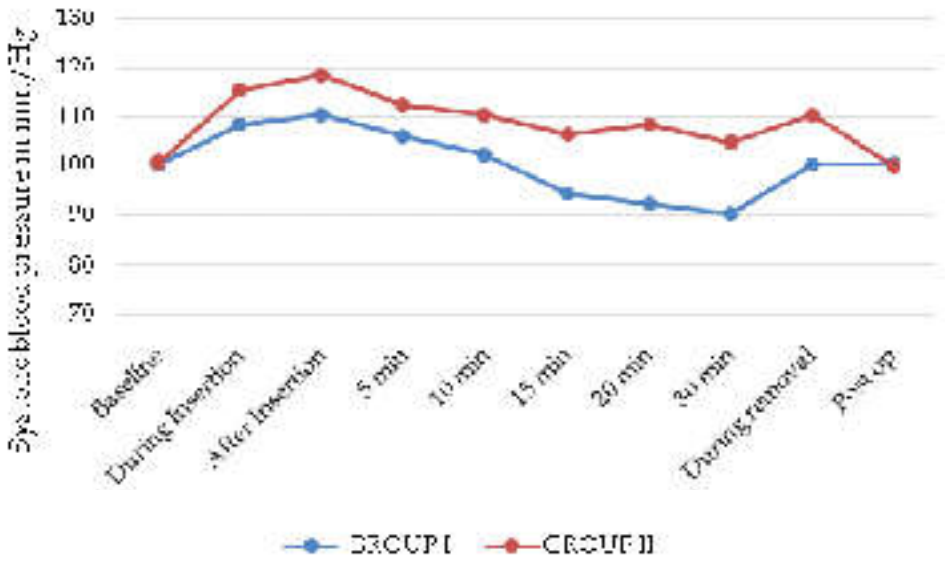

Fig. 2: Systolic Blood pressure in comparison in both groups

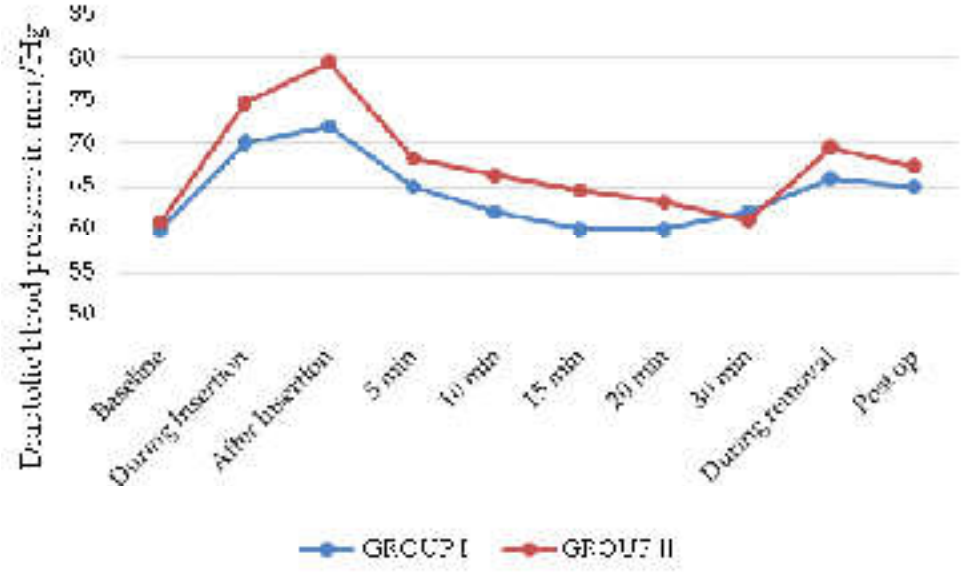

Fig 3: Diastolic Blood pressure in comparison in both groups

Table 4: Postoperative Airway Complications

	Group-I	Percentage	Group -II	Percentage
Coughing	2	6.66%	5	15%
Breath holding	1	3.33%	1	3.33%
O2 desaturation	-		1	3.33%
Laryngospasm	-		1	3.33%
Bronchospasm	-		-	

Demographic data (Table 1) like age, sex, weight, ASA status were comparable in both the groups. Males were predominant in both the groups.

We studied 47 male and 13 female patients of age 2-6 years weighing 10-18 kg with a mean age group of 2.54±1.26 in Group I and 2.68±1.30 yrs in Group II. I - gel sizes of 1.5 (ideal for infants 5-12 kg) and 2.0 (ideal for small paediatric 10-25 kg) were used according to manufacturer's recommendations.

Insertion and ease of placement was successful in first attempt in 86.66% of patients in Group I as compared to 80% in Group II (ET). 13.33% of patients in Group I (3 out of 30) required adjustment like jaw thrust, neck extension or reinsertion because of forward displacement. One patient had been recorded in Group I (I-gel) as failure because of inadequate ventilation and required endotracheal intubation. 20% in Group II required second attempt for ET tube placement because of early learning curve of anaesthesia trainees by same resident in our teaching institute.

The MAP and HR did not significantly differ from the base line values at any point of measurement in Group I patients during insertion or at the time of removal when compared to Group II patients as shown in Figure 1 to 3. There was a significant rise in HR & BP in Group II during laryngoscopy and intubation and at the time of extubation.

Airway related adverse events (coughing, breathholding, laryngospasm) were more in Group II when compared to Group I as shown in Table 4.

Discussion

The major responsibility of the anaesthesiologist is to provide adequate ventilation to the patient because airway related problems are still the most common cause of anaesthesia related morbidity and mortality. Though the tracheal intubation is the gold standard for maintaining a patent airway during anaesthesia, laryngoscopy and endotracheal intubation produce hemodynamically detrimental reflex sympathetic stimulation or response which may be detrimental in decompensated states. Pediatric respiratory adverse events often occur due to respiratory tract reactivity secondary to mechanical or chemical stimulation perioperatively [4].

Supraglottic airway devices like Laryngeal mask airway (LMA) and I- gel are less invasive compared

to endotracheal tube and has the advantage of ease of insertion without the use of direct laryngoscopy resulting in minimal hemodynamic responses and significant reduced incidence of postoperative respiratory complications [5]. Advantages of supraglottic airway devices over endotracheal tube include less incidence of sore throat and is less stimulating especially in a reactive airway [6]. The I-gel with a noninflatable cuff provides a secure airway rapidly, more protection against gastric insufflation with an inlet for gastric tube and minimal postoperative complications [7].

I-gel is very easy to insert without the use of laryngoscopy and especially useful for trainees as it has a fast learning curve and a low failure rate is [8,9]. Further endotracheal tube needs experience to master the art of tracheal intubation. In our study the success rate of insertion at first attempt was very high (86.66%) with only one failure requiring use of endotracheal tube secondary to misfit of device with considerable audible leak and inadequate tidal volume ventilation and. Lopez et al., Beringer et al., also confirm the ease of insertion with I-gel and successful maintenance of the device [2,8].

In our study there were minimal hemodynamic changes at insertion, intraoperative and immediate postoperative periods compared to children with endotracheal intubation.

Ismail et al. [10], measured Intraocular pressure (IOP), hemodynamic responses in 60 patients divided into three groups constituting LMA, I-gel, Endotracheal tube and they concluded that I-gel insertion provided a better stability of IOP and hemodynamic system when compared with LMA or E.T tube insertion. Our result was also similar with that of Ismail et al,.

Anjana Das [11] has proved that I-gel was more easily inserted than LMA-ProSeal (90% vs. 83.33% respectively). I-gel insertion time was shorter than PLMA (14.9 vs. 20.0 sec respectively) and was statistically significant. Hemodynamics (HR, BP) were less altered in I-gel than PLMA and the results were statistically significant ($p < 0.05$). The enhanced hemodynamic response in the PLMA group compared to the I gel group may be due to pressure exerted on the wall of the pharynx by the cuff of the airway device and further Shanmugavelu G et al. [12] in their study demonstrated that I- gel effectively confirms the perilaryngeal anatomy despite lack of inflatable cuff and produce less sympathetic response [14].

Thus I-gel is ideal for patients requiring minimal alteration in hemodynamics during the perioperative period.

Tait et al. [13], have demonstrated that the ability of the laryngeal mask airway to maintain a stable airway without stimulating the larynx and trachea can decrease the incidence of respiratory adverse events in children more so in children with recent or active URIs [11]. In our study postoperative complications like coughing, desaturation, breath holding and laryngospasm were less in the I-gel group compared to the endotracheal tube and observations are similar with that of Tait et al.

Conclusions

The I-gel is an innovative reliable supraglottic airway device with favourable characterstics regarding ease of insertion, success rates, minimal hemodynamic perturbations and perioperative respiratory adverse events when compared with endotracheal tube in pediatric airway management.

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Original Research Article

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Rocuronium Versus Vecuronium in Endotracheal Intubation and Maintenance in General Anaesthesia

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Abstract

Introduction: Adequate maintenance of airways in patients undergoing surgeries under general anaesthesia was through proper intubation. Succinylcholine was the most opted neuromuscular drug in the past 50 years administered for tracheal intubation. A number of adverse reactions with its use. *Aim:* To evaluate onset time, tracheal intubation conditions, duration of action and maintenance of anaesthesia using two none depolarizing muscle relaxants vecuronium and rocuronium. *Materials and methods:* The study population consisted of 50 patients of ASA physical status I and II in the age group 18 to 50 years.The present studies was undertaken to evaluate the neuromuscular and haemodynamic properties of Rocuronium bromide and to compare it with Vecuronium bromide. Of the 50 patients studies, 25 patients received 0.6 mg/kg of Rocuronium bromide for the maintenance of anaesthesia and the other 25 patients received 0.1 mg/kg of Vecuronium bromide. The top-up doses administered were 0.15 mg/kg of Rocuronium and 0.025 mg/kg of Vecuronium. In both the groups, the efficacy of nondepolarizing muscle relaxant was assessed. *Results:* The onset time was significantly shorter in the Rocuronium group (108.8 seconds /mean±SD was ±28.875) compared to Vecuronium group (188.76 seconds/ mean SD±43.78). The duration of action of first dose was significantly longer in Rocuronium group (31.5 minutes) compared to Vecuronium group (24.5 minutes). The duration of action of top-updoses was similar in both the groups ($p>0.05$). There was no significant difference in any of the haemodynamic variables (Heart rate, Systolic blood pressure, Diastolic blood pressure and meanarterial pressure) between the two groups. All the patients in both the groups were easily reversible with Neostigmine (0.05 mg/kg) and no adverse reactions were found in any patient. *Conclusion:* Rocuronium has a significantly rapid onset of action and intermediate duration of action. It is easily reversible and produces no significant cardiovascular changes. It also has a good safety profile. Therefore, inspite of its high cost. Rocuronium appears to be the safest drug, near toideal NMBA for rapid sequence intubation and routine intubation when there is no anticipated difficulty in intubation.

Keywords: Rocuronium; Vecuronium; Endotracheal Intubation.

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Introduction

The introduction of neuromuscular blocking drugs into clinical practice representsone of the most significant advances in the development of anesthesiology and has revolutionized the practice of anesthesia. The use of neuromuscular blocking drugs has increased the safety and improved the results of many established surgical procedures aswell as many new ones. Abdominal surgeries require muscle relaxation for efficacious operating conditions. Before the advent of neuromuscular blocking drugs, surgical relaxation was achieved with the use of inhalation anesthetics. At deep levels of ether anesthesia relaxation of abdominal musculature is sufficient

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to permit exploratory laparotomy. Following the introduction of d-Tubocurarine, small doses of the same were seen to amplify muscle relaxation during either anesthesia and allow reduction of inhalational anesthetic concentration The advent of neuromuscular blocking drugs in the 1940's facilitated many advances in abdominal and thoracic surgeries. Muscle relaxants not only enhance surgical exposure but also facilitate mechanical ventilation and minimize the doses of general anesthesia. As halogenated anesthetics replaced ether in common practice, a greater need torely on curare-type drugs to block neuromuscular transmission developed, since the muscle relaxing properties of the halogenated anesthetics was not adequate for abdominal surgery unless high and toxic concentrations were used.

In Nearly simultaneous introduction of the two muscle relaxants, Atracuriumbesylate and Vecuronium Bromide, both intermediate acting, non-depolarizing aminosteroid neuromuscular blocking drugs, provided a break through by a faster onset, rapid and measurable recovery with little dependence on the kidneys for elimination and great haemodynamic stability. However, there was a need for a non-depolarizing neuromuscular blocking drug, which has a rapid onset of action. Continuous search for a non-depolarizing muscle relaxant with rapid onset of action led to the synthesis of Rocuronium. Rocuronium, anewer non-depolarizing muscle relaxant was introduced in 1990s. Its similar in structure and properties to Vecuronium but had an added advantage of rapid onset of action and unchanged excretion in urine thereby eliminating the side effects of the metabolites. Its introduction is considered an added advantage over Vecuronium. Neuromuscular monitoring helps to balance adequate surgical relaxation with safe restoration of neuromuscular function at the end of the procedure. It provide ideal operating conditions with optimal doses of muscle relaxant and helps to minimize side effects like unwanted movements, prolonged paralysis and delayed recovery. In the light of the above observations Rocuronium is compared with Vecuroniumas relaxants for abdominal surgeries using peripheral nerve stimulator as an adjunct in the study.

Materials and Methods

This was a randomized, prospective clinical double blinded trial studied over a period of 2 years from November 2012 to March 2014 in the Department of Anaesthesiology, Hyderabad.

Inclusion Criteria

1. Patients in age group of 18 to 50 years.
2. ASA Gr 1 or 2
3. Mallampatti class 1 or 2.
4. Patient who underwent elective general surgeries, orthopedic surgeries, gynaecological Surgeries, urological surgeries and ear, nose and throat surgeries

Exclusion Criteria

1. Patients with difficult airway [mallampati Gr 3 or 4].
2. Gastro esophageal reflux disease.
3. Known allergy to any of these drugs or its constituents.
4. BMI >25%.
5. Heavy smokers.
6. Patients with history of cardiovascular or renal disorders.
7. Patients with neuromuscular disorders or medications known to influence neuromuscular functions.
8. Hypertensive patients.
9. Pregnant patients

Patients were randomized into one of the two groups. Group V {Vecuronium} and Group R (Rocuronium) of 25 each for induction and maintenance of anaesthesia [sample size was taken in accordance with similar type of studies done in the past]. Pre-anaesthetic assessment was done the evening prior to the day of surgery. A detailed history was taken examination and investigation were reviewed. Informed consent was obtained after explaining the procedure to the patients. Tab. Diazepam 5 mg and Tab. Ranitidine 150 mg was given night before the surgery and morning of the day of surgery 1½ hours prior to the time of surgery. All the patients were fasting for at least 6 hours before surgery. Non-invasive monitors like Electrocardiogram (ECG), Non-invasive BP, and pulseoximetry were connected to the patient. Intravenous access was established and slow infusion of crystalloids commenced.

Prior to the induction of anaesthesia, patients in both groups were premedicated with midazolam 0.025 mg/kg, inj glycopylorate 5 mcg/kg and fentanyl 1 mcg/kg. Patient were preoxygenated with oxygen 100% for a period of three minutes followed by which patient were induced with inj Thiopentone 4 mg/kg intravenously. Patients in group V received vecuronium 0.1 mk/kg [9] and those in group R received rocuronium 0.6mg/kg

[7].

After the administration of the drug the clinical efficacy of the drug will be monitored by the adequacy of relaxed jaw movements a free mouth opening followed by viewing of a relaxed vocal cord using a laryngoscope. Intubating condition were scored as excellent [8-9], good [6-7], fair [3-5], and poor [0-2] according to a system described by Cooper.

Cooper Scoring System

Score	Jaw relaxation	Vocal cords	Response to intubation
0	Impossible to open	Closed/ bucking	severe coughing
1	Opens with difficulty	Closing	Mild coughing
2	Moderate opening	Moving movement	Slight diaphragmatic
3	Easy opening	Open [relaxed]	No movement

Haemodynamic parameters like systolic, diastolic blood pressure and Heart Rate were recorded at base line during pre-oxygenation and 1st, 3, 5th and 10 minutes after induction. Trachea was intubated using a suitable size portex endotracheal tube. Anaesthesia was than maintained with 40% O_2 and 60% N_2O. After an effective tracheal intubation after 10 minutes maintenance dose of inj vecuronium 0.025 mg/kg and injrocuronium 0.15 mg/kg was anaesthesia was continued with O_2, N_2O, and halothane. During the conduct of anaesthesia patients vital were monitored regularly. Patients were administered reversal with inj neostigmine 0.05 mg/kg and injglycopylorate 5 mcg/kg. After appropriate suctioning extubation was done and readings measured.

Statistical Methods

Chi square test of significance has been used to find the significance of sex distribution between the two groups. Student t test has been used to find the significance of Haemodynamic parameters and duration of action in minutes between the two groups and to find the homogeneity of samples for age and weight between two groups.

Statistical software

The Statistical software namely SPSS 11.0 and Systat 8.0 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, Tables etc. The inferences based on 'p' value were made as follows:

p>0.05 – Not significant: p<0.05 – Significant

Results

In the present study, 50 patients aged between 18 and 50 years belonging to ASA grade I and II were randomly divided into two groups, each group consisting of 25 patients.

Group V: Patients received Inj. Vecuronium as the non-depolarizing muscle relaxant for Intubation and maintenance of anaesthesia.

Group R: Patients received Inj. Rocuronium as the non-depolarizing muscle relaxant for Intubation and maintenance of anaesthesia.

Table 1: Demographic Data

	Group V		Group R	
	No	%	No	%
<20	1	4.0	0	0
21-30	8	32.0	8	32.0
31-40	10	40.0	7	28.0
41-50	6	24.0	10	40.0
Total	25	100	25	100
Mean±SD	34.64/ SD±9.26		37.2/SD±9.2	
Interference	Samples are age matched with p=0.332			
40-50	5	20	4	16
50-60	6	24	6	24
>60	14	56	15	60
Interference	samples are weighed matched with p =0.628			
Male	15	60	10	40
Female	10	40	15	60
Interference	Samples are sex matched with p=0.258			

The mean age in Group V was 34.64 years whereas in Group R it was 37.20 years. The difference in the mean age of the patients between the two groups was not statistically significant (p=0.332). The maximum number of patients in both the groups were above 60 kgs (56% in Group V and 60% in Group R). The mean weight in Group V was 60.68 kgs and in Group R was 59.12 kgs. The difference was statistically not significant (p=0.628).

The study comprised of 25 males and 25 females. Group V comprised of 60% (15) males and 40% (10) females whereas Group II comprised of 40% (10) males and 60% (15) females. The result of sex distribution was not statistically significant (p=0.258).

Table 2: Cooper score in relation to onset of Action

Seconds	Rocuronium	SD	Vecuronium	SD
0	0		0	
30	1.12	0.44	0.72	0.46
60	1.88	0.53	1.04	0.20

90	2.46	0.59	1.6	0.50
120	2.83	0.50	1.88	0.33
180	3	0.00	2.6	0.58
240			3	0.66
300			2.67	
360				

In relation to onset of action and cooper scoring for adequacy for intubation it was found that in the present study in Group R a score of more than 2.5 was achieved by the 120th second whereas in Group V only 1.8 was achieved in 120th second. This shows the rapid onset of group R over Group V.

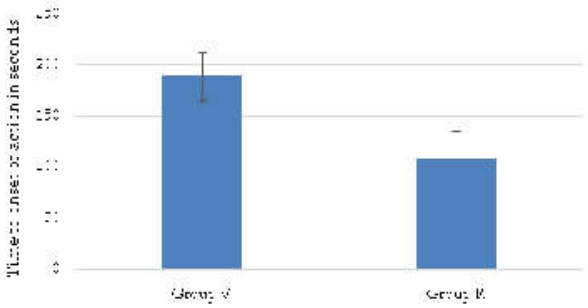

Fig. 1: Time to onset of action in both groups

Onset of action was taken as the time from the end of injection of the study drug to abolition of three responses to train of four stimulation. The maximum time to onset of action in Group V was 324 seconds and in Group R was 160 seconds. The minimum time to onset of action in Group V was 135 seconds and in Group R was 55 seconds.

The duration of action between the two groups, Group R had a longer duration of action when compared to vecuronium and also had a significant p value of 0.01. the top up doses also indicated that rocuronium seem to have a prolonged action than rocuronium.

Hemodynamic variables

In comparison between the two drugs there does not seem to be drastic variation in the heart rate systolic, diastolic blood pressure and the respiratory rate. There was only one patient who had a high systolic blood pressure before induction of anaesthesia and which later got optimized after induction of anaesthesia without any anti hypertensives.

Discussion

The introduction of neuromuscular blocking drugs into clinical practice represents one of the most significant advances in the development of anesthesiology and has revolutionized the practice of anesthesia. The use of neuromuscular blocking drugs has increased the safety and improved the results of many established surgical procedures as well as many new ones. As stated by Foldes and co-authors [1] "the first use of muscle relaxants not only revolutionized the practice of anesthesia but also started the modernera of surgery and made possible the explosive development of cardiothoracic, neurological and organ transplant surgery".

Abdominal surgeries require muscle relaxation for efficacious operating conditions. Before the advent of neuromuscular blocking drugs, surgical relaxation was achieved with the use of inhalation anesthetics. At deep levels of ether anesthesia relaxation of abdominal musculature is sufficient to permit exploratory laparotomy. Following the introduction of d-Tubocurarine, small doses of the same were seen to amplify muscle relaxation during either anesthesia and allow reduction of anesthetic depth.

As halogenated anesthetics replaced ether in common practice, a greater need to rely on curare-type drugs to block neuromuscular transmission developed, since the muscle relaxing properties of the halogenated anesthetics was not adequate for abdominal surgery unless high and toxic concentrations were used.

Booij and Crul [2] spelled out the requirements for the ideal neuromuscular blocking agent. Rocuronium has been shown to possess most of these properties of an "ideal" muscle relaxant except the high potency. Since, it has been shown

Table 3: Duration of action of intial and top up doses

Doses	Group V Mean [minutes]	Group Mean [minutes]	Group V SD	Group R SD
Intial dose	24.5	31.5	7.54	8.9
1 st top up	24.73	28.48	5.5	4.8
2 top up	24.44	28.14	6.6	5.27
3 top up	23.50	28.25	7.36	6.8
4 top up	20.50	31.50	6.65	2.12
5 top up	25			

by studies that a rapid onset of action, with a non-depolarizing muscle relaxant, is almost only produced by compounds of relatively low potency, Rocuronium which has a rapid onset has a very low potency.

The present study was undertaken to study the neuromuscular properties and cardiovascular effects of Rocuronium, the 'near-ideal' muscle relaxant and to compare it with Vecuronium, an already established drug. It is generally acknowledged that the response to neuromuscular blocking drugs is unpredictable in the population at large. This is more so in several physiologic andpathologic conditions directly or indirectly involving the neuromuscular junction. The monitoring of neuromuscular function provides valuable information to the anaesthesiologist and contributes to a more predictable and rational approach to the use of muscle relaxants, and hence to better patient care.

The study comprised of 50 patients of ASA grade I and II and patients with neuromuscular or systemic disease of significance were excluded. 25 patients each were randomly allocated to two groups for administration of the two study drugs, Group V (patients who received Vecuronium as the muscle relaxant for intubation and maintenance of anaesthesia) and Group R (patients who received Rocuronium as the muscle relaxant for intubation and maintenance of anaesthesia).

Foldes FF and colleagues [1] have studied the neuromuscular effects of Rocuronium in patients receiving balanced anesthesia with thiopental and nitrous oxide – oxygen. Both M G and colleagues while comparing the pharmacodynamics of Rocuronium and Vecuronium used halothane during maintenance of anesthesia. Maddineni VR et al [3] studied the duration of action and haemodynamic effects of Rocuronium bromide under balanced and volatile anaesthesia.

In the present study, patients were administered thiopental for induction and nitrous oxide-oxygen with halothane for maintenance of anaesthesia. The two groups are similar in terms of age, weight and sex distribution. Kreig N [4] performed a clinical study of pharmacodynamics of Vecuronium in doses of 0.06 mg/kg and 0.07 mg/kg and concluded that onset time was between 3 and 4 minutes.

In group R (Rocuronium group) the mean onset time of action was 108.8 seconds (mean±SD was ± 28.875). The present study concurs with the findings of the studies of Alvares Gomes, Mirakhur RK5 and Foldes FF [1] who have also reported the onset time similar to the present study. In relation to onset of action and cooper score for adequacy of intubation, it was found that in group R a score of 2.5 and above was achieved by 100-110 seconds whereas for group V a score of 1.7 was only achieved at at time interval of 100-110 seconds which shows the rapid onset of group R. A maximum score of 3 was obtained in group R by 120 to 150 seconds, whereas to achieve the maximum score in group V it took about 180-240 sewconds. Onset of action in Group R (Rocuronium) was rapid compared to Group V (Vecuronium) with very high statistical significance ($p<0.001$). The present study is in agreement with the study of Booth MG et al and Bartkowski RR et al. [6] who compared the onset of action of equipotent doses of Rocuronium and Vecuronium. Rocuronium onset time was found to be faster with very high statistical significance. Similar Observations were made by Bartkowski RR [6]**.** The faster onset of action of Rocuronium has been attributed to its low potency.

This necessitates a higher dose, which ensures the presence of more relaxant molecules in the bloodstream and thus due to a higher concentration gradient, the transport towards thebio phase is faster.

The duration of action of the initial dose of Vecuronium observed by various authors ranged from 22 minutes to 43 minutes depending on the dose employed. The various authors who have studied the duration of action of different initial doses of Vecuronium and the reported duration of action as follows:

In Group V (Vecuronium group) the duration of action of initial dose was 17-32 minutes (mean 24.5 minutes). The duration of action of the initial dose of Rocuronium observed by various authors ranged from 11 minutes to 40 minutes depending on the dose employed. The various authors who have studied the duration of action of different initialdoses of Rocuronium and the reported.

In Group R (Rocuronium group) the duration of action of initial dose was 13-50 minutes (mean 31.5 minutes). The duration of action of initial dose of Rocuronium in the study correlates with the findings of Mirakhur RK and Carroll MT who have found similar duration of action with a dose of 0.6mg/kg of Rocuronium. In group V (Vecuronium) the mean duration of action was 24.5 min and in group R (Rocuronium) it was 31.5 min. This difference was found to be statistically significant ($p<0.01$). In the studies of Levy JH et al., Lambalk LM et al. [7], Foldes FF et al. [1], the top-up dose of Rocuronium administered was 0.15mg/kg. In the

present study, the top-up dose administered was 0.025 mg/kg of Vecuronium and 0.15 mg/kg of Rocuronium.

There was no prolongation of duration with subsequent doses of Vecuronium inthe studies by Crul JF et al. [2] The duration of action of the maintenance doses of Vecuronium in the present study ranged from 21.8 minutes for first maintenance to 25 min for 6th maintenance and there was no prolongation of duration with subsequent doses. There was no prolongation of duration with subsequent doses of Rocuronium inthe studies by Lambalk LM et al. [7] who found no increase in the duration of the maintenance doses even after 4 to 5 doses and the duration ranged from 15.1 to 18.7 minutes. The duration of action of the maintenance doses of study ranged from 25.3 minutes for first maintenance to 27 minutes for fourth maintenance and there was no prolongation of duration with subsequent doses.

This finding of the present study is in agreement with the study of Maddineni VR et al. [3] who studied the haemodynamic effects of Rocuronium in the doses of 0.6 mg/kg and 0.9 mg/kg under balanced and volatile anaesthesia. They concluded that no significant change in heart rate occurred with both doses and both techniques.

This observation also correlates with the study by Hudson ME et al. [8] with Rocuronium in a dose of 0.6 mg/kg wherein they concluded that no changes in heart rate occurred with the given dose of Rocuronium.

Levy JH [9] studied the heart rate changes with Rocuronium in doses ranging from 0.6 mg/kg to 1.2 mg/kg and found no significant changes in heart rate even in high doses.

The heart rate differences between the two groups were compared at every 2 minute interval for the first ten minutes after onset of action of the non-depolarizing muscle relaxant and followed by every 5-minute interval for next twenty minutes and than every fifteen minutes till the end of surgery. The difference in mean heart rate between the two groups was not significant at any timeinterval ($p>0.05$).

In Group V (Vecuronium group), the systolic blood pressure at pre-induction level Was 128.16 mm of Hg? At onset of action of Vecuronium the systolic blood pressure was 130.52 mm of Hg. Throughout the study period the systolic blood pressure remained between 124.24 mm of Hg to130.88 mm of Hg, which was comparable to the pre-drug level, and there was clinically no significance in p value Ease of reversibility in the present study was assessed by clinical criteria for neuromuscular recovery.

Mirakhur R et al. [5] compared the antagonism of Vecuronium induced neuromuscular blockade by either edrophonium or neo stigmine and found adequate antagonism in all patients given neostigmine. Wicks TC [10] and Lambalk LM et al. [7] have found in their studies that neuromuscular block induced by Rocuronium is promptly reversed with conventional doses of cholinesterase inhibiting drugs.

In the present study, in both the groups, Inj. Neostigmine 0.05 mg/kg with Inj. Atropine 0.02 mg/kg was employed for reversal. There was complete and rapid recovery of neuromuscular blockade in all the patients in both the groups. No adverse effects like bronchospasm, hypotension or rashes were noted in any patient during the study.

Conclusion

Rocuronium has a significantly rapid onset of action with a mean of 108.8 seconds and intermediate duration of action. It is easily reversible and produces no significant cardiovascular changes. It also has a good safety profile. Therefore in spite of its high cost, rocuronium appears to be the safest drug for rapid sequence intubation and routine intubation and it is near to ideal NMBA when there is no anticipated difficulty in intubation and also in surgeries of prolonged duration. It provides excellent intubating conditions with completely relaxed vocal cords, and good heamodynamic stability during intubation.

It has no significant adverse cardiovascular effects and no adverse reactions on reversal with Neostigmine. The synthesis of this drug has proven to be potentially very useful for anaesthetists all over the world because of its rapid onset of action and easy reversibility.

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Original Research Article

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Intubation Sans Relaxant: Propofol VS. Triple Nerve Block

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Abstract

Aims: Methods that avoid use of muscle relaxants during intubation help us when their use would be detrimental to the patient/situation. Here we aim at intubations without muscle relaxants which could be of great significance in difficult airways. *Settings and Design:* It was a Randomised, prospective, comparative and double blinded study. *Methods and Material:* After approval by institutional ethical committee the study was conducted 60 patients of ASA I and II who were scheduled for elective surgeries under general anaesthesia. *Group P:* Direct Laryngoscopy using inducing doses of Propofol (2-3 mg/kg). *Group N:* Direct laryngoscopy using Triple nerve block technique.

- *Group P:* Direct Laryngoscopy and intubation was done with inducing doses of propofol (2-3mg/kg).
- *Group N:* The lingual branch of the Glossopharyngeal nerve, Bilateral superior and recurrent laryngeal nerve block were given.

Statistical analysis used: Haemodynamic values were analysed using the Student's unpaired't' test. Intubation grades were measured using Mann Whitney U test. *Results:* Intubating condition, ease of intubation and haemodynamic stability is better in triple nerve block group than propofol group. *Conclusions:* And Triple nerve block provides better ease and intubating conditions and haemodynamic stability compared to intubations using Propofol.

Keywords: propofol; triple nerve block; intubating condition; haemodynamic changes during laryngoscopy and intubation.

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Introduction

There are various methods of intubating an airway. It is desirable for anaesthesiologists to hone their skills in different methods as this helps an anaesthesiologist in making a judicious decision of using a particular method as justified by the situation. Broadly, we can secure the airway either using muscle relaxants or even by avoiding them. Methods that avoid use of muscle relaxants help us when their use would be detrimental to the patient/situation. Here we aim at intubations without muscle relaxants which could be of great significance in difficult airways.

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Materials and Methods

After approval by institutional ethical committee, a bilingual written informed consent was obtained from all patients. It was a Randomised, prospective, comparative and double blinded study was conducted in Hamidia Hospital, Bhopal from January to September 2015. 60 patients of both sexes, aged 18-60 years of ASA I and II who were scheduled for elective surgeries under general anaesthesia were included. H/O Hypersensitivity to any of the drugs were excluded. 30 patients each were randomly divided into two groups using sequentially numbered, sealed opaque envelope technique:

- **Group P:** Direct Laryngoscopy using inducing doses of Propofol (2-3 mg/kg).
- **Group N**: Direct laryngoscopy using Triple nerve block technique.

All patients underwent thorough pre-anaesthetic check-up and were explained the procedure. The multichannel monitor to record

i) Heart rate

ii) SpO_2

iii) ECG

iv) NIBP

v) $EtCO_2$

Were applied to the patient on arrival to the operating room. Then a suitable peripheral vein was cannulated For all patients before the procedure.

All patients were premedicated with

i) Glycopyrrolate 0.2 mg i.v.

ii) Midazolam (0.05- 0.1 mg/kg i.v)

iii) Fentanyl (1 mcg/kg)

Preoxygenation with 100% O_2 was given to all patients for 3 minutes.

Group P: Direct Laryngoscopy and intubation was done with inducing doses of propofol (2-3 mg/kg).

Group N: The lingual branch of the Glossopharyngeal nerve was blocked bilaterally by keeping cotton pledgets soaked in 4% lignocaine in contact with inferior aspect of palatoglossal arch. Superior laryngeal nerves were blocked bilaterally by infiltrating 2% Lidocaine at lateral and inferior aspect of hyoid. Finally, 3 ml of 2% Lidocaine was injected through cricothyroid membrane into the trachea which blocks the recurrent laryngeal nerve.

The intubating conditions and ease of intubation were assessed using intubation Grading Scale and number of attempts required for intubation respectively. Systolic Blood Pressure, Diastolic Blood Pressure, Pulse rate, SpO_2, ECG and Respiratory rate were recorded during intubation and then 1 and 3 minutes post intubation. All the data were tabulated and analysed statistically. Parametric values are expressed as Mean ± standard deviation. A p value < 0.05 was considered significant. Haemodynamic values were analysed using the Student's unpaired 't' test. Intubation grades were measured using Mann Whitney U test.

Intubation Grading Scale

Grade 0	No coughing/Gagging in response to intubation,
Grade 1	Mild coughing/Gagging that did not hinder intubation,
Grade 2	Moderate coughing and/or Gagging that interfered minimally with intubation,
Grade 3	Severe Coughing and/or Gagging that made intubation difficult,
Grade 4	Severe coughing and gagging that required additional dose of Propofol/additional local anaesthesia and/or other change in technique to achieve successful intubation.

Results

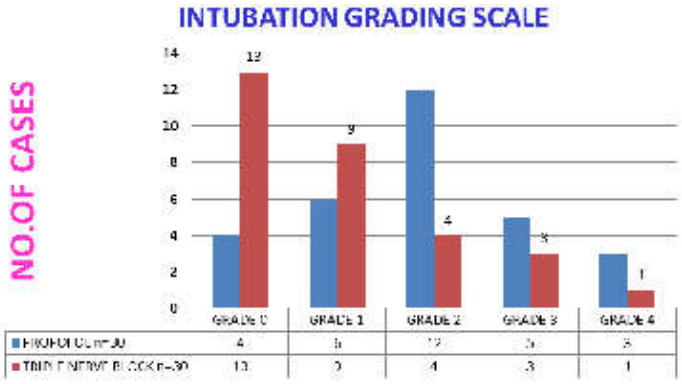


Fig. 1: The intubation Grading Scale shows intubations using Triple nerve block has better intubating conditions than Propofol.

Ease of Intubation

The ease of Intubation is assessed based on the number of attempts required for successful intubation.

Attempt – 1	Single attempt at intubation without any manipulation,
Attempt – 2	2 attempts at intubation with/without manipulation,
Attempt - 3	3 attempts at intubation with/without manipulation.

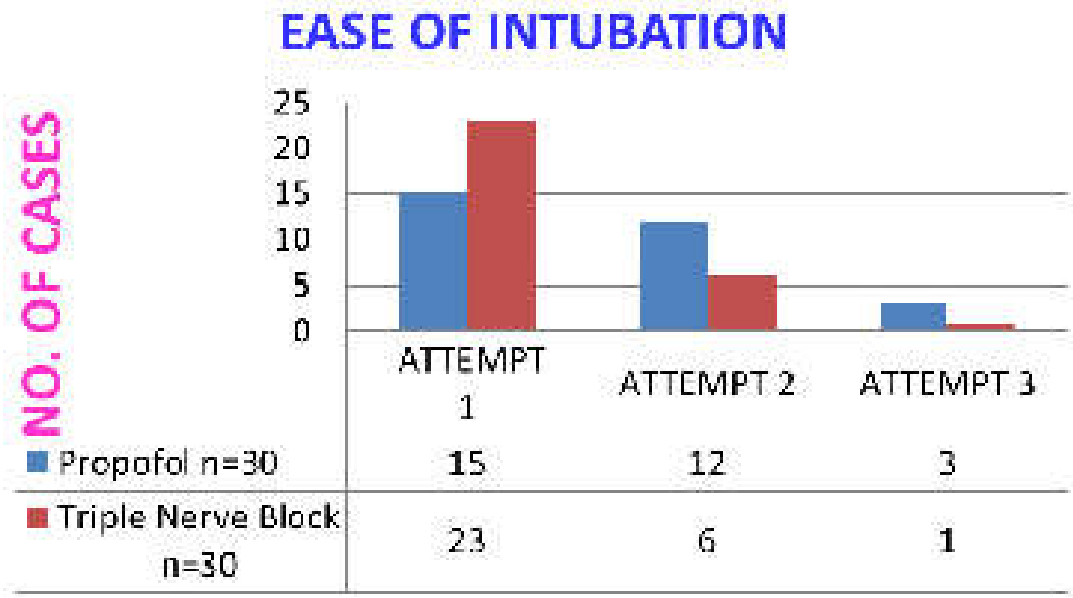


Fig. 2: The ease of Intubation chart shows Triple nerve block was better than Propofol based on the number of attempts and this was statistically significant with p value of 0.036.

Haemodynamic parameters comparison

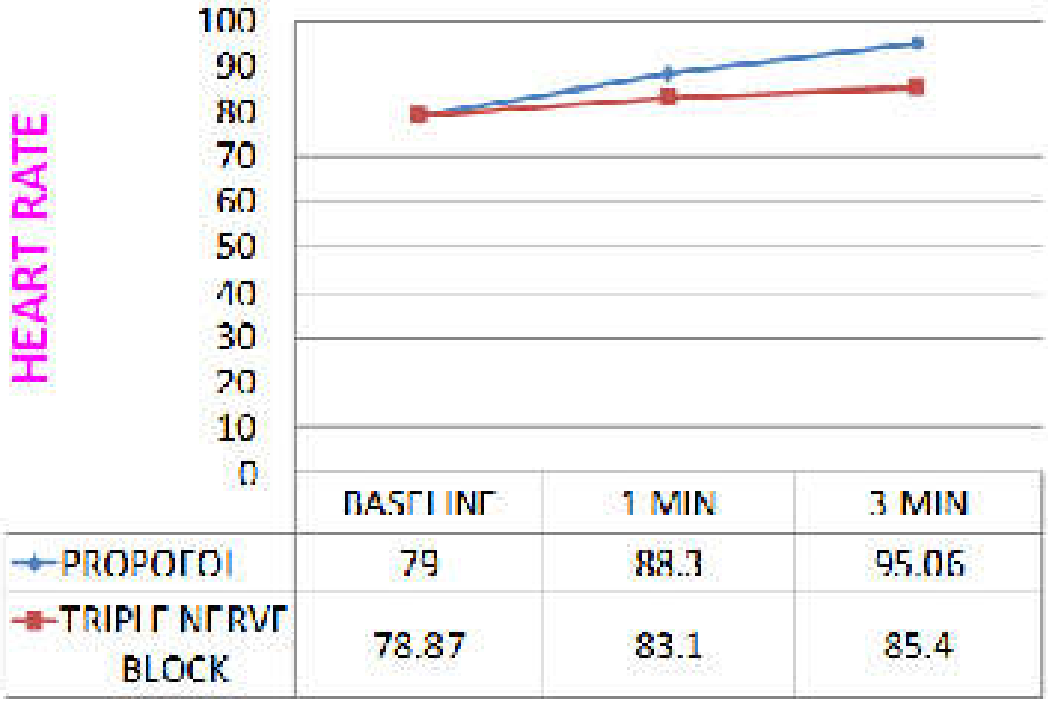
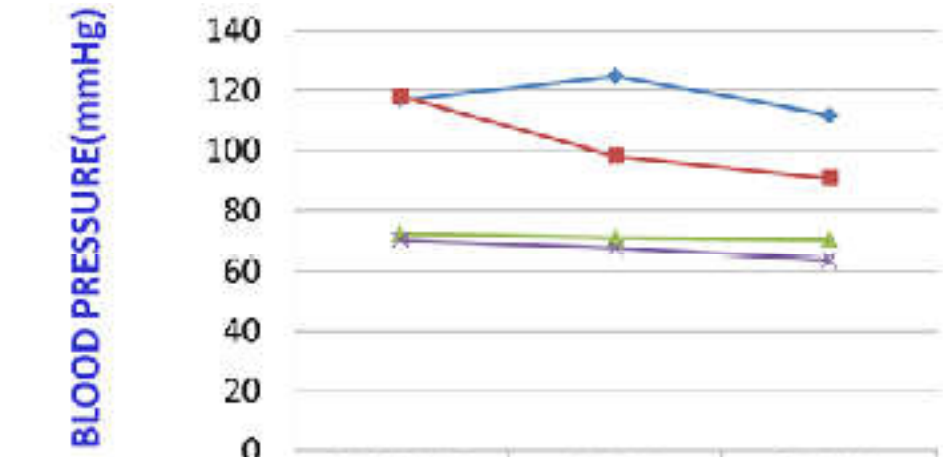
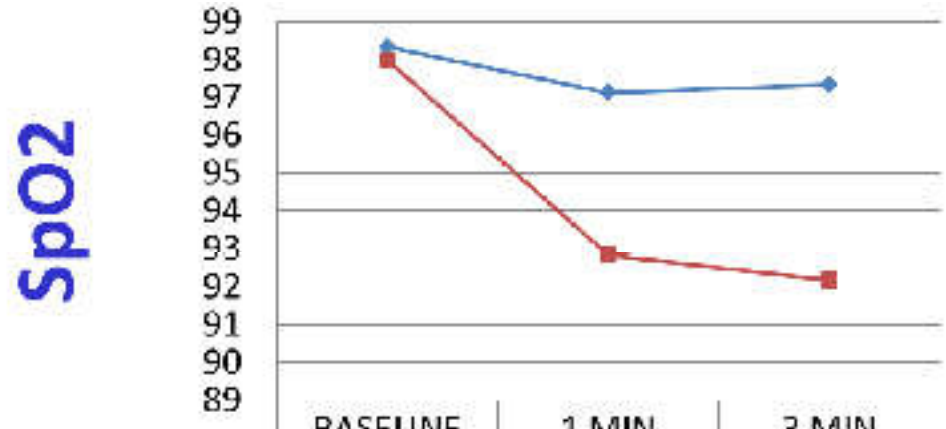


Fig. 3: Comparison of Heart rate betrween 2 groups and it was statistically significant with p value< 0.05 at 1 min and 3 mins post intubation.



	BASELINE	1 MIN	3 MIN
TRIPLE NERVE BLOCK SBP	116.73	124.67	111.73
PROPOFOL SBP	117.93	98.07	90.67
TRIPLE NERVE BLOCK DBP	72.27	71	70.4
PROPOFOL DBP	70.07	67.4	63.47

Fig. 4: Comparison of SBP and DBP between 2 groups. SBP is extremely statistically significant at 1 and 3 mins post intubation with p value <0.001.DBP is not significant at 1 min but significant at 3 mins with p value<0.05.



	BASELINE	1 MIN	3 MIN
TRIPLE NERVE BLOCK	98.33	97.13	97.33
PROPOFOL	97.97	92.83	92.17

Fig. 5: Comparison of SpO_2 between 2 groups and is statistically significant with p value <0.05.

Discussion

The routine use of succinylcholine for endotracheal intubation has been increasingly questioned. Here we aim at attaining skills of intubations using techniques which avoids the usage of muscle relaxants and could serve as an alternative for muscle relaxants in difficult airways.

- Initial studies have suggested that a combination of Propofol and Fentanyl without a muscle relaxant and nerve blocks for upper airway anaesthesia provide good intubating conditions.

Intubation using Triple nerve block has better intubating conditions than Propofol. Ease of intubation was better with Triple nerve block than Propofol with a significant p value ≤ 0.05. There is Increase in Heart rate and Decrease in Systolic and Diastolic blood pressure, 1 and 3 minutes post intubation and the values are statistically significant. Saturation (SpO_2) fall was more profoundly seen in Propofol group than Triple nerve block at 1 and 3 minutes post intubation, and it was statistically significant. There were no adverse events encountered with both techniques and all patients have been successfully intubated. Thus both these techniques serves as a good alternative to muscle relaxants which could be of utmost significance in patients with difficult airways.

Conclusion

In our study we conclude that, Intubations using both Triple nerve block and Propofol were suitable options as alternatives for intubations without muscle relaxants. And Triple nerve blocks provide better ease and intubating conditions and haemodynamic stability compared to intubations using Propofol.

Key Messages:

Triple nerve block provide better ease and intubating conditions and haemodynamic stability compared to intubations using Propofol.

Conflict of Interest: No conflict of interest

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Original Research Article

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Modified Combined Spinal and Epidural Analgesia with Buprenorphine and Bupivacaine

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Abstract

Context: Combined spinal and epidural analgesia is performed by double space or single space technique. It can also be performed through single intervertebral space with a CSE needle or a Spinal needle which is the modified technique we planned. *Aims:* To compare the effect of different doses of epidural Buprenorphine with spinal Bupivacaine in terms of Onset and duration of Sensory & Motor Block; Duration of post operative analgesia with Visual analog scale. *Settings and Design:* It is a prospective randomised control study. *Methods and Material:* A total of 30 patients who met the enrolment criteria were approached & written informed consent was obtained.Group A were given Buprenorphine in the dose of 4 micrograms per kg with 10 ml Normal saline for epidural and 15 mg of Bupivacaine for spinal and Group B given Buprenorphine in the dose of 6 micrograms per kg with 10 ml Normal saline for epidural and 15 mg of Bupivacaine for spinal. *Statistical analysis used:* Comparisons between numerical variables were made using Student's t test or the Mann-Whitney U test, accordingly. To test for potential differences in onset neural block assessments of the two concentrations, a repeated measures analysis of variance (ANOVA) was applied. *Results:* There was significant increase of mean in Onset of Sensory Block (min) in groupA compared to group B. There was significant increase of mean in Time to two Segment Regression of Sensory Level (min) in groupB compared to groupA. Mean Duration of analgesia is significantly increased in group B compared to group A. *Conclusions:* CSE can be practised safely with Buprenorphine as additive to subarachnoid block with single needle technique offering good postoperative analgesia.

Keywords: Buprenorphine; Bupivacaine; Epidural; Spinal

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Introduction

Combined spinal and epidural analgesia (CSE) can be performed by double space (DST) or single space/segment technique (SST). It can also be performed through single intervertebral space with a CSE needle or a Spinal needle which can be cost effective, single injection site with an advantage of postoperative analgesia. Using opioids for epidural is practiced and local anaesthetic like Bupivacaine/ Ropivacaine for intrathecal injections. We planned this study with a spinal needle for identifying both epidural and subarachnoid block.

Objectives

To compare the effect of different doses of epidural Buprenorphine with spinal Bupivacaine

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in terms of Onset and duration of Sensory & Motor Block; Duration of post operative analgesia; Hemodynamic changes.

Materials and Methods

Inclusion criteria were, after institutional Ethical Clearance, a total of 30 patients (15 in each group) who met the enrolment criteria were approached & written informed consent was obtained. American Society of Anesthesiologist (ASA) I & II, aged 20-60 yrs, posted for elective surgery (OBG, Surgery, Urology, orthopedic) were included. Exclusion criteria were Patient refusal, morbidly obese patients, contraindication to subarachnoid block or epidural block, patient on opioids.

Randomization done by computerized random table and double blinding method was followed. Preoperatively detailed medical, surgical history, allergies was noted. Preoperative detailed general & systemic examination was done and vitals recorded and necessary investigations were done. Demographic data like age, weight (kg), height (cm) was obtained for each case.

The patients were familiarized with the 10 cm visual analogue scale (VAS) for pain during the pre-anesthetic visit. Patients kept fasting for 6-8 hrs prior to anesthesia. Baseline monitoring of E.C.G, noninvasive blood pressure, oxygen saturation, and respiratory rate recorded, all the patients preloaded with Ringer's Lactate10 ml/kg and Group A were given Buprenorphine in the dose of 4 micrograms per kg with 10 ml Normal saline for epidural and 15 mg of Bupivacaine for spinal and Group B given Buprenorphine in the dose of 6 micrograms per kg with 10 ml Normal saline for epidural and 15 mg of Bupivacaine for spinal.

The epidural done in sitting position with 23 G Quincke spinal needle with Loss of resistance to air technique and it was followed by spinal. Modified insertion technique advocated by Ali and Samson was adopted for ease of identification of the epidural space. According to this technique, the dorsum of the operator's left hand rests on the patient's back, while the left thumb advances the spinal needle. Continuous restrain by the left three fingers thus helps in slow continuous advance movement of the spinal needle until the loss of resistance is clearly appreciated once the tip is in the epidural space [1].

The onset of Sensory, Motor block; highest level of sensory, motor block; hemodynamic changes- HR, BP; SPo2; Time to 2 segment regression; VAS scores during the postoperative period noted. If VAS >4, Rescue analgesia Inj. Tramadol 50 mg was given. Side effects- hypotension, hypoventilation, itching noted and treated appropriately.

Results

Fig. 1: Comparison of the heart rate (mean (SD) changes between groups at 0-120 min. Changes in heart rate (HR) (mean (SD)). Group A= Buprenorphine mcg and Group B = Buprenorphine 6 mcg (F=64.89, p=0.596)

Fig. 2: Comparison of the mean arterial pressure (mean (SD) changes between groups at 0-120 min. Changes in mean arterial pressure (mean (SD)). Group A = Buprenorphine 4 mcg Group B = Buprenorphine 6 mcg (F=8.496, p<0.001).

The observations made entered in to MS Excel and Demography details presented as Mean & SD; Statistical analysis was performed in SPSS 22.0 for Windows (US, Desk top Version). Comparisons between numerical variables were made using

Table 1: Comparison of age, block characteristics, in Group-A & Group-B patients

Variables	Group –A (Buprenorphine 4 mcg (mean±SD) (n=15)	Group-B (Buprenorphine 6mcg) (mean+SD) (n=15)	T Value	p
Age (years)	44.33±11.09	44.87±10.46	-0.135	0.893
Onset of sensory block (min)	2.73±0.79	2.07±0.704	2.425	0.02
Time to two segment regression of sensory level (min)	104.33±11.782	121.00±10.88	-4.024	0.001
Total duration of analgesia (min)	334.33±31.21	423±27.37	-8.271	0.001
Time for complete motor recovery (min)	323.67±34.35	314±30.89	0.810	0.424
VAS score when patient complains of pain	4.93±0.70	4.67±0.90	0.904	0.374
Number of rescue analgesia doses given during 24 hours	0.93±0.70	0.47±0.516	2.071	0.048

Student's *t* test or the Mann-Whitney U test, accordingly. To test for potential differences in onset neural block assessments of the two concentrations (Buprenorphine-4 mcg & 6 mcg), a repeated measures analysis of variance (ANOVA) was applied. Basal values for mean arterial pressure, and Heart Rate were entered as covariates in the relevant models (ANCOVA). Group assignment was entered as the between-subject factor. The Greenhouse-Geisser correction for the denominator degrees of freedom was used if the assumption of sphericity did not hold. We chose to only consider results from the Duration × group interaction, to assess for possible differences in the time course of the sensory block.

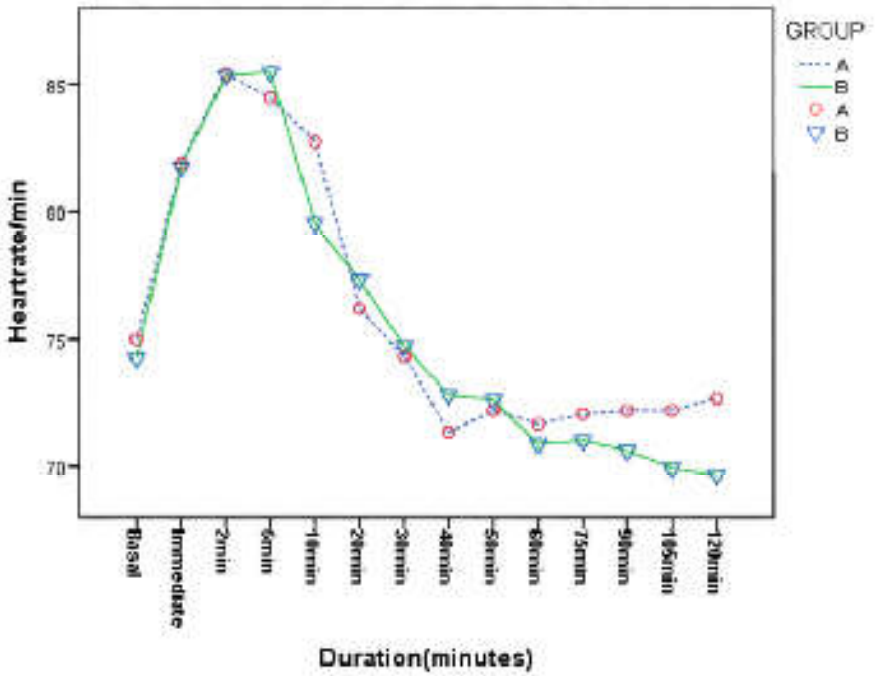

Fig. 1: shows ANOVA for repeated measures, there was no significance between-group differences in terms of heartrate (F=64.89, p=0.596)

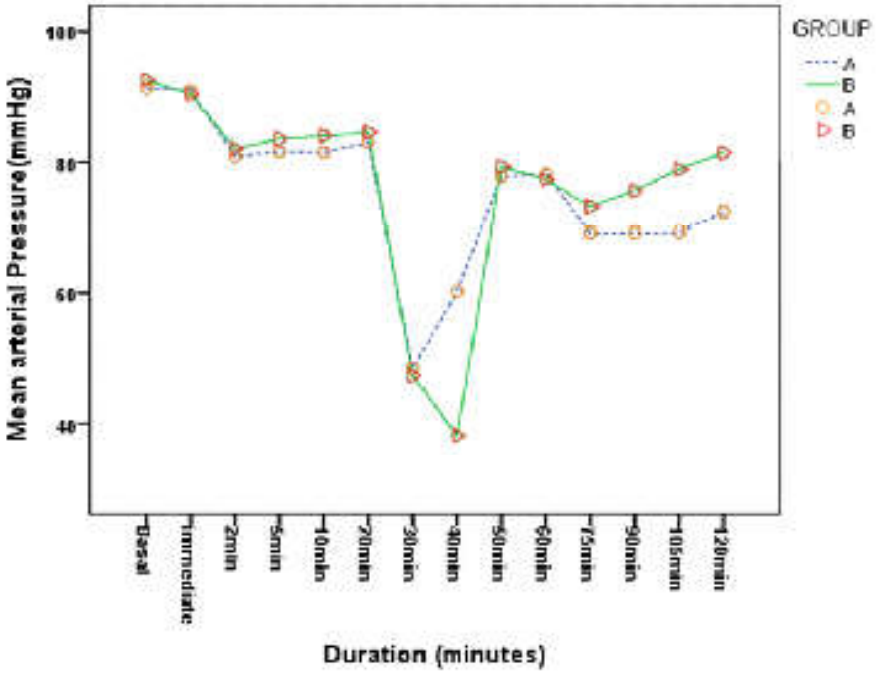

Fig. 2: shows ANOVA for repeated measures, there was significance between-group differences in terms of Mean arterial pressure (F=8.496, p<0.001)

A $p<0.005$ was considered statistically significant.

Neural block assessments are presented in Table 1. between Group-A & Group-B. The age was matched between the groups. There was significant increase of mean in onset of sensory block (min) ($p<0.02$) in group A compared to group B.

There was significant increase of mean in time to two segment regression of sensory level (min) ($p<0.001$) in group B compared to group A.

Mean Duration of analgesia is significantly increased in group B compared to group A ($p<0.001$).

The VAS scores and number of rescue analgesia doses were comparable in between the two groups.

Discussion

Different approaches for Combined spinal and epidural analgesia are practiced, like same space or 2 different spaces; Needle thorough needle or side port; use of 2 needles or single needle. We choose to use 23 Gauge spinal needles as it was difficult to identify epidural space with 25 gauge needles. We also used 2 different spaces.

One more method followed is called the modified combined spinal epidural technique or the sequential combined spinal-epidural technique, in which a spinal dose intended to be inadequate for surgery is used in an attempt to reduce hypotension and the block is then deliberately extended cephalad with the epidural drug. This is becoming popular in modern obstetric practice, because of stable haemodynamic status, also used in elderly high risk patients for orthopaedic surgery [1]. The combined spinal epidural (CSE) anaesthesia technique was first described by Soresi in 1937 [2].

Use of epidural needles may cause inadvertent dural puncture, migration of catheter in to subarachnoid space [3]. Special kit for CSE can be very costly and may not be affordable to all. To overcome this issue we have tried using a spinal needle for our study [4]. This technique of modified CSEA using a spinal needle can be cost effective and less complication prone alternative to the conventional CSEA [5].

Samaddar et al. used 25 G Quincke spinal needle for Modified CSEA in 60 adult patients subjected for lower abdominal or lower extremity surgery. Technique advocated by Ali and Samson was used while identifying epidural space. Epidural morphine 50 microgram kg-1 body weight was used. This Modified CSEA was successfully performed in 85% cases; this offered almost 24 h post of pain relief in 88.23% cases without any incidence of respiratory depression, pruritus and post dural puncture headache. They found it to be cost effective and less complication prone alternative technique and need of epidural catheter might be obviated [5].

Joshi et al. evaluated combined spinal-epidural anesthesia with a needle-through-needle technique using two different needle sets, 16-gauge Tuohy needle and a 26-gauge spinal needle that extended 13 mm beyond the tip of the Tuohy needle and other kit consisted of a 16-gauge Tuohy needle with an aperture in its curve (back hole) for the insertion of a 26-gauge spinal needle that protruded 10 mm beyond the tip of the epidural needle. They found Combined spinal-epidural technique provided satisfactory surgical and postoperative analgesia for total knee arthroplasty [6].

Rudra et al. compared of two analgesic regimens following lower abdominal surgery,extradural pentazocine 30 mg or extradural buprenorphine 0.3 mg to provide postoperative analgesia and found demand for rescue analgesia was significantly greater after extradural buprenorphine (18.96 hours) than after extradural pentazocine (8.39 hours). No serious side-effects were reported [7].

Casati et al. compared double-segment and the needle-through-needle techniques for combined spinal and epidural anesthesia (CSE), 120 patients were selected. They concluded needle-through-needle technique for CSE required less time, had no greater failure rate and resulted in greater patient satisfaction than the double-segment technique. They also observed use of a spinal needle with an adjustable locking mechanism and protruding up to 15 mm beyond the Tuohy needle improved successful spinal block in the needle-through-needle technique. No difference in the incidence of hypotension, postdural puncture headache, and back pain was observed between the two groups [8].

Kumar et al. also used 25 G Quincke spinal needle for modified CSE technique in 200 adult patients subjected for lower abdominal or lower extremity surgery. They also followed Needle insertion technique advocated by Ali and Samson. They used epidural buprenorphine 4 - 8 microgram kg-1 body weight successfully performed in 90% cases. Offered almost 20 - 24 h post of pain relief in 58.5% cases without any incidence of respiratory depression, pruritus and post dural puncture headache [4].

In our study, we planned to use epidural

buprenorphine and spinal Bupivacaine, so that postoperative analgesia is obtained without the side effects of adding additives to spinal anaesthesia. In our study we found that mean duration of onset of sensory block was earlier in group A (2.73±0.79 min) compared to group B (2.07±0.704 min). The mean time to two segment regression (A: 104.33±11.782 and B: 121.00±10.88 min) and duration of analgesia (A: 334.33±31.21 and B: 423±27.37 min) was also significant and more in group B. Group B had a significant drop in MAP at 40 minutes in 3 patients treated with Inj Mephentermine 6 m, g IV. In our study the VAS scores in between groups was not significant (4.93±0.70 & 4.67±0.90) and number of rescue analgesia doses were also less and not statistically significant.

Limitations of our study are, sample size is small and it is difficult for Novices to attempt Epidural with Spinal needle. We have used 23 gauges spinal as it is difficult to identify epidural with 25 gauge needles. Strengths of our study is using single needle for two techniques is cost effective and also provides postoperative analgesia with minimal side effects.

Conclusion

CSE can be practised safely with Buprenorphine as additive to subarachnoid block with single needle technique offering good postoperative analgesia.

Key Messages

Epidural analgesia combined with spinal anaesthesia will give an additive advantage in quality of anaesthesia and postoperative analgesia. Using spinal needle for epidural space identification needs anaesthesiologist with experience and has an advantage of cost effectiveness and post operative analgesia with a combined epidural and spinal technique.

Conflict of Interest: Nil

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Case Report

Indian Journal of Anesthesia and Analgesia
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Piriformis Syndrome a Common Cause of Buttocks Pain with Radiation to Lower Limb

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Abstract

Piriformis muscle is a muscle of gluteal region. The Piriformis syndrome is caused by compression of sciatic nerve by the muscle as it passes through sciatic notch. The pain of Piriformis syndrome is neuropathic and is often confused with pain of prolapsed intervertebral disc. We report a case of chronic pain of one and a half years treated by giving an ultrasound guided injection of local anaesthetic and steroid.

Keywords: Piriformis; sciatic nerve; Piriformis syndrome; neuropathic ultrasound; local anaesthetic; steroid.

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Introduction

Piriformis syndrome is caused by compression of the sciatic nerve by the Piriformis muscle as the nerve passes through the the sciatic notch. This entrapment neuropathy manifests as pain, numbness, paraesthesia and associated weakness in the distribution of sciatic nerve. It often begins with severe pain in the buttocks that radiates to the lower extremity and foot. Here we report a case of severe pain and heaviness in buttocks with radiation to foot [1,2].

Case report

A 28 years old male patient a computer operator with long sitting hours presented with severe pain and stiffness in left buttocks and leg for one and a half years after trauma, he was injured in a road traffic accident in March 2017. He was unable to walk on the left leg because of pain and weakness. He also had tingling sensation and numbness in the left leg. The pain also increased on sitting and his legs became numb after sitting for even 10 min. His physical examinations showed a positive straight leg raising test, FAIR test (flexion, addiction and internal rotation of hip) was positive and hyperalgesia in left leg. He also had tenderness over the left buttocks on deep palpation. He had no motor or sensory deficit. All routine blood investigation were normal. He was advised MRI lumbar spine which was normal. His Visual analogue score (VAS) was 8/10. He had no other systematic illness and no addiction. The patient is a non smoker and did not take alcohol. He had been taking analgesics and physiotherapy. He was taken to operation theatre for injection of local anaesthetic and steroid into the Piriformis muscle under ultrasound guidance. With all resuscitative measures taken an intravenous catheter 18 G in

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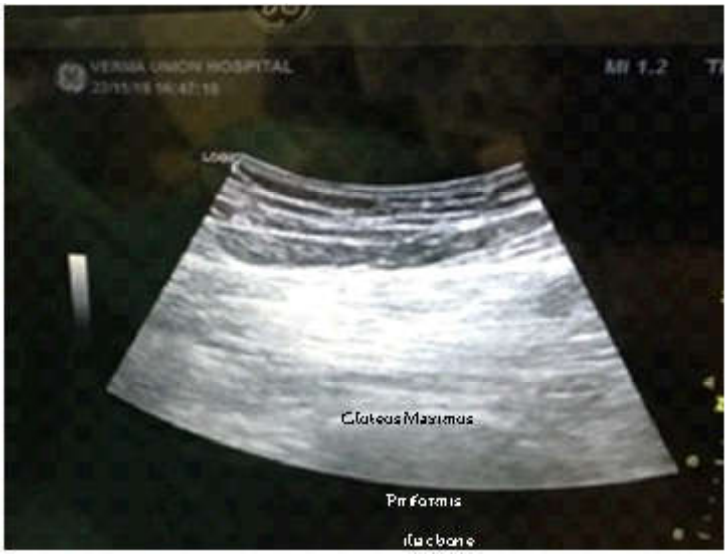

Image 1:

place. The patient was put on prone position with the affected side cleaned and draped. A Curvilinear low frequency ultrasound probe was positioned with its lateral side medial to the greater trochanter and medial side lateral to ischial tuberosity. The probe was then moved cephalad to identify the gluteus maximus muscle, Piriformis muscle and sciatic nerve were identified. Using a In plane technique a 10 cm 25 Gauge needle was inserted in the Piriformis muscle and taking precautions of not touching the sciatic nerve 40 mg of triamcinolone and 5 ml of 0.25% bupivacaine was injected. The patient was stable during and after procedure. His pain scores and stiffness decreased immediately was able to flex his hipjoint without pain. He was sent home after 2 hours of observation. He was advised simple analgesics and muscle relaxants for a week and physiotherapy was started after a week. He was followed up after a week and monthly for 6 months. He remained asymptomatic and then was lost to follow up [3].

Discussion

Piriformis muscle is a deep muscle of gluteal region deeper to gluteal maximus and medius muscle. It's origin is in three digitations from front of sacrum, gluteal surface of ilium and anterior capsule of the sacroiliac joint and extends till the the insertion at greater trochanter of femur bone [4]. The sciatic nerve is in close relation to the Piriformis muscle runs either deep to it or through it. Piriformis syndrome is caused by irritation or compression of sciatic nerve as it passes through the sciatic notch. This entrapment neuropathy will present as pain in buttocks, paraesthesia, numbness and weakness in the distribution of sciatic nerve [5,6,7]. The main symptoms are pain in buttocks with sitting, standing or lying, pain, tingling numbness radiating to the affected limb, pain when rising from sitting to standing positions. The patient may complain of difficulty in walking or alteration of gait. It may lead to development of pain in sacroiliac or hip joint. The symptoms of Piriformis syndrome usually develop after direct trauma to hip or gluteal region, repetitive motions of hip and lower extremity or continuous pressure on Piriformis muscle. Rarely there can be an occult tumour or congenital anomaly of Piriformis muscle or sciatic nerve. On physical examinations on inspection there may be signs of trauma or wasting of muscle. On palpation there can be tenderness over the sciatic notch. Tinel's sign often may be found on percussion over the sciatic nerve as it passes beneath the muscle. Various provocative tests like Lasegue test (localised pain when pressure is applied over Piriformis muscle with hip flexed at 90 degrees.), Freiburg test (pain on passive internal rotation of hip), FAIR test Piriformis syndrome provocative test (patient in modified sims position with affected side superior hip flexed at 50 degrees, pelvis stabilised and affected leg is pushed down.) straight leg raising test or SLR may be positive. Lifting or bending at the waist increases the pain in most patient with Piriformis syndrome [8]. There may be wasting of gluteal muscles in advanced stage. The differential diagnosis can be prolapsed or herniated disc, hip arthritis, sacroiliac joint dysfunction spinal canal stenosis.

The treatment of Piriformis syndrome is multimodal including analgesics, anti neuropathics antidepressant, Muscle relaxants, stretching exercises and physiotherapy. Patients who do not get relief by conservative management are taken

for intervention such as injection of steroid and local anaesthetic under ultrasound, fluoroscopy, CT or Electromyographic guidance [9,10].

Complications of procedure are rare if done under guidance but can be sciatic nerve injury, infection, hematoma.

Conclusion

Piriformis syndrome is a neuropathic condition which is usually diagnosed after excluding other conditions and often missed. Some times it coexists with other conditions. It should be kept in mind when looking for causes of back pain and the provocative tests should be done specially with a unilateral pain. Various pharmacological therapies and Physiotherapy should be done and Piriformis injection with local anaesthetic and steroid under fluoroscopy or ultrasound guidance is a good approach to treat this difficult and often neglected cause of pain and avoids spine surgery.

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Conflicts of interest: There are no conflicts of interest

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Corporate (collective) author

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[9] National Statistics Online—Trends in suicide by method in England and Wales, 1979-2001. www.statistics.gov.uk/downloads/theme_health/HSQ20.pdf (accessed Jan 24, 2005): 7-18. Only verified references against the original documents should be cited. Authors are responsible for the accuracy and completeness of their references and for correct text citation. The number of reference should be kept limited to 20 in case of major communications and 10 for short communications.

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