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Comparative Clinical Evaluation Between Intrathecal Bupivacaine (0.5%) Heavy, Bupivacaine with Nalbuphine and Bupivacaine with Butorphanol for Infra Umblical Surgeries

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Abstract

Introduction: Spinal anaesthesia is a very popular and common regional anaesthesia technique for infra umbilical surgeries. However the short duration of action of local anaesthetic drugs used for spinal anesthesia results in early postoperative analgesic intervention. Intrathecal (I/T) administration of opioids with local anaesthetics improves quality and duration of the spinal blockade, and prolongs post-operative analgesia after surgery. *Aims & objectives:* To study the onset of sensory & motor block. To study and compare intra operative quality and duration of anaesthesia and level of spinal block. To study and compare perioperative hemodynamic effects by spinal block. To study the post operative analgesia. To study the occurrence of side effects and complications if any. *Material and Methods:* The present study is a randomized prospective comparative controlled study between age group 18–50 years of both sexes belonging to ASA grade I & II for elective infra umbilical surgeries. Written and Informed consent before participation in study will be taken from all patients. 90 patients will be divided into 3 groups (n = 30), will be schedule to undergo elective infra umbilical surgeries; Group 1: Bupivacaine heavy (0.5%) 3 ml + 0.5 ml NS Group 2: Bupivacaine (3 ml) + 0.5 ml (0.5 mg) Nalbuphine Group 3: Bupivacaine (3 ml) + 0.5 ml (0.5 mg) Butorphanol. Parameters like HR, SBP, DBP (hemodynamic variables), Respiratory rate, SpO_2 will be monitor preoperatively &intraoperatively at 0, 5, 10, 15, 20 min and after that every 20 min till the end of surgery. Post operatively pain will be monitor at the end of surgery, then after every 1 hour till 1st 6 hours, then after every 6 hours till 24 hours. Sensory block level will be assess by pin prick test and motor block by Modified Bromage Scale will be use to assess the degree & duration of motor blockade. The intensity of pain will be assess by Visual analogue Scale (VAS) at the end of surgery then after every 1 hour till 1st 6 hours, then after every 6 hours till 24 hours. Patient will also be observed for any side effects and complications viz; hypotension, hypoxia, sedation, desaturation etc. These complications Sedation will be assessed by RAMSAY sedation score. *Result & Conclusion:* Statistical analysis was done by using SPSS. The difference in proportion was analyzed by one way ANOVA test and the inter group difference in means were analyzed by using post –hoc Tukey test. Significance level for tests was determined as $p < 0.05$. Onset of sensory & motor blockade remain insignificant ($p > 0.05$) whereas duration & quality of sensory & motor blockade and duration of analgesia remain significant ($p < 0.05$) in study groups. From our study we conclude that intrathecal inj. Bupivacaine combination with inj. Nalbuphine is better than inj. Bupivacaine combination with inj. Butorphanol in respect to the duration of sensory & motor blockade, quality of anaesthesia and duration of analgesia (requirement of rescue analgesia) without any significant increase in adverse effects, whereas sedation remains more with inj. Butorphanol as compare to inj. Nalbuphine.

Keywords: Bupivacaine heavy; Nalbuphine; Butorphanol; Infraumbilical surgeries; Postoperative pain; sedation; sensory and motor blockage.

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Introduction

Spinal anaesthesia has the advantage of simplicity of technique, rapid onset of action and producing effective sensory and motor blockade. However, due to the short duration of action of local anaesthetic drugs used for Subarachanoid blocks don't have the advantage of prolonged postoperative analgesia. In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient's satisfaction, decreased resource utilization compared with general anaesthesia and faster recovery. Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, enabling patients to return to their normal activity more quickly.

Intrathecal (I/T) opioids are the most commonly utilized to improve the quality and duration of neuraxial anaesthesia. The common problems encountered with the use of opioids when given intrathecally are their side-effects that include nausea/emesis, pruritus, constipation, undesirable sedation, respiratory depression and the development of tolerance/dependence [1,2].

The aim of our study was to observe the possible prompt onset of sensory/motor block and the duration of action with the use of these drugs in lower abdominal and lower limb surgeries. Our primary aim was the duration of analgesia. We have also evaluated the side-effects with the addition of intrathecalnalbuphine & butorphanol.

The consideration for adding adjuvants (Inj. Nalbuphine and inj.Butorphanol) to 0.5% hyperbaric inj. bupivacaine in patients undergoing lower abdominal and lower limb surgeries was to prolong the duration of anaesthesia and to reduce total dose of local anaesthetic used.

Material and Methods

After approval from the Institutional Ethics Committee and informed written consent from patients, the present study was carried out in the Department of Anaesthesiology, Gandhi Medical College & associated hospitals (Hamidia and Sultania), Bhopal during period from January 2016 to July 2017. It was Randomized, comparative, Prospective study. 90 patients of ASA class I and II, aged between 18-50 years, of either sex (M & F), scheduled for elective lower abdominal and lower limb surgeries were randomly divided into three groups;

Group 1: (n = 30) bupivacaine heavy (0.5%) 3 ml + 0.5 ml NS,

Group 2: (n = 30) bupivacaine (3 ml) + 0.5 ml (0.5 mg) Nalbuphine,

Group 3: (n = 30) bupivacaine (3 ml) + 0.5 ml (0.5 mg) Butorphanol.

All the patients were subjected to detailed pre-anaesthetic evaluation with clinical history, thorough physical and systemic examination, routine investigation which include complete blood count, urine (routine and microscopy), blood sugar, renal function test, serum electrolytes, X-ray chest PA view, ECG and any special investigation if required was done for the study. An informed written consent was taken from all the patients after explaining every patient in detail regarding nature and purpose of the study and also for the possible risks and complications. 0-10 point visual analogue scale (VAS) on a sheet of paper, where (0) labeled as (no pain) and (10) as (worst possible pain) was also explained.

A) Criteria for Inclusion

1. Patients of ASA I & ASA II.
2. Age group 18- 50 years of either sex.
3. Patients with average height (> 5 feet) & average weight (50-70 kg).
4. All patients going for elective infra umbilical surgeries.

B) Criteria for Exclusion

1. Patient refusal or not giving consent.
2. Patients in whom regional anaesthesia is contraindicated:
   a) Suffering from coagulopathy, blood dyscrasias and on anticoagulant therapy.
   b) Aortic and mitral stenosis
   c) Increased intra cranial pressure.
   d) Haemorrhagic shock / Hypovolemia.
3. Patient with allergy to study drugs (bupivacaine, nalbuphine or butorphanol).
4. Patient with hepatorenal, cardiovascular, respiratory or psychiatric disorders.
5. Patients with skin sepsis and spinal deformity.
6. Uncontrolled or labile hypertension.

Anaesthesia Technique: In the operation theater patients were kept in supine position, an I.V. cannula (18G) was inserted. Before starting the

procedure all the monitoring equipments (like NIBP Cuff, Pulse Oxymetry finger probe, ECG) were attached to the patient and baseline values of Heart rate, BP, SpO_2 and Respiratory rate were recorded. Patient was premedicated with inj.midazolam (0.05 mg/kg), glycopyrrolate (0.02 mg/kg), ondensetron intravenously, half an hour prior to induction. In operating room each patient received intravenous ringer lactate solution 10 ml/ kg before induction of subarachnoid block and infusion was continued during surgery. After strict aseptic precautions, skin and subcutaneous tissue was infiltrated with 2% inj. Lignocaine, then subarachnoid block was performed in sitting position. Using midline approach with 25G spinal needle in L_3-L_4 intervertebral space. After the appearance of free flow of CSF, the mixture of drugs according to assigned group was injected. Utmost care was taken to avoid any leakage of any of these drugs. The spinal needle was removed and patient was immediately turned to supine position.

Monitoring And Management

1. Pulse rate, BP, Respiratory Rate, SpO_2, pain score, discomfort and occurrence of side effects were recorded intraoperatively at 0, 5, 10, 15 min and after that every 15 min till the end of surgery. All the parameters were compared with baseline (pre-operative) value. Changes in these parameters were recorded and mean changes in each group at different period of observations were calculated for group comparison.
2. The intensity of pain was assess by Visual analogue Scale (VAS) at the end of surgery, then every 1 hour till 1st 6 hours, then after every 6 hours till 24 hours.
3. RR- Respiratory rate was monitored intra operatively in all the patients. Any variations from the pre-operative readings were recorded in the proforma.
4. Recovery room complications such as nausea/vomiting, hypotension, bradycardia, sedation, desaturation, pruritus, respiratory depression etc. Treatment was given for managing complication as and when occurs.

Hemodynamic Changes

- Any reduction in mean arterial pressure more than 20% from baseline or <90 mmHg was recorded and treated with increasing dose of fluids and 5-10 mg of intravenous administration of bolus dose of inj. mephentermine sulphate 6 mg as and when required.
- Bradycardia (Heart rate <60/min) was treated with inj.atropine (0.6 mg) i.v. as and when required.
- RR less than 10/ min and SpO_2 less than 90% was considered as significant respiratory depression.

Onset, height and duration of sensory block were assessed by pin prick method. Assessment of sensory and motor characteristics of subarachnoid block was done at 30 seconds interval till the peak of the blockade achieved.

A. Sensory Block (Grading) was assessed by pin prick method.

0. -sharp pin feel

1. -analgesia, dull sensation felt

2. -anaesthesia, no sensation felt.

B. Modified Bromage Score [3]: The onset, duration and degree of Motor Block was assessed by

Score Criteria

1. - Complete block (unable to move feet or knees)
2. - Almost complete block (able to move feet only)
3. - Partial block (just able to move knees)
4. - Detectable weakness of hip flexion while supine (full flexion of knees)
5. - No detectable weakness of hip flexion while supine
6. - Able to perform partial knee bend.

C. Quality of Block: assessed by grading

Grade 1 - (unsuccessful) patient needs general anaesthesia.

Grade 2 - (moderate) complaints that require supplemental analgesia.

Grade 3 - (good) minor complaints with no need of supplemental analgesia.

Grade 4 - (excellent) no complaints.

The duration of analgesia was recorded as the time from intrathecal injection of the drug until the patients complaining of pain or from the time of regression of sensory block level by two dermatomal segments and required additional analgesia in postoperative period which was assessed by visual analogue score of ≥ 4. Rescue analgesic used was Inj. Diclofenac Sodium 75 mg

intravenously and time for first rescue analgesic given was also noted down.

- *Visual Analogue Scale (Duration of Effective analgesia): 0 - no pain and 10 - worst pain*

Postoperative monitoring for pain was assessed by VAS Score (0-10) at the end of surgery, then every 1 hour till 1st 6 hours, then after every 6 hours till 24 hours. The duration of analgesia was assessed group-wise and compared [4].

Sedation was assessed by *RAMSAY Sedation score*

1 - Anxious agitated

2 - Cooperative, oriented & serene

3 - Sleeping, drowsy & responding easily to commands

4 - Sleeping & responding to stimuli on glabella

5 - Sleeping & responding slowly to stimuli on glabella

6 - Sleeping without response to pressure on glabella.

Statistical Analysis: Statistical analysis was done using computer software (SPSS version 20; Chicago Inc., USA). Data comparison was done by applying statistical tests to find out the statistical significance of the comparisons. The qualitative data of study groups were expressed in proportion and percentages and the quantitative data expressed as mean and standard deviations. The difference in proportion was analyzed by one way ANOVA test and the inter group difference in means were analyzed by using post –hoc Tukey test. Significance level for tests was determined as $p < 0.05$.

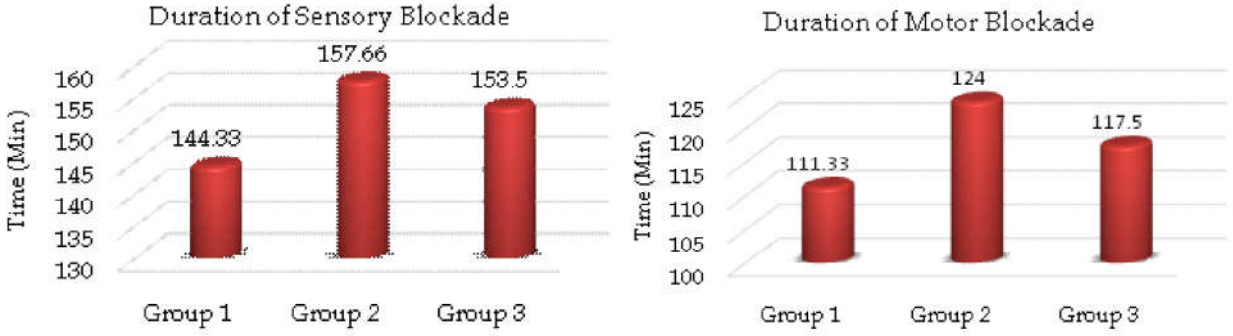
Results

Table 1: Demographic Profile of Patients in three Different Groups

Parameter	Group 1		Group 2		Group 3		p Value
	Mean	±SD	Mean	±SD	Mean	±SD	
Age (18-50 Yrs)	34.47	8.48	33.8	7.87	34.9	5.97	0.85
Height (in cm)	159.86	3.78	159.56	3.63	160.66	3.79	0.50
Weight (in Kg)	57.27	9.34	57.1	8.99	55.23	7.90	0.61
Duration of surgery (mins.)	110.33	16.07	110.67	23.03	115.67	15.01	0.456

Table 2: Table Showing Comparision of Onset Time and Duration of Sensory & Motor Blockade

Parameters	Group 1		Group 2		Group 3		p Value
	Mean	±SD	Mean	±SD	Mean	±SD	
Onset of sensory blockade (min.)	4.72	0.57	4.58	0.54	4.68	0.51	0.49
Duration of sensory blockade (min.)	144.33	7.51	157.66	12.43	153.5	11.30	0.00001
Onset of motor blockade (min.)	5.82	0.56	5.7	0.56	5.83	0.63	0.635
Duration of motor blockade (min.)	111.33	6.15	124	7.12	117.50	8.25	<0.00001

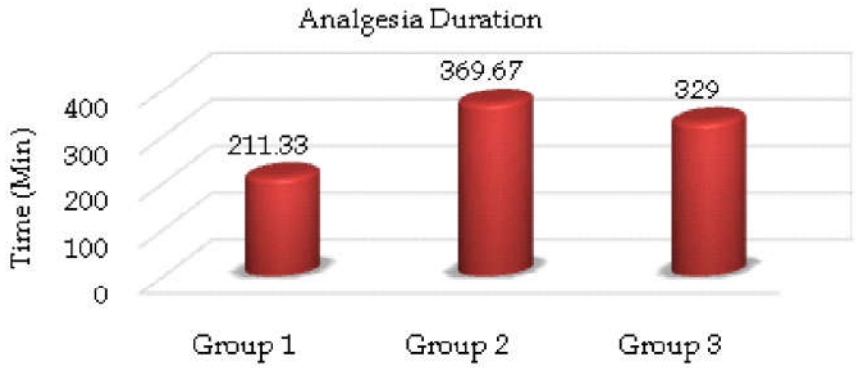


Graph 1 & 2: Bar Diagram Showing Comparision of Durationof Sensory & Motor Blockade

Table 3, Graph 3: Showing Duration of Analgesia (Min.) in three Different Groups

Parameters	Group 1		Group 2		Group 3		p Value
	Mean	±SD	Mean	±SD	Mean	±SD	
Duration of Analgesia (min.)	211.33	23.59	369.67	24.74	329	60.30	<0.00001

Table showing duration of analgesia (Mean ± SD) of three different groups. [statistically significant ($p < 0.001$)]



Graph 3:

Table 4: Intergroup Statistical Comparision of Duration of Analgesia in 3 Different Groups

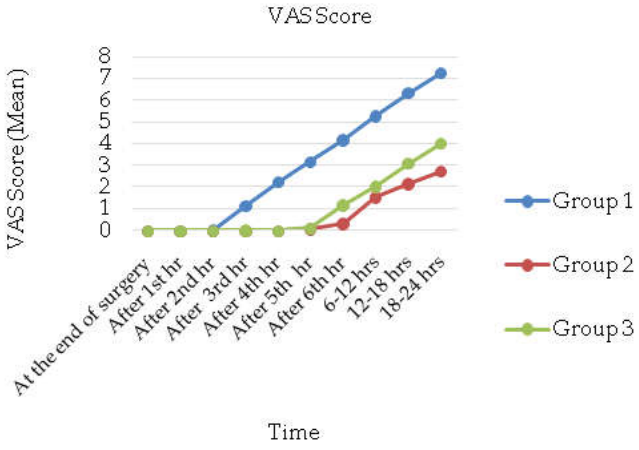
Treatments pair	Tukey HSD p-value	Tukey HSD inferfence
1 vs 2	0.0010053	*p < 0.01
1 vs 3	0.0010053	*p < 0.01
2 vs 3	0.0010053	*p < 0.01

Table 5: Showing Quality of Block in three Different Groups

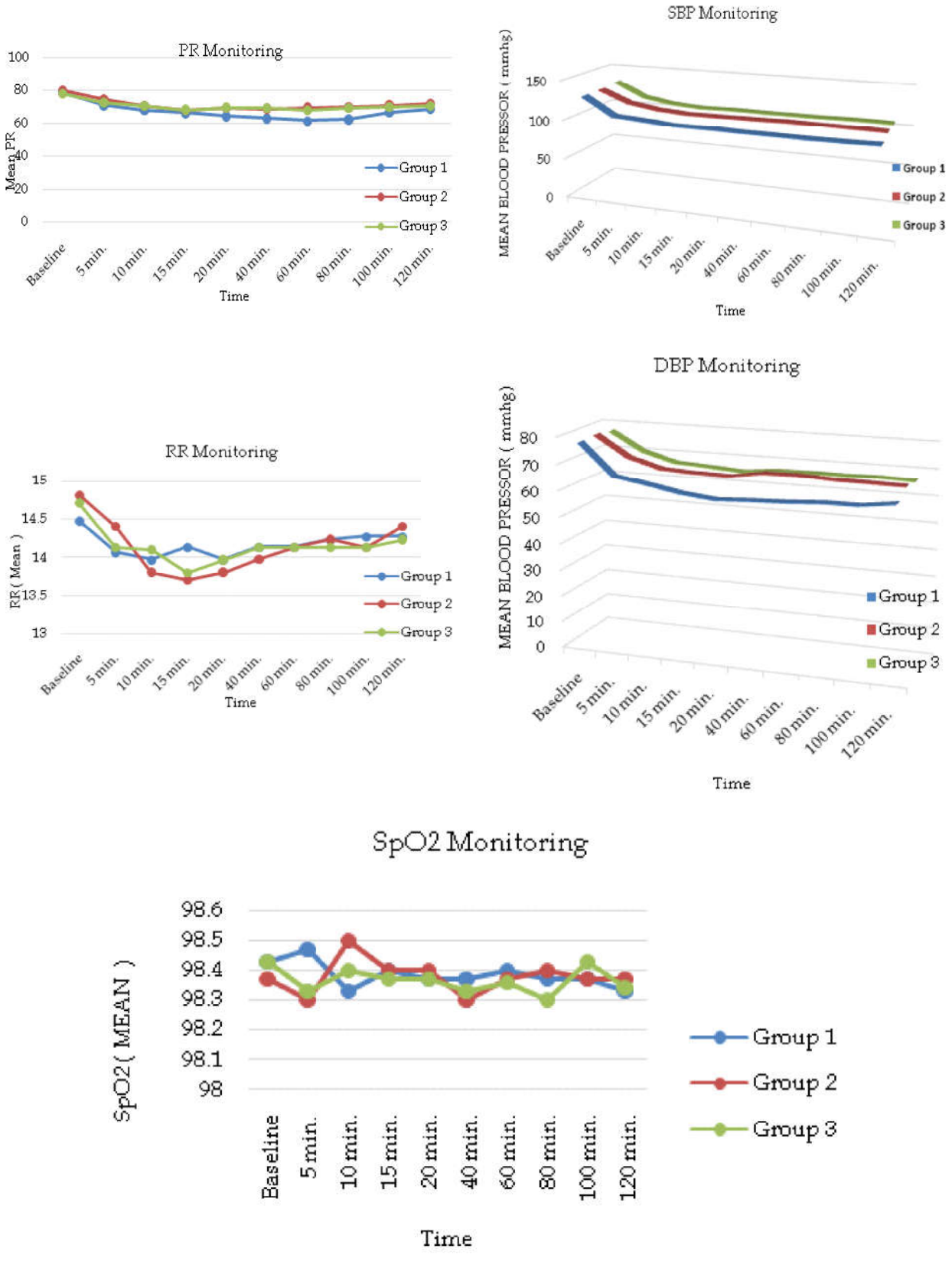
Parameter	Group 1		Group 2		Group 3		P Value
	Mean	±SD	Mean	±SD	Mean	±SD	
Quality Score	2.83	0.79	3.83	0.46	3.43	0.68	<0.00001

Table 6, Graph 4: Table & Line Diagram Showing Statistical Analysis of VAS Score in three Different Groups

VAS Score	Group 1		Group 2		Group 3		P Value
	Mean	±SD	Mean	±SD	Mean	±SD	
At the end of surgery	0.00	0.00	0.00	0.00	0.00	0.00	NA
After 1st hr	0.00	0.00	0.00	0.00	0.00	0.00	NA
After 2nd hr	0.03	0.18	0.00	0.00	0.00	0.00	0.372
After 3rd hr	1.13	0.34	0.00	0.00	0.03	0.18	< 0.00001
After 4th hr	2.23	0.43	0.03	0.18	0.07	0.25	< 0.00001
After 5th hr	3.17	0.38	0.07	0.25	0.1	0.40	< 0.00001
After 6th hr	4.17	0.38	0.33	0.54	1.17	0.38	< 0.00001
6-12 hrs	5.27	0.52	1.53	0.68	2.03	0.56	< 0.00001
12-18 hrs	6.33	0.60	2.13	0.82	3.1	0.55	< 0.00001
18-24 hrs	7.23	0.67	2.7	0.95	4.0	0.64	< 0.00001



Graph 4:



Graph 5 (A,B,C,D & E): Line Diagram Showing Hemodynamic Variation in three Different Groups

Table 7: Showing Comparison of Sedation Score in three Different Groups

Parameter	Group 1 [n=30]		Group 2 [n=30]		Group 3 [n=30]	
Sedation Score	**N**	**%**	**N**	**%**	**N**	**%**
1	17	56.66%	0	0.00%	0	0.00%
2	13	43.33%	0	0.00%	0	0.00%
3	0	0.00%	13	43.33%	4	13%
4	0	0.00%	12	40%	11	36.66%
5	0	0.00%	5	16.66%	14	46.66%
6	0	0.00%	0	0.00%	1	3.33

Table 8: Showing Side Effects and Complications in three Different Groups

Side effects	Group 1 [n=30]	Group 2 [n=30]	Group 3 [n=30]	Total [n=90]	p value
Hypotension	8	3	4	15	0.160
	26.6%	10 %	13.3%	16.6%	
Bradycardia	2	2	2	6	1.00
	6.6%	6.6%	6.6%	6.6%	
Respiratory depression	0	0	0	0	Na
	0.0%	0.0%	0.0%	0.0%	
Pruritus	0	0	1	1	0.372
	0.0%	0.0%	3.3%	1.1%	
N/V	1	1	1	3	1
	3.3%	3.3%	3.3%	3.3%	
PDPH	0	0	0	0	Na
	0%	0%	0%	0%	

Discussion

Spinal anaesthesia is the preferred technique for most of lower abdomen and lower limb surgeries. It allows the patient to remain awake, minimizes or completely avoids the problem associated with airway management during general anesthesia. Low dose bupivacaine although reduces the cardiovascular effects, it was notenough to provide adequate level of sensory blockade and prolonged postoperative analgesia. ITO used as adjuncts are capable of producing analgesia of prolonged duration but allow early ambulation of patients because of their sympathetic and motor nerve-sparing activities [2,7,9].

There are only few studies of neuraxial administration of nalbuphine that have shown to produce a significant analgesia accompanied by minimal pruritus and respiratory depression [10-13]. There are many studies of neuraxial administration of butorphanol that have shown to produce a significant analgesia and sedation as compare to other drugs [14,15].

Bupivacaine: Bupivacaine acts mainly by blockade of voltage gated Na+ channels in the axonal membrane and presynaptic inhibition of calcium channels. It reversibly decreases the rate of depolarization and repolarization of excitable membranes [5].

Nalbuphine: Nalbuphine is a semi-synthetic opioid agonist-antagonist used as an analgesic. Nalbuphine binds with high affinity to the μ-opioid receptor and κ-opioid receptor and has relatively low affinity for the δ-opioid receptor. It behaves as a moderate-efficacy partial agonist (or mixed agonist-antagonist) of the μ-opioid receptor and as a high-efficacy partial agonist of the κ-opioid receptor. Activation of supraspinal and spinal κ receptors results in limited respiratory depression, and sedation. It is particularly advantageous because of the potential to maintain or even enhance opioid-based analgesia while simultaneously eliminating the common μ-opioid side effects [3,4]. Kappa receptors are distributed throughout the brain and spinal cord, responsible for nociception. Nalbuphine binds intensely to kappa-receptors in these areas to produce analgesia [6,7].

Butorphanol: Butorphanol is a synthetic opioid analgesic, shows partial agonist and antagonist activity at the μ opioid receptor, as well as competitive antagonist activity and partial agonist activity at the κ opioid receptor. Stimulation of these receptors on CNS neurons leads to intracellular inhibition of adenylatecyclase, closing of influx membrane calcium channels, and opening

of membrane potassium channels. This will result in hyperpolarization of the cell membrane potential and suppression of action potential transmission of ascending pain pathways. Additionally, κ agonism of butorphanol can cause dysphoria at therapeutic or supertherapeutic doses; this gives butorphanol a lower potential for abuse than other opioid drugs [7,8].

Both butorphanol and nalbuphine exert their action by opening K+ channels and reducing the Ca++ influx, resulting in inhibition of transmitter release. A combination of these effects may explain the observed synergism between bupivacaine and butorphanol/nalbuphine. The synergism is characterized by enhanced somatic analgesia without an effect on the degree of level of local anaesthetic induced sympathetic or motor blockade.

We chose the dose 0.5 mg of Nalbuphine as this dose provided better postoperative analgesia with significantly lower side effects compared to other doses, which has been concluded from previous studies [13].

After applying one way ANOVA test on the data, the p value obtained was statistically insignificant ($p>0.05$). Thus the randomly selected groups were similar in terms of age ($p = 0.849$), height ($p = 0.502$), weight ($p = 0.610$), duration of surgery ($p = 0.456$), sex ($p = 0.552$) and ASA grade ($p = 0.870$) as their difference is statistically insignificant and therefore they are comparable for this study.

Sensory & Motor Blockade

1. Onset of sensory blockade ($p=0.49$) & motor blockade ($p=0.635$) were found to be statistically insignificant ($p>0.05$), shows no difference of mean time of onset of sensory & motor blockade between Group 1, 2 & 3. On inter group analysis of onset of sensory & motor blockade in three groups with the help of post hoc TUKEY test, were statistically insignificant ($p > 0.05$).

2. Duration of sensory blockade was found to be statistically significant as $p =0.00001$ ($p<0.05$), shows significant difference of mean time of duration of sensory blockade between Group 1, 2 & 3. On inter group analysis, difference of duration of sensory blockade between group 1 vs 2 and group 1 vs 3 were statistically significant p (< 0.01), whereas between group 2 vs 3 it was insignificant ($p > 0.01$). Though duration of sensory blockade is prolonged in both group 2 & 3, but it is more prolonged in Group 2.

3. Duration was found to be statistically significant in all three groups as $p< 0.00001$. On inter group analysis, difference of duration of motor blockade between group 1 vs 2, between group 1 vs 3 and between group 2 vs 3 were statistically significant p (< 0.01). Though duration of motor blockade is prolonged in both group 2 & 3, but it is more prolonged in Group 2.

Duration of Analgesia: The duration of analgesia as assessed by VAS score was prolonged in Group 2 & 3 as compared to Group 1 which was statistically significant as $p= 0.00001$ ($p<0.05$). On intergroup analysis, difference between group 1 vs 2, between group 1 vs 3 and between group 2 vs 3 were statistically significant ($p < 0.001$). Though duration of analgesia is prolonged in both group 2 & 3, but it is more prolonged in Group 2.

Quality of Block: The quality of block as assessed by Quality Score was high in Group 2 & 3 as compared to Group 1, ($p < 0.00001$). On intergroup comparison these changes were found to be statistically significant between group 1 vs 2 and group 1 vs 3 $p= 0.001$ ($p<0.01$) but statistically insignificant between group 2 vs 3 ($p = 0.05388$). So the quality of block is better in group 2 & 3.

Sedation Score: It was found that inj. nalbuphine and inj.butorphanol added to inj. Bupivacaine causes more sedation than inj. Bupivacaine alone which is statistically significant ($p<0.00001$). On inter group analysis, difference of sedation between group 1 vs 2, between group 1 vs 3 and between group 2 vs 3 were statistically significant ($p < 0.01$). Thus it was found that inj. butorphanol added to inj. Bupivacaine causes more sedation than inj. nalbuphine added to inj. Bupivacaine which is statistically significant ($p < 0.01$).

Hemodynamic Parameters

a) *Pulse Rate:* Changes in pulse rate in Group 1, 2 & 3 were remain statistically insignificant ($p > 0.01$) upto 15 mins. After subarachnoid block but there after differences were become statistically significant. ($p < 0.01$) in group 1, 2 & 3. On inter group analysis, difference in change in pulse rate between group 1 vs 2 and between group 1 vs 3 remain insignificant up to 15 mins after subarachnoid block but it become significant afterward ($p <0.01$). In group 1 PR goes on decreasing or change is significant ($p <0.01$) whereas in group 2 & 3 changes in pulse rate were remain insignificant as ($p >0.01$). So the pulse rate remains stable in group 2 & 3 throughout the surgery and in postoperative period also.

b) *Systolic Blood Pressure:* There was significant fall in the systolic blood pressure in Group 1 as compare to group 2 & 3 ($p<0.01$). On statistical analysis these changes were significant in Group 1. On intergroup analysis changes in SBP between Group 1 & 2 and Group 1 & 3 were statistically significant. ($p \geq 0.01$), whereas between Group 2 & 3 were statistically insignificant ($p \leq 0.01$), so the SBP remains stable in group 2 & 3 throughout the surgery and in postoperative period also.

c) *Diastolic Blood Pressure:* There was significant fall in the diastolic blood pressure in Group 1 as compare to group 2 & 3 ($p<0.01$). On statistical analysis these changes were significant in Group 1. Group 2 and 3 changes in mean Diastolic Blood Pressure were insignificant from basal value till the end of surgery. On statistical analysis these changes were statistically insignificant in both the Groups.On intergroup analysis changes in DBP between Group 1 & 2 and Group 1 & 3 were statistically significant. ($p \geq 0.01$), whereas between Group 2 & 3 were statistically insignificant ($p \leq 0.01$), so the DBP remains stable in group 2 & 3 throughout the surgery and in postoperative period also.

d) *Respiratory Rate:* Changes in respiratory rate between Group 1, 2 & 3 were statistically insignificant. ($p \geq 0.05$) even on inter group analysis.

c) *SpO_2:* Changes in SpO_2 between Group 1, 2 & 3 were statistically insignificant. ($p \geq 0.05$) even on inter group analysis.

The difference in mean pulse rate, mean systolic blood pressure, mean diastolic pressure, mean respiratory rate and mean SpO2 in all three groups in whole of the study is not statistically significant ($p > 0.05$). So we concluded that Butorphanol and Nalbuphine when used intrathecally have stable and similar haemodynamic characteristics.

Side Effects: In present study incidence and frequency of side effects and complications were closely monitored perioperatively as well as postoperatively.

- *Bradycardia:* There were 2 patients in each group i.e. 1, 2 & 3 respectively; who had suffered with bradycardia, which was effectively treated by inj. Atropine 0.6 mg i.v.
- *Hypotension:* There were 8 patients in group 1, 3 patients in group 2 and 4 patients in group 3, who had suffered with hypotension, it was transient and treated by i.v. fluids and inj. Mephentermine sulphate 6 mg i.v. Hypotension was seen more pronounced in patients of group 1; whereas patients in group 2 & 3 were remain stable hemodynamically throughout surgery and thereafter.
- *Nausea And Vomiting:* There were 1 patient in each group i.e. 1, 2 & 3 respectively; who had suffered with nausea and vomiting but that was not severe and the difference is insignificant.
- *Pruritus:* There was only 1 patient in group 3, but that was very mild and not required any treatment.
- *Respiratory depression:* None of the patient was suffered with respiratory depression in this study.
- There was no incidence of PDPH in any patient. No incidence of urinary retention could be identified as all patients were catheterized intraoperatively till postoperative period.

All three groups have no statistically significant ($p > 0.05$) incidence of complications which is similar to other studies.

Conclusion

There was no study protocol deviation and all patients successfully completed the study protocol and were cooperative with subsequent assessment. Hence, all patients were included for data analysis. Surgical procedures were performed uneventfully and there were no surgical or anaesthetic complications.

Following conclusions are drawn from the present study:

1. Onset of sensory and motor blockade remain similar with bupivacaine added with inj. Butorphanol, with inj. Nalbuphine and with NS.
2. Duration of sensory and motor blockade prolongs with inj. Nalbuphine and inj. Butorphanol as compare to bupivacaine with NS and more with inj. Nalbuphine as compare to inj. Butorphanol.
3. Duration of analgesia prolongs with inj. Nalbuphine and inj. Butorphanol as compare to bupivacaine with NS and more with inj.

Nalbuphine as compare to inj. Butorphanol.

4. Quality of block becomes better with inj. Nalbuphine and inj. Butorphanol as compare to bupivacaine with NS; and remains same with inj. Nalbuphine and inj. Butorphanol.
5. Hemodynamic parameters (Pulse rate, Systolic blood pressure, Diastolic blood pressure, respiratory Rate and SpO_2) remain stable throughout the surgery and postoperatively with inj. Nalbuphine and inj. Butorphanol as compare to bupivacaine with NS.
6. Sedation remains much better with inj. Nalbuphine and inj. Butorphanol as compare to bupivacaine with NS; and remains more with inj. Butorphanol as compare to inj. Nalbuphine.
7. There was no significant occurrence of complications or any other side effects in all three groups when used intrathecal as adjuvants to inj. Bupivacaine.

Thus, from our study we conclude that intrathecal inj. Bupivacaine combination with inj. Nalbuphine is better than inj. Bupivacaine combination with inj. Butorphanol in respect to the duration of sensory & motor blockade, quality of anaesthesia and duration of analgesia (requirement of rescue analgesia) without any significant increase in adverse effects, whereas sedation remains more with inj. Butorphanol as compare to inj. Nalbuphine.

So that both study drugs can be used intrathecally along with hyperbaric Bupivacaine to effectively prolong duration of postoperative analgesia but prolongation is more with Nalbuphine than with Butorphanol. To conclude, both Nalbuphine and Butorphanol in combination with 0.5% hyperbaric bupivacaine (3 ml) are efficacious in patients undergoing lower limb orthopaedic surgeries instead of bupivacaine alone.

So, finally we have concluded from this study that inj. *Nalbuphine* is more efficacious than inj. *Butorphanol* as an adjuvant with bupivacaine.

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