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Clinical Evaluation of Adding Fentanyl versus Dexmedetomidine to Intrathecal Isobaric Levobupivacaine on Spinal Block Characteristics in Patients Scheduled for Lower Abdominal Surgeries

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Abstract

Background: Fentanyl, an opioid and dexmedetomidine, an alpha 2 agonist added to local anaesthetics in spinal anaesthesia potentiates local anaesthetics action, have analgesic properties and reduces the requirement of local anaesthetics. *Aim:* To evaluate the effect of adding fentanyl and dexmedetomidine to intrathecal isobaric levobupivacaine. *Materials and Methods:* 60 patients scheduled for lower abdominal surgeries at our institute belonging to ASAgrade I-II satisfying inclusion criteria were recruited for the study and randomised to receive levobupivacaine 15mg with dexmedetomidine 5µg in group LD or levobupivacaine 15mg with fentanyl 25 µg in group LF. Sensory and motor block characteristics, haemodynamic changes and side effects were recorded. *Results:* Onset of sensory block was shorter, time taken to attain maximum sensory block was shorter in group LD as compared to group LF with no stastistical significance. Maximum sensory block achieved was T4 in both the groups. Onset of motor blockade was faster and time taken to attain maximum bromage score 3 was faster in group LD as compared to group LF. Two segment regression duration, duration of analgesia, duration of sensory blockade and motor blockade were stastistically significantly prolonged in group LD as compared to groupLF. Patients maintained haemodynamic stability. Sedation scoring and side effects were insignificant. Data was analysed using Chi-square test and Independent t test. *Conclusion:* Dexmedetomidine as an adjuvant to isobaric levobupivacaine for spinal anaesthesia fastens sensory, motor onset and enhances the block duration without any significant side effects as compared to fentanyl.

Keywords: Isobaric Levobupivacaine; Dexmedetomidine; Fentanyl; Spinal Anaesthesia.

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Introduction

Spinal anaesthesia is a safe inexpensive common technique used to perform infraumbilical surgeries. It provides excellent surgical anaesthesia and prolongs post operative pain relief by the use of adjuvants with local anesthetics. It provides better operative pain relief and attenuates autonomic, somatic and endocrine responses [1].

Bupivacaine is available as a racemic mixture of its enantiomers, dextrobupivacaine and levobupivacaine. It has been found that dextro enantiomer is the cause for cardiotoxicity and the levobupivacaine the pure S (-) enantiomer does not have the cardiotoxicity. Levobupivacaine has similar pharmacodynamic properties of racemic bupivacaine but a documented reduced central nervous system and cardiovascular toxicity [2, 3,4]. It has emerged as a safer alternative for regional anaesthesia than its racemic parent in recent years [2,3].

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Different drugs like opioids and non- opioids are used as adjuvant drugs along with local anaesthetic agents [2]. Opioids and alpha2-receptor agonists are important as neuraxial adjuvants not only to improve the quality of perioperative analgesia but also to minimize the local Anesthetic dose, particularly in high-risk patients and in ambulatory procedures [5]. Opioids when given along with local anaesthetics prolongs sensory block without any prolongation in motor and sympathetic blockade.

Fentanyl is a potent mu opioid receptor agonist with improved analgesia overmorphine [6].The addition of fentanyl 10-15 microgram demonstrates a sparing effect on the requirement of levobupivacaine while maintaining excellent clinical efficacy with less hemodynamic variation [7,8,9]. Álpha-2 adrenoreceptor agonists have sedative, analgesic and haemodynamic stabilizing effect hence they have been used as additives to local anaesthetics. They are also found to decrease the sympathetic tone, attenuate stress response to surgery and anaesthesia and also prolong the duration of spinal block [10].

Dexmedetomidine being an alpha-2adrenergic agonists is pharmacologically related to clonidine, was approved by FDA in the year 1999 for its usage as analgesic and sedative [11]. Dexmedetomidine is a highly selective alpha 2 agonist. It has 10 times more affinity for alpha 2 receptors than clonidine. It potentiates local anaesthetic effect, prolongs postop analgesia and has a dose dependent sedative effect without respiratory depression [12].

Here we have designed a randomized clinical study to evaluate and compare the efficacy of addition of fentanyl or dexmedetomidine to levobupivacaine intrathecally in patients scheduled for lower abdominal surgeries.

Objectives

To compare the time taken for the onset, duration of sensory and motor block, two segment regression duration, total duration of analgesia, haemodynamic changes, sedation scoring, any side effects and complications following intrathecal administration of 15 mg of 0.5% isobaric levobupivacaine with either of 25 μg fentanyl or 5μg dexmedetomidine in patients undergoing lower abdominal surgeries.

Material and Methods

After obtaining the permission from institutional ethical committee, 60 patients scheduled for lower abdominal surgeries under spinal anaesthesia aged Between 20 to 60yrs with ASA physical status grade I –II were recruited for this prospective randomized, double blind controlled clinical study. Patient refusal for surgery, unco-operative patient, patients of age less than 20 years and more than 60 years, ASA grade III, IV and V, pregnant females, emergency surgeries, diabetes, hypertension, morbid obesity, local infection, hypovolemic shock, bleeding and clotting disorders, emergency surgeries, known allergy to any of the test drugs, pre-existing neurological deficits in the lower extremities, respiratory, neurological, psychological, hepatic and renal disease were excluded from the study. Informed written consent was obtained from all the patients. Patients were randomly allocated into 2 groups of 30 each using computer generated randomization table.

Group LD: 5μg dexmedetomidine was added to15 mg of 0.5% isobaric levobupivacaine intrathecally.

GroupLF: 25 μg fentanyl was added to15 mg of 0.5% isobaric levobupivacaine intrathecally.

Total volume of drug was 3.5 ml.

One day prior to surgery, preanaesthetic check-up was done for each patient, advised nil by mouth for solids at least 6hrs and clear fluids 2 hrs before surgery premedicants tablet ranitidine 150mg and tablet alprazolam 0.5mg were given at night.

On the day of surgery in the preoperative room, an intravenous line was secured with 18 gauge cannula and preloaded with 10 ml/kg ringer lactate solution half an hour before anaesthesia. After shifting the patient on to the ot table multiparameter monitor having pulse oximetry, ECG and NIBP was connected.

Under aseptic precautions spinal block was performed on patients at level of L3-L4 through a midline approach using 25G Quincke spinal needle in lateral position and study drug was injected with operative table kept flat. Immediately patients were turned to supine posture. The completion of the injection was taken as zero time of anaesthesia.

Parameters such as onset of sensory blockade (when patient does not feel pin pick at T10 level) and motor blockade, maximum level of sensory and motor blockade attained and the time taken for the same, two segments sensory regression time, total duration of analgesia(time at which patient demanded first dose of rescue analgesic,VAS >4) , total duration of sensory blockade(regression to S1dermatome)and motor blockade (recovery to

bromage 0), level of sedation, total duration of surgery and if any side effects like nausea vomiting, hypotension and bradycardia were noted.

Sensory blockade was tested in midclavicular line both the sides using pinprick method with a blunt tipped 27G needle. Quality of motor blockade was assessed by modified Bromage scale [13]. (Bromage 0 – patient is able to move the hip, knee and ankle, Bromage 1- patient is unable to move the hip but is able to move the knee and ankle, Bromage 2 – patient is unable to move the hip and knee but is able to move the ankle,Bromage 3- patient is unable to move the hip, knee and ankle). Level of sedation was assessed by Ramsay sedation scale [14].

Scale 1–patient is anxious, agitated or restless, Scale 2–patient is co-operative, oriented and tranquil alert, Scale 3- patient responds to commands, Scale 4 –patient is asleep but with brisk response to light glabellar tap or loud auditory stimulus, Scale 5- patient is asleep with sluggish response to light glabellar tap or loud auditory stimulus, Scale 6– patient is asleep, with no response.

Haemodynamic monitoring was done initially before block, after the block every 5 mins for first 15 mins and every 10 mins for next 60 mins and once in 15 mins till the end of surgery and every hour post operatively in PACU. Hypotension was defined as mean arterial pressure falling more than 20% mm Hg of preoperative value or SBP less than 100 mmHg and was treated by increasing the fluid infusion and with inj. mephenteramine 3-6 mg in bolus doses and bradycardia was defined as heart rate less than 60 beats/min and was treated with 0.6mg of inj. Atropine [12].

Post operative pain was assessed by Visual Analogue Scale (VAS), duration of analgesia was assessed by VAS scores, rescue analgesic Inj diclofenac 75mg intramuscularly was given if VAS was more than 4.

Statistical Analysis

Statistical Analysis was done using SPSS, Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version (IBM SPSS Statistics, Somers NY, USA) software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

Result

In our study, demographic profile was comparable among both the groups as depicted in the Table 1.

Time taken for the onset of sensory block to achieve T10 level and time taken for maximum sensory blockade were shorter in group LD as compared to group LF with no statistical significance between the groups (p=0.125 and p=0.123 respectively).There was no difference between the groups with regard to maximum level of sensory blockade (p=0.960) as shown in table 1. Maximum sensory level attained in both the groups was T4 accounting up to 6.7% in each group . In groupLD and group LF majority of subjects had maximum level of sensory block at T6 level (53.3% and 50% respectively).

Ttime taken for the onset of motor block and time taken for maximum motor blockade were faster in group LD as compared to group LF but there was no statistical significant difference between the groups (p=0.42 and p=0.262 respectively). Maximum motor blockade attained in both the groups was bromage 3 (Table 2).

The time taken for sensory regression by two segments, total duration of analgesia, total duration of sensory blockade and total duration

Table 1: Demographic profile of patients in group LD and group LF

Parameters	Group LD	Group LF	P value
Mean age in years	42.7 ±10.4	39.4±12.6	0.274
Sex ratio in %			
Male	15(50%)	15(50%)	1
Female	15(50%)	15(50%)	1
Mean weight in kgs	80.2±8.2	79.6±8.4	0.426
Mean height in cms	175.7±3.6	170±6.2	0.086
Mean duration of surgery in minutes	94.7±37.3	68±40.5	0.01

Table 2: Sensory, Motor block and Analgesia

Parameters	Group LD	Group LF	P value
Onset of sensory block to T10 dermatome in mins	2.1±1.0	2.6±1.3	0.125
Time taken to achieve maximum Sensory Block in mins	7.3±2.4	8.5±3.3	0.123
Onset of motor block in mins	1.6±0.9	1.8±1.0	0.420
Time taken to achieve maximum motor block in mins	5.4±3.0	6.4±3.6	0.262
Time taken for sensory regression by two segments in mins	135.8± 22.0	98.5± 24.7	<0.001*
Total duration of analgesia in mins	411.43 ±18.81	212.00±21.94	<0.001*
Total duration of sensory blockade in mins(S1segment regression)	486.72 ±22.0	272.00±12.3	<0.001*
Total duration of motor blockade in mins	355.14±1 7.38	170.57±22.74	<0.001*

*P value significant

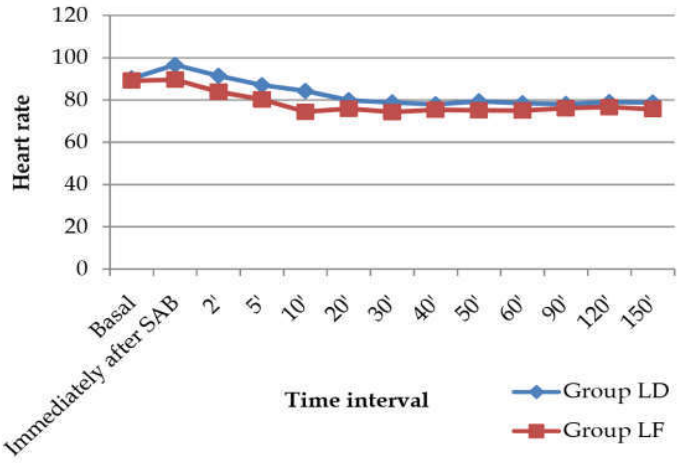

Fig. 1: Line diagram showing heart rate comparison between two groups at various intervals of Follow-up

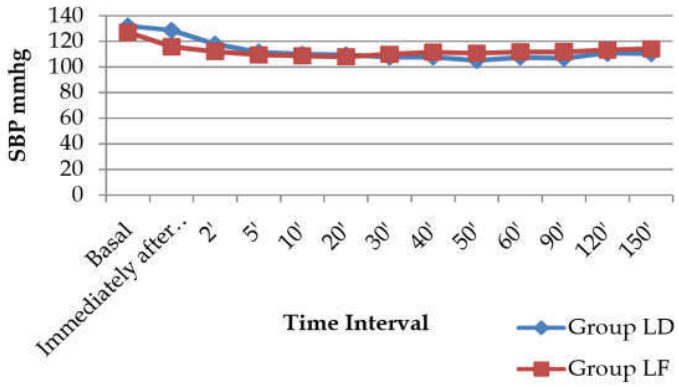

Fig. 2: Line diagram showing SBP comparison between two groups at various intervals of Followup

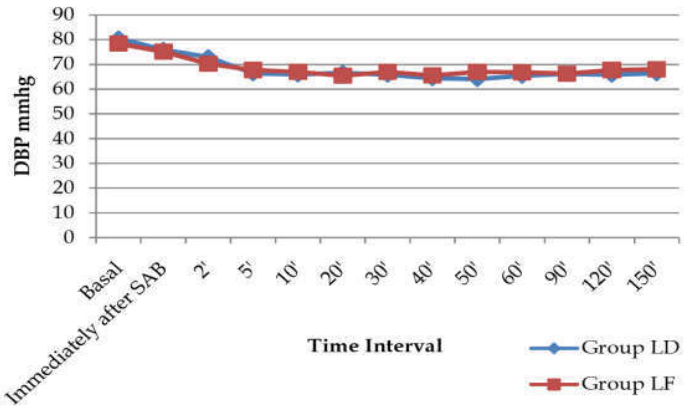

Fig. 3: Line diagram showing DBP comparison between two groups at various intervals of Followup

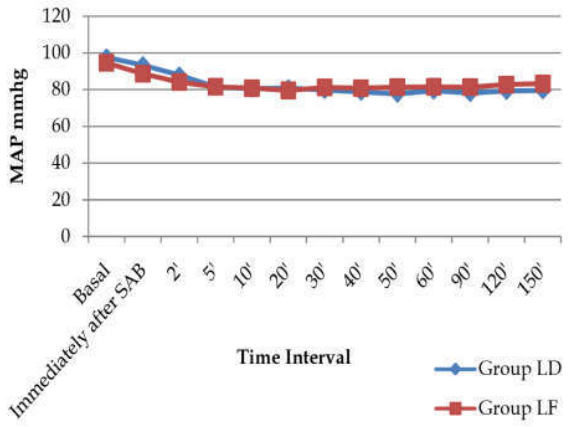

Fig. 4: Line diagram showing MAP comparison between two groups at various intervals of followup

of motor blockade were statistically significantly prolonged ($p< 0.001$) in group LD as compared to group LF (Table 2).

Patients hemodynamics were monitored at varying intervals starting from baseline till 24 hours , there was no significant change with regard to heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure as depicted in figures 1,2,3 and 4. Bradycardia was noted in about 5 patients (16.6%) in group LD and 2 patients (6.6%) in group LF within first 30 mins of spinal block intraoperatively , was treated with inj atropine 0.6mg intravenously. Hypotension was noted in 3 patients (10%) in group LD and 2 patients (6.6%) in group LF, patients were treated with oxygen, i.v fluids and inj.mephentramine as 6mg incremental doses. The sedation score was 2 in both the groups. Respiratory rate and SpO_2 were monitored and comparable. Patients were monitored for side effects and adverse effects.

Discussion

Spinal anaesthesia is most commonly performed technique for lower abdominal surgeries because of its early and effective onset of sensory and motor block and excellent prolonged post op analgesia [15]. Levobupivacaine, is being preferred in infraumbilical surgeries for its lower cardiovascular and CNS toxicity, lesser motor blockade and prolonged sensory blockade [16]. Levobupivacaine blocks the transmission of action potential in sensory, motor and sympathetic nerve fibers by inhibiting the passage of sodium through voltage sensitive ion channels in the neuronal membrane [16]. Alpha 2 adrenergic exert their action by binding to pre synaptic C fibers postsynaptic dorsal horn neurons and potentiate neuraxial local anaesthetics [10]. They produce analgesia by depressing the release of C fibers transmitters and hyperpolarisation of post synaptic dorsal horn neuron. Opioids related side effects are not seen when these agonists are given intrathecally along with local anaesthetics. They have antinociception for both somatic and visceral pain [17].

Fentanyl is a lipophilic μ receptor agonist opioid. It acts by combining with opioid receptors in the dorsal horn of spinal cord and it also has a supra spinal spread and action [18,19]. Fentanyl in dosage of 25μg for supplementation of spinal anaesthesia produces excellent quality of perioperative analgesia [17,20-22]. Kim et al., observed that fentanyl beyond 25 μg produce no benefit with regard to duration of analgesia [23]. Hence, we have chosen 25 μg as a supplementation for spinal anaesthesia.

Dexmedetomidine is highly selective alpha 2 adrenoceptor agonist and more specific ,hence used as a safe adjunct in diverse clinical application [24]. Dexmedetomidine in small doses (3,5,10 μg) as an additive to intrathecal bupivacaine has shown to produce a shorter onset of motor block and a prolonged sensory and motor block with preserved haemodynamics with lack of sedation and minimal side effects [17,25,26]. We have chosen 5μg in our study based on previous human studies [17,25,26]. In studies done by Sathikarnmanee T et al., and Mantouvalou M et al., authors used 15mg of levobupivacaine and concluded that 15mg is adequate to provide sensory and motor block for abdominal surgeries [27,28]. Hence we chose 15mg of levobupivacaine in our study.

In our study mean time of onset of spinal block was faster without any statistical significant difference and there was statistically significant prolongation of time taken for two segment regression, duration of analgesia, duration of sensory and motor block, with good post op analgesia and stable haemodynamics without any significant side effects in group LD as compared to group LF which is similar to the studies done by A.S. Basuni et al. [12], Al –Ghanem et al. [17] and Gupta. R.et al. [29].

A.S. Basuni, HAA Ezz et al. [12], found that dexmedetomidine 3μg with isobaric levobupivacaine 4mg improved the quality of anaesthesia and post op analgesia for knee arthroscopy as compared

with 10μg fentanyl added to levobupivacaine 4mg. Al –Ghanem et al. [17], in his study reported that under spinal block 10mg plain bupivacaine supplemented with 5μg dexmedetomidine produced prolonged motor and sensory block compared with 25 μg fentanyl in gynaecological procedures. In a comparative study by Gupta R et al. [29], dexmedetomidine 5μg was found to be a better alternative than 25 μg fentanyl as adjuvants to bupivacaine as it provided better quality of intra operative and post operative analgesia, haemodynamic stability and fewer side effects.

In a study done by Atrri J.P. et al. [30] author compared 10mg levobupivacaine and levobupivacaine with 25μg fentanyl given intrathecally for infraumbilical surgeries and found adding fentanyl fastens the onset and prolongs sensory and motor block with excellent post op analgesia, maintained haemodynamics and lesser side effects.

Author Vania K et al. [31], in her study added and compared dexmedetomidine 10 μg and clonidine 15μg as adjuvants to 15mg levobupivacaine intrathecally and found dexmedetomidine when compared to clonidine significantly prolongs motor and sensory block and increases duration of postop analgesia. Tiwari J.P. et al. [32], in patients undergoing gynaecological surgeries evaluated the efficacy and safety of addition of dexmedetomidine 5μg to 15mg levobupivacaine and reported that dexmedetomidine shortens the onset and provides intense sensory and motor block with maintained haemodynamics Aliye Esmaoglu and Sumeyra et al. [33], in their study added 3 μg dexmedetomidine to intrathecal 15mg levobupivacaine for transurethral endoscopic surgery and found dexmedetomidine prolongs the duration of sensory and motor block.

Haemodynamics remained stable during intaoperative and postoperative period. Bradycardia was seen in 5 (16.6%) patients in group LD and 2 patients in group LF(6.6%). Similar incidence of bradycardia with dexmedetomidine about 17.5 % was seen in a study conducted by Tiwari J.P et al. [32]. About 10% incidence of bradycardia with fentanyl was reported by Atrri et al. [30].

In our study hypotension was more in group LD than in group LF but there was no statistical significant difference between the group which is similar to study by Gupta et al. [29] slight reduction of MAP was observed in both the groups without any significance.

Kanazi et al. [25], reported insignificant effect of dexmedetomidine on mean blood pressure when added to intrathecal bupivacaine. Bradycardia and hypotension were managed successfully [25]. Sedation scores remained comparable among the groups, sedation scale was 2 among the patients. There was no incidence of respiratory depression, pruritis, delayed micturition and any other side effects and adverse effects observed in both the groups.

Conclusion

Dexmedetomidine 5μg is a good and safe adjuvant to spinal levobupivacaine as compared to 25μg fentanyl, it enhances sensory and motor block with better quality of post op analgesia, preserved haemodynamics and minimal side effects.

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Conflicting Interest: None

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