Original Article

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Comparison between Dexmedetomidine and Buprenorphine as Adjuvants to Isobaric Levobupivacaine in Spinal Anaesthesia for Elective Lower Limb Surgeries

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Abstract

Background: Levobupivacaine and racemic bupivacaine are equally effective in spinal anaesthesia with less systemic toxicity seen with levobupivacaine. Buprenorphine and Dexmedetomidine now being evaluated as a potential neuraxial adjuvant. This study has been designed to study various effects and any adverse effects of addition of either dexmedetomidine or buprenorphine to 2 ml of 0.5% isobaric levobupivacaine intrathecally for lower limb surgeries.

Methods: In this randomized, double-blind prospective study, 60 patients of ASA I and II were randomized into two groups: group LD and LB (n=30). All patients received a drug volume of 2.5 ml containing 2 ml isobaric levobupivacaine (15 mg). They received dexmedetomidine 10 µg (Group LD) or 60 µg of buprenorphine (Group LB) diluted to 0.5 ml with distilled water added to levobupivacaine in the same syringe.

Results: It was found that the onset of sensory block upto T10 and motor block is statistically significantly faster in group LD (109.33 and 153.5, in sec) over group LB (133 and 167.67, in sec). The mean time for two segment regression, the mean time to sensory regression to L1, the mean duration of analgesia and the mean duration of motor blockade is significantly prolonged in Group LD (106.67, 322, 343, 330.5, in min) over Group LB (132.67, 259.67, 290.67, 253.34, in min) with $p<0.001$.

Conclusion: 10µg of dexmedetomidine added to local anaesthetic in subarachnoid block has proved to be a better adjuvant in prolonging the sensory and motor blockade intraoperatively and the duration of postoperative analgesia compared to 60µg of buprenorphine, without significant adverse effects.

Keywords: Spinal anaesthesia; Levobupivacaine; Buprenorphine; Dexmedetomidine.

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Introduction

Pain is a complex, multidimensional perception. It is a dynamic process, involves actions at multiple sites starting from peripheral tissue injury provoking peripheral sensitization leading to central sensitization. Ultimately the inflammatory response leads to release of chemical mediators that act synergistically to convert high thresh-hold nociceptors to low thresh-hold nociceptors.[1]

Prevention and treatment of postoperative pain

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plays an important role. It enables early ambulation, reduces morbidity, duration of hospital stays and improves the surgical outcome. The adequacy of postoperative pain control is one of the most important factors in determining safe discharge from Day care surgery.[2] Systemic analgesia by nature is associated with numerous side effects like drowsiness, dizziness and disorientation. This may not allow the patient to ambulate early. Some drugs may cause nausea, vomiting and itching.

Spinal anaesthesia is the most commonly used technique for lower abdominal and lower limb surgeries. It is easy to administer, has rapid onset of action, low risk of infection as from catheter in situ, less failure rates. Spinal is safe and economical.[3-4] Patient is awake and conscious, so can describe and relate timely indicators of complications.

Spinal anaesthesia using traditional local anaesthetics only, without adjuvants have a shorter duration of action and so lead to an early analgesic requirement in the postoperative period.

Intrathecal narcotics potentiate the sensory blockade of local anaesthetics without affecting the sympathetic activity.[5] They provide prolonged post-operative analgesia but are associated with increased risk of nausea, vomiting, itching and respiratory depression.[6]

Buprenorphine, a μ receptor partial agonist with low intrinsic activity can be safely used in subarachanoid block. Buprenorphine is compatible with CSF. It is lipophilic and has high molecular weight. This may prevent its rostral spread and thus respiratory depression.[7]

Dexmedetomidine, a new highly selective 2 – agonist is under evaluation as a neuraxial adjuvant as it provides sedation, stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.[8-9] Dexmedetomidine, has a high ratio of α_2/α_1 activity. It possesses many properties of an ideal adjuvant but lacks respiratory depression thus making Dexmedetomidine a safe adjuvant.[10] Based on the findings in a few human studies, it is hypothesized that intrathecal 10 μg of Dexmedetomidine would produce significant postoperative analgesic effect when combined with hyperbaric Bupivacaine in spinal anaesthesia with minimal side effects.[8-9]

This study has been designed to compare the sensory and motor effects of Dexmedetomidine and Buprenorphine as adjuvants to 0.5% levobupivacaine for spinal anaesthesia in lower limb surgeries.

Objectives and Aim of the Study

This study aims to investigate and compare the effect of intrathecal administration of Dexmedetomidine (10 μg) or Buprenorphine (60μg) to 2 ml of 0.5% isobaric levobupivacaine intrathecally for elective lower limb surgeries.

The objective of the study was to evaluate the following parameters in both the groups:

- Time to onset of sensory and motor block
- Duration of sensory and motor block
- Duration of effective post-operative analgesia
- Side effects.

Materials and Methods

Study setting

This study was conducted at the Basaveshwar Teaching & General Hospital, Gulbarga attached to Mahadevappa Rampure Medical College, Gulbarga between January 2016 to march 2017.

This study was done after Ethical Committee approval and written informed consent from all patients included in the study.

Study design

This study was done in a prospective double blinded randomized manner.

Inclusion criteria

- American Society of Anesthesiologists [ASA] grade 1 and 2 patients.
- Adult patients aged between 18-60 years of both sex
- Patients undergoing elective lower limb surgeries

Exclusion criteria

- Patients belonging to ASA grade III, IV and V
- Patient refusal
- Liver and renal dysfunction
- Patients with cardiac dysarrhythmias
- Patients using adrenergic receptor blockers, calcium channel blockers
- Weight >120 kg or height < 150 cm
- Patients with contraindications for spinal anaesthesia
- Allergy to drugs

Source of data

This study was conducted in adult patients aged between 18-60 years undergoing elective urological, perineal and lower extremity surgeries under spinal anaesthesia in Basaveshwar Teaching & General Hospital And Sangameshwar Hospital, attached to Mahadevappa Rampure Medical College. 60 patients were divided into 2 groups by permuted block randomisation technique in the ratio 1:1.

Group LD- received 10 milligrams (2 ml) of 0.5% isobaric levobupivacaine and 10 micrograms (in 0.5 ml of distilled water) of Dexmedetomidine. Total volume was made to 2.5 ml.

Group LB- received 10 milligrams (2 ml) of 0.5% isobaric levobupivacaine and 60 micrograms (in 0.5 ml of distilled water) of Buprenorphine was drawn from the ampoule of buprenorphine containing 300 µg/mL. Total volume was made to 2.5 ml.

Procedure

In the O. T, appropriate equipment for airway management and emergency drugs were kept ready. The horizontal position of the operating table was checked and patient shifted to the table.[18] G i.v cannula was inserted and the patient was preloaded with 500 ml of Lactated Ringer's solution. NIBP, SpO2, ECG leads were connected to the patient. Preoperative baseline systolic and diastolic BP, PR, SpO2 and RR were recorded. Under strict aseptic precautions, a midline lumbar puncture was performed using a 25 G Quincke needle in sitting position. The patient was then immediately placed in supine position. The time for intrathecal injection was considered as 0 and the following parameters were observed – sensory blockade, motor blockade, duration of analgesia.

The PR, systolic and diastolic BP, SpO2 and RR were recorded every 2 min for 10 min and then every 5 min throughout the intraoperative period. The above vital signs at the completion of surgery were noted.

Hypotension was defined as fall in systolic BP >30% from baseline or MAP <60 mmHg. This was managed with i.v Mephentermine 6mg in increments. Bradycardia was defined as HR < 60 / min and was managed with Inj. Atropine 0.01mg/ kg i.v. Respiratory depression was defined as RR < 8/min and or SpO2 < 85%. This was planned to be managed with bag and mask ventilation or intubation and IPPV if necessary. Blood loss more than the allowable loss was replaced with blood.

Monitoring and follow up of the patients

Patient was shifted to recovery room after completion of surgery. The vital signs were recorded, every 15 min in the 1st hour after surgery and 30 min interval for next 2 hours and thereafter at hourly intervals for next 3hrs. Sensory and motor block were assessed every 15 min till recovery of pin prick sensation to L1 and Bromage score of 1 respectively. Patients were shifted to post operative ward after complete resolution of motor blockade.

Patients were monitored for 24 hours to detect the occurrence of side effects - respiratory depression, nausea, vomiting, dry mouth, urine retention and pruritis. Patients were also enquired about the occurence of transient neurological symptoms which was described as pain / paraesthesia in the neck, buttocks, legs or pain radiating to lower extremities after initial recovery from SAB within 72 hrs.

Assessment of sensory blockade

Following subarachnoid block, sensory block was assessed by loss of sensation to pinprick using 23 G sterile needle. The assessment was started immediately after injection and continued every 15 sec till loss of pinprick sensation at T10 level. Onset of sensory block was taken as time from intrathecal injection to loss of pinprick sensation at T10. At 20 mins interval after SAB, the dermatomal level of sensory block noted and this was considered as maximum level of sensory block.

Assessment of Motor blockade

Motor block was assessed using the Bromage score:

Grade 1: full flexion of knees and feet possible.

Grade 2: just able to flex knees with free movement of feet.

Grade 3: unable to flex knees but with free movement of feet.

Grade 4: unable to move legs and feet.

Assessment of motor block was started immediately after the intrathecal injection. It was tested every 15 sec till Bromage Score of 4 was reached. Onset of motor block was taken as time taken to achieve Bromage score of 2 from subarachnoid block. The degree of motor block after 20 min of injection was noted and this was considered the maximum degree of motor block. Thereafter, motor block regression was noted and duration of motor block was taken as time from initiation of SAB to return of Bromage Score to 1.

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Assessment of Pain

At the end of surgery, the degree of pain was assessed using VAS scale till VAS score >4 was reached. Whenever the patient complained of pain, the rescue analgesic, Inj. Diclofenac 75 mg i.m was given. Duration of effective analgesia was defined as time interval between onset of SAB and the time to reach VAS ≥4. (Fig.1)

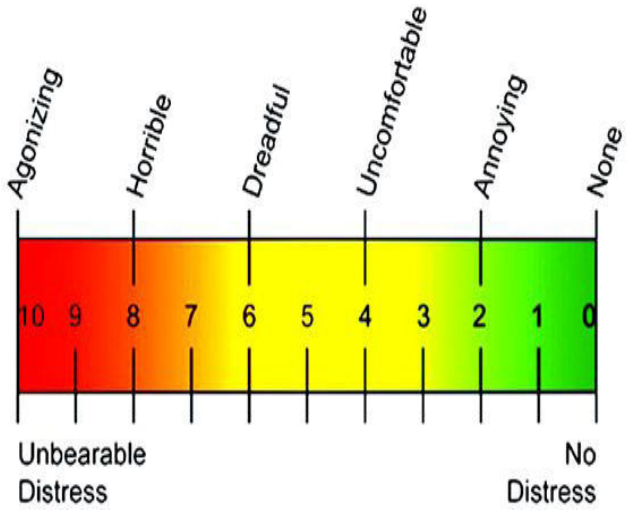


Fig 1: Visual Analogue Scale.

Statistical analysis

All recorded data were entered using MS Excel software and analysed using SPSS 16 version software for determining the statistical significance. Analysis of Variance was used to study the significance of mean of various study parameters between the three groups.

Chi-square test with Yates correction was used to study the significant association between sex distributions among the groups. The p-value taken for significance is less than 0.05. A p-value < 0.001 was considered to be highly significant.

The median was used to compute the maximum sensory and motor block and the sedation scores.

Patient characteristics

The groups were comparable with respect to their age because there was no statistical significant difference among the groups (p>0.05). The demographic profile of both the groups showed no significant differences statistically (table no.01)

Both the groups were comparable in terms of the sex distribution and there was no statistical significant difference (p>0.05). Both the groups were comparable on the basis of duration of surgeries.

Observations and Results

Table 1: Comparison of age, BMI and ASA among the two groups.

Parameters	Group D (n=30)	Group B (n=30)	P value
	Mean ± SD	Mean ± SD	
Age in years	33.87 ± 10.19	37.27 ± 10.31	0.204
BMI	23.04 ± 1.2	23.23 ± 1.25	0.553
ASA	Group D	Group B	P value
	n (%)	n (%)	
Grade 1	20 (66.7%)	20 (66.7%)	1.00
Grade 2	10 (33.3%)	10 (33.3%)	
Total	30 (100%)	30 (100%)	

Onset of sensory block

There is a significant difference between groups with regard to onset of sensory block, with Group LD having a rapid onset compared to Group LB ($p < 0.0001$). (table 02)

Onset of motor block

There is no significant difference between groups in the onset of Motor block. (table 02)

Time to two segment regression

There is significant difference between groups in two segments Regression, with Group LB requiring a much longer time compared to Group LD ($p<0.0001$). (table 02)

Time to sensory regression to l_1

There is significant difference between the groups in mean time to sensory regression to L1– with Group D requiring a much longer time compared to Group B ($p<0.0001$). (table no 02)

Mean duration of analgesia

There is a significant difference between the groups in the mean duration of analgesia with Group LD having a much longer duration compared to Group LB ($p<0.0001$). (table no 02)

Maximum level of sensory block

The median of the maximum level of sensory block reached in both the groups is T6., Therefore, there is no significant difference between the groups in this respect. (table no 02)

Mean duration of motor block

There is significant difference between groups in duration of motor block with group LD having longer duration compared to group LB (p<0.0001). (table no 02)

Table 2: Comparison of sensory, motor analgesia parameters among the two groups.

Parameter	Group LD (n=30)	Group LB (n=30)	P value
	Mean ± SD	Mean ± SD	
Sensory parameters			
Onset of sensory block (sec)	109.33 ± 12.98	133 ± 15.35	<0.001
Two segment regression (min)	132 ± 14.6	106.67 ± 15.77	<0.001
Time to sensory regression to L1	322 ± 40.39	259.67 ± 22.51	<0.001
Motor parameters			
Onset of motor block (sec)	153 ± 59.83	167.67 ± 18.46	0.2202
Duration of motor block (min)	330.5 ± 39.85	253.34 ± 22.48	<0.001
Duration of analgesia			
Analgesia (min)	343 ± 43.02	290.67 ± 22.88	<0.001

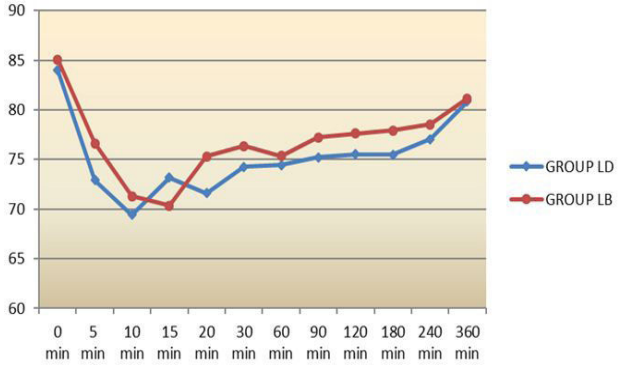
Hemodynamic parameters

These included heart rate, systolic blood pressure, diastolic blood pressure and respiratory rate recorded at definite time intervals of 0 and every 5 minutes for first 30 minutes and there after every 10 minutes for the next 90 minutes.

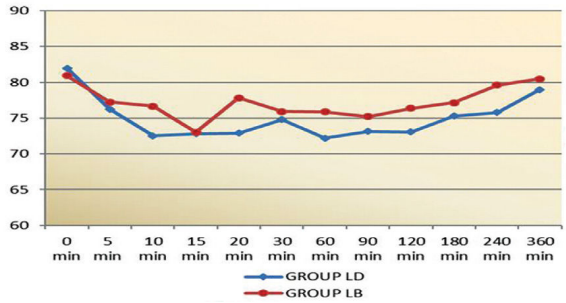
Variation of heart rate among the groups

There is no significant difference between both the groups with respect to intra-operative and postoperative mean heart rates with p>0.05. (Graph 1)

Both the groups have similar mean SBP, DBP and MAP values throughout the intra-operative and postoperative periods with p >0.05.(graph 2)



Graph 1: Variation of heart rate among the groups.



Graph 2: Variation of MAP by groups.

Mean respiratory rate

There was no statistically significant difference in the mean respiratory rate between Group D and Group B at any point of time during the study.

Mean Oxygen saturation

There was no statistically significant difference in the mean oxygen saturation between the two groups at any point of time during the study.

Adverse effects

There was no statistically significant difference in the adverse effects among the two study groups. (table no. 03). Six patients in Group LD and five patients in Group LB had Bradycardia. Three patients in group LD and two patients in group LB had hypotension. None of the patient s in Group LD had nausea, vomiting or Pruritis. In group LB one patient had Pruritis, one patient had nausea and two patients had vomiting.

Table 3: Comparison of adverse effects among the two groups.

Side effects	Group LD		Group LB		P value
	Frequency	Percent	Frequency	Percent	
Bradycardia	6	20.0%	5	16.7%	0.494
Hypotension	3	10.0%	2	6.7%	
Nausea	0	0.0%	1	3.3%	
Pruritis	0	0.0%	1	3.3%	
Vomiting	0	0.0%	2	6.7%	
Nil	21	70.0%	19	63.3%	
Total	30	100.0%	30	100.0%	

Discussion

In our study, we compared the sensorimotor effectiveness of addition of buprenorphine (60 µg) or dexmedetomidine (10 µg) to intrathecal isobaric levobupivacaine (0.5%). We chose to use this dose of Dexmedetomidine as it was found to be safe according to study by B maharani et al.[14] We chose dexmedetomidine 10 µg as this has been found to provide good, prolonged analgesia.[11]

Onset of sensory block

The mean time to onset of sensory block is 109.34 sec in Group LD and is 133 sec in group LB . Onset of sensory block upto T10 is statistically significantly faster in Dexmeditomidine group over buprenorphine group with p <0.0001.

It correlates with the study by B maharani et al[14] who found that the mean time of sensory block to reach T10 was 1.67+0.52 min in D10 group D(10 µg dexmedetomidine) and 2.04+0.6 min in group B (buprenorphine).

Onset of motor block

The mean time to onset of Bromage 2 motor block is 153.5 sec in group LD and 167.67 sec in group LB. There was no statistically significant difference among the three groups (p = 0.2202).

It correlates with the study by B maharani et al[14] who found that the mean time to reach Bromage 3 scale was 3.56+1.13 with 10 µg Dexmedetomidine, 3.66+1.19 min with 60µg buprenorphine which was statistically insignificant (p 0.740).

Mean time to two segment regression and time to sensory regression to l_1

The mean time taken for two segment regression was 132.67 min in group LD compared to 106.67 min in group LB. The time for two segment regression is significantly prolonged in group LD compared to Group LB (p< 0.0001).

In our study, there is significant difference between the groups in terms of the time to sensory regression to L1 – with Group LD requiring a much longer time 322 min) compared to Group LB (259.7 min) which is highly significant with p<0.0001.

B maharani et al[14] also found that the regression time to S1 dermatome was 377.5+48.54 min in group D and 304.6+73.67 min in group N (p< 0.001).

Hala E A Eid MD et al[12] also concluded that Dexmedetomidine significantly prolonged time to two segment regression, sensory regression to S_1.

Mean duration of analgesia (min)

There is significant difference between groups in total duration of analgesia with Group LD having a much longer duration compared to Group LB (p <0.0001). Group LD has a mean duration of analgesia of 343 min and Group LB has 290.6 min. Thus, the analgesic requirement in the first 24 hours postoperatively in Group LD was significantly lesser than that in Group LB.

B maharani et al[14] concluded that intrathecal dexmedetomidine in doses of 10 µg significantly prolong the anaesthetic and analgesic effects of spinal hyperbaric bupivacaine compared to 60 µg buprenorphine.

Addition of 10 ug increased the duration of analgesia provided by spinal bupivacaine by about 375.83+48.59 min compared to 302.57+75.74 min with 60 µg buprenorphine (p <0.001).

Mean duration of motor block

The mean duration of motor block in Group LD and Group LB are 330.5 min, 253.34 min respectively (p<0.0001) which was statistically significant.

It correlates with the study by B maharani et al[14] who found that motor block regression to modified Bromage 0 were significantly prolonged in group D 342.11 + 48.67 (10 µg dexmedetomidine) than in group B 266.98 + 73.47 (60 µg buprenorphine)

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA et al[11] observed that the regression to Bromage 0 was 302.9±36.7 min in D10 (10 µg dexmedetomidine) which was similar to our study.

Haemodynamic Parameters

In our study, there is no significant difference between both the groups with respect to intraoperative and postoperative mean heart rates with p>0.05.Both the groups have similar mean SBP,DBP and MAP values throughout the intraoperative and postoperative periods with p>0.05.

Thus, the haemodynamic stability is maintained even in the presence of Dexmedetomidine.

It correlates with the study by B maharani et al[14] who found that the mean values of MBP and HR were comparable between the two groups throughout the study duration.

Side effects

In a study by F A Khan Gauhar[7] the incidence of nausea and vomiting was higher with intrathecal buprenorphine which correlates with the findings of our study.

Three patients who received intrathecal dexmedetomidine developed transient hypotension that was easily treated with intravenous mephentermine. Six patients in Dexmedetomidine and 5 patients in Buprenorphine group had transient bradycardia which responded

to Intravenous atropine.

Conclusions

The following conclusions were drawn

The time to two segment regression was significantly prolonged with the addition of intrathecal Dexmedetomidine to hyperbaric Bupivacaine.

The time to motor regression was significantly prolonged with the addition of Dexmedetomidine. This was a major advantage in our study on perineal and lower limb surgical procedures where immobility is important during intraoperative and post operative period.

Addition of either Dexmedetomidine or Buprenorphine along with hyperbaric Bupivacaine intrathecally does prolong duration of analgesia especially in dexmeditomidine group and reduce postoperative analgesic requirements.

There was no appreciable difference in the time to onset of either sensory or motor block.

The incidence of adverse effects like nausea, vomiting and pruritis was higher in the Buprenorphine group though it was not statistically significant.

Addition of Dexmedetomidine or Buprenorphine to intrathecal hyperbaric Bupivacaine is safe as both maintain hemodynamic stability without producing excessive sedation or respiratory depression.

Further studies to validate our findings recruiting larger patient population is considered essential.

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