Section: Anaesthesia

Original Research Article

ANALGESIC EFFECT OF INTRATHECAL MORPHINE VS. DEXMEDETOMIDINE AS AN ADJUVANT TO LEVOBUPIVACAINE IN PATIENTS UNDERGOING LOWER LIMB SURGERIES -A RANDOMISED CONTROL TRIAL

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Abstract

Background: Various adjuvants to local anesthetics are used in spinal anesthesia for improving the quality and prolonging postoperative analgesia. We aim to compare the analgesic efficacy of morphine or dexmedetomidine given intrathecally as adjuvants to isobaric levobupivacaine undergoing lower limb surgeries. **Materials and Methods:** 105 patients of age group 18-60 years, ASA Grade 1 and 2 undergoing elective lower limb surgeries, were randomized into 3 groups. Group L received spinal anesthesia with 0.5% isobaric levobupivacaine .Group LM received spinal anesthesia with 3 mL of 0.5% isobaric levobupivacaine with 100 µg of preservative-free morphine. Group LD received 3 mL of 0.5% isobaric levobupivacaine with 5 µg of dexmedetomidine. Quality of anesthesia, sensory and motor block characteristics, duration of effective analgesia, and incidence of side effects were compared. **Result:** The mean duration of surgery was observed to be statistically comparable among the 3 study groups (p>0.05). It was 175.86±23.53 min in group LM; 174.57±28.32 min in group LD and 173.86±23.329 min in group L. The mean time for sensory block onset was 61.43±31.683min in group LM; 66±31.97min in group LD and 69.57±26.606min in group. Maximum level achieved is T10 by most of the patients in group LM, LD and L. T8 was reached by only 1 patient in group LD. **Conclusion:** In our study we conclude that both morphine and dexmedetomidine as adjuvants to spinal anesthesia increases the duration of analgesia compared to levobupivacaine alone. Duration of sensory block is more with dexmedetomidine. Time to achieve maximum level is lesser with dexmedetomidine with fewer post-operative side effects.

INTRODUCTION

Neuraxial blockade is the preferred mode of anesthesia for lower limb and lower abdominal surgeries out of which Spinal anesthesia is the preferred due to its rapid onset, superior blockade, lower failure rate and cost effectiveness.[1] The main drawbacks are short duration of block and short period of postoperative analgesia. With side effects such as hypotension and bradycardia resulting due to sympathetic blockade.

Bupivacaine is the most common local anesthetic agent used for spinal anesthesia because of prolong duration of action.[2] Its usage limited by adverse effects on the cardiovascular and central nervous system.[3] Levobupivacaine the S (-) enantiomer of bupivacaine has lesser side effects than racemic bupivacaine due to more selective neuraxial blockade.[4]

Intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block and post-operative analgesia. Different drugs such as epinephrine, neostigmine, magnesium sulphate, opioids, midazolam, ketamine and clonidine have been added to intrathecal local anesthetics in an attempt to prolong analgesia and reduce the incidence of adverse events.

Opioids are one of the most frequently used class of adjuvant in neuraxial space.it acts in intrathecal space by activating opioid receptor in the dorsal grey matter of spinal cord which modulates the function of afferent pain fibers.[5] Intrathecal morphine is most widely used hydrophilic opioid adjuvant as it provides prolonged post-operative analgesia however, over the years, it is losing popularity due to

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dose dependent side effects such as pruritus, nausea, vomiting, urinary retention and the most feared risk of delayed respiratory depression.[6]

Intrathecal α 2 adrenergic agonist's are also commonly used adjuvants, act by binding to presynaptic C-fibers and post synaptic dorsal horn neurons.[7] Dexmedetomidine is a highly selective α 2 agonist which possesses sedation, analgesic and sympatholytic properties and gives prolonged analgesia when used intrathecally without respiratory depression.[8]

Limited Studies are available on literature on comparison of analgesic efficacy of dexmedetomidine and morphine with isobaric levobupivacaine in this study we planned to compare post-operative analgesic efficacy of intrathecal morphine and intrathecal dexmedetomidine with isobaric levobupivacaine in the patients undergoing lower limb surgeries under spinal anesthesia.

MATERIALS AND METHODS

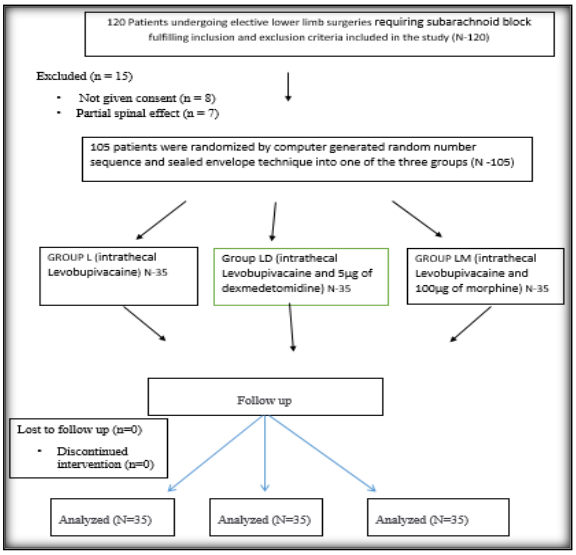
After obtaining institutional ethical clearance we conducted hospital based Randomized Double Blinding control trial in tertiary hospital between 2020-2022.

Patients aged above 18 years with ASA: I & II undergoing traumatic lower limb orthopedic surgery (surgical duration of up to 2 hours) are included in our study.

A patients with infection at the site of injection, history of allergy to study drug, Spine abnormalities (like scoliosis), cardiac diseases (like heart block, dysrhythmias), head injuries, Pregnant females, patients taking β- Blocker and α-antagonists medication, patients with any contraindication to spinal anesthesia like abnormal coagulation profile, sepsis. Are excluded from the study. Informed consent was obtained from all patients.

The patient underwent thorough pre anesthetic evaluation assessment and patients detailed history, general physical examination and systemic examination were carried out to rule out exclusion criteria. Basic demographic data like age, sex, height, weight were recorded. Routine investigations such as complete blood count, blood sugar, renal function test, liver function test, bleeding time, clotting time, chest x-ray, ECG carried out. Patients were explained in detail about the anesthesia procedure. All the patients planned for elective procedure will be instructed for fasting as per ASA guidelines before surgery

Pre-medication: All patients were kept nil per oral for 8 hours and premedicated with Inj. Midazolam 0.03mg/kg, given 5 minutes before procedure to reduce the anxiety.



Randomization: In this proposed study 105 patients, who were posted for elective lower limb surgeries requiring subarachnoid block was randomized by computer generated random number sequence and sealed envelope technique into one of the three groups: Group L Group LD and Group LM (35 in each group).

Group L: Received 0.5ml NS with 3ml(15mg) of Levobupivacaine intrathecally

Group LD: Received 5µg of dexmedetomidine with 3ml(15mg) of Levobupivacaine intrathecally.

Group LM: Received 100µg of morphine with 3ml(15mg) of Levobupivacaine intrathecally.

BLINDING: This trial is DOUBLE BLINDED so planned that neither the doctor nor the patient was aware of the groups and the drug used.

All solutions were prepared in sterile manner. The drug solution was be prepared by an anesthesiologist not involved in the study.

During intra operative period following para meter were assesed

1. Onset of sensory block
2. Duration of sensory block
3. Onset of motor block
4. Duration of motor block
5. Sedation
6. Visual Analogue Scale (VAS)
7. Duration of analgesia
8. Intraoperative hemodynamic parameters and adverse effects

RESULTS

Total 120 patients were selected for this study out of which 8 patients not given consent to participate in the study and 7 patients had partial spinal effect and converted to general anesthesia. So 15 patients were excluded from the study. 105 Patients were participated in the study, 35 patients in each group. Demographic variable like age, sex, height, weight are comparable with 3 groups with no statistical significance

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Mean Time for Sensory Block Onset: The mean time for sensory block onset was observed to be statistically comparable among the 3 study groups (p>0.05) in our study. The mean time for sensory block onset was 61.43±31.683min in group LM; 66±31.97min in group LD and 69.57±26.606min in group.

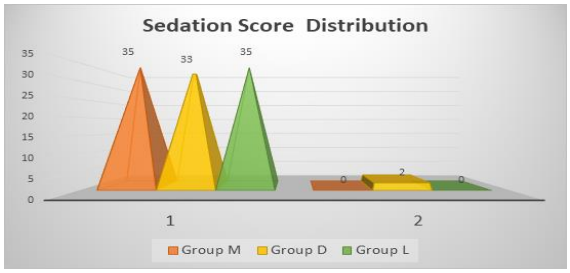

Figure 1: Sedation Score distribution

Above table shows distribution of patients on the basis of sedation score. All the three groups were statically compared by using Chi square test , no significant difference (P value - 0.130) in weight among three groups was observed .The sedation score at 60 min was 1 for all 35 patients in group LM and L, and for 33 patients of group LD. 2 patients of group LD had sedation score of 2 in the current study.

VAS (Visual Analogue Scale) Score: VAS scores are evaluated from baseline to 24 hours. The pattern was observed to be similar in all the 3 groups. There was no significant difference in mean VAS score between LM and LD groups from baseline to 24 hours in the current study (p>0.05).

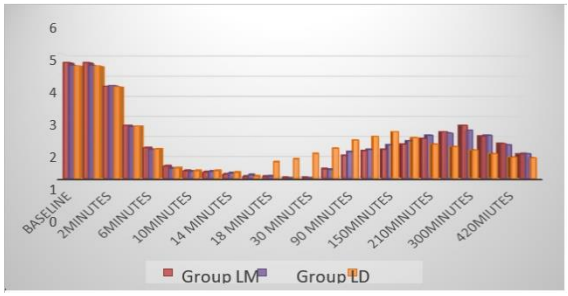

Figure 2: Mean VAS Score

Mean Time to Reach Maximum Level: It was maximum in group L (30.46±6.065 min). There was statistically significant difference (p=0.0001 between LM and LD; 0.0377 between LM and L and 0.0001 between LD and L group).

Maximum level reached: Maximum level achieved is T10 by most of the patients in group LM, LD and L. T8 was reached by only 1 patient in group D.

Mean Onset of Motor Block: All the three groups were statically compared by using Chi square test, no significant difference was found in the mean onset of motor block.

Mean Time for Two Segment Regression: The mean time for two segment regression was highest in dexmedetomidine (LD) group 99.43 min followed by morphine (LM) group 89.43 min and levobupivacaine (L) 79.86 min alone. The difference was found to be statistically significant with p value of 0.0218 in between LM and LD groups.

Mean Time for Rescue Analgesia: The mean time for demand for first rescue analgesia was observed to be more in LM group (298.86 min) and LD group (279.71 min) followed by L group (145.71 min) Among LM and LD groups, the difference was not found to be statistically significant (p>0.05) while L group showed lesser mean time for rescue analgesia as compared to LM and LD groups (p<0.0001 in both cases).

Mean HR (Heart Rate): There is no significant difference in mean heart rate between LM and LD groups from baseline to 90 mins and at 4 hrs., 8 hrs., 12 hrs. and 24 hours. There is significant difference in mean heart rate between LM and LD groups at 120 min.

Mean SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure), MAP (Mean Arterial Pressure): There was no significant difference in mean SBP between LM and LD groups at 0min, 2 min, and from 6 min to 24 hours. There was no significant difference at baseline and at 4min between LM and LD groups.

There was no significant difference in mean DBP between LM and LD groups at baseline to 24 hours.

There was no significant difference in mean blood pressure between LM and LD groups from baseline to 24 hours.

Mean RR (Respiratory rate), SPO2 (Oxygen saturation): There was no significant difference in mean respiratory rate between LM and LD groups from baseline to 24 hours. The mean oxygen saturation is 100% for all patients in all 3 groups from baseline to 30minutes. It is 100% till 18 hours in LM group and till 12 hours in L group. There is no significant difference in spo2 between LM and LD groups from baseline to 24 hours.

Post-operative complications: Incidence of nausea/vomiting, pruritus was significantly higher in LM group, while incidence of Hypotension and bradycardia were lower in LD group. Respiratory Depression was zero in all the groups.

Table 1: Mean Time for Sensory Block Onset.

Duration (Seconds)		Group LM	Group LD	Group L
Mean		61.43	66	69.57
Standard deviation		31.683	31.97	26.606
P value	LM vs LD	0.5501(NS)		
	LM vs L	0.2485(NS)		
	LD vs L	0.6132(NS)		
Tvalue	LM vs LD	0.6007 with df=68		
	LM vs L	1.164 with df=68		

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	LD vs L	0.5078 with df=68

Sedation Score

Sedation Score	Group LM	Group LD	Group L
1	35	33	35
2	0	2	0
Total	35	35	35

Chi square = 4.078 with 2 degrees of freedom; P=0.130 (NS)

Table 2: Post –Operative Complication wise Distribution

Post-Operative Complication	Group LM		Group LD		Group L	
	Yes	No	Yes	No	Yes	No
Nausea/ vomiting	15	20	0	35	0	35
Pruritis	8	27	0	35	0	35
Hypotension	2	33	10	25	1	34
Bradycardia	0	35	2	33	0	35
Respiratory Depression	0	35	0	35	0	35
P value	LM vs LD vs L	<0.0001(S)				
	LM vs LD	<0.0001(S)				
	LM vs L	<0.0001(S)				
	LD vs L	0.0002(S)				
Chi square value	LM vs LD vs L	76.863 with df 20				
	LM vs LD	72.840 with df 12				
	LM vs L	43.22 with df 12				
	LD vs L	37.663 with df 12				

Chi square test applied; df=degree of freedom; S=Significant

DISCUSSION

A subarachnoid block is an established technique for surgeries on the Lower limb and lower abdomen. The short duration of postoperative analgesia after spinal anesthesia is a limitation. Numerous adjuvants have been used intrathecally to extend the duration of analgesia of the subarachnoid block.

Levobupivacaine and bupivacaine are equally effective local anesthetics for spinal anesthesia. However, many studies have reported fewer adverse effects, e.g. hypotension and bradycardia, with intrathecal levobupivacaine as compared to bupivacaine.[9]

Morphine injected intrathecally results in analgesia by acting on opioid receptors in the dorsal horn of the spinal cord. Analgesia is adequate and long lasting due to its hydrophilicity, decreased systemic absorption, cephalad spread in the cerebrospinal fluid and slow rate of clearance from the opioid receptors.[10]

The antinociceptive properties of intrathecal α2 agonists are produced by inhibiting the release of c fiber transmitters, by inhibition of release of substance P and by hyperpolarizing post synaptic dorsal horn neurons. Dexmedetomidine is highly specific, potent and selective α2 agonist. Hence, intrathecal dexmedetomidine results in potent analgesia as compared to clonidine with lesser side effects such as bradycardia, hypotension and sedation.[11]

We compared the duration of analgesia of intrathecal morphine (100 µg) and intrathecal dexmedetomidine (5 µg) as an adjuvant to isobaric levobupivacaine in our study. Onset and duration of sensory and motor block, hemodynamic effects, post-operative 24 hours analgesic consumption, sedation score and adverse effects were also noted.

Mean time for onset of sensory block was recorded to be 61.43±31.683 sec in group LM; 66±31.97 sec in group LD and 69.57±26.606 sec in group L. No statistically significant difference was observed among the 3 groups in respect to mean time of onset of sensory block. Our results are similar with Prinjal et al,[12] who reported mean time for sensory block onset as 0.58 min in group LM and 0.56 min in group LD.

Time to reach maximum sensory level was observed to be statistically different among the 3 study groups. It was maximum in group L (30.46±6.065 min). Pranjal et al,[12] reported mean time to reach maximum sensory levels as 19.36 min in group LM and 24.16 min in LD group patients.

Maximum level reached was T10 in the current study. Maximum level achieved was T8 in Pranjal et al study.[12] The difference could be due to higher dose of intrathecal dexmedetomidine (5µg versus 2.5µg) used in our study which could have result in quicker achievement of highest level of block up to T10.

Our results are comparable with study done by Qi X et al,[13] which showed was time to achieve maximum level faster in dexmedetomidine group as compared to morphine.

Time to reach motor block -the difference was observed to be not statistically significant (p>0.05). In group LM it was 98.86±44.690 sec; in group LD it was 106.86±35.739 sec and in group L it was calculated to be 110.86±32.865 sec.

The mean time for demand for first rescue analgesia was observed to be more in LM group (298.86 min) and LD group (279.71 min) followed by L group (145.71 min).

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Compared to intrathecal alpha 2 agonist, intrathecal morphine was found to be better post-operative analgesic with far less rescue analgesic consumption in 24 h. in our study The mean time for demand for first rescue analgesia was observed to be more in LM group (298.86 min) and LD group (279.71 min) followed by L group (145.71 min). Our results are similar to study done by Ashraf Amin Mohamed et al,[14] and Pranjal et al.[12]

Intrathecal morphine and dexmedetomidine both are known to cause hypotension by action on adrenergic receptors. In our study, hypotension was seen more frequently in dexmedetomidine group than morphine. In our study No statistically significant differences were observed among the 3 study groups related to Hemodynamic parameters (p>0.05).

Our results were similar to study done by Qi X et al,[13] In their study, the incidence of bradycardia and hypotension were not significant, and patients did not require additional treatment.

Post operative complications like nausea, vomiting and pruritus were seen more in LM group observation similar to Manal et al study,[15] they reported pruritus and dry mouth were more commonly reported in LM group patients.

Vomiting, pruritus, hypotension and bradycardia were more in morphine group compared to LD group in Xian et al study.[16]

Hypotension and bradycardia were seen more in LD group with No statistically significant differences.

CONCLUSION

In our study we conclude that both morphine and dexmedetomidine as adjuvants to spinal anesthesia increases the duration of analgesia compared to levobupivacaine alone. Duration of sensory block is more with dexmedetomidine. Time to achieve maximum level is lesser with dexmedetomidine with fewer post-operative side effects.

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