

Comparison of the analgesic and hemodynamic effects of intrathecal ropivacaine with dexmedetomidine in lower limb surgeries



Medical Science

KEYWORDS : Intrathecal, Dexmedetomidine, Ropivacaine

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ABSTRACT

Objective: To compare the analgesic and hemodynamic effects of intrathecal with dexmedetomidine in lower limb surgeries.

Methods: Patient aged 18-50 years belonging to ASA physical status 1 or 2 planned for lower limb surgery were included in this study. On the basis of computer generated random table, patients were divided in to following two groups (25 in each): Group R+D was given intrathecal dexmedetomidine (3ml of ropivacaine 0.5% plus 3mic.gm dexmedetomidine intrathecally) and Group R had been the control group.

Results: On comparing, the age, sex, height, weight and ASA grade of the groups were found similar i.e. did not differed significantly ($p > 0.05$). The mean HR in Group R and R+D increased just after the surgery while in Group R+D, it remains almost similar to baseline. The mean MAP in Group R increased just after the spinal anesthesia while mean MAP in group R+D remained similar as compared to baseline. The mean time to achieve T10 sensory block lowered significantly in Group R+D ($p < 0.001$) as compared to Group R. There was significant difference in the mean intra-operative VAS ($p = 0.01$) and maximum sedation ($p < 0.001$) between both the groups. A significantly difference in time to 1st analgesic requirement ($p < 0.001$) and the time to 1st analgesia requirement was observed in both the groups. Not much difference was observed in the proportion of adverse effects between the groups.

Conclusion: Our study establishes dexmedetomidine as superior drug as an adjunct to intrathecal ropivacaine 0.5% for patients undergoing lower limb surgery as it provides faster onset of anesthesia, better intraoperative and postoperative analgesia and prolonged duration of motor and sensory blockade without significant increase in adverse effects.

INTRODUCTION

Neuraxial blockade (spinal or epidural) is the preferred mode of anesthesia for lower limb surgeries. Spinal block is still the first choice because of its rapid onset, superior blockade, low risk of infection as from catheter in situ, less failure rates and cost-effectiveness, but has the drawbacks of shorter duration of block and lack of 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 satisfaction, decreased resource utilization compared with general anesthesia 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. The quality of the spinal anesthesia has been reported to be improved by the addition of opioids such as morphine, fentanyl and sufentanil^{1,2} and other drugs such as dexmedetomidine^{3,4} and magnesium sulfate⁵.

Dexmedetomidine (DXM) is a new generation highly selective α_2 -adrenoreceptor agonist that dose-dependently reduces blood pressure (BP) and heart rate (HR) and has sedative effect. It might permit sedation and analgesia without the unwanted vascular effects from activation of α_1 receptor. Kanazi et al⁴ found that 3 μ g DXM added to 12 mg spinal bupivacaine produced the significant short onset of sensory and motor block as well as significantly longer duration of sensory and motor block than bupivacaine and Al-Mustafa et al³ reported that intrathecal DXM as an adjuvant to 12.5 mg bupivacaine in spinal anesthesia has a dose-dependent effect on the onset and regression of sensory and motor block. Intrathecal α_2 -receptor agonists are found to have antinociceptive action for both somatic and visceral pain.

The present study was designed to compare the analgesic and hemodynamic effects of intrathecal ropivacaine with dexmedetomidine in lower limb surgeries.

MATERIAL AND METHODS

Study Design

The study was conducted after getting approval from ethical committee of the institute. An informed consent was taken from the patient before including in the study

Study participants

Patient aged 18-50 years belonging to ASA physical status 1 or 2 planned for lower limb surgery were included in this study. However, the patients with contraindication of spinal anesthesia, sensitive to local anesthetics and studying drugs, neurological disease, and on analgesic, antidepressant, steroid, alfa agonist, studying drugs were excluded from the study.

On the basis of computer generated random table, patients were divided in to following two groups (25 in each): Group R+D was given intrathecal dexmedetomidine (3ml of ropivacaine 0.5% plus 3mic.gm dexmedetomidine intrathecally) and Group R had been the control group.

Twenty five patients per group was required to detect a significant difference of 25% or more in the requirement of rescue analgesia between the two groups (power of 85%, $\alpha = 0.05$).

Monitoring

All the were monitored for- Heart rate, Blood pressure (systole/diastole), Mean arterial pressure (MAP) and other outcome parameters.

Technique of spinal anesthesia

With all aseptic precautions, a midline spinal puncture was performed at $\frac{3}{4}$ interspace (at $\frac{2}{3}$, if for an anatomical reason it was not possible at $\frac{3}{4}$) with 25G pencil point needle (Pancan, B. Braun, Melsungen, Germany) with patient in sitting position and anesthetic solution were injected without barbotage or aspiration at the beginning or at the end of injection.

All injections were made with hole in the spinal needle facing upward. The patient and the anaesthesiologist who delivered the drug was blinded to the study solution. The injection was given over a span of 15 seconds and the patients were returned to supine position immediately after the completion of the block.

The measurements were performed at 10, 15, 20 and 30 min before surgery and every 15 min after surgery. The time to complete motor recovery (modified Bromage scale-6) was noted.

The quality of intra operative analgesia was evaluated by patient using the following 4-point scale: 1: perfect analgesia 2: adequate analgesia sensation of motion only, 3: inadequate analgesia, discomfort, but the patient decline additional analgesia 4: major discomfort , additional analgesics necessary. Patient at rest was assessed using a visual analogue scale (VAS) (0 for no pain , 10 for worst pain the patient had ever experienced). Level of sedation was determined using the following scale: 1= wide awake; 2= sleepy but easily aroused; 3= sleepy and difficult to arouse; VAS and sedation scores was assessed hourly for the first 8 hr after operation, and every 4hr thereafter for a total of 24 hr.

In the post anesthesia care unit, pain was treated with IV injection of tramadol 50-100 mg, titrated with patient comfort. No other analgesic and/or sedative agents, including non-steroidal anti-inflammatory drugs, was allowed during the first 24 hr after surgery. Ondansetron 4mg IV and diphenhydramine 25 mg IM as needed was prescribed for nausea/ vomiting and itching, respectively.

The amount of tramadol administered after operation, time to first analgesic dose, post operative length of stay and occurrence of any intraoperative or post operative adverse event, including (but not limited to) nausea, vomiting, itching respiratory depression (defined as a respiratory rate <12 bpm) and post dural puncture headache, was documented and treated accordingly.

Statistical analysis

The results are presented in mean±SD and percentages. The categorical/dichotomous variables were compared by using Chi-square test and continuous variables were compared by Unpaired t-test. The paired t-test was used to compare the changes from baseline to different time intervals. The p-value<0.05 was considered significant. All the analysis was carried out by using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

On comparing, the age, sex, height, weight and ASA grade of the groups were found similar i.e. did not differed significantly ($p>0.05$) (Table-1).

The mean HR in Group R and R+D increased just after the surgery while in Group R+D, it remains almost similar to baseline. Further, after spinal anesthesia, the mean HR decreased in both the groups and the decrease was evident highest in R+D group as compared to Group R. For each time, comparing the mean HR between the groups, lower HR was observed in Group R+D from 2 min to till end (210 min) as compared to Group R (Fig.1).

The mean MAP in Group R increased just after the spinal anesthesia while mean MAP in group R+D remained similar as compared to baseline. Here after (from 2min), the mean MAP in both the groups decreased up 20 min and then increase gradually in both the groups till end with highest being lowest in Group R+D. For each time, comparing the mean MAP between the groups, lower MAP in Group R+D was found as compared to Group R at most of the periods (Fig.2).

The mean time to achieve T10 sensory block lowered significantly in Group R+D ($p<0.001$) as compared to Group R. In contrast, mean time to 2-segment regression delayed significantly in group R+D ($p<0.001$) as compared to group R. Like time to 2-segment regression, the duration of regression to L4 was also significantly delayed in R+D ($p<0.001$) ($p<0.01$) as compared to group R. The mean maximum modified Bromage score ($p<0.001$), Bromage score at 2 hr ($p<0.001$) and time to motor recovery ($p<0.001$) were found to be significantly different between the groups. The total fentanyl and total midazolam required only in Group R. There was significant difference in the mean

intra-operative VAS ($p=0.01$) and maximum sedation ($p<0.001$) between both the groups. A significantly difference in time to 1st analgesic requirement ($p<0.001$) and the time to 1st analgesia requirement was observed in both the groups. The Surgeon's assessment of motor block was lowered significantly in Group R+D ($p<0.001$) as compared to Group R (Table-2).

Not much difference was observed in the proportion of adverse effects between the groups (Fig.3).

DISCUSSION

Alpha 2-adrenoceptor agonists are being increasingly used in anesthesia and critical care as they not only decrease sympathetic tone and attenuate the stress responses to anesthesia and surgery; but also cause sedation and analgesia. They are also used as adjuvant during regional anesthesia. Dexmedetomidine is the most recent agent in this group approved by FDA in 1999 for use in humans for analgesia and sedation. The mechanism of action of dexmedetomidine differs from clonidine as it poses selective alpha 2-adrenoceptor agonism especially for the 2A subtype of this receptor, which causes it to be a much more effective sedative and analgesic agent than clonidine. Dexmedetomidine produces a powerful antinociception effect, mediated at the spinal level, while systemic redistribution of the drug leads to hypnotic state with significant cardiorespiratory effects.

The present study was conducted in 80 patients of either sex aged between 18-50 years belonging to ASA physical status I and II undergoing lower limb surgeries.

In the present study, the mean HR decreased in both the groups and the decrease was evident highest in R+D group as compared to Group R. Similar observation was also noted by Gupta et al⁶ in which Intrathecal dexmedetomidine was associated with hemodynamic stability during the period of anesthesia. However, Kanazi et al⁴ showed in their study that addition of 3µg dexmedetomidine or 30 µg clonidine to 12 mg bupivacaine did not produce significant change in heart rate.

In this study, for each time, comparing the mean MAP between the the groups, there was significant ($p<0.001$) difference and lower MAP in Group R+D as compared to Group R. Salgado et al⁷ studied the effect of adding dexmedetomidine to ropivacaine 0.75% for epidural anesthesia and found that dexmedetomidine did not cause hemodynamic instability.

In our study, the mean time to achieve T10 sensory block, time to 2-segment regression and duration of regression to L4 significantly different between the groups. Salgado et al⁷ studied the effect of adding dexmedetomidine to ropivacaine 0.75% for epidural anesthesia and found that dexmedetomidine increases sensory block duration during epidural anesthesia with ropivacaine. In another study⁴, 3µg DXM added to 12 mg spinal bupivacaine produced the significant short onset of sensory blockade.

In the present study, maximum modified Bromage score, Bromage score at 2 hrs and Time to motor recovery (min) were compared between the groups and statistical differences between the groups were significant. Similar observation was found by Al-Mustafa et al³ in which the effect of adding dexmedetomidine to spinal bupivacaine (12.5 mg) for urological procedures were studied. The mean time to reach Bromage 3 scale was 10.4±3.4 minutes in group D10 (10 mcg dexmedetomidine), 13.0±3.4 minutes in D5 (5 mcg dexmedetomidine), and 18.0±3.3 minutes in group N (normal saline). Similarly, Calasans-Maia et al⁸ investigated the duration of motor nerve block induced by spinal injection of 0.5% levobupivacaine (LVB) associated with intrathecal or intraperitoneal administration of DEX and found that motor block induced by spinal injection of LVB was prolonged by in-

trathecal and systemic administration of DEX.

In this study, the Surgeon's assessment of motor block was lowered significantly in Group R+D (1.24 ± 0.52 , $p < 0.001$) as compared to Group R (3.48 ± 0.51). Similarly, the patient's assessment of intra-operative analgesic lowered significantly in Group R+D (1.12 ± 0.33 , $p < 0.001$) than to Group R (3.56 ± 1.04). It signifies that dexmedetomidine is better than control group regarding surgeon's and patient's assessment of anesthesia. The maximum sedation was significantly higher in Group R+D as compared to both Group R ($p < 0.001$) in the present study. So, it is evident dexmedetomidine produces much more sedation than control when used with ropivacaine. Salgado et al⁷ studied the effect of adding dexmedetomidine to ropivacaine 0.75% for epidural anesthesia and found that sedation and no respiratory depression is an advantage of the association between ropivacaine and dexmedetomidine.

In our study, the highest intra-operative VAS (pain level) lowered significantly in R+D group ($p < 0.05$) as compared to group R. Further, the time to 1st analgesia requirement in Group R+D ($p < 0.05$) was also found to be significantly delayed as compared to Group R. However, total dose of tramadol did not differ between the groups. Overall, dexmedetomidine produced better intra and post-operative analgesia than control. Salgado et al⁷ studied effect of adding dexmedetomidine to ropivacaine 0.75% for epidural anesthesia and found that dexmedetomidine prolongs postoperative analgesia. Gupta R et al⁶ showed that Intrathecal dexmedetomidine is associated with reduced demand for rescue analgesics in 24 h as compared to fentanyl. There was no difference in the adverse effects between the groups in this study.

CONCLUSION

Our study establishes dexmedetomidine as superior drug as an adjunct to intrathecal ropivacaine 0.5% for patients undergoing lower limb surgery as it provides faster onset of anesthesia, better intraoperative and postoperative analgesia and prolonged duration of motor and sensory blockade without significant increase in adverse effects.

Table-1: Patient characteristics

Characteristics	Group R (n=25)	Group R+D (n=25)	P value
Age (yrs)	36.20 ± 7.96 (24-48)	32.72 ± 8.39 (19-17)	0.198
Sex: Males	14 (56.0%)	19 (76.0%)	0.136
Females	11 (44.0%)	6 (24.0%)	
Height (cm)	168.00 ± 9.70 (153-180)	166.64 ± 7.97 (151-177)	0.874
Weight (kg)	62.76 ± 8.88 (47-78)	65.76 ± 5.95 (53-74)	0.354
ASA physical status: 1	9 (36.0%)	8 (32.0%)	0.182
2	16 (64.0%)	17 (68.0%)	
Duration of surgery (min)	171.60 ± 13.75 (150-180)	163.20 ± 17.49 (120-180)	0.083

Numbers in parenthesis indicates the range (min-max)

Table-2: Comparison of secondary outcomes between the groups

Characteristics	Group R (n=25)	Group R+D (n=25)
Sensory block characteristics		
Time to achieve T10 sensory block (min)	14.68 ± 3.47	5.96 ± 1.54*
Time to 2-segment regression (min)	89.44 ± 16.59	174.48 ± 12.52*
Duration of regression to L4 (min)	176.00 ± 14.87	360.28 ± 37.29*
Motor block characteristics		
Maximum modified bromage score	3.92 ± 0.81	1.52 ± 0.51*
Bromage score at 2 hrs	4.60 ± 0.58	2.56 ± 0.51*

Time to motor recovery (min)	165.52 ± 14.79	370.68 ± 29.22*
Intraoperative drug requirement		
Total fentanyl requirement (µg)	29.17 ± 10.21	0.00 ± 0.00
Total midazolam requirement (mg)	3.50 ± 1.22	0.00 ± 0.00
Total dose of ephedrine (mg)	8.00 ± 2.74	10.00 ± 3.54
Total dose of atropine (mg)	0.45 ± 0.21	0.68 ± 0.15
Intraoperative VAS and Sedation score		
Highest intraoperative VAS	1.36 ± 0.99	0.56 ± 0.65*
Maximum sedation	1.12 ± 0.33	2.76 ± 0.60*
Postoperative analgesia requirement		
Time to 1st analgesic requirement (min)	245.04 ± 36.66	390.68 ± 29.34*
Total dose of tramadol (mg)	83.33 ± 25.00	75.00 ± 35.36
Surgeon's and patient's assessment of anesthesia		
Surgeon's assessment of motor block	3.48 ± 0.51	1.24 ± 0.52*
Patient's assessment of intraoperative analgesia	3.56 ± 1.04	1.12 ± 0.33*

*Significant

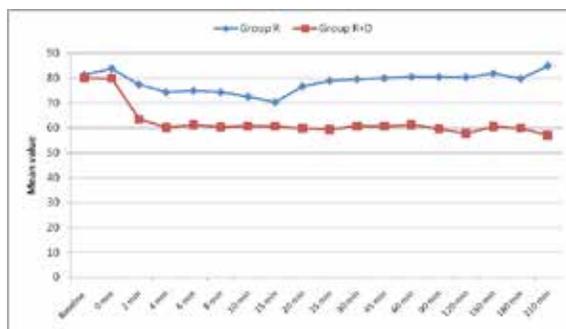


Fig.1: Comparison of heart rate between the groups

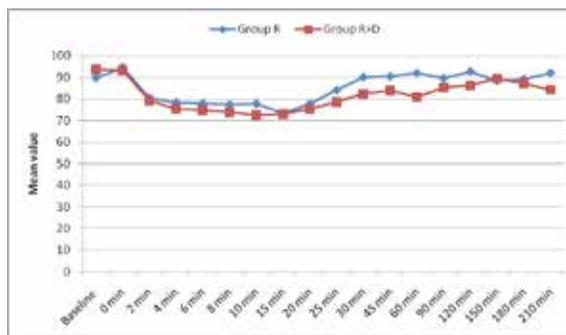


Fig.2: Comparison of MAP between the groups

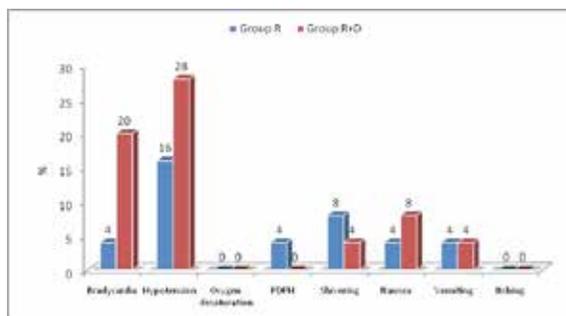


Fig.3: Frequency distribution of adverse effects in both the groups

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