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Original Research Article

Comparison of adjuvant effects of intrathecal magnesium sulfate and dexmedetomidine with hyperbaric bupivacaine

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ABSTRACT

Background: Surgeries involving infraumblical regions are commonly done under spinal anaesthesia. No single adjuvant to bupivacaine found to prolong the duration of analgesia and to reduce its limitations.
Objectives: To compare the block characteristics of intrathecal administration of dexmedetomidine and magnesium sulfate as an adjuvant with bupivacaine in infraumblical surgeries.
Materials and Methods: This is a prospective randomized double-blinded study. Around 90 American Society of Anaesthesiologist physical status I and II patients, scheduled for infraumblical surgeries were enrolled in this study. Patients were randomly assigned into Group B (bupivacaine), Group D (bupivacaine plus dexmedetomidine) and Group M (bupivacaine plus magnesium sulfate). In the operating theatre, baseline values were recorded. Onset and duration of sensory and motor block, time of rescue analgesia were noted.
Results: The onset of sensory block was rapid in Group D (2.63 ± 0.66 min) and slow in Group M (6.35 ± 0.87 min) when compared to Group B (2.93 ± 0.785 min) with a statistically significant difference. Motor duration (min) was prolonged in Group D (423.00 ± 12.360) and early in the Group M (165 ± 31.55) when compared to Group B (219.23 ± 14.875).
Conclusion: For the surgery, which requires prompt onset and long duration of analgesia,dexmedetomidine can be used as an adjuvant. However, surgical procedures that permit delayed onset block and shorter duration of analgesia,magnesium sulfate can be preferred.

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1. Introduction

Infraumblical surgeries are commonly done under central neuraxial blockade. Spinal anaesthesia is preferred for its rapid onset, higher block, fewer failure rates, and cost -efficiency. However, the role of spinal anaesthesia is restricted in prolonged procedures, for its shorter duration of action and less postoperative analgesia when only local anaesthetics are used. This is overcome by adding adjuvants to local anaesthetics. Hence,various adjuvants like opioids, magnesium sulphate, clonidine, and dexmedetomidine were studied to prolong spinal anaesthesia.[1–4] Each adjuvant has its limitations and requires strict observation for any adverse effects. Best modality would be to deliver better analgesia with lesser opioid use and augment patient satisfaction and early rehabilitation.

Dexmedetomidine is an α2-adrenergic receptor agonist, with a relatively higher selective ratio of α2 to α1 receptor (1620:1 as compared to 220:1 for clonidine).[5] Intrathecal α2 agonists exerts its antinociceptive effects on somatic and visceral pain.[6] It has been the focus of interest in anaesthetic procedures, as it produces dose-dependent analgesia,sedation(involving spinal and supraspinal sites) without respiratory depression, secondary to activation of central α2-adrenoceptors in the locus coeruleus.[7] Based on earlier studies, it is clear that 5 μg dexmedetomidine when added to hyperbaric bupivacaine would provide better postoperative analgesia, at the same time with minimal side effects.[8–10] In the present study, the appropriate dosage of

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intrathecal dexmedetomidine with no neurotoxic effects was administered to study participants.[11,12]

Magnesium sulfate prevents the development of central sensitization of pain by antagonistic action on spinal cord N-methyl-D-aspartate receptors. The calcium channel blocking property of magnesium sulfate also contributes to its antinociceptive effect.[13] Intrathecal magnesium sulfate improved postoperative analgesia in orthopaedic cases.[14,15] Magnesium sulphate plus 25 μg fentanyl added to 10 mg bupivacaine enhanced spinal anaesthesia duration in lower extremity surgery.[16] Similarly, a study done by Khezri et al, shows optimal dosage of spinal magnesium sulfate to prolong the intrathecal opioid analgesia duration without additional side effects.[17]

In our study, we have compared the adjuvant effects of intrathecal magnesium sulphate and intrathecal dexmedetomidine added to hyperbaric bupivacaine, on block characteristics.

2. Materials and Methods

The prospective, randomized, double-blind, placebo-controlled study was conducted in the Annapoorna Medical College and hospital between June 2019 to December 2019. 90 patients planned for elective surgeries involving infraumbilical regions by spinal anaesthesia were involved in our study. Patients aged 18-50 years of both gender with American society of Anaesthesiologist physical status(ASA)PS I and II were included for our study. Exclusion criterion was contraindications for spinal anaesthesia, patients taking antihypertensives and antidepressant medications, dysrhythmias, and pregnant patients.

Institutional ethical committee approval obtained. Consent (written informed) of all the participants was obtained. Patients were allocated into three groups randomly (Group B, D, and M). Patients in 3 groups received drugs as follows. Group B- 15 mg hyperbaric bupivacaine +0.5 ml normal saline. Group D-15 mg hyperbaric bupivacaine +5 μg dexmedetomidine in 0.5 ml normal saline. Group M-15 mg hyperbaric bupivacaine +50 mg magnesium sulphate in 0.5 ml normal saline. All patients were given anxiolytic tablet alprazolam 0.5 mg, the night before surgery.

In the operation room, electrocardiogram (ECG), pulse oximeter(Spo2),and non-invasive blood pressure monitor were connected to patients and baseline values noted. Intravenous (IV) cannula was secured and preloading with ringer lactate 10 ml/kg was done. The study drug loaded in a 5 ml syringe was given in a coded form to the anaesthesiologist giving anaesthesia who was blinded to the drug given to him/her. Under strict asepsis, a lumbar puncturewas done at L_{2-3} or L_{3-4}interspace using a 26-gauge Quincke spinal needle with patients in sitting position. Immediately after injecting the study drug, patients were placed supine. Oxygen 2 L/min given through face mask if saturation falls below 90%.

Hypotension, defined as >30% fall in systolic blood pressure from baseline value or mean arterial blood pressure <60 mmHg was treated with i.v. fluids, inj.ephedrine 6 mg i.v based on response. Bradycardia, if heart rate < 50 beats per min patient was awakened and when heart rate does not increase, was treated with Inj.Atropine 0.3-0.6 mg i.v. Other adverse effects such as nausea, vomiting, shivering, respiratory depression, sedation, and pruritus were noted.

Intraoperative data were noted by the anaesthesiologist. The sensory level was assessed by the absence of pinprick sensation, using a 25-gauge blunt needle every 2 minutes till it reaches the highest dermatomal level. Surgery was started after the accomplishment of the loss of pinprick sensation at the T8 level. Time to two dermatomes sensory regression was noted. Time taken to return of pinprick sensation at S1 dermatome was taken as duration of sensory blockade.

The motor block level was examined by Modified Bromage score.[18] (the duration to reach Bromage score 3 was considered as motor block onset time) Motor block onset was when Bromage 3 score attained. Time to achieve full regression of motor block which corresponds to the score of Bromage 0 was taken as duration of motor block. The time of spinal injection was taken as time zero and all durations were assessed.

The pain was assessed using the visual analogue scale (VAS).[19] Time when the first request for rescue analgesics made or VAS Score > 4 was noted as period of effective analgesia. Rescue analgesia was an intravascular infusion of paracetamol 1gm and repeated 8^{th} hourly.

The data recorded were collected and tabulated. Analysis of data was done using Statistical Package for Social Sciences (SPSS Inc. Chicago, IL, USA) Windows-based version 16.0. Fisher's exact test or chi-square test was used to study nominal categorical data between groups. Data were tabulated as either means and standard deviations. The comparisons of continuous variables which were normally distributed amongst the groups was done by one-way analysis of variance (ANOVA) and, if relevant, the Bonferroni test was used for post hoc analysis. $p< 0.05$ values were considered statistically significant.

3. Results

A total of 30 participants in each group were included in the study. Group B received bupivacaine alone, Group D bupivacaine with dexmedetomidine and Group M bupivacaine with magnesium sulfate.

The demographic profile (Table 1) was compared among the three study Groups. The gender distribution ASA distribution of study participants was depicted in Figure 1 and Figure 2 respectively. The mean sensory onset time (min) was achieved earlier in Group D (2.63 ± 0.66) and delayed in Group M (6.35 ± 0.87) when compared to Group

B (2.93 ± 0.785) (Table 2). When compared to Group B (11.23 ± 1.331), maximum sensory block (min) was attained faster in Group D (9.27 ± 1.172) and delayed in Group M (12.40 ± 1.32) (Table 2). Time to 2 segment regression (min) was prolonged in Group D (152.03 ± 10.307) when compared to Group B (71.70 ± 9.520) and Group M (90.43 ± 7.060) (Table 2). There was a significant delay in time for rescue analgesia (min) in Group D (363.00 ± 22.537) and Group M (261.25 ± 21.75). When compared to Group B (6.60 ± 1.163), the motor onset time in (min) was early in the Group D (5.33 ± 0.711) and delayed in the Group M (7.45 ± 1.35). Motor duration (min) was less in Group M (165 ± 31.55) and prolonged in Group D (423.00 ± 12.360) and when compared to Group B(219.23 ± 14.875) (Table 2). There was no significant change in heart rate and mean arterial pressure in all the three study groups. (Figure 3 and Figure 4).

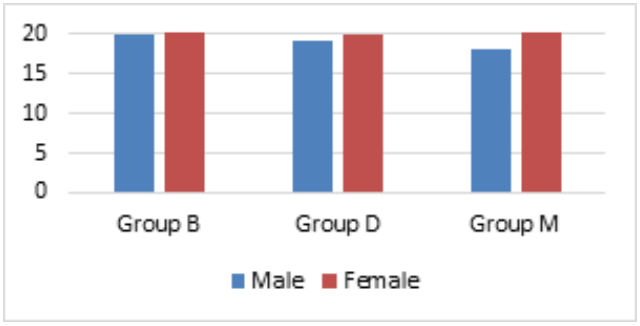

Fig. 1: Gender wise distribution of study participants

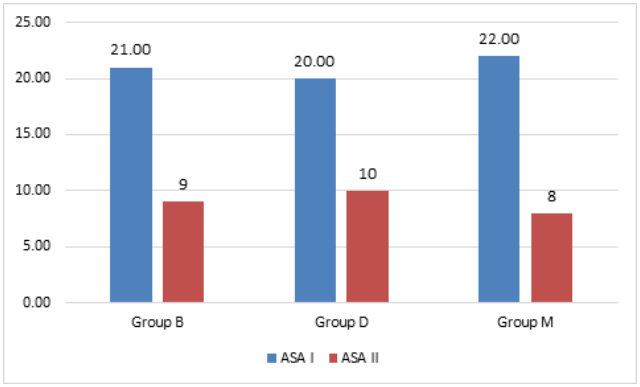

Fig. 2: ASA grade distribution of study participants

4. Discussion

The effects of spinal bupivacaine, when supplemented with intrathecal dexmedetomidine, revealed the shorter onset time for both sensory and motor block. Also, the period of sensory and motor blocking effects of spinal bupivacaine was prolonged when supplemented with intrathecal dexmedetomidine. Our study concurs with Kaya et al.[20] and Kanazi et al.,[2] where there is prolonged bupivacaine spinal anesthesia when dexmedetomidine was used as an adjuvant.[20] Moreover, Al-Mustafa et al. 2009[21] showed that prolonged duration of motor block was attributed to the appropriate dosage and volume of intrathecal dexmedetomidine. Furthermore, a study done in animals showed significant analgesic effect and increased duration of the sensory and motor block when intrathecal dexmedetomidine was given along with bupivacaine.[22] The sensory block prolongation by intrathecal dexmedetomidine was by depressing the C-fibre transmitter release and also

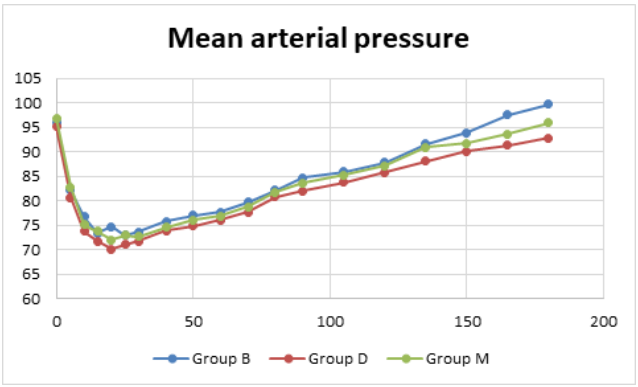

Fig. 3: MAP Changes during the study in three Groups

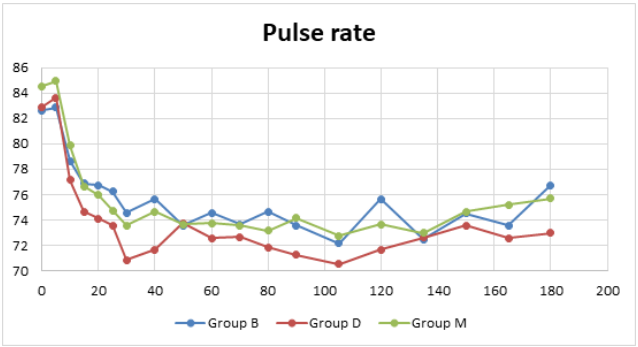

Fig. 4: Pulse rate changes during the study in three Groups

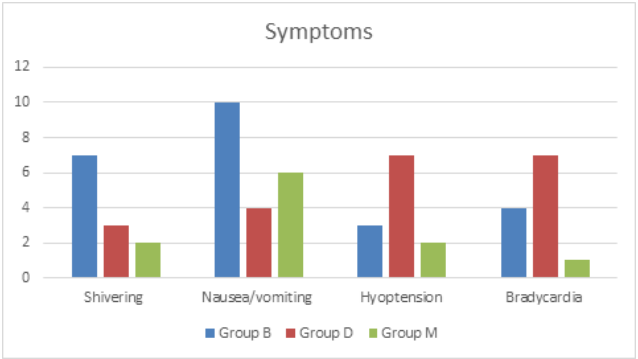

Fig. 5: Number of cases with symptoms in different Groups

Table 1: Demographic profile of the study participants

Parameters	Group B	Group D	Group M	p value
Age in years	40.16±10.12	41.85 ± 9.85	42.56 ± 7.5	0.5876
Height in cms	161.70 ± 8.38	165.23 ± 7.32	163.73 ± 9.32	0.1625
Weight in kgs	60.33 ± 7.21	64.32 ± 8.56	63.54 ± 7.64	0.0960

Table 2: Characteristics of spinal anaesthesia in study participants

Parameters	Group B (mean ± SD)	Group D(mean ± SD)	Group M (mean ± SD)	F value	p value
Sensory onset time (min)	2.93 ± 0.785	2.63 ± 0.66	6.35 ± 0.87	638.892	0.000*
Time to maximum sensory block (min)	11.23 ± 1.331	9.27 ± 1.172	12.40 ± 1.32	138.174	0.000*
Time to 2 segment regression (min)	71.70 ± 9.520	152.03 ± 10.307	90.43 ± 7.060	1933.144	0.000*
Time for rescue analgesia (min)	230.83 ± 13.332	363.00 ± 22.537	261.25 ± 21.75	679.176	0.000*
Motor onset time (min)	6.60 ± 1.163	5.33 ± 0.711	7.45 ± 1.35	83.503	0.000*
Motor duration (min)	219.23 ± 14.875	423.00 ± 12.360	165 ± 31.55	3648.37	0.000*

p< 0.05 value considered statistically significant.

by postsynaptic dorsal horn neurons hyperpolarization.[23] Intrathecal dexmedetomidine prolong motor block by binding to $\alpha 2$ adrenoreceptors of motor neurons located in the spinal cord dorsal horn.[24] Although there was no significant bradycardia and hypotension intraoperatively, postoperative hypotension and bradycardia were obvious in participants receiving intrathecal dexmedetomidine with bupivacaine (Figure 5). Compared with the use of bupivacaine for spinal anaesthesia for lower segment caesarean section, adding intrathecal dexmedetomidine during spinal anaesthesia can significantly shorten the onset time and decrease the rate of shivering during anesthesia.[25]

The sensory and motor blockade onset time was delayed in Group M compared to other two groups as depicted in Table 2. The sensory block duration was prolonged, whereas motor block duration was less when compared to Group B. Our study is supported by Zhong et al., who showed intravenous magnesium sulfate can accelerate the sensory block onset and lenghthen the sensory block and spinal anesthesia duration.[26] Banihashem et al., reported that the intrathecal magnesium sulfate delayed the onset of sensory blockadewhich was not advisable for cesarean section.[27] Ozalevli M et al. observed in lower extremity surgery patients, that there was a significant delay in the onset of motor and sensory blockade but prolonged the period of anaesthesia without additional side-effects when intrathecal magnesium sulfate was added to bupivacaine and fentanyl spinal anaesthesia.[15] Compared to three Groups, in Group M, shivering, hypotension, and bradycardia were less marked (Figure 5). These findings are supported by Omar et al.[28] and He L at al,[29] who showed magnesium sulfate causes peripheral vasodilation which improves the cutaneous circulation thereby decreasing the incidence of shivering. In a randomized control trial, reported by Morrison AP, et al., it was found that the incidence of hypotension and pruritus was similar in Group which bupivacaine alone and Group which received both bupivacaine plus magnesium sulfate. This is contrary to what is reported in this study.[30] The slow rate of injection would induce lower incidence of hypotension and thus better hemodynamic stability induced by spinal Bupivacaine for Caesarean section.[31]

In our study, both Group D and Group M have produced remarkable intraoperative analgesia with stable hemodynamics. The hemodynamic stability that was observed in this study is attributed mainly to good preloading. Furthermore, the associated sympathetic block is usually near-maximal with the doses used for spinal anaesthesia. Moreover, the time required for the first dose of rescue analgesic was more for Group D when compared to Group M. The duration of two-segment sensory block regression was remarkably slower in Group D when compared to Group M and Group B**.** However, different doses of the local anaesthetic with the same adjuvants were not considered in the study and the same can be done in the future studies.

5. Conclusion

Thus our study proved the superiority of bupivacaine and dexmetidomidine combination over bupivacaine alone for the surgeries which require prompt onset and longer duration of analgesia. However, bupivacaine with magnesium sulfate can be preferred over bupivacaine alone for short surgical procedures that permit sensory blockade onset delay.

6. Source of Funding

None.

7. Conflict of interest

None.

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