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Comparison between Intrathecal Dexmedetomidine and Magnesium Sulphate in Reduction of Post-Operative Analgesia Requirement among the Patients Undergoing Surgeries under Spinal Anaesthesia: A Prospective Randomized, Double Blinded Comparative Study

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ABSTRACT
Dexmedetomidine can be used as an adjuvant in epidurals with local anesthetic sparing effects. Its use during nerve blocks results in reduced postoperative pain. Also, local infiltration of IV dexmedetomidine is associated with earlier discharge from PACU. Similarly, magnesium the blockade of N-methyl-D-aspartate (NMDA) receptor and calcium channel has an important meaning to anesthesia. However, side effects could be cardiac or respiratory complications. Therefore, we compared the intrathecal dexmedetomidine and magnesium sulphate for post-operative analgesia requirement reduction in patients undergoing spinal anaesthesia and analysing hemodynamic changes. All three drugs (dexmedetomidine, magnesium sulphate and hyperbaric bupivacaine) proved to be haemodynamically stable as clinically significant bradycardia and hypotension were not observed in any of the groups. The incidences of side effects were negligible in all the three groups. In conclusion, although longer duration of effect can be obtained by the addition of either dexmedetomidine or magnesium to intrathecal hyperbaric bupivacaine, dexmedetomidine showed a significantly prolonged effect and a faster onset with fewer side effects.

Key words: Intrathecal, dexmedetomidine, magnesium sulphate, ASA grade I & II, post op analgesia, spinal anaesthesia

INTRODUCTION

According to International Association for the study of pain, pain is defined as an unpleasant network activity occurring in sensory brain and emotional personal experience influence to varying degrees by biological, psychological, and social factors that are associated with actual or potential tissue damage.

Pain is the most devastating experience to patient post-surgery though analgises are administered via spinal anesthesia. However, recent interest is found with magnesium and dexmedetomidine drugs which have proved its efficiency in curing pain.[1]Dexmedetomidine, a selective alpha$_2$ agonist, possesses analgesic effects and has a different mechanism of action when compared with opioids. When dexmedetomidine is initiated at the end of a procedure, it has a better hemodynamic stability and pain response than ropivacaine. Dexmedetomidine can be used as an adjuvant in epidurals with local anesthetic sparing effects. Its use during nerve blocks results in reduced postoperative pain. Also, local infiltration of IV dexmedetomidine is associated with earlier discharge from PACU.[2] Similarly, magnesium the blockade of N-methyl-D-aspartate (NMDA) receptor and calcium channel has an important meaning to anesthesia. However, side effects could be cardiac or respiratory complications.[3]

The 2017 Global Burden of Disease study found that the age standardised rates for point prevalence of neck pain was 3551.1 per 100 000. The highest burden for neck pain was found in Norway, Finland, and Denmark.[4] Recent studies have found that pain remains a prevalent and serious problem in older age, demonstrated by the following data: the prevalence of chronic pain in older people (>65 years) living in the community ranges from 25.0% to 76.0%, while the prevalence of chronic pain in older people living in residential care is much higher and ranges from 83.0% to 93.0%.[5]

Therefore, we proposed to compare the intrathecal dexmedetomidine and magnesium sulphate for post-operative analgesia requirement reduction in patients undergoing spinal anaesthesia and analysing hemodynamic changes in terms of heart rate (HR), systolic BP (SBP), diastolic BP (DBP), mean arterial pressure (MAP), Respiration rate, Oxygen saturation variability.

METHODOLOGY

The present study was a prospective randomized, double blind study entitled “Comparison Of intrathecal Dexmedetomidine and Magnesium Sulphate in Requirement of Post-Operative Analgesia in Patients Undergoing Surgeries In spinal Anaesthesia" conducted among 60 patients undergoing surgeries under spinal anaesthesia to compare the use of dexmedetomidine versus magnesium sulfate as adjuvants; in the Department of Anaesthesiology and Critical Care, Jhalawar Medical College and Associated Groups of Hospitals, Jhalawar from a period of November 2021 to November 2022.

INCLUSION CRITERIA: After hospital's ethical committee's approval and written informed consent from the patient's attendant, the present study was conducted on 60 adult patients of either sex aged 20-50 years, ASA grade I & II, who were scheduled for surgery under spinal anaesthesia, of duration about 30 minutes to 2 hours and 30 controls were also included.

EXCLUSION CRITERIA: Patient’s with ASA Grade III, IV, patients refusing to take part in the study, diagnostic evidences of having diabetes mellitus, neurological, psychiatric, neuromuscular, cardiovascular, pulmonary, renal or hepatic disease, known hypersensitivity to local anaesthetic drugs/magnesium sulphate/α agonist, showing coagulopathy, associated head injury and chronic pain sensitivity with prolong analgesic treatment.

Patients included in the study were grouped into two categories Group A (30) and Group B (30) administered 10ug of dexmedetomidine along with 2.5ml(12.5mg) hyperbaric bupivacaine intrathecally and administered 75mg of magnesium sulphate along with 2.5ml(12.5mg) hyperbaric bupivacaine intrathecally respectively. Group C (30) remained control who received only hyperbaric bupivacaine intrathecally. Pre-anaesthetic evaluation

was done to examine the patient physically fit for the study, visual analogue score (VAS) was done to assess the pain tolerance, further, haemodynamic monitoring was done to know patient's cardio-respiratory parameters of heart rate, blood pressure, SpO2 and ECG were monitored continuously and recorded before (baseline) and every 5 min after administration of drugs till 30 minutes and then every 15 minutes until the end of surgery.

Hypotension was defined as a fall in systolic blood pressure of more than 20% of baseline value or less than 100 mm Hg and were treated with volume expansion and if required, by incremental doses of mephentramine 3-6 mg. Bradycardia (heart rate <55/min) was treated with 0.6 mg of intravenous atropine. Duration of analgesia, was observed for intensity of pain in post-operative period and was measured using a 10 cm VAS (where 0 = no pain and 10 = worst). The VAS was measured at 1, 2, 4, 8, 12 and 24 hours respectively. The rescue analgesia was given by injection tramadol (2.5mg/kg i.v) SOS. When VAS was more than 4, total analgesic consumption in 24 hours was recorded. Side effects were also noted in case patients had any complaints of pruritus, nausea, vomiting, respiratory depression, and shivering was carefully observed, recorded, and managed symptomatically.

STATISTICAL ANALYSIS: Appropriate statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 22.0. Continuous data was expressed in the form of mean and standard deviation and categorical data was expressed in the form of percentage. Student's unpaired t-test was used to establish level of significance for differences in haemodynamic variables between the groups and ANOVA for intergroup evaluation. Nominal data was analyzed using the Chi-Square test. P value <0.05 was considered statistically significant.

RESULTS

Present study included three groups each 30 patients as stated above, all the three groups were similar in terms of age, gender, weight, Mallampatti Grade Wise Distribution and ASA classification and type of surgery. No statistically significant difference was seen with respect to these parameters.

ONSET OF SENSORY AND MOTOR BLOCK: In our study, a statistically significant quicker onset of sensory block was observed in Group A (Dexmedetomidine). 2.34 minutes was the mean onset time of sensory block in Group A,while in Groups B and C, it was 5.99 and 4.02 minutes respectively ,resulting in a statistically significant difference with P<0.001. Group A (Dexmedetomidine) took 3.96 min for the appearance of motor block. In Groups B and C it was 6.71 and 4.91 minutes, respectively with P <0.001. (Table 1)

TOTAL DURATION OF SENSORY BLOCK, MOTOR BLOCK AND ANALGESIA: In the current study, sensory block lasted for 352.6 mins in Group A. The duration was 273.87 and 190 mins in Group B and C respectively with P<0.001. This statistically significant difference proves that the duration of sensory block can be prolonged by adding dexmedetomidine. **M**otor block lasted for 333 mins in Group A. The duration was 284 and 137 mins in Group B and C respectively with P<0.001. This statistically significant difference proves that the duration of motor block can be prolonged by adding dexmedetomidine. Analgesia lasted for 379 mins in Group A in the present study, while it was 305 and 211 mins in groups B and C respectively. (Table 2)

QUALITY OF ANALGESIA: It was observed that the dexmedetomidine group had significantly lower VAS scores compared to the other two groups indicating better analgesia. This difference attained a higher significance from 4 to 48 hours, indicating that the addition

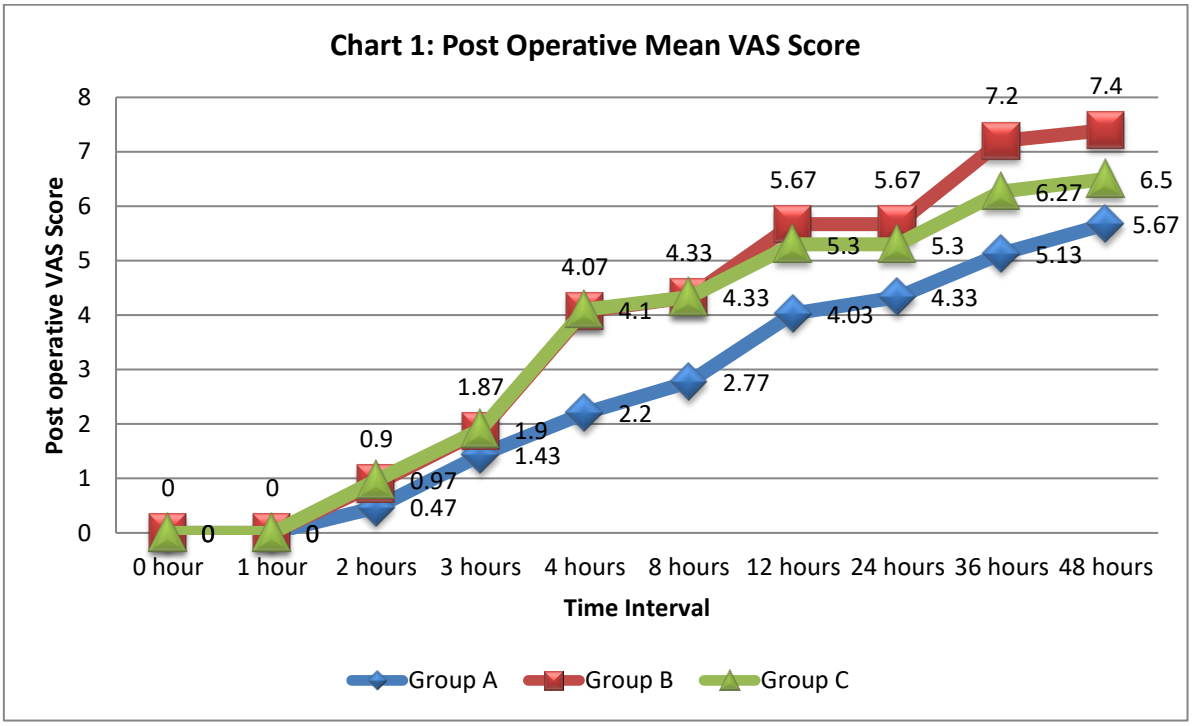
of dexmedetomidine provides better analgesia compared to Magnesium sulfate and plain Bupivacaine. (Chart 1)

Table 1: Mean Onset of Sensory and Motor Block:

Mean onset time (in minutes)	Group A N=30	Group B N=30	Group C N=30	P value (ANOVA)
Sensory Block	2.34±0.16	5.99±0.22	4.02±0.34	<0.0001(HS)
Motor Block	3.96±0.14	6.71±0.11	4.19±0.25	<0.0001(HS)

Table 2: Mean Duration of Sensory Block, Motor Block and Analgesia:

Mean duration (in minutes)	Group A N=30	Group B N=30	Group C N=30	P value (ANOVA)
Sensory Block	352.6±6.02	273.87±3.64	190±5.23	<0.0001(HS)
Motor Block	332.5±2.92	284.13±3.75	137±3.43	<0.0001(HS)
Analgesia	379.8±2.64	305.93±4.83	211±4.27	<0.0001(HS)



HEMODYNAMIC VARIABLES: There was no difference in the baseline HR, SBP, DBP and MAP among the groups. In the subsequent recordings, lower values were observed for these parameters in group A. The same pattern was seen in the post-operative recordings of these variables.Significant hypotension and bradycardia were observed in only 1 patient in the dexmedetomidine group and in 3 patients in the magnesium group and hemodynamic stability was maintained in rest of the patients.

SIDE EFFECTS: Only 2 patients each in groups A and B and 3 in group C had nausea and vomiting. Other side effects like headache, pruritus or seizures were not observed.

DISCUSSION

Subarachnoid or spinal block is straight forward to carry out. Advantages include need for minimal dose of medication, quick onset and dependable surgical conditions with

appropriate muscle relaxation.However, the disadvantages include a brief period of action and complaints of postoperative pain as effect reduces.

The efficacy of regional anaesthetics may be improved with the usage of adjuvants inclusive of opioids, α 2 agonists, magnesium, neostigmine, ketamine. Prolonging the effect of spinal block is desirable for surgeries of long duration and for remedy of postoperative pain. In the present study, we aimed to compare the effect of intrathecally administered magnesium and dexmedetomidine with Bupivacaine with respect to time of onset, duration and hemodynamic profile, in addition to the side effects .

DEMOGRAPHIC DATA: All the three groups were similar in terms of age, gender, ASA classification and type of surgery.No statistically significant difference was seen with respect to these parameters.

ONSET OF SENSORY BLOCK: In our study, a statistically significant quicker onset of sensory block was observed in Group A (Dexmedetomidine). 2.34 minutes was the mean onset time of sensory block in Group A,while in Groups B and C,it was 5.99 and 4.02 minutes respectively ,resulting in a statistically significant difference with P<0.001. The observations of the present work correlated with other similar studies. Mahesh Kumar et al[6], undertook a study in which dexmedetomidine was added to ropivacaine. An early onset of sensory block at T10 was observed. The time taken to achieve T10 sensory level was 4.85 minutes vs. 6.52 minutes, the difference being statistically significant.

In the study by Deepika Shukla et al[7], magnesium sulfate had a delayed onset (6.46 ± 1.33 minutes) in contrast to dexmedetomidine (2.27 ± 1.09 minutes).The time to attain sensory block at T10 in group plain bupivacaine was found to be 4.15±1.14 minutes in the study performed by Sunil et al[8],whereas in groups with magnesium sulfate and dexmedetomidine it was 6.46±1.32 min and 3.27±0.86 min ,respectively (p <0.05) which become statistically significant.

Srinivasan et al[9] carried out a study to assess the usage of dexmedetomidine as adjuvant with intrathecal ropivacaine.The author observed that compared to plain ropivacaine, sensory block wasfaster in group dexmedetomidine,5.58±3.56 min vs 8.0±1.8 min (P<0.0001).

ONSET OF MOTOR BLOCK: In the present study,Group A (Dexmedetomidine) took 3.96 min for the appearance of motor block.In Groups B and C it was 6.71 and 4.91 minutes,respectively with P <0.001.

Kavitha Jain et al[10] also made similar observation, in their study;time of onset of motor block in Group Dexmedetomidine was 3.73 ± 0.43 min, whereas in Group Magnesium sulphate it was 7.72 ± 0.48 min. 5.92 ± 1.48 min,8.8 ± 1.54 min and 6.33 ± 1.37 minutes were the mean time for onset inDexmedetomidine; Magnesium and control groups in the study by Raviprakash et al[11], these studies show that adding dexmedetomidine with hyperbaric bupivacaine results in a faster onset of motor block.

Onset of motor block was similarly shown to be hastened in group with dexmedetomidine in a study conducted by Mahesh Kumar et al[6].It was faster (9.93 min) compared to group with magnesium sulfate (12.11 min) with a statistical significance (p<0.001). In a comparative study,Eloraby RMet al[12] also observed thatthe motor block was delayed in Magnesium sulfate group 5.80±1.47 min, versus 5.50±0.61 min and 3.95±1.47 min in Bupivaccaine plain and Dexmedetomidine groups.

TOTAL DURATION OF MOTOR BLOCK: In the current study of motor block lasted for 333 mins in Group A.The duration was 284 and 137 mins in Group B and C respectively,with P<0.001.This statistically significant difference proves that the duration of motor block can be prolonged by adding dexmedetomidine.

A significantly prolonged motor block was also observed by Kavitha Jain et al[10] in the Dexmedetomidine Group (314.38 ± 14.93 min) compared to Magnesium sulfate (228.81 ± 11.01 min) Group (P < 0.05). In line with these studies, Mahesh Kumar et al[6] found a statistically significant(p<0.001) prolongation in group with dexmedetomidine 226.03 min, versus bupivacaine 171.17 minutes. Vani et al[13] obtained a longer duration by using dexmedetomidine as an additive to isobaric ropivacaine. 182.9 ± 18.4 min was the total duration in Group D dexmedetomidine in contrast to 104 ± 12.1 min in Group R Ropivacaine. Similar observation was made by Deepika Shukla et al[7]. They showed that complete wear off took 331 ± 35 min in the group Dexmed,pointing to a longer duration.

TOTAL DURATION OF ANALGESIA: Analgesia lasted for 379 mins in Group A in the present study,while it was 305 and 211 mins in groups B and C respectively.This was in concordance with the study by Kavitha Jainet al[10]. The duration of analgesia was significantly longer In Group D (348.26 ± 22.35 min) than Group M (268.01 ± 11.31 min) (P < 0.001).

Addition of dexmedetomidine increased the analgesia duration in the study done by Mahesh Kumar et al[6].In this study, 390.17 min was the mean duration of analgesia in group A(ropivacaine with dexmedetomidine) whereas in group B (ropivacaine with magnesium sulfate) it was 199.27 min. A statistically significant difference (P<0.05) with respect to duration of analgesia was seen in the study carried out by Vani et al[13]which was 430.9±33.08 minutes in Group D (ropivacaine with dexmedetomidine) versus 204.7± 20.61minutes in Group R(plain ropivacaine)

QUALITY OF ANALGESIA: It was observed that the dexmedetomidine group had significantly lower VAS scores compared to the other two groups indicating better analgesia. This difference attained a higher significance from 4 to 48 hours, indicating that the addition of dexmedetomidine provides better analgesia compared to Magnesium sulfate and plain Bupivacaine. Similar observation was made by Reena Makhni et al[14] wherein the VAS started increasing after 4th hour. However, the requirement for analgesia was earlier in the magnesium sulfate group compared to the dexmedetomidine group.

HEMODYNAMIC VARIABLES: There was no difference in the baseline HR,SBP, DBP and MAP among the groups. In the subsequent recordings, lower values were observed for these parameters in group A. The same pattern was seen in the post-operative recordings of these variables. Significant hypotension and bradycardia were observed in only 1 patient in the dexmedetomidine group and in 3 patients in the magnesium group and hemodynamic stability was maintained in rest of the patients. This correlated with the studies conducted by Deepika Shukla et al[7].

SIDE EFFECTS: Only 2 patients each in groups A and B and 3 in group C had nausea and vomiting. This incidence is slightly higher than that observed by Omar et al[15]. Other side effects like headache,pruritus or seizures were not observed. Raviprakash et al[11] and Eloraby RMet al[12]also came across similar findings wherein significant side effects were not observed by adding dexmedetomidine.

The above results of our study are in line with the study by Sunil B.V et al[8].Similar to our study,the authors used 10 µg of dexmedetomidine intrathecally with 15 mg hyperbaric

bupivacaine (total volume: 3.5 ml) .The onset of the block was quicker with a longer duration as compared to magnesium and plain bupivacaine.A delayed onset in magnesium sulfate observed in this studyis similar to the observations made by Ozalevli et al[16] and Malleeswaran et al[17]. Addition of magnesium sulfate results in a change in pH and baricity of bupivacaine which could account for the delayed onset of action in magnesium group. All the three study groups had stable haemodynamic.

Wang J et al[18] conducted a meta-analysis to look into the utilization of Dexmedetomidine and magnesium sulfate as an additive to bupivacaine in spinal anesthesia. This study demonstrated that intrathecal dexmedetomidine is associated with longer durations of sensory and motor block and shorter onsets of sensory and motor block than intrathecal magnesium sulfate without an increased risk of adverse effects. Therefore, dexmedetomidine is superior to magnesium sulfate as a local anesthetic adjuvant for spinal anesthesia.

Dexmedetomidine is a useful adjuvant to intrathecal bupivacaine as it results in an early onset of sensory and motor block. Magnesium sulfate (Group B) has a delayed onset of sensory and motor blockade in contrast to dexmedetomidine (Group A). Dexmedetomidine is a better additive compared to magnesium as the total duration of analgesia and motor block is significantly longer.

CONCLUSION

In conclusion, although longer duration of effect can be obtained by the addition of either dexmedetomidine or magnesium to intrathecal hyperbaric bupivacaine, dexmedetomidine showed a significantly prolonged effect and a faster onset with fewer side effects

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