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Comparison Of The Hemodynamic Effects And Assess The Adverse Effects Of Intrathecal Dexmedetomidine And Midazolam In Lower Limb And Abdominal Surgeries

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ABSTRACT

Background: Various adjuvants have been used with local anesthetics in spinal anesthesia to avoid intraoperative visceral and somatic pain and to provide prolonged postoperative analgesia. Dexmedetomidine, the new highly selective α2-agonist drug, is now being used as a neuraxial adjuvant. The aim of this study was to evaluate the onset and duration of sensory and motor block, hemodynamic effect, postoperative analgesia, and adverse effects of dexmedetomidine or fentanyl given intrathecally with hyperbaric 0.5% bupivacaine.

Aim and Objective: To study the hemodynamic effects and assess the adverse effects of intrathecal dexmedetomidine and midazolam in lower limb and abdominal surgeries.

Methodology: The Department of Anaesthesiology at Santosh Medical College & Hospital in Ghaziabad, Uttar Pradesh, conducted this prospective, randomised clinical study for a full year from May 2016 to May 2017. 60 patients underwent elective procedures on their lower limbs and

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abdomen. Patients must be between the ages of 18 and 60 in order to undergo surgery on the lower limbs and the abdomen. The patients were given ASA grades I and II.

Result: The three groups' MAP means were examined. Group D baseline MAP was 92.60±6.524 mm Hg, group M was 93.25±8.187, and group C was 90.80 ±8.519 mm Hg.

Conclusion: Intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 h as compared to fentanyl.

Keywords: Bupivacaine, dexmedetomidine, fentanyl, spinal anaesthesia,

INTRODUCTION

Spinal anesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action, and thus early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as clonidine and midazolam, and others have been studied to prolong the effect of spinal anesthesia.[1,2] A common problem during lower abdominal surgeries under spinal anesthesia is visceral pain, nausea, and vomiting.[3] The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block.[4] The addition of opioids to local anesthetic solution have disadvantages, such as pruritus and respiratory depression. Dexmedetomidine, a new highly selective α2- agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.[5-7] Dexmedetomidine has been approved by Food and Drug Administration (FDA) as a short-term sedative for mechanically ventilated intensive care unit (ICU) patients. Based on earlier human studies, it is hypothesized that intrathecal 5 µg dexmedetomidine would produce more postoperative analgesic effect with hyperbaric bupivacaine in spinal anaesthesia with minimal side effects.[5-7],there has been no study

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comparing the addition of dexmedetomidine to hyperbaric bupivacaine with hyperbaric fentanyl to bupivacaine, although various studies have compared dexmedetomidine and fentanyl with isobaric bupivacaine.[5,6]

Midazolam, a benzodiazepine derivative, modulates antinociception through gamma-amino butyric acid (GABA) receptors present in the dorsal horn of the spinal cord and through the activation of spinal delta opioid receptors. In contrast to sympatholytic effects of dexmedetomidine, Intrathecal midazolam keeps the function of sympathetic nervous system intact [17,18] but may result in excessive sedation due to its GABA mimetic and opioid induced analgesia.

Dexmedetomidine, an imidazoline compound is a D-isomer of medetomidine, which is pharmacologically active and exhibits selective alpha 2 adenoreceptor agonistic activity.[8,9]. From earlier studies [10,11] we understand that 5 mcg dexmedetomidine would produce prolonged sensory blockade with bupivacaine 0.5% in spinal anaesthesia with less side effects. Dexmedetomidine binds to pre synaptic C fibres and post synaptic dorsal horn neurons.[12,13] Intrathecal dexmedetomidine produces analgesia by suppressing the release of C fibres pro-nociceptive neurotransmitters, substance P and glutamate from primary afferent terminals and by hyper polarisation of post synaptic dorsal horn neurons through G protein mediated activation of potassium channels.[14]. An alpha 2 agonist administered intrathecally or epidurally provides prolonged analgesia effect in post operative period without severe sedation.[15,16]. Its effects are reversible with atipamezole, an alpha 2 adrenoreceptor antagonist. Potential desirable effects include decreased requirement of anaesthetics and analgesics, a diminished sympathetic response to stress and the potential for cardio protective effects against myocardial ischemia with minimal effects on respiration.

Despite the fact that dexmedetomidine and midazolam both modulate spinal analgesia by various mechanisms, there aren't many human studies that compare their effects on postoperative analgesia following neuraxial administration. Dexmedetomidine and midazolam

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were therefore compared in the current study to intrathecal hyperbaric bupivacaine as adjuvants in lower limb and abdominal surgeries.

MATERIALS AND METHODS

The Department of Anaesthesiology at Santosh Medical College & Hospital in Ghaziabad, Uttar Pradesh, conducted this prospective, randomised clinical study for a full year from May 2016 to May 2017. 60 patients underwent elective surgeries on their lower limbs and abdomen. Patients must be between the ages of 18 and 60 in order to undergo surgery on the lower limbs and the belly. The patients were given ASA ratings I and II.

Following preloading, under all aseptic precautions, lumbar puncture was performed with 25G Quincke's spinal needle in L3-L4 interspace or L4- L5 interspace, through a midline approach in a sitting position. After confirming the free flow of Cerebrospinal fluid (CSF) through the spinal needle, patients in the dexmedetomidine group D received 3 ml of 0.5% hyperbaric bupivacaine combined with 5 mcg of dexmedetomidine, patients in the midazolam group M received 3 ml of 0.5% hyperbaric bupivacaine and 1 mg of midazolam while patients in the control group C were given 3 ml of 0.5% hyperbaric bupivacaine and 0.5 ml of 0.9% saline in the intrathecal space. The total volumes of intrathecal injections were made 3.5 ml by adding the appropriate amount of 0.9% saline.

The comparison of normally distributed continuous variables between the groups was performed using one-way analysis of variance (ANOVA) and, if appropriate, followed by post hoc analysis to see the significance between each pair of groups. SPSS analysis (version 10.0) was used. p value of less than 0.05, i.e, $p<0.05$ was considered statistically significant.

RESULTS

Table 1: Demographic data distribution of study subject.

Demographic Distribution	Number (Percentage)

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		Group D	Group M	Group C
ge Groups	21-30 Years	%)	5 (25%)	4 (20%)
	31-40 Years	%)	7 (35%)	4 (20%)
	41-50 Years	%)	3 (15%)	6 (30%)
	51-60 Years	%)	5 (25%)	6 (30%)
Gender	Male	12 (60%)	11 (55%)	11 (55%)
	Female	08 (40%)	09 (45%)	09 (45%)
Age	Mean±SD	41.55 ± 14.376	39.35±14.224	43.75±14.163
Weight	Mean±SD	64.90±6.773	65.50±6.261	69.20±5.952

This table shows that the majority of patients in group D were between the ages of 21 and 30, while group M had the highest proportion of patients between the ages of 31 and 40, and group C had six patients in each of the age groups between 41 and 50 and 51 to 60. The distribution of patients by age within these 3 categories was discovered to be comparable and statistically insignificant (p=0.786). Males outnumbered females in all three groups, and the difference was statistically insignificant (p=0.876).

Table 2: Comparison of mean heart rate and mean map (mean arterial pressure) among study subjects.

	Time Intervals	Group D	Group M	Group C	p value
Mean Heart Rate	Baseline	81.55±8.17	84.85±6.11	86.10±8.54	0.089
	0 Minute	82.45±7.97	85.90±9.70	84.00±7.75	0.198
	30 Minutes	69.05±6.668	68.55±5.316	64.20±7.409	0.564
	60 Minutes	69.61±6.203	66.47±6.397	68.65±8.138	0.987

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	120 Minutes	74.40±4.623	70.00±4.708	70.84±6.902	0.123
	180 Minutes	73.50±4.434	74.66±0.577	70.75±7.588	0.235
Mean Map	Baseline	92.60±6.524	93.25±8.187	90.80±8.519	0.878
	0 Minute	92.20±6.932	88.65±4.625	86.70±7.547	0.001
	30 Minutes	82.15±5.88	81.90±5.220	76.95±5.355	0.056
	60 Minutes	81.72±6.007	82.88±5.143	78.55±4.957	0.076
	120 Minutes	86.45±5.520	84.91±5.107	81.76±4.323	0.065
	180 Minutes	90.00±3.162	84.00±2.645	81.00±.000	0.076

In Table 2, it shows that the mean heart rate at baseline was assessed. It was 81.55±8.17 per minute in group D, 84.85±6.11 per minute in group M and 86.10±8.54 per minute in group C. The p value being > 0.05, difference in the mean value in three groups at base line was statistically not significant. There was a fall in heart rate in all three groups, but the drop being maximum in group C. The mean of MAP in the three groups was analyzed. The baseline MAP in group D was 92.60±6.524 while in group M was 93.25±8.187 and in group C was 90.80±8.519 mm of Hg. Though there was a fall in MAP in all three groups intra operatively but the maximum fall was noted in group C which was not statistically significant (p>0.05).

Table 3: Side Effects in 3 groups.

Side Effects	Group D	Group M	Group C	p value
Hypotension	02 (10%)	03 (15%)	05 (25%)	
Bradycardia	01 (5%)	03 (15%)	03 (15%)	

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Respiratory Depression	00 (00%)	01 (5%)	01 (5%)	0.362
Shivering	02 (10%)	02 (10%)	04 (20%)	
Nausea	01 (5%)	01 (5%)	03 (15%)	
Vomiting	01 (5%)	02 (10%)	03 (15%)	
Other Effects	01 (5%)	02 (10%)	04 (20%)	

This table compares the side effects in 3 groups. Hypotension developed in 2 out of 20 subjects in group D, while 5 subjects in group C had hypotension which was seen in only 3 subjects of group M. 1 out of 20 patients in group D had bradycardia while 3 patients in group M and 3 patients in group C had bradycardia. None in group D had respiratory depression while 1 each in group M and group C suffered respiratory depression. 1 each out of 20 in group D and M and 3 in group C had nausea. While 1 in group D, 2 in group M and 3 in group C had vomiting. 4 out of 20 patients in group C developed shivering while only 2 patients each in group D and M were noted to develop shivering.

DISCUSSION

In our study, the largest number of patients (7 or 35%) in group D belonged to the 21–30 age range, while 7 (or 35%) of the patients in group M belonged to the 31–40 age range, and 6 (30%) of the patients in group C belonged to the 41–50 and 51–60 age ranges, respectively. The average age of the patients in group D was 41.55 years, compared to 39.35 and 43.75 years for groups M and C, respectively.

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In our study there was a fall in mean heart rate in all three groups. The fall was most significant at 30min in group C, the mean heart rate being 64.20±7.409 per minute. In group M the fall was maximum at 60 minute the mean heart rate at this point was 66.47±6.397 per minute. The minimum mean heart rate in group D was 68.05±6.235 per minute at 45min. Amongst the three groups the fall in mean heart rate was least in group D as compared to the baseline though the difference was not statistically significant (p>0.05). we also observed that a maximum fall in mean MAP at 45th minute in all three groups. The mean values being 76.50±4.382 mm Hg in group C, 80.90±5.25 mm Hg in group M while it was 80.11±4.921 mm Hg in group D. Though there was a fall in mean MAP in all three groups but the fall was least in group D followed by that in group M and maximum in group C as compared to baseline. There was no statistically significant difference (p=0.084) in the three groups regarding the fall in MAP.[20]

In our study, 2 patients (10%) out of 20 patients experienced hypotension, and 1 patient (5%), in the dexmedetomidine group, experienced bradycardia, however the number was higher in group M, where 3 patients (15%) experienced both hypotension and bradycardia. However, 3 (15%) patients in group C experienced bradycardia, while 5 (25%) of them experienced hypotension. While none of the patients in group D experienced respiratory depression, 1 (5%) each in groups M and C did. Between the three groups, there was no statistically significant difference (p=0.362).

In a study conducted by Shukla U et al.[19] 20% of patients in group D developed hypotension and bradycardia whereas in group M 12.5% had hypotension and 10% patients had bradycardia, that is contrary to the findings in our study where the patients in dexmedetomidine group were comparatively more haemodynamicaly stable, though the difference was not statistically significant.

CONCLUSION

Dexmedetomidine administered as an adjuvant intrathecally with bupivacaine extends the duration of effective analgesia in the early post-operative period with effective hemodynamic

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stability and without any noticeable adverse effects among the three groups studied. As a result, it may be a desirable intrathecal adjuvant for extending the effects of bupivacaine.

In conclusion, 5 µg dexmedetomidine seems to be an attractive alternative to 25 µg fentanyl as an adjuvant to spinal bupivacaine in surgical procedures. It provides good quality of intraoperative analgesia, hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia.

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