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A COMPARATIVE STUDY OF EVALUATING TWO DIFFERENT DOSES OF INTRAVENOUS DEXMEDETOMIDINE IN SPINAL ANAESTHESIA

Anaesthesiology

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ABSTRACT

Background: Neuraxial anesthesia offers valuable alternatives to general anesthesia and can be combined with it for post-operative pain relief. Subarachnoid blocks with hyperbaric bupivacaine are preferred for their quick onset and dense block lasting 2-2.5 hours. Adjuvants, especially opioids and α2 agonists, enhance spinal anesthesia. Increasing evidence has shown that Intravenous dexmedetomidine, an α2 agonist, prolongs spinal anesthesia, induces sedation, and improves post-operative pain relief with minimal cardiovascular and respiratory effects. **Aims:** To observe and compare the effects of intravenous dexmedetomidine in two different doses of 0.5 mcg/kg and 1.0 mcg/kg diluted in 10ml of normal saline, given slowly over 10 mins as a premedication before spinal anaesthesia with 0.5% hyperbaric bupivacaine in the dose of 15mg in regard to anaesthesia. **Methods:** A prospective, randomized study was done in the Department of Anaesthesia at SVPIMSR Hospital, Ahmedabad. 40 patients of ASA grade I & II, age 20-50 undergoing lower abdominal and lower limb surgeries under spinal anaesthesia were divided into two groups: Group D1- received 0.5 mcg/kg of dexmedetomidine and Group D2- received 1.0 mcg/kg of dexmedetomidine. **Results:** Patients receiving dexmedetomidine has significantly prolonged sensory block (1.0 mcg/kg > 0.5 mcg/kg). Motor blockade is also prolonged but not statistically significant. Dexmedetomidine does not affect the onset and maximum level achieved of the sensory or motor block. It significantly prolonged the time to first rescue analgesia (1.0 mcg/kg > 0.5 mcg/kg). Hemodynamics were stable both intra and post operatively and no more than usual complications were observed. **Conclusion:** Our study adds to the existing evidence supporting the efficacy and safety of sub-arachnoid block with 0.5% hyperbaric bupivacaine supplemented with intravenous α2 agonist for lower abdominal and lower limb surgeries, by prolonging sensory and motor blockade duration and prolonging time to first rescue analgesia, without any significant complications. Effects more prolonged with 1 mcg/kg dexmedetomidine compared to 0.5 mcg/kg.

KEYWORDS

Intravenous dexmedetomidine, Spinal Anaesthesia, Sensory and Motor blockade, First rescue analgesia, Hemodynamic parameters.

INTRODUCTION

Subarachnoid block is quite popular, as is generally well tolerated by all patients, producing less post-operative adverse effects like pulmonary complications, nausea, vomiting, confusion and delirium than general anaesthesia. Also associated with lesser incidence of post-operative thromboembolism. However, subarachnoid block has got its own inherent complications, especially related to cardiovascular stability.

Today, central neuraxial blocks are routinely employed for labor analgesia, caesarean delivery, lower abdominal surgery, lower limb orthopaedic surgery, peri-operative analgesia and chronic pain management[1]. Adjuvants from different pharmacological classes of drugs are used intravenously/ intrathecally to prolong the action of analgesia and enhance the efficacy of spinal anaesthesia, among which opioids and α2 agonist are most commonly used[2].

Dexmedetomidine is a potent, highly selective α2 adrenergic agonist[3]. One of the highest densities of α2-receptors is located in the pontine locus ceruleus,[4]an important nucleus mediating sympathetic nervous system function, vigilance, memory, analgesia and arousal. The effects produced by dexmedetomidine are largely due to inhibition of this nucleus. Few studies suggest that I.V Dexmedetomidine supplementation prolongs the effect of spinal anaesthesia. It is used as adjuvant to regional anaesthesia.

METHODOLOGY

Study Design

This prospective, randomized controlled trial conducted at SVP Hospital Ahmedabad from Jan 2021 to June 2021, included 40 ASA Grade I and II patients, aged 20-50 years, undergoing lower abdominal and lower limb surgeries under spinal anaesthesia. The patients were randomly assigned into two groups.

Group D1: Bupivacaine and Dexmedetomidine (0.5 mcg/kg) group

Patient in this group received 0.5mcg/kg of dexmedetomidine, diluted in 10ml saline, given slowly over 10 mins, 10 mins before giving spinal anaesthesia with bupivacaine 0.5% - 15 mg.

Group D2: Bupivacaine and Dexmedetomidine (1.0 mcg/kg) group

Patient in this group received 1mcg/kg of dexmedetomidine, diluted in 10ml saline, given slowly over 10 mins, 10 mins before giving spinal anaesthesia with bupivacaine 0.5% - 15mg.

Study Protocol

A comprehensive preoperative history was taken, including a general and systemic examination of each patient. Laboratory investigations, such as complete blood count, blood sugar levels, renal function tests, serum bilirubin, serum electrolytes, chest X-ray, and ECG, were reviewed. The procedure, including potential pain and discomfort during surgery, was explained to each patient, and the Visual Analog Scale (VAS) for pain, ranging from 1 to 10, was introduced. Written informed consent was obtained from both the patient and their relative. All patients were advised to be Nil by mouth (NBM) for a minimum of 6 hours prior to the scheduled surgery time. They were also educated about the procedure beforehand. Upon arrival in the operating room, intravenous (IV) access was established using an 18G or 20G cannula. Each patient received a preload of 10 to 15 ml/kg of lactated Ringer's solution before the procedure commenced. Dexmedetomidine was then administered intravenously over 10 minutes before the spinal anaesthesia was given. During this period, patients' vital signs were recorded at 1, 5, and 10-minute intervals.

Under strict aseptic and antiseptic conditions, with the patient in either a lateral or sitting position, a lumbar puncture was performed at the L3-L4 or L2-L3 interface via a midline approach using a 23-gauge Quincke's spinal needle. After confirming free and clear flow of cerebrospinal fluid (CSF), the selected amount of anaesthetic drug was injected slowly, and the time of injection was recorded and subsequently vitals were monitored.

Exclusion Criteria

Patients were excluded if they were younger than 20 years or older than 50 years, pregnant, had an infection at the block site, had a history of allergy to local anaesthetic drugs, suffered from severe cardiac or respiratory disease, had coagulation disorders, or were undergoing surgeries lasting more than three hours. Additionally, patients on medications that modify pain perception were also excluded from the study.

RESULTS

Statistical Analysis:

Statistical analysis was conducted using the unpaired Student's t-test to compare the means and standard deviations of the parameters between

the two groups. A p-value of <0.05 was considered statistically significant, and a p-value of <0.001 was considered highly significant. A p-value of >0.05 indicated a statistically non-significant difference. The unpaired Student's t-test was chosen due to its suitability for comparing the means of two independent groups, ensuring that differences observed were not due to random chance.

Patient Demographics and Baseline Characteristics (Table 1) were comparable between Group D1 and Group D2. There were no statistically significant differences observed in mean age mean weight, BMI, male to female ratio (12:8 vs. 11:9, p=0.74), ASA grades I and II distribution (8:12 vs. 11:9, p=0.34), and mean duration of surgery showing the homogeneity of study groups.

Preoperative hemodynamic parameters (Table 2) were similar between Group D1 and Group D2. There were no significant differences observed which suggest comparable baseline cardiovascular stability between the groups.

Characteristics of Sensory Block (Table 3): No statistically significant difference was observed in the time to onset of sensory block and time to reach the T10 level ($p > 0.05$), but time to two-segment regression was significantly prolonged in Group D2 ($p < 0.001$). The highest level of sensory blockade achieved was T8 in both groups. The mean time to onset of block was 1.06 ± 0.24 minutes in Group D1 and 0.94 ± 0.18 minutes in Group D2 (p=0.08).

Characteristics of Motor Blockade (Table 4): Both the groups were comparable in the time to achieve Grade 3 block as per modified bromage criteria. Although the total duration of motor blockade was longer in Group D2, the difference was not statistically significant(p>0.05).

Sedation Score (Ramsay Sedation Score) (Table 5): In Group D1, 75% of patients showed an RSS of 2, 20% showed RSS 3 (sleeping comfortably but easily arousable), and 5% showed RSS 4 (in deep sleep). In Group D2, 50% of patients showed RSS 3, and 45% showed RSS 4. There was a higher proportion of patients with higher sedation scores in Group D2 compared to Group D1. Also, both the groups were comparable with regards to postoperative hemodynamic parameters (HR, BP, RR, SpO2) with no statistically significant difference (P>0.05).

Complications (Table 6) such as hypotension were observed in 20% of patients in Group D2 and 10% in Group D1. Bradycardia occurred in 10% of patients in Group D2 and 5% in Group D1. No cases of nausea, vomiting, respiratory depression, or shivering were reported in either group.

Hemodynamic Parameters:
We observed an initial increase in heart rate post-administration of the study drug for the first 5 minutes, followed by a decline from 10 minutes onwards. This reduction was significantly more pronounced in Group D2 compared to Group D1 ($P < 0.05$). Similarly, there was an initial rise in mean arterial pressure (mm Hg) after drug administration, followed by a decrease from 10 minutes up to one hour, with a more notable reduction in Group D2 than Group D1 ($P < 0.05$). Intraoperative respiratory rate and SpO2 levels remained stable in both groups, with no statistically significant differences observed (P>0.05).

Time to First Rescue Analgesia:
The study found a significantly prolonged time to first rescue analgesia (VAS ≥ 3) in Group D2 patients (318.5 ± 16.63 minutes) compared to Group D1 (267 ± 12.18 minutes) ($P < 0.001$). This indicates that administering dexmedetomidine at the higher dose (1.0 mcg/kg) prolonged the duration until the need for additional analgesia post-operatively, compared to the lower dose (0.5 mcg/kg).

TABLES

Table-1: Demographic Characteristics

Parameters	Group D1	Group D2	p Value
Age in Years	35.55 ± 6.52	35.95 ± 9.07	0.87
Weight in Kg	57.65 ± 3.31	59.70 ± 4.19	0.97
Height in cm	157.80 ± 4.82	159.35 ± 4.28	0.29
BMI in kg/m2	23.22 ± 2.06	23.55 ± 1.95	0.61
Male: Female	12:8	11:9	0.74
ASA Grade I: II	8:12	11:9	0.34
Duration of Surgery in Hrs	2.06 ± 0.32	1.95 ± 0.24	0.23

Table-2: Pre-operative Hemodynamic Parameters (Mean +/- Sd)

Parameter	Group D1	Group D2	p Value
Pulse (beats / min)	83.60 ± 6.01	84.70 ± 5.60	0.55
Blood pressure (Systolic/Diastolic) (mm Hg)	125.10 ± 5.82 / 77.00 ± 4.88	125.90 ± 5.71 / 78.50 ± 3.94	0.66 / 0.29
SpO_2 %	98.80 ± 0.41	99.00 ± 0.56	0.60
Respiratory rate (per min.)	14.30 ± 1.03	14.45 ± 0.76	0.21

Table 3: Characteristics Of Sensory Block

Parameters	Group D1	Group D2	p Value
Time to onset of block (Mean ± SD) minutes	1.06 ±0.24	0.94 ± 0.18	0.08
Time to reach T10 level (Mean ± SD) minutes	5.53 ± 0.90	5.21 ± 0.62	0.20
Time taken for two segment regression (Mean ± SD) minutes	144.90 ± 16.87	174.60 ± 10.81	<0.0001

Table-4: Characteristics Of Motor Blockade

	Group D1	Group D2	p Value
Time to achieve Grade 3 block (Mean ± SD) minutes	6.68 ± 0.59	6.38 ± 0.46	0.08
Time taken for regression to Grade 0 level (Mean ± SD) minutes	182.35± 12.41	188.95± 9.16	0.06

Table- 5: Sedation Score (According to Ramsay Sedation Score)

Sedation score	No. (%) of patients	
	Group – D1	Group – D2
6	0	0
5	0	0
4	1(5%)	9(45%)
3	4(20%)	10(50%)
2	15(75%)	1(5%)
1	0	0

Table-6: Complications

Complications	No. of Patients			
	Group-D1		Group-D2	
	Intra-Op.	Post-Op.	Intra-Op.	Post-Op.
Nausea / Vomiting	0	0	0	0
Hypotension	2 (10%)	0	4(20%)	0
Bradycardia	1 (5%)	0	2 (10%)	0
Respiratory depression	0	0	0	0
Shivering	0	0	0	0

FIGURES

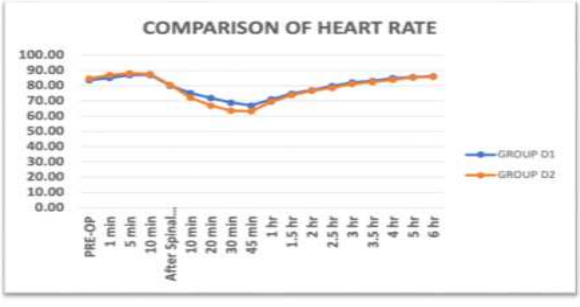

Figure1: Comparison of Heart Rate

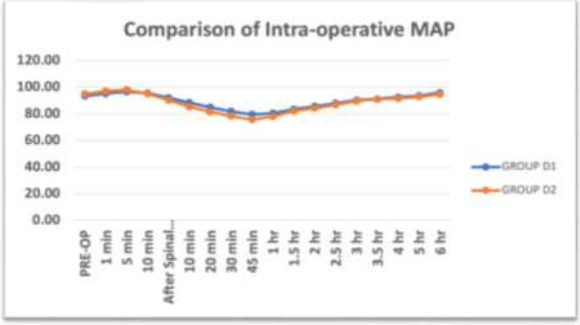

Figure 2: Comparison of Intraoperative MAP

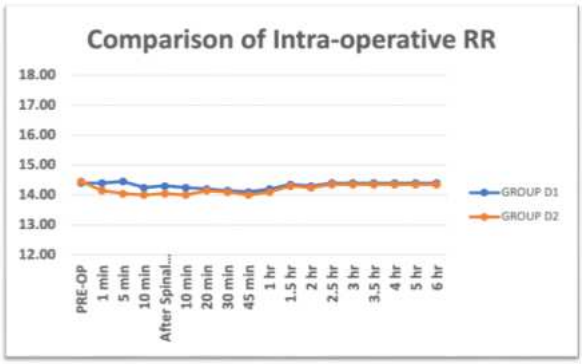

Figure 3: Comparison of Intraoperative RR

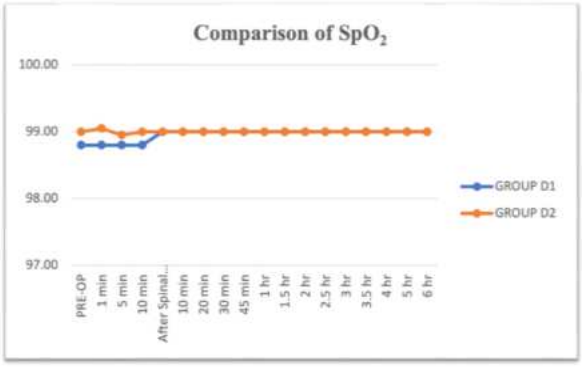

Figure 4: Comparison of SpO_2

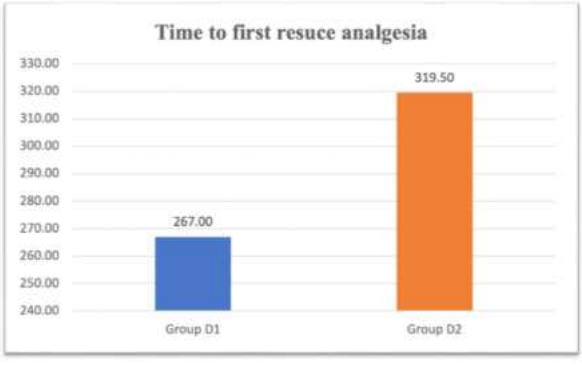

Figure 5: Time to first rescue analgesia

DISCUSSION

Dexmedetomidine, a potent α2-adrenoceptor agonist known for its analgesic and sedative properties, is widely utilized in intravenous sedation during spinal anesthesia and as an adjunct to local anesthetic agents across various administration routes including intrathecal, epidural, and peripheral nerve blocks. The use of dexmedetomidine as a local anaesthetic adjuvant has been increasingly reported to extend the duration of motor and sensory blockade produced by single injection neuraxial and peripheral nerve blockade[2]. Dexmedetomidine, binds to the presynaptic alpha-2 adrenoceptors, inhibits the release of norepinephrine, thereby, terminate the propagation of pain signals. Also, activation of the postsynaptic alpha-2 adrenoceptors inhibits the sympathetic activity which decreases blood pressure and heart rate[5].

At the spinal cord, stimulation of α2 receptors at the substantia gelatinosa of the dorsal horn leads to inhibition of the firing of nociceptive neurons and inhibition of the release of substance P. It affects the locus ceruleus area, which causes sleep termed as cooperative sleep, and the drug does not disturb the sleep architecture, as well as the respiratory drive. However, it produces a greater degree of differential blockade by preferentially blocking the myelinated A α-fibers involved in sensory conduction over the unmyelinated C fibers involved in motor conduction.[4]

In a study by Bhirud et al., which compared two different doses of intravenous dexmedetomidine (0.5 mcg/kg bolus followed by maintenance infusions of 0.25 mcg/kg/hr and 0.5 mcg/kg/hr), no statistically significant differences were observed in the onset of sensory block, or the time taken to reach T10 between the groups[6]. Our study similarly found no significant differences in these parameters between Group D1 and Group D2 ($p > 0.05$), consistent with their findings.

In a systemic review and meta-analysis by AL Nobani MK et al. found that the duration of sensory block was significantly prolonged regardless of the administered dose of dexmedetomidine or the type and dose of the used local anaesthetic, by a mean difference of 47.583 min, 95% CI (33.133–62.033), P<0.001[1]. Our study similarly showed a statistically significant difference regarding duration of regression of sensory blockade. ($P < 0.001$).

Kavya UR et al. studied the effect of intravenous dexmedetomidine given either as a bolus or a bolus-plus-infusion on subarachnoid anaesthesia with intrathecal hyperbaric bupivacaine in 75 patients and observed that the onset of motor blockade was comparable in all three (dexmedetomidine, midazolam and control) groups[7]. Similarly, our study showed no statistically significant difference regarding to time of onset of motor blockade as well as time to reach grade 3 bromage score (P>0.05).

A study conducted by Lee MH et al. observed that the time for regression of the motor block (modified bromage scale from 3 to 0) was significantly prolonged in the D-0.5 group (132.9 $\pm$ 43.4) and the D-1 group (130.4 $\pm$ 50.4) compared to the control group but was statistically insignificant in between both the groups[8]. In our study, no statistically significant difference was found regarding total motor duration which is time to grade 0 from grade 3 modified bromage motor block in both the groups (p>0.05). Also, our study showed, preoperative & postoperative vitals were comparable in both the groups with no statistically significant difference. (P>0.05).

In a randomized study on 212 patients undergoing scheduled lower abdominal or lower limb surgery under spinal anaesthesia, reported that the time for rescue analgesia was significantly prolonged in Group D (197.26 mins) compared to Group C (120 mins)[2]. Our study showed the time for 1st rescue analgesia was statistically significant between both the groups (p<0.001).

Overall, our findings align with existing literature, confirming that dexmedetomidine prolongs sensory blockade duration and delays the need for rescue analgesia. The absence of significant differences in motor blockade and vital signs between doses underscores the consistent safety profile of dexmedetomidine across varied dosages.

CONCLUSION

From this study, we concluded that intravenous dexmedetomidine bolus before spinal anaesthesia significantly prolonged sensory and to some extent motor blockade duration with no effect on onset and highest achieved level of sensory and motor block. It also increased the duration of requirement of the first rescue analgesia. Also, dexmedetomidine provided arousable sedation intraoperatively with no significant respiratory depression and with lesser complications like hypotension and bradycardia. These effects were more prolonged with 1.0 mcg/kg dexmedetomidine as compared to 0.5 mcg/kg.

Disclosure

The authors report no conflicts of interest for this work.

Financial or Other Competing Interests None.

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