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Effect of intravenous vs intrathecal dexmedetomidine on 0.5% hyperbaric bupivacaine spinal anaesthesia

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Abstract
Objective: It has been demonstrated that dexmedetomidine can extend the time that spinal anaesthesia and postoperative analgesia last. The study's objective was to examine the impact of dexmedetomidine delivery via intrathecal vs intravenous routes on patients posted for lower extremities surgery under spinal anaesthesia with 0.5% hyperbaric bupivacaine.
Methods: A prospective observational study involving 60 ASA PS I & II adults between the ages of 18 & 60 years posted for elective lower extremity surgeries under spinal anaesthesia was conducted from January to June 2022.The participants were randomly assigned to two groups: (1) IT group (n=30) patients received 3 ml of 0.5% hyperbaric bupivacaine and 5 µg of dexmedetomidine intrathecally (100 µg/1 ml ampoule raised in a 40 IU/ml insulin syringe, giving 5 µg=2 IU=0.05 ml) and (2) the IV group (n=30) received 3 ml of 0.5% hyperbaric bupivacaine and 0.05 ml normal saline intrathecally, followed 5 minutes later by IV dexmedetomidine 0.5 µg/kg via infusion pump over 10 minutes as a single dose.
Results: In the IT group, the time from injection to the greatest sensory level was shorter and the sensory beginning occurred statistically substantially sooner at T10 (p 0.001). The IT group had substantially shorter regression times for two dermatomes, to the S1 dermatome, and to the Bromage 3 motor block, however the regression time to the Bromage 0 dermatome was longer (p 0.001). In comparison to the IV group, the IT group demonstrated a considerably longer duration to the need for rescue analgesia and reduced analgesic intake in the first 24 hours (p 0.001). In addition, the IT group experienced much less discomfort than the IV group (p 0.001). The IT group experienced fewer total side effects and a lower sedation score when compared to the IV group, although these differences were not statistically significant (p>0.05).
Conclusion: Dexmedetomidine, when given intrathecally instead of intravenously (IV), had superior analgesic qualities, better hemodynamic stability, and fewer overall adverse effects when used for lower extremities surgeries under bupivacaine spinal anesthesia.

Keywords: Bupivacaine, spinal anaesthesia, dexmedetomidine, intravenous, intrathecal

Introduction
For lower abdomen, perineal, and lower limb surgery, spinal anaesthesia is a type of regional anaesthesia that includes injecting a local anaesthetic into the subarachnoid space.
It offers a number of benefits, including simplicity in administration, affordability, reduced risk of pulmonary aspiration, elimination of the need for intubation, decreased intraoperative blood loss, decreased perioperative cardiac dysrhythmia, post-operative hypoxic episode, as well as arterial and venous thrombosis [1-3]. Numerous adjuvants have been utilised to extend the duration of bupivacaine's effect, including phenylephrine, epinephrine, clonidine, magnesium sulphate, neostigmine, and opioids [4, 5].
Dexmedetomidine is a highly selective α2-adrenoceptor agonist that alleviates pain and induces drowsiness in a dose-dependent manner without depressing breathing [6–9]. Through a number of administration methods, it has been found to increase the duration of local anaesthetics [10, 11]. Dexmedetomidine can extend spinal anaesthesia and enhance postoperative analgesia when delivered intravenously (IV) or intrathecally (IT), according to studies [10, 12]. Dexmedetomidine was added to IT bupivacaine, according to Kanaji *et al*., and this prolonged the time that the patient was under spinal anaesthesia [5]. When given intravenously before to spinal anaesthesia [13] or as a loading dose followed by continuous infusion during surgery [14], dexmedetomidine also extended the duration of spinal anaesthesia.

In the current study, we compared the effects of dexmedetomidine given intravenously (IV) vs intrathecaly (IT) in patients undergoing lower extremity surgeries under hyperbaric bupivacaine spinal anaesthesia, which has been sparsely documented to date

Materials and Methods

This was a descriptive observational study conducted in Sree Gokulam Medical College hospital over a 6-month period from January 2022 to June 2022.Sixty ASA PS I & II adults between the ages of 18 and 60 years were enrolled in this study after obtaining written informed consent and approval from the institutional ethics committee

Only consenting ASA I & II adults between ages of 18 & 60 years posted for elective lower extremity surgeries under spinal anaesthesia were included in this study. Participants with allergy to bupivacaine or dexmedetomidine, non-consenting, obesity (BMI > 30 kg/m^2), extremes of height (> 1.8 m or < 1.5 m), recent analgesic, sedatives, or antidepressants use were excluded from the study.

All patients were divided into two groups at random: (1) The IT group (n = 30) Patients received 3 ml of 0.5% hyperbaric bupivacaine and 5 µg of dexmedetomidine intrathecally (100 µg/1ml ampoule drawn up in 40 IU/ml insulin syringe, giving 5 µg=2 IU=0.05 ml) and (2) the IV group (IV group) (n=30) received 3 ml of 0.5% hyperbaric bupivacaine and 0.05 ml of normal saline intrathecally, followed by IV dexmedetomidine 0.5 µg/kg via an infusion pump over 10 minutes as a single dose. A non-study anesthesiologist prepared the research medications, which were then put in unlabeled syringes to be kept at room temperature and utilized within 30 minutes after preparation. The post anesthesia care unit nurse (PACU) and anesthesiologist engaged in the trial were both blinded to the patient groups.

All research participants completed thorough pre-anesthetic examinations, were told of the study's purpose, and provided with signed consent. Preoperatively the participants were fasted overnight. In the OR suite, Pulse oximeter, 3-lead ECG lead, NIBP cuff attached & baseline HR, NIBP, SpO2, RR recorded and continuously monitored. An 18G peripheral IV access obtained in non-dominant forearm and all participants were co-loaded with 20 ml/kg Ringer Lactate IV fluid. Under strict asepis, a sitting median lumbar subarachnoid block performed at L3 – L4 intervertebral space with 25 G Quincke Babcock needle & intrathecal injection administered. Time zero (T0) was the moment the intrathecal injection was administered. Depending on the group to which the patients were assigned, the IV medication regimen was begun.

After successful lumbar subarachnoid block at L3-L4 intervertebral space, vital signs were recorded 0 minute, 5 minute and every 5 minutes in the operating room and every 15 minutes in the PACU. Hypotension [> 25% fall in baseline mean arterial pressure (MAP)] was treated with fluid bolus and intravenous 6 mg of mephentermine IV. Bradycardia [heart rate <50 beats/min] and was treated with 0.6 mg of atropine IV. Hypoxia [oxygen saturation value below 90%] was treated with a 6 L/min O2 via Hudson facemask.T10 onset time and the Maximum dermatome sensory loss time was recorded. Motor block was measured using a Modified bromage score [16]. Prior to surgery, the time to Bromage 3 motor block was timed, and following surgery, the time to Bromage 0 was timed. In both lower extremities, the patient's motor function and response to cold were assessed using an alcohol solution up to the T10 dermatome. By employing a pinprick test with a blunt 25G needle, another researcher who was blind to the study evaluated the sensory level at midclavicular line bilaterally for each patient. Calculations for all times used the timing of the spinal injection as the starting point. The level of sensory and motor block was assessed after administering the spinal block every 2 minutes until the maximal level of block was reached, and then every 5 minutes after that. Bromage scale and sensory level were assessed every 15 minutes in the PACU. Every 15 minutes, intra-operatively and postoperatively, sedation was assessed using the Ramsey level of sedation scale [17].

Initially every hour for 2 hours, then every 2 hours for the following 8 hours, then every 4 hours until 24 hours, pain was measured postoperatively using a visual analogue scale (VAS) on a range from 0 to 10 (0 = no pain, 10 = the most severe pain). Total duration of analgesia was measured from the moment subarachnoid block was administered until the patient's first complained of discomfort (VAS > 4). As a last-resort painkiller, a 75 mg intramuscular injection of diclofenac sodium was employed. Any adverse symptoms, such as headaches, nausea, vomiting, itching, shivering, or respiratory or cardiovascular problems, were noted.

Statistical analysis

In order to tabulate and analyse the data, SPSS ver 21.0 was used. Results were presented as means, standard deviations, or percentages. The Student's t-test and Chi-square tests were used for statistical studies on parametric and non-parametric data, respectively. P values of 0.05 or higher were regarded as statistically significant, and p values of 0.001 or higher as very significant.

Results

In terms of demographics, length of surgery, and ASA physical state, both patient groups were equivalent (p>0.05) (Table 1). Both groups' pre-operative MAP and HR values were comparable. The MAP and HR values during the first hour following spinal anaesthesia and the first hour in the recovery room did not significantly differ between the groups (p>0.05) (Figs. 1 and 2).

Table 1: Demographics (n=60)

Parameters	Group IT (n=30)	Group IV (n=30)	p value
Age (years)	42.21±3.8	44.35±4.08	0.418
Sex (Male/Female)	15/10	18/07	0.551
Height (cm)	168.3±8.6	170.0±10.2	0.488
Weight (kg)	65.13±13.4	64.42±9.6	0.814
Duration of surgery (min)	63.84±30.5	69.40±40.34	0.549
ASA I/ASA II	22/08	26/04	0.333

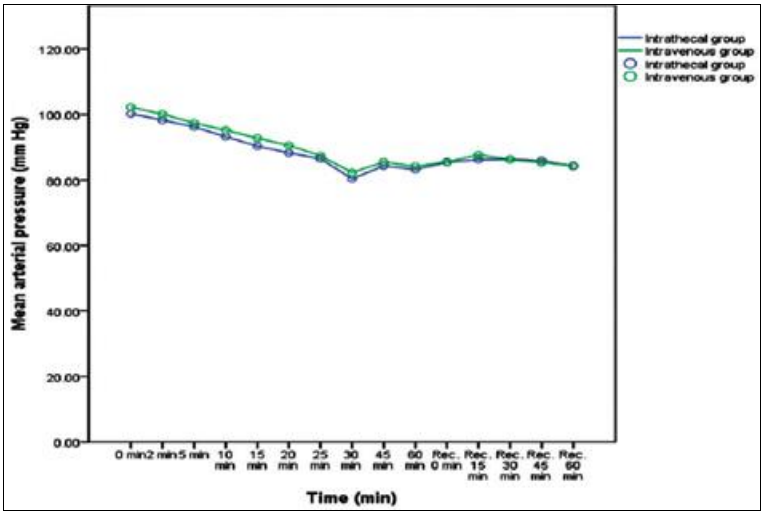

Fig 1: MAP changes (mm Hg) between groups

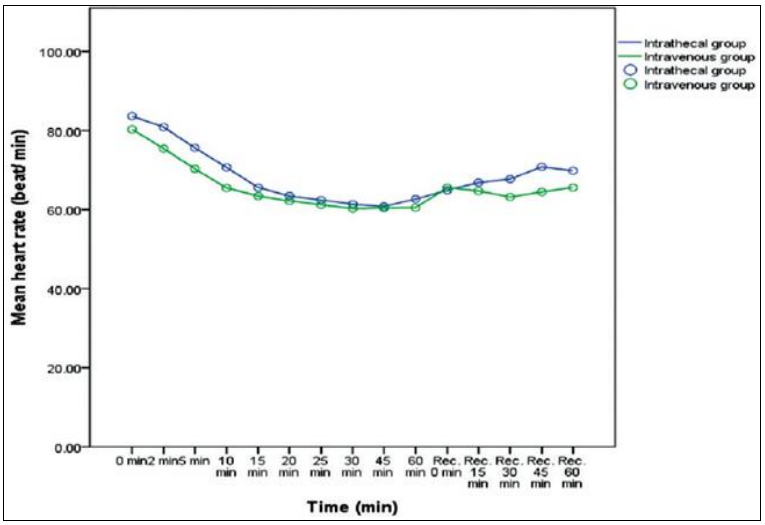

Fig 2: HR changes (beats/min) between groups

The IT group had a statistically substantially shorter duration from injection to the greatest sensory level (p 0.001) and earlier sensory start to T10 (p0.001). Regression periods for two dermatomes and the S1 dermatome were also considerably shorter in the IT group than in the IV group (p 0.001). The regression time to Bromage 0 was substantially longer in the IT group than in the IV group, whereas the mean onset time to reach Bromage 3 motor block was significantly quicker in the IT group (p0.05) (Table 2).

Table 2: Block characteristics (n=60)

Parameters	Mean ±SD		p value
	Group IT (n=30)	Group IV (n=30)	
Time to reach T10 sensory block level (min)	5.69±0.43	6.35±0.41	<0.001
Time from injection to highest sensory level (min)	21.38±0.42	22.97±0.45	<0.001
Bromage 3 motor block (min)	5.18±1.13	6.23±1.45	0.003
Time of two segment regression	134.0±10.17	98.80±11.56	<0.001
From highest sensory level (min)			
Regression time to S1 Dermatome (min)	319.23±24.11	197.53±17.82	<0.001
Regression time to Bromage 0 (min)	381.77±33.03	213.1±21.16	<0.001

In comparison to the IV group, the IT group demonstrated a considerably longer duration to the need for rescue analgesia (p 0.001) and reduced analgesic intake in the first 24 hours (p 0.001). In addition, the IT group experienced considerably less pain (VAS score over 8 hours) than the IV group did (p 0.001). Although the IV group's sedation score was greater than the IT group's, this difference was not statistically significant (p>0.05). The IT group experienced fewer total side effects than the IV group, however this difference was statistically insignificant (p>0.05) (Table 3).

Table 3: Analgesia & adverse effects

Parameters	Group IT (n=30)	Group IV (n=30)	p value
Time of rescue analgesia (Min)	451.47±46.81	227.67±33.11	<0.001
Analgesic consumption in first 24 h	1.12±0.23	2.94±0.56	<0.001
Sedation score over 2 h	2.3±0.42	2.6±0.74	0.283
VAS score over 8 h	0.96±0.49	1.65±0.74	<0.001
Hypotension	2 (6.7)	3 (10.0)	1.0
Bradycardia	0 (0)	1 (3.3)	1.0
Shivering	0	0	-
Respiratory depression	0	0	-
Nausea and vomiting	0	0	-

Discussion

In this study, we examined the impact of dexmedetomidine administered intravenously (IV) versus orally (IT) on bupivacaine spinal anaesthesia. Comparing IT administration of dexmedetomidine to intravenous administration, we found that it improved the anaesthetic effects of bupivacaine. The IT group considerably increased the sensory regression time to the S1 dermatome while dramatically decreasing the duration to the T10 sensory block. In addition, the IT group greatly increased the length of the motor block while significantly reducing the time it took for it to start. These conclusions concur with those of other research [15, 18].

Dexmedetomidine has reportedly been used as a local anaesthetic adjuvant to extend the duration of peripheral nerve blockade and single injection neuraxial blockade's effects on both motor and sensory function [19, 20].

It is hypothesized that dexmedetomidine given intravenously (IT) or intravenously (IV) lengthens the bupivacaine-induced motor and sensory block through an additive or synergistic effect. Dexmedetomidine has a supraspinal effect when administered intravenously (IV) [21], but intrathecaly it inhibits the release of C-fiber transmitters by binding to presynaptic C fibres and hyperpolarizing postsynaptic dorsal horn neurons (PSDH) [22]. Dexmedetomidine has been administered intravenously [12, 23, 24] or intrathecaly [5, 25], and it has been shown to hasten the onset of sensory block and lengthen the duration of sensory and motor block in several trials.

According to the findings of our study, IT dexmedetomidine increased the analgesic effects of bupivacaine and decreased the need for analgesics when compared to IV dexmedetomidine in terms of time to rescue analgesia, total analgesic use, and VAS score. This shows that the spinal level may be where the analgesic action of α2 agonists occurs most frequently. Dexmedetomidine is quickly absorbed into the cerebrospinal fluid and binds to the spinal cord's α2 adrenoceptor because of its high lipophilicity. Dexmedetomidine has been demonstrated to have strong antinociceptive effects in mice when administered intravenously (IT) [26, 27]. To cause analgesia, the α2 agonists act on three separate areas, including the brain and brainstem, the spinal cord, and peripheral tissues. Different hypothesised mechanisms, including activation of the descending medullospinal noradrenergic pathways, reduction of the spinal sympathetic outflow at presynaptic ganglionic sites, interaction between opioids and α2 agonists at the spinal cord level, and inhibition of substance P release in the nociceptive pathway, have been proposed to explain how stimulation of α2 receptors at the spinal cord level causes analgesia [18, 28].

Throughout the course of the trial, the hemodynamic values of the HR and MAP were comparable. Our findings are consistent with the fact that bradycardia and hypotension are the negative effects of α2 agonist usage that are most often reported. In comparison to the IT group, the IV group experienced both adverse effects more often. As in other research [18, 29], these differences weren't statistically significant, though. In our investigation, there was no shuddering in either group. In their research, Affifi *et al*. [18] demonstrated that the α2 adrenergic drugs had anti-shivering properties. Both groups did not report any cases of respiratory depression, and this conclusion is consistent with those of earlier research [18, 30], which have also been supported by the findings of our investigation. Previous research [18, 31] have found that the incidence of nausea/vomiting during spinal anaesthesia ranges from 0% to 18%. In contrast, none of the trial participants experienced nausea or vomiting.

The current study has a few drawbacks, however adding a control group that exclusively used bupivacaine for spinal anaesthesia would have given the study more power. Furthermore, because this study was done on a narrower, more concentrated sample of patients in a single institution, its findings cannot be generalized to other patient types, operations, or older age groups.

Conclusion

IT dexmedetomidine is preferable to IV dexmedetomidine when used as an adjuvant in bupivacaine spinal anaesthesia for lower extremity procedures. Compared to IV routes of administration, IT dexmedetomidine administration offers stronger enhancement to sensory and motor block, more hemodynamic stability, better analgesic characteristics, and less overall adverse effects.

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Author's Contribution

Not available

Conflict of Interest

Not available

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