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Original Research Article

# A COMPARISON BETWEEN THREE DIFFERENT DOSES OF INTRATHECAL DEXMEDITOMEDINE ADDED TO HYPERBARIC BUPIVACAINE FOR INFRA-UMBILICAL SURGERIES

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## Abstract

**Background:** The relatively short duration of action associated with spinal anaesthesia using local anaesthetics necessitates early analgesic intervention in the postoperative period. We include adjuvants to enhance the quality, expedite the initiation of drug activity, and address the issues that arise during spinal analgesia. Much attention has been paid to α2-adrenergic receptor agonists like dexmedetomidine and their effects on sedation, pain relief, perioperative sympatholysis, and stabilizing blood flow. Dexmedetomidine is a novel and very specific medication that functions as an agonist for the alpha-2 adrenergic receptor. **Aim:** This study aims to compare three different intrathecal dexmedetomidine doses added to hyperbaric bupivacaine for infra-umbilical surgeries. **Materials and Methods:** The trial consisted of sixty patients divided into three groups of twenty each, using a randomized, prospective, parallel-group, double-blind design. We administered 0.5% hyperbaric bupivacaine at 2.4 ml (12 mg) to each patient, along with dexmedetomidine at 5 µg, 10 µg, or 15 µg in 0.6 ml of normal saline. The intraoperative vital signs, the time and extent of sensory and motor blockade, the duration of analgesia, the postoperative sedation score, and the need for rescue analgesics were monitored. **Results:** The 5 µg groups showed a significantly increased time of sensory blockade onset compared to the other two groups. The 15µg group exhibited a significantly reduced time of motor blockade onset compared to the other two groups. The 15µg group had significantly longer durations of motor blockade and analgesia. The 15µg group had significantly higher postoperative sedation scores. **Conclusion:** Intrathecal dexmedetomidine added to bupivacaine for intraabdominal surgeries has a dose-dependent effect on the sensory and motor blockade, with earlier onset and increased duration of the blockade, prolonged post-operative analgesia, a better level of sedation, and stable hemodynamics.

## INTRODUCTION

Administering local anaesthetics for spinal anaesthesia has a relatively brief duration of effect, thereby requiring early analgesic care during the postoperative phase. Frequent complications encountered with infra-umbilical surgery under spinal anaesthesia include visceral discomfort, nausea, and vomiting.[1,2] We include adjuvants to enhance the quality, expedite the initiation of drug activity, and address the issues that arise during spinal analgesia. Initially, we used adrenaline as the spinal adjuvant. Adrenaline mitigates its toxicity, but it does not significantly extend the duration of the action. Local anaesthetics include different adjuvants such as morphine, fentanyl, sufentanil, clonidine, midazolam, ketamine, neostigmine, etc. The most recent addition is dexmedetomidine.[3,4] Specific methods such as epidural, intrathecal, and intravenous can deliver adjuvants effectively. The present study involves adding an adjuvant to local anaesthesia via the intrathecal route. An α2-


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adrenergic receptor agonist called dexmedetomidine has gotten a lot of attention because it can calm people down, ease pain, relax the body before surgery, and keep the blood flow stable. Dexmedetomidine is a novel and very specific therapeutic agent that acts as an agonist for the α-2 adrenergic receptor. The Food and Drug Administration (FDA) has approved the use of this compound to provide short-term sedation to mechanically ventilated ICU patients. Thus far, there have been no documented neurological abnormalities in both human and animal research investigating the use of intrathecal administration. The point of this study is to look at what happens when three different amounts of intrathecal dexmedetomidine are mixed with hyperbaric bupivacaine during infra-umbilical procedures, such as vaginal hysterectomies and operations to fix two inguinal hernias.

## MATERIALS AND METHODS

This is a randomized, prospective, double-blinded study. We used computer-generated random numbers for simple randomized sampling. We examined a cohort of sixty patients. The study comprised ASA I and II patients aged 18–60 years of both genders who were undergoing elective procedures, namely infra-umbilical surgery. We excluded from the study patients with documented hypersensitivity to any of the study drugs, documented contraindications to regional anaesthesia, documented or suspected coagulopathy, renal disorders, hypertension, ischemic heart disease (IHD), heart blocks, arrhythmias, and cardiac valvular abnormalities, patients on -blockers, patients on any long-term analgesic therapy, and patients on drugs known to interact with the study molecules Once receiving clearance from the Institutional Research and Ethical Committee (Gandhi Medical College/Hospital), the study was done from September 2022 to March 2024.

We randomly assigned the patients to three groups.

Group A administered 0.5% hyperbaric bupivacaine 2.4 ml (12 mg) and 5 µg of dexmedetomidine in 0.6 ml of normal saline to twenty patients.

Group B (n = 20) subjects received 0.5% hyperbaric bupivacaine 2.4 ml (12 mg) and 10 µg of dexmedetomidine in 0.6 ml of normal saline.

Group C administered a 0.5% hyperbaric bupivacaine dosage of 2.4 ml (12 mg) to twenty patients, along with 15 µg of dexmedetomidine in 0.6 ml of normal saline.

Both the anesthesiologist responsible for medication administration and the observer were unaware of the research design. Another anesthesiologist, who was not involved in the trial, filled sterile syringes with 3.0 ml of the pharmacological substance. The anesthesiologist who provided the medication also conducted intraoperative and postoperative surveillance while unaware of the contents of the syringes. We prepared emergency medications and equipment in advance. We preloaded the patients by administering an intravenous infusion of Ringer lactate at a rate of 20ml/kg. We attached monitors to the patients and recorded initial measurements of heart rate, systolic, diastolic, mean arterial pressures, and oxygen saturation. We strictly performed the sub-arachnoid block under aseptic precautions, using a 26-gauge quincke's needle through the L3-L4 interspace. Once we confirmed the free flow of cerebrospinal fluid (CSF), we administered the study drug to the designated group. After administering the medication, the surgeon repositioned the patient in a supine posture. Once the surgeon achieves the maximum level of sensory block, they proceed accordingly. We measured the pulse rate, systolic blood pressure, mean blood pressure, diastolic blood pressure, respiratory rate, and SPO2 at intervals of 5, 10, 15, and 20 minutes until the surgery concluded. We then took these measurements every hour, every second hour, and every fourth hour until 24 hours into the postoperative period. Hypotension was defined as a systolic blood pressure below 90 mm Hg or a reduction in mean arterial pressure below 20% of the initial value. We managed it by administering progressive boluses of Inj. Ephedrine (6 mg). We evaluated the sensory blockade by puncturing the skin with a small hypodermic needle every minute until the block reached the T10 level. We recorded the upper limit of the sensory block at 20 minutes. We determined the onset of sensory blockade as the duration between the drug injection and the attainment of the T10 level. We assumed the offset of sensory block to occur when the pinprick sensation at the S1 dermatome recurred. Sensory block duration was defined as the time period between sensory block commencement at T10 and sensory block regression to S1. We used a modified Bromage score to evaluate motor blockade at 1-minute intervals until we achieved total motor block. We determined the onset of motor block as the duration between the medication administration and the occurrence of total motor blockade, as measured by the Bromage score-3. Complete recovery from the motor block is defined as achieving a Bromage score of 0, whereas the duration of motor block refers to the period from the beginning of complete motor blockade and the complete recovery of the motor block. We conducted the pain assessment using the Visual Analogue Scale. When the pain score exceeded 4, we administered an intramuscular injection of 75 mg of Diclofenac as a rescue analgesic. We evaluated the duration of analgesia as the time elapsed from the initiation of a subarachnoid block to the point at which the patient requires the initial dosage of rescue analgesic medication. We conducted the evaluation of sedation using the Ramsay Sedation Score. We monitored the patients for up to 24 hours after the surgery to detect any problems such as


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nausea, vomiting, pruritus, respiratory depression, neurological issues, and urine retention.

**Statistical Analysis**

We executed the statistical operations using the quantitative software IBM SPSS Statistics 20. Statistical significance was defined as p-values below 0.05 ($p<0.05$). We randomly assigned three groups by matching their ages, demographic characteristics, and hemodynamic parameters such as pulse rate, systolic blood pressure, mean arterial pressure, suction pressure, and surgical time using ANOVA (Analysis of Variance). We conducted a statistical analysis of the differences between them using the Bonferroni post hoc test. Furthermore, we used the ANOVA to examine the onset times of sensory block and motor block across groups. We used analysis of variance (ANOVA) to compare the pulse rates, systolic blood pressure (SBP), mean arterial pressure (MAP), and systolic blood pressure (SPO2) across groups at various time points. We interpreted the found differences using post hoc Bonferroni analysis. Statistical analysis and interpretation of the sensory level and sedation score among three groups were conducted using the chi-square test. We conducted statistical analysis and interpretation of the analgesic duration in the groups using the Kaplan-Mayer survival function.

## RESULTS

After matching the three groups based on their age for randomization, it was shown that there was no significant difference in the mean ages among Groups A, B, and C (44.4 ± 10.7, 46.0±5.6, 44.4±8.1, and $P > 0.05$). We detected no statistically significant differences among the three groups ($P > 0.05$) when comparing the average pre-operative pulse rate, systolic blood pressure, mean arterial pressure, systolic arterial pressure, and surgical time. Significantly increased mean onset time of sensory blockade was observed in group A compared to groups B and C (A>B&C; 226.1±28.7>206.8±20.2&197.2±14.9 and $p<0.05$). The mean values of the B & C groups were roughly the same (206.8± 20.2, 197.2 ± 14.9, and $p > 0.05$). Significantly decreased mean initiation time of motor blockade was seen in the C group compared to the other two groups (190.4±14.2<233.0 ±23.3 & 228.2 ± 16.8 and P<001). Motor block onset times in groups A and B were not statistically significant (233.0±23.3 ± 228.2 ± 16.8 and P>0.05).

The maximum sensory level attained by the A group was T6, whereas the C group reached T4. Fifty-five per cent of the patients in the A & B group and forty per cent of the subjects in the C group attained the T8 sensory level. The values shown above were statistically highly significant ($P<0.001$). We found no significant differences in the mean pulse rates, mean SBP, mean MAP, and mean SPO2 among the three groups ($P > 0.05$).

Table 1 displays the durations of the sensory and motor blocks. The sensory block duration of the C group was much greater than that of the B group and equally longer than that of the A group (341.5±47.6 > 290±56.2 > 241.0±48.9 and $P <0.001$). Likewise, there was a statistically significant difference in the length of motor block between the C group and B groups and between the A group and C group (362.5±16.5>318.0±31.0>260.6±41.5 and P <0.001). The regression times for the two segments across the three groups were 139.7±28.2, 143.2±28.8, and 172.7±30.2 minutes, respectively. In comparison to the other two groups, group C had a substantially longer regression time (172.7±30.2.> 143.2±28.8 &139.7±28.2, and P<0.00). Nevertheless, the regression periods between groups A and B did not show statistical significance (143.2±28.8 ≈139.7±28.2 and $P<0.05$). A significant difference was seen in the mean duration of analgesia between the C group and B group (740.5 65.9 > 471.0 24.6 > 347.5 101.4 and $P<0.001$). [Table 1]

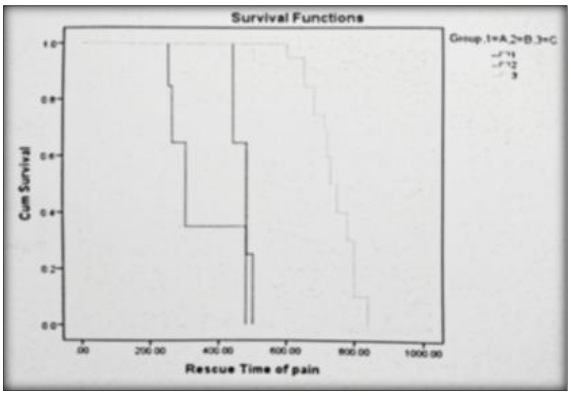


**Figure 1: Comparison of Analgesia survival functions between three groups. [Kaplan-meier survival function curve]**

Figure 1 illustrates the duration of analgesia from the onset of anaesthesia to the emergence of a VAS pain score of 4. The time intervals for groups A, B, and C were 250 to 480 minutes, 440 to 500 minutes, and 600 to 840 minutes, respectively. The A group attained a maximum sedation score of 2, whereas the C group obtained that of 4. Within the C group, 55% attained sedation levels of 3, while 45% obtained sedation levels of 4. The values shown above were statistically highly significant ($P<0.001$). Bradycardia and hypotension were the sole reported side effects, predominantly observed in the C group. Nevertheless, the correlation between the groups did not show any statistical significance ($P > 0.05$).


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**Table 1: Comparison of duration of Sensory and Motor blocks between groups**

| Block | Groups | N | Mean(Min.) | SD | ANOVA 'F' | Df | P |
|---|---|---|---|---|---|---|---|
| DSB | A | 20 | 241.00 | 48.9 | 19.37 | 2.57 | 0.001 |
| | B | 20 | 290.00 | 56.2 | | | |
| | C | 20 | 341.50 | 47.6 | | | |
| DMB | A | 20 | 260.60 | 41.5 | 52.84 | 2.7 | 0.001 |
| | B | 20 | 318.00 | 31.0 | | | |
| | C | 20 | 362.50 | 16.5 | | | |

DSB=Duration of Sensory block; DMB=Duration of Motor blocks

## DISCUSSION

Recent studies have shown that using α2-agonists in the neuraxial blockade results in extended postoperative pain relief without excessive sedation. We can attribute the observed effect to the preservation of supraspinal central nervous system (CNS) sites from excessive drug exposure, which results in pain relief without significant sedation. It's still not clear exactly how intrathecal α2-adrenergic agonists increase the motor and sensory blocking effects of local anaesthetics. Intrathecal α2-adrenergic agonists induce analgesia by inhibiting C-fiber transmitter release and hyperpolarizing postsynaptic dorsal horn neurons. When combined with spinal anaesthetics, the anti-nociceptive effect is likely to account for the extension of the sensory block. Spinal anaesthetics may extend the duration of the motor block by interacting with two motor neurons in the dorsal horn through -adrenergic agonists. Most clinical experience with intrathecal adrenoceptor agonists documents clonidine's strong synergistic effect with local anaesthetics. There are only a few studies on the use of intrathecal dexmedetomidine in conjunction with local anaesthetics. The reported epidural/caudal dexmedetomidine dosage is within the range of 1.5–2 µg/kg2. The receptor binding affinity of dexmedetomidine is tenfold greater than that of clonidine. We used extrapolations to estimate an equipotent dosage of intrathecally delivered dexmedetomidine. Adding intrathecal clonidine to spinal local anaesthetics has been shown in many clinical trials to extend the time of sensory and motor spinal block. Furthermore, the dosage of clonidine influences its impact. Toxic doses over 75 mcg result in severe drowsiness, hypotension, and bradycardia. The experiments undertaken by the aforementioned authors have shown that the addition of intrathecal dexmedetomidine up to 10 µg to local anaesthetics does not result in any significant side effects. Anand et al,[5] established a suggested dosage of 15–45 mcg of clonidine to augment spinal anesthesia. This dosage successfully extends the duration of the spinal block with minimum sedation and adverse effects. Researchers have attempted to administer increased intrathecal dosages of clonidine. Notably, there is no existing research on intrathecal dosages over 10µg of dexmedetomidine. The equivalent dosage of dexmedetomidine at 5, 10, and 15µg relative to clonidine would be about 50, 100, and 150µg, respectively. Researchers James et al,[6] looked at spinal anaesthesia in humans and thought that giving dexmedetomidine (3 µg) or clonidine (30 µg) through an IV would work just as well as bupivacaine spinal anaesthesia and have similar effects. The authors carefully considered prior animal research using intrathecal dexmedetomidine to reach these results. The authors administered a modest dosage of either 3µg of dexmedetomidine or 30µg of clonidine in conjunction with 12 mg of intrathecal bupivacaine. The researchers observed no statistically significant difference in blocking characteristics, analgesia, and sedation between the groups. The researchers validated their hypothesis that the intrathecal dosages of dexmedetomidine and clonidine employed in the experiment are equivalent in potency. According to Al-Mustafa et al.'s hypothesis,[5] 5 µg and 10 µg of intrathecal dexmedetomidine may be equivalent to 50 µg and 100 µg of intrathecal clonidine, respectively. The researchers delivered dexmedetomidine intrathecally in combination with bupivacaine at a maximum dosage of 10µg. Researchers reported a dose-dependent impact of dexmedetomidine when given as an adjuvant to bupivacaine in spinal anaesthesia, on the onset and regression of sensory and motor block. Ashraf Amin Mohamed et al,[7] conducted an investigation to examine the effects of adding 5µg dexmedetomidine and 25µg fentanyl to bupivacaine for abdominal procedures. Researchers found that intrathecal administration of 5 µg dexmedetomidine improved both the quality and duration of postoperative pain relief. Subhi Al-Ghanemet et al,[8] conducted further research on the impact of incorporating 5µg dexmedetomidine compared to 25µg fentanyl into intrathecal bupivacaine during vaginal hysterectomies. The researchers came to the conclusion that adding 5µg of dexmedetomidine to 10 mg of plain bupivacaine and ropivacaine intravenously makes the motor and sensory nerve block last longer. Mahmoud et al,[9] conducted a comparison between 10µg of intrathecal dexmedetomidine and magnesium sulfate as adjuvants to bupivacaine. They found that dexmedetomidine resulted in a faster onset and longer duration of sensory and motor blockade, without any notable changes in hemodynamics. The current investigation revealed that the period at which sensory and motor blockage began varied depending on the dosage. The sensory onset time of group A (226.1±28.7 seconds) was substantially


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different (P<0.001) from that of group B (197.2±14.9 seconds) and group C (206.8±20.2 seconds). This suggests that administering greater dosages led to the initiation of sensory blockage earlier. With larger dosages, the start time of motor block also occurred sooner. The time shown by Group C (190.4±14.2 seconds) was considerably different (P<0.001) from that of Group A (233.0±23.3 seconds) and Group B (228.2±16.8 seconds). We observed a dose-dependent rise in the degree of sensory blockade (C>B>A). Differences in the duration of sensory and motor blocks across the groups were dose-dependent and statistically significant (P<0.001). Group C exhibited the longest duration of both sensory and motor blockade, with a mean sensory blockade of 341.5±47.6 minutes and a mean motor blockade of 362.5±16.5 minutes. Group C obtained the longest 2-segment regression times, with a mean of 172.7±30.2 minutes. A dose-dependent mean duration of analgesia was seen with C>B>A (740.5 ±65.9>471.0±24.6> 347.5± 101.4 minutes; P<0.001). The effectiveness of postoperative sedation varied depending on the dosage, with group C showing a minimum score of 3 and a maximum score of 4. Not a single patient exhibited any indications of respiratory depression. The current study demonstrates that the combination of intrathecal dexmedetomidine and spinal bupivacaine not only reduces the time it takes to induce anaesthesia but also extends the period of blockade, resulting in a longer duration of pain suppression. None of the patients reported any adverse effects such as nausea, vomiting, pruritus, or urine retention. Out of 60 patients, 10 experienced bradycardia and hypotension, with group C exceeding group B by 5, 3, and 2, respectively, despite the lack of statistical significance in these occurrences. Bradycardia required no therapy, and progressive boluses of less than 12–18 mg of ephedrine corrected the hypotension. Otherwise, the patients maintained their hemodynamic status throughout. A statistical analysis of the three groups' pre-, intra-, and post-operative blood flow parameters, such as PR, SBP, MAP, and SPO2, showed that there were no statistically significant differences. The current investigation's findings, in comparison to the trials conducted by the aforementioned authors, show comparable results in terms of sensory and motor block initiation and length, analgesia duration, and hemodynamic profile.

## CONCLUSION

Intrathecal dexmedetomidine, when combined with bupivacaine, has a dose-dependent impact on the sensory and motor blockade during infra-umbilical procedures. This results in earlier onset and longer duration of blockade, as well as extended post-operative analgesia, improved sedation levels, and stable hemodynamics.

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