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COMPARISON OF TWO DIFFERENT DOSES OF INTRATHECAL DEXMEDETOMIDINE (5 µG VERSUS 10 µG) AS AN ADJUVANT TO HYPERBARIC BUPIVACAINE FOR SPINAL ANAESTHESIA IN LOWER LIMB ORTHOPAEDIC SURGERIES: A PROSPECTIVE RANDOMIZED DOUBLE-BLIND STUDY

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ABSTRACT

Background: Intrathecal dexmedetomidine (Intrathecal Dexmedetomidine) is increasingly used as an adjuvant to hyperbaric bupivacaine (Hyperbaric Bupivacaine) to increase the extent and spinal anaesthesia's quality. However, the optimal intrathecal dose for elective orthopaedic procedures on the lower limbs remains uncertain.

Objective: To compare the safety and efficacy of 5 µg and 10 µg Intrathecal Dexmedetomidine as an adjuvant to 12.5 mg of 0.5% Hyperbaric Bupivacaine in patients undergoing lower limb orthopaedic surgeries.

Methods: Sixty patients aged 18–60 years undergoing elective lower limb orthopaedic surgeries were randomized to receive either 5 µg or 10 µg Intrathecal Dexmedetomidine as an adjuvant to Hyperbaric Bupivacaine. Comparisons were made between block properties, postoperative analgesia, hemodynamic parameters, sedation, VAS Score, and adverse events.

Results: Group D10 confirmed faster onset of sensory block (3.70 ± 0.50 vs. 4.53 ± 0.38 min) and motor block [5.50 (5.03–5.80) vs. 6.45 (6.20–6.88) min], along with longer sensory block duration (306.37 ± 26.15 vs. 259.07 ± 26.74 min) and motor block duration (259.77 ± 27.15 vs. 224.23 ± 28.08 min), compared with Group D5 (**$p < 0.001$**). Group D10 also had a lower VAS score and provided better postoperative analgesia, with acceptable sedation and a comparable incidence of adverse events.

Conclusion: Intrathecal dexmedetomidine 10 µg provided superior spinal block characteristics and postoperative analgesia compared with the 5 µg dose while maintaining acceptable haemodynamic stability and a favourable safety profile. Therefore, 10 µg dexmedetomidine may be considered the preferred intrathecal adjuvant to 12.5 mg of 0.5% Hyperbaric Bupivacaine for elective lower limb orthopaedic surgeries.

KEYWORDS: Dexmedetomidine; bupivacaine; intrathecal; postoperative analgesia; spinal anaesthesia and Orthopaedic surgeries.

1. INTRODUCTION

In the world, lower limb orthopaedic surgery is the most often used surgical operation for the treatment of fractures, degenerative joint diseases, ligament injuries and musculoskeletal disorders. An anaesthetic technique which allows haemodynamic stability, sufficient sensory and motor blockage, and efficient pain management following surgery, is required for successful perioperative management of these procedures. Spinal anaesthesia is the best of the available regional anaesthetic techniques due to rapid onset, reliable neural blockade, less blood loss, less incidence of thromboembolic complications and early postoperative recovery [1]. In recent years, there have been several clinical trials showing that spinal anaesthesia is a suitable option in orthopaedic procedures of the lower limbs with excellent operating conditions and high patient satisfaction when the appropriate adjuvants are added to the local anaesthetic solution [2].

For spinal anaesthesia, the most widely used local anaesthetic is hyperbaric bupivacaine (HB) 0.5% because of its ability to generate extensive sensory and motor blockage and its consistent spread in cerebrospinal fluid. In an orthopaedic procedure of the lower limbs, a dose of 12.5 mg is commonly used to achieve good surgical anaesthesia. But postoperative analgesia is rather short-lived after bupivacaine alone and might require further postoperative administration of analgesics [3]. Consequently, a number of intrathecal adjuvants have been investigated to prolong the duration of spinal blockade, enhance the quality of the analgesia, and decrease postoperative analgesic requirements [4].

Dexmedetomidine is an extremely selective α_2-adrenergic receptor agonist and is a good intrathecal adjuvant due to its analgesic, sedative, and sympatholytic characteristics. Dexmedetomidine binds to the spinal α_2 receptors and inhibits the nociceptive neurotransmission in the dorsal horn, increasing the effects of the local anaesthetic and extending sensory and

motor blockade [5]. Experimental studies have demonstrated that dexmedetomidine added to HB increases the speed of onset of spinal block, increases the duration of postoperative analgesia, decreases rescue analgesic use, and has beneficial haemodynamic effects [6]. Furthermore, comparative randomized trials have shown that dexmedetomidine has better analgesic effects, and it is also known to have a good safety profile for patients having orthopaedic procedures on their lower limbs [7]. The results of double-blind clinical trials comparing dexmedetomidine to other intrathecal drugs have also yielded similar results that support its clinical utility in spinal anaesthesia [8].

Despite the consistent reports of beneficial effects of ID, the optimal dose of Intrathecal dexmedetomidine (ID) in clinical practice is yet to be determined. Several randomized studies have looked at dexmedetomidine versus fentanyl or other adjuvants, but not directly at different dose levels of dexmedetomidine [9]. Low-dose dexmedetomidine has positive impacts on the features of spinal anaesthesia, according to a comprehensive review and meta-analysis, but there is still no consensus on the best ratio of effectiveness and safety of dexmedetomidine [10]. Likewise, studies that compared the different routes of dexmedetomidine administration have shown some differences in clinical outcome, but still have not set the optimal intrathecal dosage of dexmedetomidine [11]. Variations in administration methods have also been demonstrated to affect block properties and dose standardization is difficult [12]. Moreover, there is limited data available on the use of intrathecal 5 µg and 10 µg dexmedetomidine as compared to 12.5 mg of 0.5% HB in lower limb orthopaedic surgeries [13].

Finding the right dosages of ID may allow for better quality spinal anaesthesia with fewer adverse effects associated with dose. Comparative clinical studies showed dexmedetomidine to be superior for postoperative analgesia and for the period of spinal block as associated to some conventional intrathecal adjuvants [14]. There are also other studies that have shown the beneficial impact of dexmedetomidine on the features of spinal block and postoperative pain in orthopaedic surgery [15]. Previous studies have suggested that dexmedetomidine with HB is more effective at providing analgesia than dexmedetomidine with fentanyl [16], while others have highlighted the need to maintain adequate analgesia whilst ensuring patient safety [17]. Randomized trials done more recently continue to confirm the clinical benefits of dexmedetomidine in lower limb orthopaedic surgery [18]. In this context, the current investigation was done to measure the use of dexmedetomidine of 5 µg and 10 µg as an adjuvant to 12.5 mg 0.5% HB concerning the qualities of block, postoperative pain, haemodynamic stability, sedation, and any other perioperative complications.

Objectives of the Study

To compare the efficacy of 5 µg versus 10 µg intrathecal dexmedetomidine as an adjuvant to 12.5 mg of 0.5% hyperbaric bupivacaine for spinal anaesthesia in patients undergoing lower limb orthopaedic surgeries.

To compare the characteristics of sensory and motor blockade and postoperative analgesia between patients receiving 5 µg and 10 µg intrathecal dexmedetomidine.

To assess the incidence of perioperative adverse events, sedation profile and haemodynamic parameters between patients receiving 5 µg and 10 µg ID.

2. METHODOLOGY

2.1 Study Design

This prospective, randomized, double-blind comparative clinical study evaluated the safety and efficacy of two doses of Intrathecal Dexmedetomidine (5 µg and 10 µg) as an adjuvant to 12.5 mg of 0.5% Hyperbaric Bupivacaine in patients undergoing elective lower extremity orthopaedic surgeries under spinal anaesthesia. The study looked at the differences between the two doses of dexmedetomidine on block characteristics, postoperative analgesia, haemodynamic parameters, sedation, and perioperative adverse events.

2.2 Study Population

The study included 60 adult patients aged 18–60 years undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia.

2.3 Eligibility Criteria

Patients of either sex, aged 18–60 years, with ASA physical status I or II and undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia were included in the study. The individuals who had an allergic reaction to any of the drugs like dexmedetomidine and bupivacaine, contraindications for spinal anaesthesia such as coagulopathy, and infections at the puncture point, significant diseases related to heart, liver, kidney, and nervous system, pregnancy and breastfeeding, and those on opioids and medicines affecting pain measurement were excluded from the investigation.

2.4 Randomization and Blinding.

Ethical approval was obtained from the Institutional Ethics Committee prior to commencement of the study. Written informed consent was obtained from all participants before enrolment. Eligible patients were randomly allocated into two equal groups of 30 patients each. Computer generated random number table was used to allocate the individual to one of the study groups in a 1:1 allocation ratio. Distribution was concealed using opaque, sealed envelopes with sequential numbers. The anaesthesiologist responsible for preparing the study drugs was not involved in patient management or outcome assessment. Both the patients and the researcher responsible for intraoperative monitoring, data collection and outcome assessment were blinded to the group allocation throughout the study.

2.5 Study Intervention
Group D5 received 5 µg intrathecal dexmedetomidine as an adjuvant to 12.5 mg of 0.5% HB, whereas Group D10 received 10 µg ID as an adjuvant to the same dose of HB. Baseline demographic and clinical characteristics were recorded before surgery to ensure comparability between the groups.
To ensure blinding and uniform administration, the total quantity of the intrathecal drug was kept the same in both groups.

2.6 Anaesthetic Procedure
Pre-anaesthetic assessment was completed and baseline heart rate, SBP, DBP, MAP and peripheral oxygen saturation was obtained. Intravenous access was obtained and routine peri-operative fluid management was done as per institutional protocol. Using a 25-gauge Quincke spinal needle and stringent aseptic measures, spinal anaesthesia was administered at the L3–L4 or L4–L5 intervertebral region in the "sitting" position. The assigned intrathecal study drug was given over a duration of 10 to 15 seconds upon confirmation of free cerebrospinal fluid flow. Individuals were put in the supine position as soon as the injection was administered, and they were closely watched during the procedure.

2.7 Outcome Measures
The important outcome variable was duration of postoperative analgesia which was demarcated as the time interval from the intrathecal drug administration to the initial call for analgesic rescue. The Visual Analogue Scale (VAS) pain scores, mean arterial pressure, heart rate, sedation score, and the frequency of peri-operative adverse events like hypotension, bradycardia, nausea and vomiting and shivering were among the secondary outcomes.

2.8 Data Collection
Pre-operative demographic information was documented, including ASA physical condition, Body mass index (BMI), age, sex, and length of operation. The pin prick test was used to assess sensory block, and the most cephalad sensory dermatome was recorded. The Modified Bromage Scale was used to evaluate motor block and VAS was used to gauge the degree of postoperative discomfort. Patients were monitored for haemodynamic parameters and adverse events during the intraoperative and early postoperative phases, and sedation was evaluated using a standard sedation grading system.

2.9 Data Analysis
Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± SD or median with interquartile range, contingent on data dispersal. For normally distributed continuous variables, the independent samples t-test was used to compare the two groups; for non-normally distributed continuous variables, the Mann-Whitney U test was used. A two-sided p-value of less than 0.05 was considered statistically significant. The outcomes obtained from statistical analysis were presented in relevant tables and figures for easy comparisons between the two groups.

3. RESULTS
3.1 Demographic Features
Sixty patients undergoing elective lower limb orthopaedic surgeries under spinal anaesthesia were incorporated into the research and equally allocated to Group D5 and Group D10, with 30 patients in each group. There were no statistically substantial variances in distribution of age groups, gender or ASA physical status. Similarly, the mean BMI was 24.67 ± 2.49 kg/m² in Group D5 and 25.17 ± 2.96 kg/m² in Group D10 (**p = 0.487**). The mean duration of surgery was 100.07 ± 20.63 minutes in Group D5 and 100.07 ± 21.30 minutes in Group D10 (**p = 1.000**). These data show that both groups were similar at baseline and reduced the possibility for confounding factors to potentially affect the outcomes of this study (Table 1).

Table 1. Demographic features

Variables	Category	Group D5 (n = 30)	Group D10 (n = 30)	p-value
Age	18–30	10 (33.3%)	8 (26.7%)	**0.801**
	31–45	12 (40.0%)	12 (40.0%)	
	46–60	8 (26.7%)	10 (33.3%)	
Gender	Male	18 (60.0%)	17 (56.7%)	**1.000**
	Female	12 (40.0%)	13 (43.3%)	
ASA Grade	I	17 (56.7%)	16 (53.3%)	**1.000**
	II	13 (43.3%)	14 (46.7%)	

Two treatment groups were given in Figure 1 to provide a visual comparison of the study population with regard to the baseline demographic characteristics.

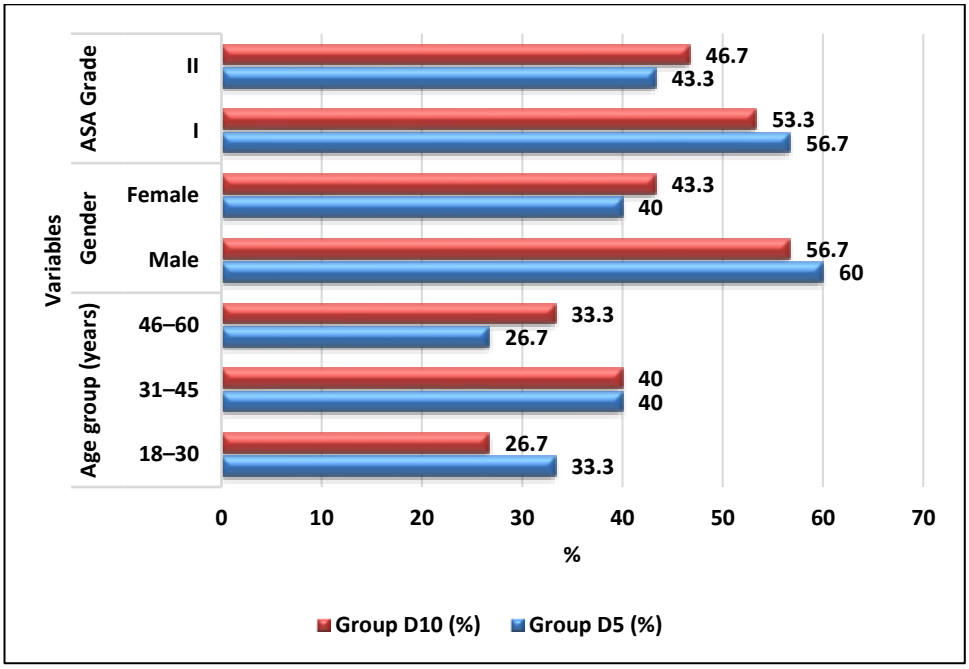

Figure 1. Distribution of Baseline Demographic and Clinical Characteristics

Both study groups had a similar age category range, gender and ASA grade distribution as shown in Figure 1. Group D5 and Group D10 appear to have a similar distribution of participants overall, suggesting that the randomization procedure was successful and that the baseline characteristics were comparable.

3.2 Comparison of Characteristics of Sensory Block

The onset of sensory block was pointedly faster in Group D10 than in Group D5 (3.70 ± 0.50 min vs. 4.53 ± 0.38 min; **p < 0.001**). The time to peak sensory block was also significantly shorter in Group D10 than in Group D5 (7.49 ± 0.88 min vs. 8.65 ± 1.04 min; **p < 0.001**). Furthermore, the duration of sensory block was significantly longer in Group D10 than in Group D5 (306.37 ± 26.15 min vs. 259.07 ± 26.74 min; **p < 0.001**), indicating a prolonged period of spinal anaesthetic action with the higher dose of ID (Table 2).

Table 2. Assessment of Sensory Block Features

Variables	Group D5	Group D10	p-value
Onset of sensory block (min)	4.53 ± 0.38	3.70 ± 0.50	**<0.001**
Time to peak sensory block (min)	8.65 ± 1.04	7.49 ± 0.88	**<0.001**
Duration of sensory block (min)	259.07 ± 26.74	306.37 ± 26.15	**<0.001**

Figure 2 shows the distribution of the highest sensory block level obtained by patients in both study groups.

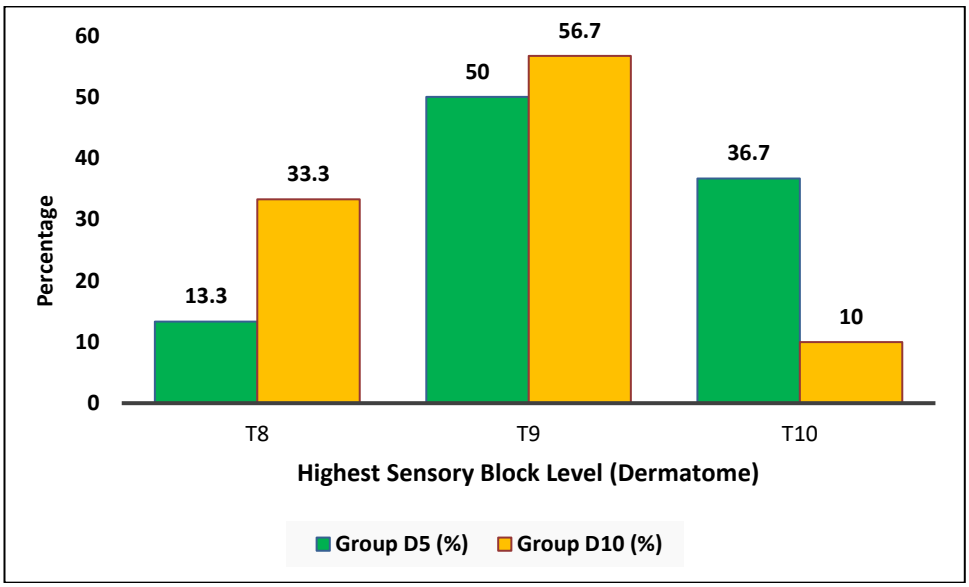

Figure 2. Distribution of the Highest Sensory Block Level (Dermatome)

The T8 sensory block level was achieved more frequently in Group D10 than in Group D5 (33.3% vs. 13.3%). The T9 dermatome was the most frequently achieved sensory block level in both Group D10 and Group D5 (56.7% vs. 50.0%, respectively). In contrast, the T10 sensory block level was more frequently observed in Group D5 than in Group D10 (36.7% vs. 10.0%). Overall, patients receiving 10 µg intrathecal dexmedetomidine tended to achieve a higher sensory block level than those receiving the 5 µg dose.

3.3 Comparison of Motor Block Characteristics

The onset of motor block was significantly faster in Group D10 than in Group D5. The median onset of motor block was 5.50 minutes (IQR: 5.03–5.80) in Group D10 and 6.45 minutes (IQR: 6.20–6.88) in Group D5 (**$p < 0.001$**). Furthermore, the mean duration of motor block was significantly longer in Group D10 than in Group D5 (259.77 ± 27.15 min vs. 224.23 ± 28.08 min; **$p < 0.001$**). These outcomes indicate that 10 µg ID produced a faster onset and longer duration of motor block than the 5 µg dose.

3.4 Comparison of Postoperative Analgesic Outcomes

The analgesic outcomes in the postoperative period are detailed in Table 3. Individuals in the D10 group had longer duration of postoperative analgesia and had a delayed time of rescue analgesia compared with the 5 µg group. Furthermore, the total amount of analgesics utilised in Group D10 was considerably less within the first 24 hours following surgery. Group D10 had a lower VAS score compared with Group D5, indicating better postoperative pain control.

Table 3. Postoperative Analgesic Outcomes Comparisons

Variables	Group D5	Group D10	p-value
Duration of analgesia (min)	354.50 (343.25–383.25)	468.50 (432.75–494.25)	**<0.001**
Time to first rescue analgesic (min)	354.50 (343.25–383.25)	468.50 (432.75–494.25)	**<0.001**
Total analgesic consumption (mg/24 h)	125.00 (100.00–150.00)	87.50 (75.00–100.00)	**<0.001**

3.5 Comparison of Haemodynamic Parameters and Sedation Profile

Haemodynamic parameters and sedation profile are revealed in Table 4. There were no statistical alterations among the two groups at baseline when average heart rate and arterial pressure were measured (**$p > 0.05$**). These results indicate that the baseline haemodynamic profile of the two groups was similar. However, group D10 had considerably greater sedation scores than Group D5, showing a higher sedative effect of the higher dose of dexmedetomidine, but within clinically acceptable limits.

Table 4. Comparison of Haemodynamic Parameters and Sedation Profile

Variables	Group D5 (n = 30)	Group D10 (n = 30)	p-value
Baseline heart rate (beats/min)	79.73 ± 8.54	79.00 ± 7.14	**0.720**
Baseline mean arterial pressure (mmHg)	92.17 ± 5.64	90.57 ± 4.44	**0.227**
Sedation score	1.00 (1.00–2.00)	2.00 (2.00–2.00)	**0.007**

3.6 Comparison of Adverse Events

Perioperative adverse events were relatively rare in both study groups. A higher percentage of patients treated with 10 µg ID had numerical hypotension, bradycardia, and nausea as compared to those receiving 5 µg, while vomiting and shivering were rare in each group. Figure 3 displays the distribution of perioperative adverse events for both the study groups.

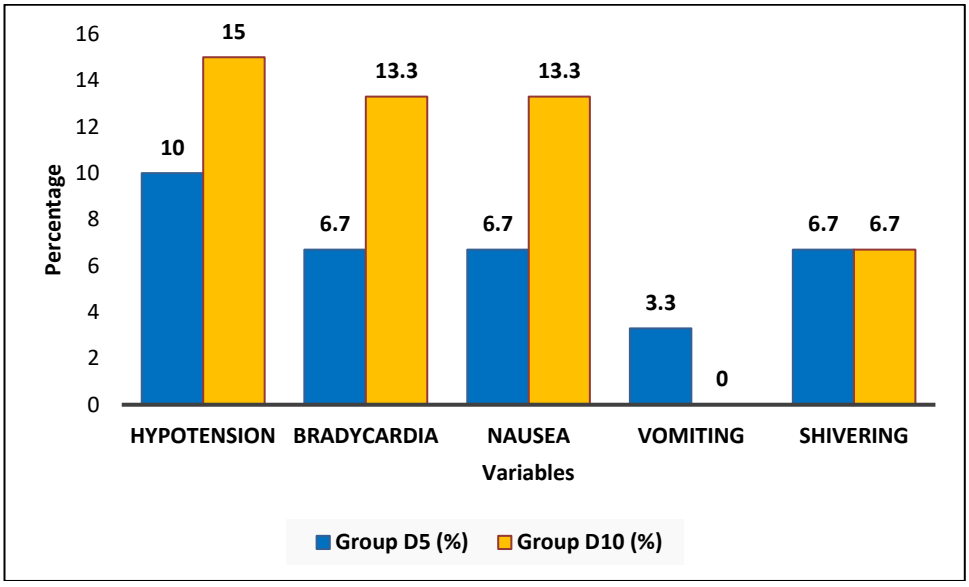

Figure 3. Comparison of Adverse Events

15.0% of Group D10 and 10.0% of Group D5 experienced hypotension as seen in Figure 3. Bradycardia occurred in 13.3% of patients in Group D10 and 6.7% in Group D5. Nausea occurred in 13.3% of patients in Group D10 and 6.7% in Group D5. One patient (3.3%) in Group D5 vomited and none in Group D10, and the occurrence of shivering was the same in both groups (6.7%). Although there were alterations in the numbers of adverse events, none were statistically diverse among study groups (**$p > 0.05$**) and both doses of dexmedetomidine had a favourable safety profile.

4. DISCUSSION

The effectiveness and safety of 5 µg versus 10 µg ID as an adjuvant to 12.5 mg of 0.5% HB were compared in patients undergoing lower limb orthopaedic surgeries in this prospective, randomised, double-blind trial. The onset of sensory block was significantly faster in Group D10 than in Group D5 (3.70 ± 0.50 min vs. 4.53 ± 0.38 min; **$p < 0.001$**). The onset of motor block was also significantly faster in Group D10 than in Group D5 [5.50 min (IQR: 5.03–5.80) vs. 6.45 min (IQR: 6.20–6.88); **$p < 0.001$**]. The results also showed that the 10 µg dose produced significantly longer durations of sensory block (306.37 ± 26.15 min vs. 259.07 ± 26.74 min) and motor block (259.77 ± 27.15 min vs. 224.23 ± 28.08 min), prolonged postoperative analgesia, delayed the requirement for rescue analgesics, reduced postoperative analgesic consumption, and produced slightly higher sedation scores without a clinically significant increase in perioperative adverse events. Both groups were comparable in terms of demographic characteristics and baseline haemodynamic parameters, suggesting that the observed differences were attributable to the intervention rather than baseline differences. The results indicate that a higher dose of ID, 10 µg, provides improved quality and duration of spinal anaesthesia without major adverse effects.

The present study outcomes are known to the outcomes of MiShra et al., [19], who showed that advanced doses of ID resulted in a substantial improvement in postoperative analgesia and sensory and motor blockage when associated to lower doses in lower limb surgeries. Similarly, Gupta et al. [20] found that the property of the subarachnoid block was dose dependent with 10 µg dexmedetomidine being able to produce longer sensory and motor blockade without any major side effects. Biekhet et al. [21] also reported comparable improvement in the quality of the spinal anaesthetic with the increase in the dosage of ID in ambulatory spinal anaesthetic, which extended the duration of the block and the postoperative analgesic effect. All these findings are in line with the current observation of better spinal block characteristics and longer duration of analgesia with the higher dose of dexmedetomidine.

Results of the postoperative analgesia in the present investigation are also in line with earlier comparative investigations which compared dexmedetomidine with other intrathecal adjuvants. Rahimzadeh et al. [22] showed dexmedetomidine significantly reduced the need for postoperative analgesics and had a longer duration of postoperative analgesia over fentanyl in patients undergoing lower limb orthopaedic surgery. Likewise, when used as an intrathecal adjuvant, dexmedetomidine was found to be superior in analgesic efficacy and duration of spinal anaesthesia than dexamethasone by Elshahawy et al. [23]. Moreover, the use of dexmedetomidine is related with better sensory and motor block features than clonidine and was found to be safe during the perioperative period [24]. The results of the current investigation have been supported by the findings of these studies, and dexmedetomidine has been found to be an effective intrathecal adjuvant to improve spinal anaesthesia.

This study has clinical implications in routine anaesthetic practice in lower limb orthopaedic surgery. 10 µg of ID combined with 12.5 mg of 0.5% HB may improve the surgical condition, with the advantages of faster onset of sensory and motor block, longer postoperative analgesia, and less postoperative consumption of analgesics. The higher dose also resulted in only minimal increase in sedation and similar haemodynamics and adverse event rates, indicating safety in the appropriately selected patient. Thus, to optimize the intrathecal dose of dexmedetomidine might improve patient comfort, consumption of other analgesics and perioperative management.

5. Limitations: However, there are some caveats to these positive outcomes. Because of the study's small sample size (n = 60), the findings might not be broadly applicable. The results may not apply to higher-risk patients or other surgical populations because only patients with ASA physical status I and II undergoing elective lower extremity orthopaedic surgeries were involved. Also, postoperative outcomes were only measured during the initial postoperative phase and long-term recovery or functional outcomes were not examined.

6. CONCLUSION

The present study demonstrated that both 5 µg and 10 µg ID were effective as an adjuvant to 12.5 mg of 0.5% HB for spinal anaesthesia in patients undergoing lower extremity orthopaedic surgeries. However, the 10 µg dose produced a better clinical response than the 5 µg dose. Patients receiving 10 µg dexmedetomidine experienced a faster onset of sensory and motor block, a longer duration of sensory block (306.37 ± 26.15 min vs. 259.07 ± 26.74 min), and a longer duration of motor block (259.77 ± 27.15 min vs. 224.23 ± 28.08 min). The 10 µg dose also prolonged postoperative analgesia, delayed the requirement for rescue analgesics, reduced postoperative analgesic consumption, and had a lower VAS score compared with Group D5. Although sedation scores were marginally higher with the 10 µg dose, they remained clinically acceptable. Baseline haemodynamic parameters were comparable among the groups, and there was no statistically substantial alteration in the incidence of perioperative adverse events. Therefore, 10 µg ID may be considered a more effective adjuvant than the 5 µg dose when combined with 12.5 mg of 0.5% HB for elective lower limb orthopaedic surgeries.

7. **Recommendations:**

Larger, multicentric randomized controlled trials with more diverse patient groups are needed to authorize these conclusions in the future. Future studies should also evaluate other intrathecal doses of dexmedetomidine, make

comparisons with other new spinal adjuvants and evaluate long-term postoperative recovery, patient satisfaction, and cost effectiveness. These studies would contribute to the development of uniform dosage guidelines and further fine-tune spinal anaesthetic techniques for lower limb orthopaedic procedures.

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Conflict of Interest: Authors declare no conflicts of interest.

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