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Original Article

Anaesthesia Section

Comparison of Intrathecal Dexmedetomidine and Fentanyl as Adjuvants to 0.5% Heavy Ropivacaine for Lower Limb Surgeries: A Randomised Controlled Study

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ABSTRACT

Introduction: Spinal Anaesthesia (SA) is a suitable Regional Anaesthesia (RA) for lower limb surgery, but is limited by its comparatively short analgesic duration. Adjuvants like fentanyl and dexmedetomidine can be administered intrathecally with local anaesthetics like ropivacaine to assist in modulating block parameters, extend the duration of analgesia and decrease systemic administration of opioids.

Aim: To compare and evaluate the safety and efficacy of intrathecal fentanyl and dexmedetomidine as adjuvants to ropivacaine in lower limb orthopaedic surgery.

Materials and Methods: This double-blinded, randomised controlled study was carried out at the Department of Anaesthesiology, Jawaharlal Nehru Medical College, Acharya Vinoba Bhave Rural Hospital, Datta Meghe Institute of Higher Education and Research (DMIHER), Sawangi (Meghe), Wardha, Maharashtra, India. It was performed in 60 American Society of Anaesthesiologists (ASA) I-II patients aged 18-50 years undergoing elective lower limb operations. The patients were divided into two groups: Group-RD was administered 15 mg 0.5% hyperbaric ropivacaine with 10 µg dexmedetomidine and Group-RF was administered 15 mg 0.5% hyperbaric ropivacaine with 20 µg fentanyl. Haemodynamic parameters, sensory and motor block characteristics, sedation {as measured by the Ramsay Sedation Score (RSS)}. Duration of analgesia and side-effects were recorded. Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) v22.0 and GraphPad Prism v6.0 and $p<0.05$ was considered statistically significant.

Results: The mean age was 38.43±8.31 years in Group-RF and 37.27±8.75 years in Group-RD. Group-RD showed a significantly earlier onset of sensory block (4.33±0.64 min vs 5.58±0.59 min). Motor block onset was also earlier in Group-RD (5.04±0.75 min) than in Group-RF (7.57±0.60 min), with a longer motor block duration (207.26±6.58 min vs 148.9±8.22 min). Postoperative analgesia lasted significantly longer in Group-RD (391.86±9.89 min) compared with Group-RF (213.3±3.79 min). Haemodynamic parameters remained clinically stable in both groups, with only slight transient decreases in PR and blood pressure and no significant bradycardia or hypotension.

Conclusion: Dexmedetomidine is a better adjuvant to ropivacaine compared to fentanyl in SA. It provides better onset, longer sensory and motor block duration and increased analgesia without inducing further haemodynamic instability or respiratory depression.

Keywords: Analgesia, Pain relief, Spinal anaesthesia

INTRODUCTION

Pain is an unpleasant sensory phenomenon characterised by actual or potential tissue damage [1]. Effective, safe and long-duration pain relief during surgery has remained the mainstay of anaesthetic and perioperative practice [2]. With the increasing use of technology and more invasive surgery, as well as minimal access surgery, greater attention has been given to anaesthetic methods designed to maximise patient comfort, minimise postoperative complications and facilitate earlier recovery [3]. Among the various modalities of RA, SA is among the most commonly used for lower-limb surgeries [4].

The SA entails direct intrathecal injection of local anaesthetic into the cerebrospinal fluid in the subarachnoid space [5]. SA offers sensory and motor block via inhibition of nerve conduction and sympathetic block, resulting in vasodilation and hypotension, which reduce blood loss but necessitate careful haemodynamic monitoring [6]. SA's widespread application in orthopaedic, vascular and trauma surgery of the lower limb is due to its rapid onset, predictable block, systemic exposure at low doses and avoidance of airway manipulation [7].

One of the most significant drawbacks of SA is its short duration of analgesia, which may be suboptimal with prolonged surgery or in postoperative pain treatment. Once the block wears off, patients are at the mercy of systemic opioids with emesis, vomiting, pruritus, urinary retention, respiratory depression and sedation. Therefore, prolongation of quality and duration of SA without side-effects has been a significant clinical issue [6,8].

To overcome this shortcoming, the addition of adjuvants to the local anaesthetic solution used in SA has become increasingly popular. Adjuvants are pharmacological substances that, when added to local anaesthetics, can extend the duration of sensory and motor block, enhance postoperative analgesia, decrease the need for systemic analgesics and even improve haemodynamic stability [9]. The amide type of local anaesthetic, which has a delayed onset of sensory blockade, reduced cardiotoxicity and bupivacaine-resistant sensory-motor selectivity, is therefore appropriate for elderly or cardiac patients and ropivacaine is the preferred choice. However, ropivacaine is inadequate to cause postoperative analgesia and adjuvants thus need to be used [10]. This study was undertaken because of limited comparative evidence on the optimal intrathecal adjuvant with ropivacaine to improve block characteristics and prolong postoperative analgesia while maintaining haemodynamic stability. Fentanyl is a highly lipophilic opioid that acts by binding with dorsal horn µ opioid receptors to cause severe analgesia. Combined with ropivacaine, it provides analgesia with minimal

potentiation of motor blockade and causes a rapid onset of action with synergism [11]. Its brief duration of action and possible opioid-type side-effects like pruritus, nausea, urinary retention and mild respiratory depression are its drawbacks [12]. Dexmedetomidine, an ultra-selective α adrenergic agonist, causes long-acting sensory and motor blockade, non depressant sedation and enhanced haemodynamic stability by sympatholysis. It can produce bradycardia and hypotension in susceptible patients and should be monitored closely [13,14].

The present study aimed to compare the effectiveness and safety of dexmedetomidine (10 mcg) and fentanyl (20 mcg) as an adjuvant with intrathecal ropivacaine 0.5% heavy in lower limb surgery. The primary objective was to find the onset and duration of sensory and motor block in both groups. Secondary outcomes included assessing analgesia duration, haemodynamic stability, sedation using the modified Ramsay Sedation Score (RSS) and side-effects.

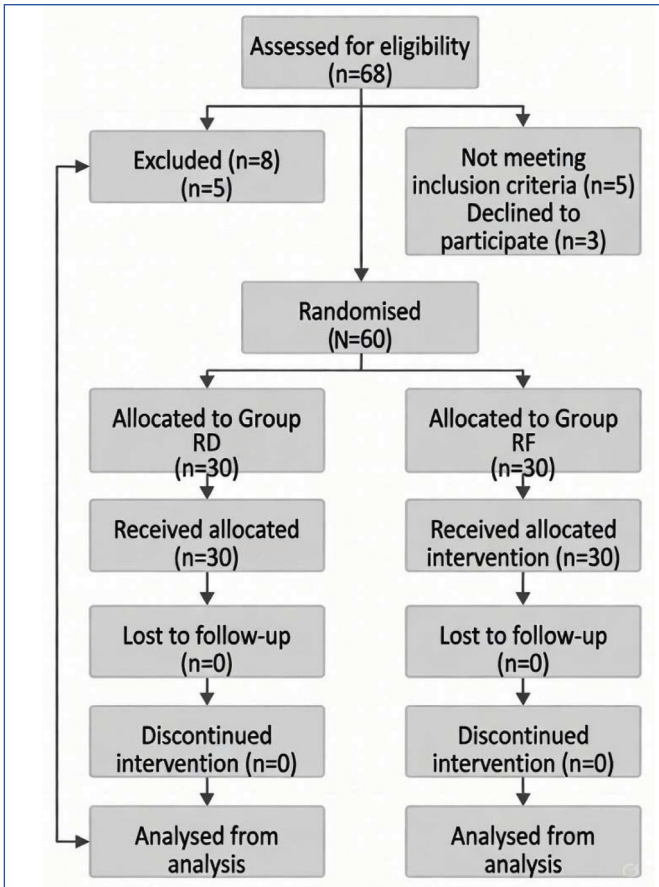
MATERIALS AND METHODS

The present double-blinded, randomised controlled study was carried out at the Department of Anaesthesiology, Jawaharlal Nehru Medical College, Acharya Vinoba Bhave Rural Hospital, Datta Meghe Institute of Higher Education and Research (DMIHER), Sawangi (Meghe), Wardha, Maharashtra, India, after Institutional Ethics Committee approval (Ref No: IEC/2022/04/17) and Clinical Trials Registry- India (CTRI) Registration (CTRI- 2024/07/071589). Informed written consent was obtained from all the participants in the study after explaining the procedure, the benefits, the risks and the right to withdraw without prejudice.

The participants were either female or male, aged 18 to 50 years, with an ASA physical status of I or II and were posted for elective lower limb surgery. Local infection at the puncture site, hypersensitivity to study medication, renal or hepatic impairment, ischaemic heart disease or valvular heart disease, uncontrolled hypertension, sepsis, coagulopathy, or chronic opioid dependence were exclusion criteria.

Sample size calculation: The sample size was calculated based on data on sensory blockade reported by Ravipati P et al., [15]. In that study, the mean time required to achieve sensory blockade at T10 was 156.4667±33.78 s in Group-RD and 185.2000±35.17 s in Group-RF, showing a clinically and statistically significant difference (p=0.002). Using a two-tailed α error of 0.05, a study power of 80% and an anticipated minimum difference of 20% in the mean time between the two groups, the required sample size was estimated to be 23 patients per group, as shown in [Table/Fig-1]. To improve the reliability of the study outcomes and to compensate for possible dropouts, 30 patients were included in each group.

Randomisation was carried out using a computer-generated block randomisation sequence prepared by an independent investigator not involved in patient recruitment, drug preparation, or outcome assessment. The Consolidated Standards of Reporting Trials (CONSORT) diagram of the study is shown in [Table/Fig-1]. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. These envelopes were opened immediately before SA by a designated anaesthesiologist who was not involved in intraoperative monitoring or postoperative assessment. Blinding was achieved by preparing the intrathecal study drugs in identical syringes with the same total volume (3.4 mL) and identical appearance. The anaesthesiologist administering the SA was aware of the group allocation but had no role in postoperative evaluation. In contrast, the patients and the anaesthesiologist assessing intraoperative and postoperative outcomes were blinded to the group assignment, thereby ensuring double blinding. Group-RD received 15 mg of 0.5% hyperbaric ropivacaine with 10 μg dexmedetomidine diluted with 0.2 mL normal saline (total volume 3.4 mL) and Group-RF received 15 mg of 0.5% hyperbaric ropivacaine with 20 μg fentanyl (total volume



[Table/Fig-1]: CONSORT diagram of the study.

3.4 mL). The dosages of dexmedetomidine and fentanyl were selected based on previously published studies demonstrating their safety and efficacy as intrathecal adjuvants [16,17].

Study Procedure

preparation: A preanaesthetic check-up, comprising a history, clinical examination and various investigations (complete blood count, renal and liver function tests, coagulation profile, random blood sugar, urinalysis, chest X-ray and electrocardiogram), was performed in all patients. A local anaesthetic skin sensitivity test was conducted. Preoperative premedication with intravenous (i.v.) pantoprazole 40 mg and ondansetron 8 mg was given at night before surgery. The standard fasting routine was followed.

Anaesthetic technique: Standard monitors (electrocardiography, pulse oximetry and non invasive blood pressure) were used in the operating room and the first readings were obtained. Intravenous access was established using an 18-gauge cannula and a 500 mL Ringer's lactate preload was administered. The patient received SA in the lateral or sitting position. Under aseptic cover, local infiltration of 2 mL 1% lignocaine was administered, followed by localisation of the L3-L4 interspace by palpation. Midline access was obtained using a 25-G Quincke spinal needle until a free flow of cerebrospinal fluid was achieved. The study drug was given slowly over 10-15 seconds without barbotage. The patients were then positioned for the surgery. Facemask supplemental oxygen was administered if SpO_2 was less than 90 percent.

Intraoperative monitoring and management: Pulse Rate (PR), Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were measured at 2-minute intervals for the initial 10 minutes, 5-minute intervals for the subsequent 30 minutes and 15-minute intervals thereafter until the conclusion of surgery. Hypotension (SBP >20% below baseline or <90 mmHg) was managed with i.v. mephentermine in 6-mg boluses. Bradycardia (PR < 50 bpm) was treated with i.v. atropine 0.6 mg. Nausea and vomiting were managed with ondansetron 4 mg i.v., shivering was treated with butorphanol 500 μg i.v. and an allergic reaction was treated with

hydrocortisone 100 mg i.v. and pheniramine maleate 25 mg i.v.. The primary endpoints were the time to onset and duration of sensory block, as well as the onset and duration of motor block. The secondary endpoints included sedation score (RSS), intraoperative haemodynamic stability and the incidence of side-effects, including hypotension, bradycardia, nausea, vomiting, pruritus, shivering and anxiety.

Postoperative care and rescue analgesia: Patients were observed in the post-anaesthesia care unit at 30-minute intervals for the first six hours and then at 12-hour intervals for the next 24 hours. The i.v. tramadol 100 mg was administered as required.

STATISTICAL ANALYSIS

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 22.0 and GraphPad Prism version 6.0. Continuous-type data were reported as mean±standard deviation and compared between groups using appropriate tests as required. Categorical data were reported as percentages and numbers and compared by appropriate tests. A p-value of <0.05 was used as the level of significance.

RESULTS

The examination and laboratory investigations of all patients revealed normal results. Demographic characteristics of the RF and RD groups are presented in [Table/Fig-2]. Age, gender, weight and height were not significantly different between groups. ASA physical grading showed no statistical significance. The above observation benefits both groups, as they are demographically equal for future comparison.

Parameters	RF (n=30)	RD (n=30)	χ^2/t-test	p-value
Age (years)	38.43±8.31	37.27±8.75	0.789	0.674
Gender (M/F)	26 / 4	20 / 10	3.354	0.067
Height (cm)	164.4±4.26	162.0±4.74	3.751	0.290
Weight (kg)	59.53±10.62	61.06±9.30	3.910	0.418
ASA Grade (I/II)	23 / 7	21 / 9	0.340	0.560

[Table/Fig-2]: Demographic characteristics of study participants. Data are presented as mean±SD for continuous variables and as counts for categorical variables. Comparisons between groups were performed using the independent t-test for continuous variables (age, height and weight) and the χ^2 test for categorical variables (gender and ASA grade). A p-value ≤ 0.05 was considered statistically significant.

Group-RD showed a significantly faster onset of sensory and motor block compared to Group-RF. The duration of sensory and motor block was markedly longer in Group-RD than in Group-RF. These differences were statistically significant (p<0.01). The results are depicted in [Table/Fig-3].

Parameters	RF (n=30)	RD (n=30)	p-value
Onset of sensory block (min)	5.58±0.59	4.33±0.64	<0.01
Duration of sensory block (min)	210.8±0.72	378.4±0.84	<0.01
Onset of motor block (min)	7.57±0.60	5.04±0.75	<0.01
Duration of motor block (min)	148.9±8.22	207.26±6.58	<0.01

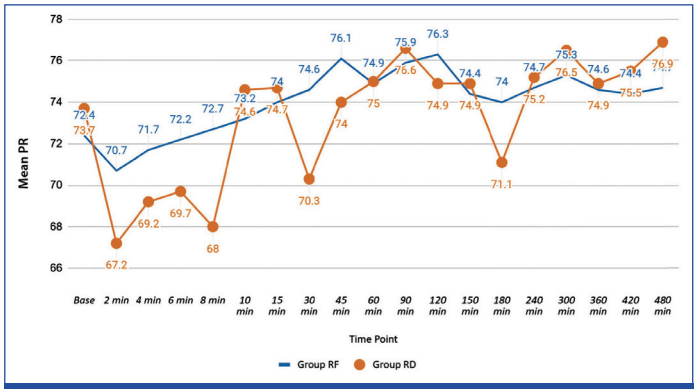
[Table/Fig-3]: Characteristics of sensory block and motor block. Data are presented as mean±SD. Comparisons were performed using the independent t test. A p-value<0.05 was considered statistically significant.

The duration of analgesia was significantly greater in the Group-RD than in the RF group, as seen in [Table/Fig-4]. All RF patients required the first rescue analgesic at 200-240 minutes, whereas all RD patients required it at 375-425 minutes.

Duration of analgesia (min)	RF (n=30)	RD (n=30)	Mean±SD (RF)	Mean±SD (RD)	p-value
<300	30	0	213.3±3.79	391.86±9.89	<0.01 S
>300	0	30			

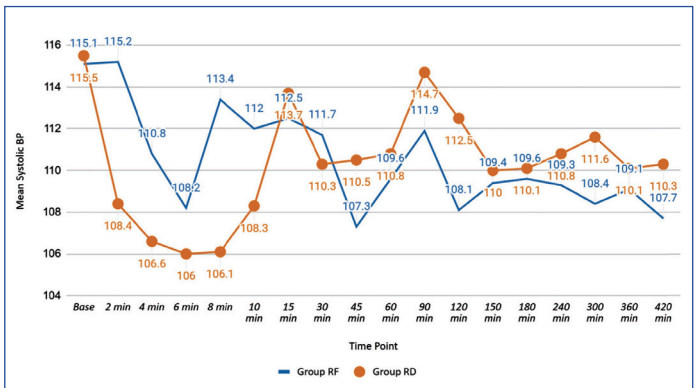
[Table/Fig-4]: Analgesia duration (minutes). Data are presented as mean±SD. Comparisons were performed using the independent t test. A p-value<0.05 was considered statistically significant.

Mean PR decreased minimally from baseline during the initial 2-10 minutes in both groups, with a reduction of <15%. A statistically significant difference between the groups was observed at two minutes (p=0.0019), four minutes (p=0.0192), 6 minutes (p=0.0029), 8 minutes (p<0.001) and 10 minutes (p=0.0274). Additional significant differences were noted at 30 minute (p<0.001), 45 minute (p=0.0011), 120 minute (p=0.0235), 180 minute (p=0.0015) and 480 minute (p=0.0177), while values at other time points were not statistically significant. Overall, PR values remained comparable and clinically stable in both groups throughout the study period, as shown in [Table/Fig-5].



[Table/Fig-5]: Comparison of mean PR (in minutes). Data are presented as mean±SD. Comparisons between groups were performed using one-way Analysis of Variance (ANOVA). A p-value<0.05 was considered statistically significant.

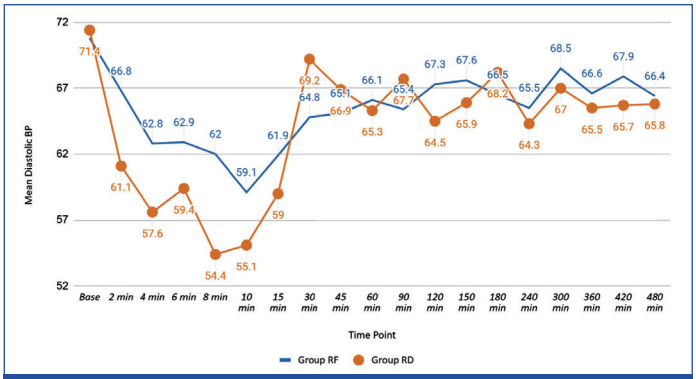
There were minor reductions in SBP in both groups during the first 10 minutes, with a fall of <16% from baseline. A statistically significant difference between the groups was observed at 2 minute (p<0.001), 4 minute (p=0.0004), 8 minute (p<0.001) and 10 minute (p=0.0012). Additional significant differences were noted at 120 minute (p=0.0002) and 300 min (p=0.0358), while values at other time points were not statistically significant. Overall, SBP remained clinically stable in both groups without episodes of significant hypotension, as shown in [Table/Fig-6].



[Table/Fig-6]: Comparison of mean SBP (in minutes). Data are presented as mean±SD. Comparisons between groups were performed using one-way ANOVA. A p-value<0.05 was considered statistically significant.

The DBP also showed a trivial decrease within the first 10 minutes in both groups. A statistically significant difference between the groups was observed at 2 min (p=0.0001), 4 min (p=0.0076), 6 min (p=0.0017), 8 min (p<0.001) and 10 min (p=0.0069). Additional significant differences were noted at 15 min (p=0.0002), 30 min (p=0.0252) and 120 min (p=0.0418), while values at other time points were not statistically significant. Overall, DBP remained clinically stable in both groups throughout the study period, as shown in [Table/Fig-7].

Most patients were side-effect-free, with 76.7% of RF and 66.7% of RD experiencing no adverse effects. Bradycardia (10%) and hypotension (6.7%) occurred only in RD and pruritus (6.7%) only in RF. Dry mouth, nausea/vomiting and shivering occurred in small, comparable numbers for both groups. The variation in the side-



[Table/Fig-7]: Comparison of mean DBP (in minutes). Data are presented as mean±SD. Comparisons between groups were performed using one-way ANOVA. A p-value<0.05 was considered statistically significant.

effect profile between the two groups was not statistically significant (χ^2=7.209, p=0.302), as seen in [Table/Fig-8].

Side-effects	RF (n=30)	RD (n=30)	χ^2	p-value
None	23 (76.7%)	20 (66.7%)	7.209	0.302
Bradycardia	0	3 (10%)		
Dry mouth	1 (3.3%)	1 (3.3%)		
Hypotension	0	2 (6.7%)		
Nausea & vomiting	2 (6.7%)	2 (6.7%)		
Pruritus	2 (6.7%)	0		
Shivering	2 (6.7%)	2 (6.7%)		

[Table/Fig-8]: Distribution of side-effects. Data are presented as the number of participants (n) and the percentage. Comparisons between groups were performed using the χ^2 test. A p-value<0.05 was considered statistically significant.

The RSS was mildly higher in RD. All subjects in both groups were two or three, with a maximum of three. Mean RSS was 2.67±0.48 for RD and 2.40±0.50 for RF, reflecting marginal and clinically acceptable deepening of sedation by dexmedetomidine, as seen in [Table/Fig-9].

Sedation Score (RSS)	RF (n=30)	RD (n=30)	Mean±SD (RF)	Mean±SD (RD)	χ^2	p-value
2	10	12	2.40±0.50	2.67±0.48	3.28	0.07
3	20	18				

[Table/Fig-9]: Distribution of Ramsay Sedation Score (RSS). Data are presented as the number of participants (n) and mean±SD. Comparisons between groups were performed using the χ^2 test. A p-value<0.05 was considered statistically significant.

DISCUSSION

Demographic and anthropometric profile: No differences were found between groups for ASA grade, sex, weight, height, Body Mass Index (BMI), or age, verifying the appropriateness of randomisation and the comparability of the study groups. Homogeneity of demographic features excludes confounding variables and verifies that the differences between block characteristics and analgesic effect are adjuvant-related. Kalbande JV et al. and Gupta R et al., noted that age did not significantly affect the efficacy of intrathecal dexmedetomidine or fentanyl, thereby minimising the possibility of age bias in SA responses [18,19]. Shukla U et al., (2024) did not report gender differences in the outcome [20]. The outcomes on weight and height reported by Shukla U et al., (2024) and Shaikh M et al., (2024) show similar results, regardless of demographic effects [20,21].

Sensory block onset and duration: Dexmedetomidine elicited a more rapid onset and peak of sensory block than fentanyl, revealing its efficient α2-adrenergic receptor effect on presynaptic inhibition and postsynaptic hyperpolarisation. The results of Divya VS et al., (2021), Alipour M et al., (2022) and Sun S et al., (2017) confirm the efficacy of dexmedetomidine in accelerating the onset of sensory block [22-24]. Although differing in timing, both groups attained identical peak levels of block, as shown by Shen Q et al., (2020) and Rahimzadeh P et al., (2018), that dexmedetomidine accelerates the onset of block without altering cephalad spread [25,26].

Motor block characteristics: The motor block had a faster onset and was prolonged with the addition of dexmedetomidine as an adjuvant, exhibiting enhanced synergy with ropivacaine. The same trends were observed by Sun S et al., (2017), Shen Q et al., (2020) and Gautam B et al., (2018), with a much earlier onset of motor activity with dexmedetomidine [24,25,27]. Prolonged motor block was described by Tsaroucha A et al., (2021) [28]. However, Urooj S et al., (2022) warned that such prolonged blocks are a step backward toward early ambulation of ambulatory patients and proposed individualised adjuvant selection based on surgical requirements [29].

Quality and duration of postoperative analgesia: Dexmedetomidine provided extended postoperative analgesia to a greater degree than fentanyl, resulting in a delayed need for rescue analgesic and improved pain control. Ahmed SA et al., (2024) equated similar durations of prolonged analgesia with intrathecal dexmedetomidine to fentanyl [30]. Gupta P et al., (2024), Sun S et al., (2017), Hosseini R et al., (2023) and Pramathesh A et al., (2024) also demonstrated longer analgesic duration and lower opioid use, favoring dexmedetomidine for improved recovery and opioid sparing [24,31-33].

Haemodynamic profile: The two adjuvants were haemodynamically stable. Both drugs induced slight reductions in SBP, DBP and HR, resulting from their sympatholytic effects. These were not clinically significant and did not require pharmacological treatment, as illustrated by the transient and controlled effects reported by Emam MWM et al., (2023) and Shukla U et al., (2024) [20,34].

Side-effects and sedation: The side-effects were minimal and similar between groups, with pruritus alone for the fentanyl group. Similar findings were reported by Peddapally A et al., (2024) [35]. Nausea, vomiting and mouth dryness were transient and self-limiting. At the same time, bradycardia and hypotension frequently occurred with dexmedetomidine, in line with earlier reports of Sun S et al., (2017) and Hosseini R et al. (2023) [24,32]. Sedation scores increased with dexmedetomidine but not to levels that precluded cooperation, without affecting respiration, as seen by Peddapally A et al., (2024) [35].

Limitation(s)

Only ASA I and II patients aged 18 to 50 years were studied and are thus not generalisable to high-risk, paediatric, or geriatric patients. It was conducted in a single centre, limiting its generalisability to other centres with heterogeneous patient populations or different protocols. Orthopaedic lower limb surgery alone was included in the study and the results could not be extended to any other surgical field. Adjuvant fixed doses were employed, which did not permit the establishment of dose-response relationships. Follow-up was limited to the postoperative period alone and chronic pain or late complications were not investigated. Sedation was measured using subjective devices rather than objective devices, such as the bispectral index, which is subject to observer bias.

CONCLUSION(S)

The present study confirms intrathecal dexmedetomidine as a superior adjuvant to ropivacaine compared to fentanyl, providing shorter sensory onset, longer sensory and motor blockade duration and prolonged postoperative analgesia without inducing marked haemodynamic or respiratory distress. The anthropometric and demographic equivalence of groups ensures that any differences are due to pharmacological action rather than patient heterogeneity. Dexmedetomidine's pharmacological profile sets it as a better adjuvant for SA, particularly in procedures that need extended analgesia or in situations where opioid-related side-effects should

be avoided. Additional large-scale, multicentric studies with dose titration and long-term follow-up can further enhance its clinical usefulness.

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