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ORIGINAL RESEARCH REGIONAL ANESTHESIA

Dexmedetomidine versus fentanyl as an adjuvant to bupivacaine in saddle anesthesia for anoplasty: a correlative randomized double-blinded trial

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ABSTRACT

Background: A saddle block is a preferred choice for peri-anal surgical procedures including anoplasty. Anesthesiologists have experimented by adding different adjuvants like dexmedetomidine and fentanyl to local anesthetics for spinal anesthesia, in an attempt to maintain balanced hemodynamics, fast recovery and prolonged post-operative pain relief. We compared the effect of dexmedetomidine with fentanyl on these parameters when added to hyperbaric bupivacaine for saddle block for anoplasty.

Methodology: Fifty-eight adult patients were categorized into two groups. Group-Fen, consisting of 29 patients, underwent a saddle block with 2.5 ml hyperbaric bupivacaine combined with fentanyl 0.5 ml (25 µg). Second group, the Group-Dex, consisted of 29 patients, received 2.5 ml hyperbaric bupivacaine mixed with dexmedetomidine 10 µg (0.5 ml). Monitoring of HR and SpO_2 was conducted every min for 10 min, then every 10 min. Evaluation of sensory blockage was done by using the pinprick technique, and the motor block was done utilizing the Bromage scale. Following surgery, assessments were conducted. Postoperative pain was determined utilizing the visual analog scale (VAS) in the ward and PACU.

Results: The Group-Dex exhibited significantly longer duration of two-segment retrogression and sensory retrogression to S1 compared to Group-Fen. Group-Dex exhibited a significantly prolonged duration until reaching Bromage 0 compared to the Group-Fen. A notable difference between groups was noted in terms of the time to request analgesia. The total consumption of tramadol and analgesic requirement frequency in Group-Dex was more alleviated than in Group-Fen, with highly substantial differences between groups.

Conclusion: Dexmedetomidine is recommended over fentanyl as adjunctive medication to bupivacaine for spinal anesthesia in anoplasty surgeries and procedures, in terms of duration of two-segment retrogression and sensory retrogression to S1.

Abbreviations: Anoplasty; BMI - Basal Metabolic Rate; IV - Intravenous; LA - Local anesthetics; PACU - Post-anesthesia care unit; VAS - Visual Analog Scale

Keywords: Dexmedetomidine; Regional Anesthesia; Spinal block; Bromage scale

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1. INTRODUCTION

Subarachnoid anesthesia, utilizing a minimal volume and anesthetic dose, is a viable option for anoplasty surgeries.[1] This technique effectively maintains stable hemodynamics, especially in older patients, and facilitates a painless recovery.[2] Numerous drugs are utilized as adjuvants to subarachnoid local anesthetics (LA) to enhance spinal anesthesia effectiveness. These drugs include opioids (sufentanil, fentanyl, and morphine), α2 adrenergic agonists (clonidine and dexmedetomidine), magnesium sulfate, neostigmine, midazolam, and ketamine.[3]

Fentanyl, a potent lipophilic synthetic opioid, is frequently utilized as an adjuvant medication for subarachnoid anesthesia due to its specific rapid onset, half-life, and limited propensity to induce respiratory depression.[4] The intravenous administration of opioids can alleviate pain without causing a notable impact on somatosensory evoked potentials, dorsal root axons, or nociceptive afferent inputs from C and δ fibers.[5] Dexmedetomidine acts as an agonist for α2 receptors in both the central as well as peripheral nervous systems.[6] The analgesic effect of α2-adrenoceptor agonists' subarachnoid injection is achieved by attenuating hyperpolarizing postsynaptic dorsal horn neurons as well as C-fiber transmitter release.[7] Stimulating the brain and spinal cord receptors hinders neuronal firing, resulting in bradycardia, hypotension, analgesia, and sedation.[8]

This study aimed to assess the impact of incorporating dexmedetomidine vs. fentanyl to bupivacaine in spinal anesthesia for anoplasty surgeries. Items evaluated are the duration of postoperative analgesia, hemodynamic changes, total postoperative tramadol consumed, and postoperative complications.

2. METHODOLOGY

This comparative, randomized, prospective trial was performed as per the guidelines established by the Faculty of Medicine's Research Ethics Committee at Al-Azhar University, Cairo, Egypt. Approved by the Ethical Committee of the Anesthesia, Critical Care, and Pain Management Department at Al-Azhar University (Registration number: 00395/2023). All patients in the research gave knowledgeable written consent. Registered in the ClinicalTrials.gov under the number of (NCT06216197).

Patient enrollment commenced in April 2021 and concluded in December 2022. All study procedures adhered to the principles outlined in the Declaration of Helsinki. In addition, the trial was performed at the General Surgery Department at Al-Azhar University Hospitals. Before participation, all participants gave informed, explicit consent.

The study included 58 adult patients of both sexes. Inclusion criteria for the study included ages between 20 and 60, both ASA-II and ASA-I, and Scheduled for anoplasty surgeries. Exclusion criteria included subjects who refused to participate and participants who had uncontrolled hypertension and heart failure (class IV or III) based on the New York Heart Association (NYHA), participants with BMI > 30 kg/m2, patients with uncorrected coagulopathy, Neuropathy or any spinal anesthesia contraindication (such as infection or a pelvic fracture), patients had any study's drug allergy, and patients having a history of drug abuse.

The primary outcome in this trial included the duration until the first call for analgesia, while the secondary outcomes included the duration from spinal injection until reaching the maximal sensory level, the duration needed for sensorial block regression seen over two spinal from the maximal sensory level, the time required for sensory regression until reaching the S1 level (from the maximal sensory level), The duration from injection to achieving Bromage 0, the total tramadol consumption (until the first 24 h), and side effects occurrences like vomiting, respiratory depression, shivering, and nausea, within 24 h following the administration of spinal anesthesia, as well as sedation level as determined utilizing the modified Ramsay scale.

The subjects were randomly categorized into two groups utilizing random numbers generated by computer software. A sealed envelope (containing the allocation numbers of groups) was (prepared by an anesthesiologist who was not sharing in the procedure) and opened at the time of patient enrollment. The Group-Fen, consisting of 29. In contrast, the Group-Dex, consisting of 29 patients. An anesthesiologist (at least five years of experience in regional anesthesia) administered the spinal blocks. This anesthesiologist was blinded to the medication being used.

Following the insertion of a wide-bore intravenous (IV) cannula, a normal saline solution (10 ml/kg) was administrated. Vital signs, specifically heart rate (HR), blood pressure (BP), and oxygen saturation (SpO_2), were assessed. Patients were set in a spine position on the operating table. Spinal anesthesia was done using a 25-gauge Quincke needle (with midline access) and bevel facing up. All subjects were administered subarachnoid hyperbaric bupivacaine along with the designated adjuvant based on group allocation. The Group-Fen, consisting of 29 patients, underwent saddle block spinal anesthesia utilizing (2.5 ml) hyperbaric bupivacaine combined with fentanyl (25 µg; 0.5 ml). In contrast, the Group-Dex, consisting of 29 patients, was administrated (2.5 ml) hyperbaric bupivacaine combined with

dexmedetomidine (10 µg; 0.5 ml). Following the injection, patients in both groups were gently repositioned (as required for the procedure).

Hypotension, MAP < 20% of the initial value, was managed by administering 250 ml of normal saline and intravenous ephedrine at a dosage of 3-6 mg. In addition, Bradycardia with HR<50 beats/min was managed by intravenous atropine at 0.01 mg/kg dose.

Measurements of the study are as follows: HR & SpO2 were continuously monitored, with measurements recorded at one-minute intervals for the initial 10 min and after that at 10-min intervals, BP was measured at 5-min intervals. The assessment of the sensory block was conducted by employing a pinprick technique with a 27G-hypodermic needle, whereas the motor block assessment was performed utilizing the Bromage scale.

The assessments were conducted before the subarachnoid injection and then at 2-min intervals following the injection until the maximum sensory level, as well as Bromage III, were achieved. Following surgery, evaluations were performed at 10-min intervals until a decrease of 2 sensory levels was observed. After that, assessments were conducted every 20 min until a decrease in the S1 dermatome and a Bromage motor scale score of 0. Subsequently, every patient was sent to the post-anesthesia care unit (PACU) and monitored by an anesthetist who was blinded to the study's procedures. Pain in the ward and PACU was determined using VAS. We requested patients to rate their degree of pain by putting a tick on one line with markers from 0 to 10, we used a ruler for that purpose with 10 centimeters from No pain (0 on the ruler) to the actual pain score. If the VAS score exceeded 3, analgesia was provided with a dose of 50 mg tramadol, and the total amount administered was recorded.

2.1. Sample size justification

Power analysis was utilized to calculate the required sample size. A prior meta-analysis comparing the effectiveness of two adjuvants found that dexmedetomidine substantially elevated the interval of pain-free periods, motor blocks, and stable sensory blocks.[5] The effect size for all four parameters was determined to be significant. Therefore, to obtain a power of 0.81 and 0.05 significance level, it is recommended that a two-independent samples t-test be utilized with a minimum sample size of 29 cases (per group), totaling at least 58 cases.

2.2. Statistical analysis

Data collection, input, coding, and editing were done utilizing the 23rd version of the IBM SPSS software. The presentation of parametric quantitative data included ranges or mean ± standard deviations, whereas non-parametric quantitative data was expressed utilizing interquartile ranges (IQR) as well as medians. Qualitative variables were represented using both numerical values and percentages. The chi-square test and Fisher exact test were utilized for the evaluation of qualitative data between groups when the predicted

Table 1: Comparative demographic data in both groups

Variable	Group-Dex (n = 28)	Group-Fen (n = 28)	Test value	P-Value
Gender				
• Female • Male	7 (27.4) 21 (72.6)	8 (28.6) 20 (71.4)	0.000*	1.001
Age (y)	37.43 ± 11.22	36.17 ± 7.43	-0.337•	0.718
BMI (kg/m^2)	27.21 ± 3.22	27.83 ± 3.21	0.554	0.499
ASA				
• I • II	22 (81.3) 6 (18.7)	23 (85.5) 5 (14.5)	0.157*	0.672
Type of surgery				
• Hemorrhoidectomy • Internal sphincterotomy • Rectopexy • Resection of anal mass	9 (32.1) 6 (21.4) 6 (21.4) 7 (25.0)	8 (28.5) 7 (25.0) 5 (17.8) 8 (28.5)	1.897*	0.781
Duration of surgery (min)	28.01 ± 0.45	29.33± 0.74	-1.446•	0.142

Data expressed as mean ± SD or n (%); P < 0.05 expressed as significant (S) • Independent t-test;

** Chi-square test*

count in a cell was < 5. The Independent t-test was utilized to correlate two independent groups (with a parametric distribution and quantitative data), whereas the Mann-Whitney test was utilized for non-parametric data. Furthermore, the confidence interval was 95%, and the accepted margin of error was 5%. A p-value over 0.05 signifies non-significance (NS), a p-value of 0.05 indicates significance (S), and a p-value below 0.01 signifies high significance (HS).

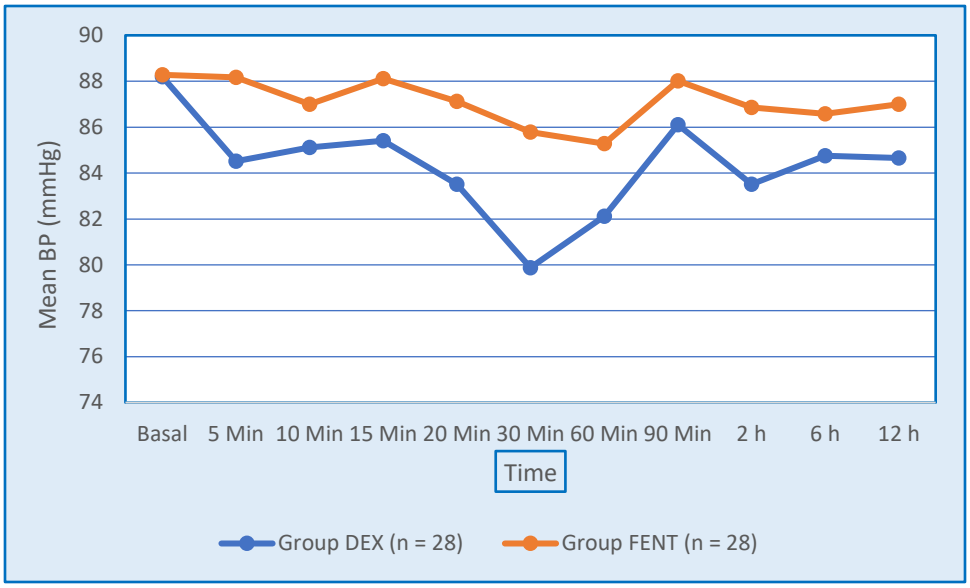

Figure 1: Comparative mean blood pressures in two groups.

3. RESULTS

The study assessed the eligibility of 74 patients in total. Out of these, nine patients were excluded due to non-compliance with inclusion criteria, and seven patients declined participation. The final analysis included 58 subjects who fulfilled the inclusion criteria. Subjects were randomly divided into one of the two groups; the Group-Dex and the Group-Fen, each including 29 patients. All subjects completed the trial.

The demographic data (Sex, BMI, age, and ASA classification) were comparable between both groups. Additionally, surgery time did not alter significantly between the groups (Table 1).

There were no substantial variations in MAP and HR between both groups before performing the block (basal), intraoperatively, or after the saddle block, as illustrated in Figure 1 & 2.

Table 2 indicates no substantial difference between both groups concerning the maximal sensory level, as well as the time until obtaining Bromage III as well as maximal sensory level. Nevertheless, Group-Dex exhibited considerably longer durations for both sensory regression and two-segment regression to S1 compared to Group-Fen. Furthermore, the duration for the return to Bromage 0 was notably extended in Group-Dex in comparison to the Group-Fen.

Furthermore, there were highly substantial differences between both groups concerning the time needed to rescue analgesia, with Group-Dex necessitating a more prolonged time compared to the Group-Fen. In Group-

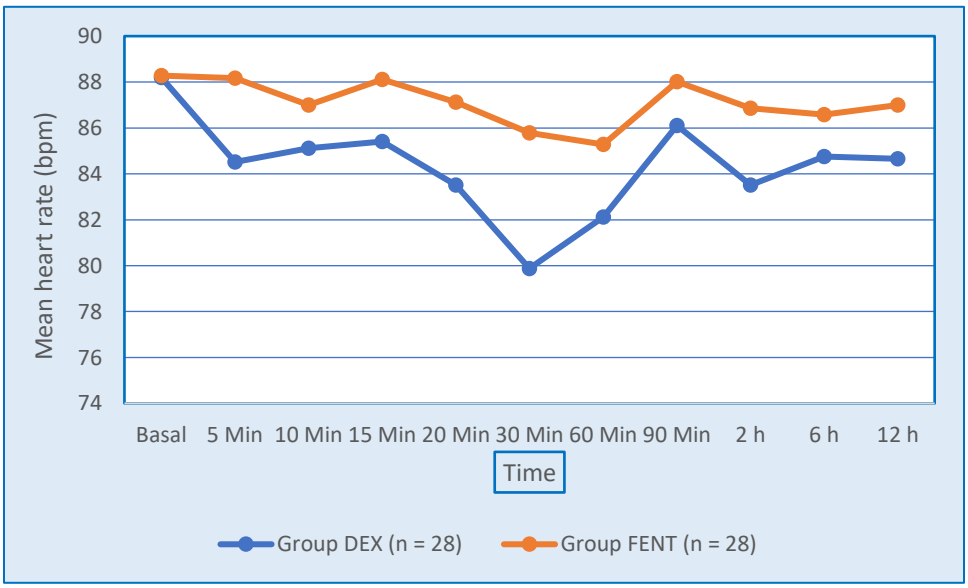

Figure 2: Comparative mean heart rates in two groups.

Table 2: Correlative block indicatives

Block Indicatives	Group-Dex (n = 28)	Group-Fen (n = 28)	Test value	P-value
Maximal sensory level				
• T4 • T5 • T6 • T7 • T8	3 (8.6) 4 (10.6) 10 (35.8) 3 (17.3) 8 (28.4)	4 (10.6) 5 (18.5) 7(22.2) 7 (22.2) 5 (18.5)	3.321•	0.532
Time to approach the maximum sensory level (min)	7.21 ± 1.67	6.89 ± 1.15	-1.651•	0.082
Time to two-segment retrogression (min)	148.11 ± 41.34	90.19 ± 7.02	6.608•	0.001**
Time for sensory retrogression to S1(min)	469.83 ± 42.33	170.50 ± 22.02	31.763•	0.001**
Time to approach Bromage III (blocked side) (min)	10.36 ± 3.29	10.6 ± 2.73	0.169	0.851
Time to retrogression to Bromage 0 (blocked side) (min)	372.43 ± 53.62	172.45 ± 26.04	18.153	0.000**

Data expressed as mean ± SD or n (%); P < 0.05 expressed as significant (S)

*• Independent t-test; ** Chi-square test*

Table 3: Correlative analgesic demands

Analgesic demands	Group-Dex (n = 27)	Group F ENT (n = 27)	Test value•	P-value
Time to call for analgesia (min)	399.63 ± 72.41	288.78 ± 35.54	7.123	0.000***
Total tramadol (mg) used per 24 h	50.41 ± 1.29	95.62 ± 2.50	-8.882	0.000***
Frequency of rescue analgesia (per 24 h)	1.65 ± 0.39	2.69 ± 0.37	-8.231	0.000***

****P < 0.01: strongly significant; •: Independent t-test*

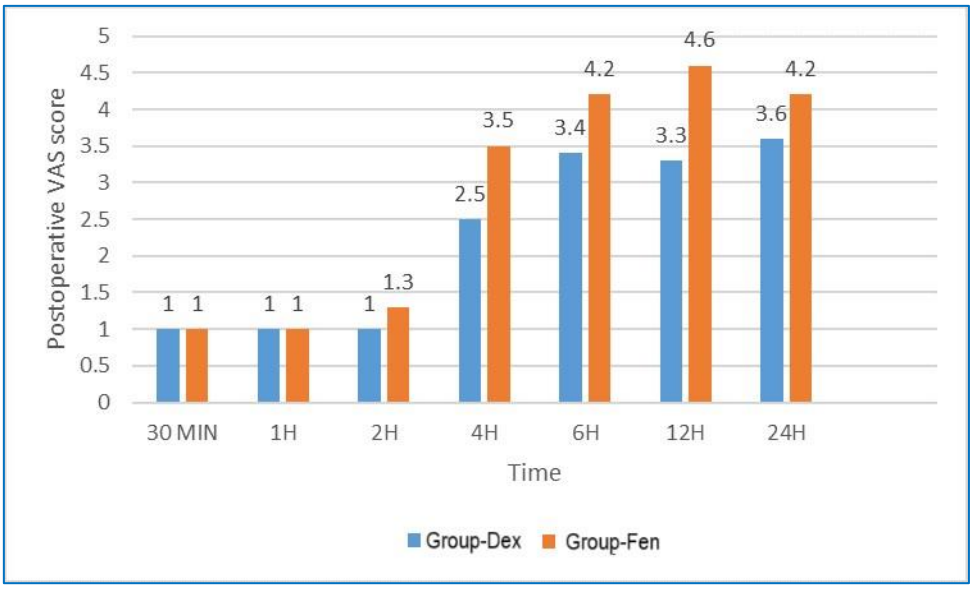

Figure 3: Postoperative VAS scores in the two groups.

Dex, the amount of tramadol administered was lower compared to Group-Fen. Additionally, the need for analgesics was less frequent in Group-Dex than in Group-Fen. This difference in values was found to be substantial, as depicted in Table 3.

No statistically substantial differences were observed in VAS scores between 30 min and one hour following surgery. Nevertheless, there was a highly substantial difference in the postoperative period, with Group-Dex showing lower scores compared to Group-Fen (Figure 3). Patients' sedation scores in the Group-Dex were between 1 and 3, higher than those in the Group-Fen (1-2), with no statistical differences.

No cases of respiratory depression were observed in either group. However, one subject in the Group-Dex and three in the Group-Fen exhibited symptoms of vomiting and nausea. The occurrence of shivering was less frequent in the Group-Dex (one case) in comparison to the Group-Fen (two cases), with no statistical significance. Pruritus was absent in Group-Dex, whereas one patient in Group-Fen experienced pruritus with no statistical differences.

4. DISCUSSION

This prospective, randomized double-blind study indicated that the duration required to rescue analgesia administration was more prolonged in the group receiving dexmedetomidine compared to the group receiving fentanyl. Moreover, tramadol's total dose needed for postoperative pain was substantially lower in the Group-Dex compared to the Group-Fen, and administration frequency was also alleviated in the Group-Dex than in the Group-Fen. Furthermore, VAS scores measured within the initial 24 h postoperatively were notably downregulated in Group-Dex compared to the Group-Fen.

Our findings agree with the outcomes of prior investigations conducted by Rahimzadeh et al.[9], which examined utilizing fentanyl (25 µg) and intrathecal dexmedetomidine (5 µg as adjuvants to bupivacaine) in cases undergoing lower limb as well as lower abdominal surgeries, respectively.

The findings of Mostafa et al.[10] indicated that the group receiving dexmedetomidine had substantially decreased VAS scores than the group receiving magnesium sulfate. Additionally, the dexmedetomidine group experienced a considerably longer period until the initial request for postoperative pain relief, and a higher number of patients in this group needed a second dosage of pain relief compared to those who were administered magnesium sulfate. Mazy et al.[11] conducted a comparison between the utilization of dexmedetomidine combined with fentanyl versus dexmedetomidine (as adjuvants to bupivacaine) in cases undergoing orthopedic procedures that were anticipated to last longer than 4 h. The outcomes indicated no discernible variations between both groups concerning the duration until the initial request for analgesia, VAS scores, and the overall amount of morphine needed. Yektaş and Belli[12] examined the impact of administering 4 µg & 2 µg of dexmedetomidine, combined with subarachnoid hyperbaric bupivacaine during elective inguinal hernia repair surgeries. The study revealed that the average duration until the pain started was more significant in the group that was administered 4 µg compared to the other group. Rai and Bhutia[13] found that the addition of 5 µg of dexmedetomidine to spinal anesthesia in orthopedic patients (during lower limb operations) was more effective than 3 µg in increasing time to rescue analgesia. Finally, Taher-Baneh et al.[14] performed a study on individuals who underwent elective calf surgeries while under unilateral spinal anesthesia. The study determined that the quantity of meperidine administered as a supplementary medication for pain management over 24 h was similar in both groups, with no substantial differences.

The current study found that the hemodynamic outcomes of HR and MBP were reduced in Group-Dexmedetomidine compared to Group-Fenanyl within the first hour following spinal anesthesia. Nevertheless, it is crucial to acknowledge that no marked differences were observed between both groups. These results align with Gupta et al.[8] as they also detected an elevated occurrence of hypotension in the Group-Dex compared to the fentanyl group, with no statistical significance. Likewise, Ravipati et al.[15] conducted a comparison of the impacts of subarachnoid isobaric ropivacaine (0.75%) combined with (5 µg) dexmedetomidine and (0.75%) isobaric ropivacaine combined with fentanyl (20 µg) in lower limb surgeries. They discovered that the reduction in SBP, MBP, and DBP was comparable in both groups. These changes were deemed clinically or statistically non-significant.

Contrary to these results, Rahimzadeh et al.[9] found that the decrease in SBP and DBP was notably more significant in individuals who were administered fentanyl as opposed to those who were given dexmedetomidine. The varying outcomes were ascribed to individual variations in drug reactions, demographic characteristics, the quantity of anesthetic combination administered intrathecally, and the amount of diluent utilized. In addition, Kalbande et al.[16] detected a higher and more pronounced decline in DBP, SBP, and HR in the group administered fentanyl 25 µg compared to those receiving dexmedetomidine 5 µg, and these differences reached statistical significance. Based on block characteristics, our findings indicated no substantial variations between both groups concerning the maximal

sensory level and the time to reach the maximal sensory level and Bromage III (in the side blocked). However, the time to two-segment regression, as well as the time for sensory regression to S1 and Bromage 0 in the side blocked, were more extended in Group D than Group F, with highly significant differences between groups. These results align with the meta-analysis conducted by Shen et al.[1,7] which demonstrated that intrathecal dexmedetomidine administration in cases undergoing cesarean section resulted in a substantial reduction in the onset time of motor block and sensory block while prolonging the block duration. Furthermore, Mostafa et al.[10] illustrated that dexmedetomidine decreased sensory block onset and extended the regression duration to S1. Taher-Baneh et al.[14] found that administering 5 µg of intrathecal fentanyl had a more significant impact on the quality and length of both sensory and motor block in the dependent limb compared to dexmedetomidine (5 µg).

The findings of this study align with Elshahawy et al.[18], who compared the utilization of dexamethasone and intrathecal dexmedetomidine (in emergency orthopedic surgeries of lower limbs). They illustrated that dexmedetomidine reduced the time for the sensory and motor block to occur with no differences in the maximum sensory block level. Additionally, dexmedetomidine led to a more prolonged sensory and motor block duration. Furthermore, a meta-analysis conducted by Liu et al.[19] supported these findings, showing that intrathecal dexmedetomidine 5 µg prolonged sensory and motor blocks' duration while accelerating both blocks' onset. It also delayed the time at which the first analgesic was requested. Nevertheless, it is important to highlight that the clinical importance of the initiation of sensory and motor block was not detected in this investigation.

Dexmedetomidine has a hypnotic impact that is similar to natural sleep. This effect is achieved by activating neurotransmitters that decrease histamine levels by inhibiting the descending noradrenergic inhibitory pathways.[20] In this study, the sedation scores were comparable between the two groups, with no substantial difference observed.

5. CONCLUSION

Dexmedetomidine is recommended over fentanyl as adjunctive medication to bupivacaine for saddle block spinal anesthesia in anal surgeries and procedures. It has favorable implications for pain management and minimal adverse effects.

6. Data Availability

All numerical data generated in the current study are available with the corresponding author.

7. Acknowledgment

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8. Conflict of Interest

No conflict of interests declared by the authors. The study involved no external or industry funding.

9. Authors' contribution

SSHA: Concept, Supervision, Design, Drafting the manuscript

IMA: Design, Data Collection and/or Processing, Literature Review

MAA: Materials, Literature Review,

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