Comparative Study Between Ketamine and Dexmedetomidine as Additives to Local Anesthetic in Ultrasound-Guided Combined Sciatic and Femoral Nerve Blocks for Below-Knee Surgeries. A Prospective Double-Blind Randomized Clinical Trial

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ABSTRACT

Background: Ultrasound-guided sciatic and femoral nerve blocks are widely used for below-knee surgeries, with adjuvants often added to local anesthetics to improve block efficacy and duration. Ketamine and dexmedetomidine are two commonly used adjuvants with distinct mechanisms and clinical profiles.

Objective: This study aimed to compare the efficacy and safety of ketamine and dexmedetomidine as additives to bupivacaine in ultrasound-guided combined sciatic and femoral nerve blocks for below-knee surgeries.

Patients and methods: This study involved 80 patients aged 18–60 years (ASA grade I–II) who were scheduled for below-knee surgeries. Patients were randomly assigned to receive a combination of 40 mL of 0.5% bupivacaine with either 0.5 mg/kg ketamine (Group K) or 50 μ g/kg dexmedetomidine (Group D). The measured outcomes included the onset and duration of sensory and motor blockade, pain scores (VAS), hemodynamic parameters, and adverse effects.

Results: A total of 80 patients were enrolled, with no significant differences in demographic characteristics between group K and group D groups. Heart rate and mean arterial blood pressure remained stable, with no significant intergroup differences. Sensory block duration was significantly longer in group K (14.21 \pm 0.35 hours) than in group D (13.94 \pm 0.29 hours) (p = 0.0003), while motor block duration was similar (13.81 \pm 1.46 vs. 13.3 \pm 0.9 hours, p = 0.064). VAS scores showed no significant differences at any time point (p > 0.05). Sedation levels were significantly higher in group D, with scores of 2.5 \pm 0.03 vs. 2 \pm 0.02 at 15 minutes (p < 0.001), maintaining significance up to 6 hours. Bradycardia was more frequent in Group D (20% vs. 5%, p = 0.043), while other adverse events, including hypotension (30% vs. 20%, p = 0.302), vomiting (12.5% vs. 5%, p = 0.235), and agitation (10% vs. 2.5%, p = 0.166), were comparable between groups. **Conclusion:** Both ketamine and dexmedetomidine effectively prolonged sensory and motor block durations, with ketamine providing a longer sensory block and dexmedetomidine inducing deeper sedation but a higher incidence of bradycardia.

Keywords: Ketamine, Dexmedetomidine, Bupivacaine, Sciatic nerve block, Femoral nerve block, Ultrasound-guided anesthesia.

INTRODUCTION

Peripheral nerve blocks (PNBs) have become a cornerstone in modern regional anesthesia, providing superior analgesia, reducing opioid consumption, and improving postoperative recovery in lower limb surgeries ^[1]. Among these, the ultrasound (US)-guided combined sciatic and femoral nerve block is widely used for surgeries involving the knee, leg, or ankle due to its efficacy in achieving complete anesthesia of the lower extremity. While, bupivacaine, which is a longacting local anesthetic, is a popular choice for PNBs, its duration of action remains a limiting factor in extended procedures or for prolonged postoperative analgesia^[2]. Thus, the addition of adjuvants to bupivacaine has garnered significant interest in optimizing the quality and duration of nerve blocks. Ketamine, a noncompetitive N-methyl-D-aspartate (NMDA) receptor antagonist, is recognized for its analgesic and anti-inflammatory properties, making it an appealing adjuvant in regional anesthesia^[3].

By modulating central sensitization and providing peripheral analgesia, ketamine enhances the efficacy of local anesthetics, while potentially reducing their systemic toxicity ^[4]. Similarly, dexmedetomidine, a selective alpha-2 adrenergic agonist, has been extensively studied for its sedative, analgesic, and nerve-block potentiation effects. It prolongs the action of local anesthetics through vasoconstriction at the injection site and by hyperpolarizing nerve cell membranes ^[5]. While, both agents have shown promise in enhancing bupivacaine-induced nerve blocks, their relative efficacy when combined in a dual nerve block setup warrants further investigation. The use of ultrasound guidance in nerve blocks has revolutionized regional anesthesia by increasing precision and reducing complications. US-guided techniques not only facilitate accurate deposition of the anesthetic agent around the nerve but also allow for real-time monitoring of the spread of the injectate ^[6].

This advancement ensures consistent outcomes and provides a robust platform to explore the benefits of adjuvants like ketamine and dexmedetomidine in combined nerve blocks. However, the interplay between these adjuvants and their impact on the duration and quality of sensory and motor blockade remains an area of ongoing research. Therefore, our rationale was to evaluate the impact of adding ketamine versus dexmedetomidine to bupivacaine in US-guided combined sciatic and femoral nerve blocks.

MATERIALS AND METHODS

This randomized, double-blind clinical trial was conducted at Sohag University Hospitals (May 2023–

October 2024). Eighty adults (18–60 years, ASA grade I–II) scheduled for below-knee surgery under US-guided femoral and sciatic nerve blocks were included.

Exclusion criteria: Patient refusal, neurological or psychiatric disorders, pregnancy/lactation, substance abuse, coagulopathy, morbid obesity, drug allergies, and infections at the block site.

Randomization and study groups: Patients were randomly assigned to one of two groups using a computer-generated sequence: Group K (Ketamine) received 40 mL of 0.5% bupivacaine with 0.5 mg/kg ketamine, while group D (Dexmedetomidine) received 40 mL of 0.5% bupivacaine with 50 µg/kg dexmedetomidine (Precedex®, Hospira, USA).

Preprocedural protocol: All participants received a thorough preoperative evaluation, including a medical history review and baseline vital sign assessment. Anxiolysis was provided with midazolam (0.03 mg/kg) as needed, and paracetamol (1 g) was administered for multimodal analgesia unless contraindicated. A peripheral IV cannula (18 G) was inserted, and lactated Ringer's solution was infused at 5 ml/kg/h, with continuous monitoring of HR, BP, RR, and SpO₂. The ultrasound machine (SonoSite, Nanomax, USA) was calibrated for femoral (3-5 cm depth, 8-12 MHz) and sciatic (3-9 MHz) nerve blocks, and sterile equipment, including anesthetic agents (bupivacaine 0.5% with ketamine 0.5 mg/kg or dexmedetomidine 50 μ g/kg), was prepared. The surgical site was disinfected, and patients were positioned based on the nerve block technique: supine with the leg abducted and externally rotated for femoral blocks, and lateral with the surgical side uppermost and the hip and knee partially flexed for sciatic blocks.

Procedural techniques

Femoral nerve block: An 8–12 MHz linear highfrequency probe was placed perpendicular to the femoral nerve, with the femoral artery identified below the midpoint of the inguinal ligament. Imaging depth was adjusted to 3–5 cm. The femoral nerve was located beneath the fascia iliaca and targeted using an in-plane technique. 15 ml of the assigned anesthetic solution was injected.

Sciatic nerve block: For the sciatic nerve block, the Labat approach was utilized. The patient was positioned laterally with the surgical side uppermost. A 3–9 MHz curvilinear low-frequency probe was used to scan the sub-gluteal region, identifying the sciatic nerve beneath the gluteus maximus and above the quadratus femoris muscle. The ischial tuberosity and greater trochanter served as anatomical references. 25 mL of the assigned anesthetic solution was injected around the sciatic nerve.

Block assessment and outcome measures: Sensory block was evaluated using the pinprick test and graded

on a 3-point scale (Grade 0: normal sensation, grade 1: loss of pinprick sensation and grade 2: loss of touch sensation). Motor block was assessed by evaluating foot and knee movements, using the modified Bromage scale (Grade 0: normal motor function, grade 1: partial motor impairment and grade 2: complete motor block). Sensory and motor block onset was measured from anesthetic administration to full block, while duration was recorded from full block to complete recovery.

Postoperative pain and analgesia: Pain intensity was evaluated using the Visual Analogue Scale (VAS) at 0, 1, 2, 4, 6, 12, and 24 hours postoperatively. Patients with VAS \geq 4 received 1 g IV paracetamol, while those with VAS \geq 7 received 0.1 mg/kg IV morphine. Recorded parameters included time to first analgesic request, number of patients requiring analgesia, and total analgesic consumption in the first 24 hours.

Sedation assessment: Sedation levels were assessed using the Modified Ramsay Sedation Scale, which ranges from 1 to 6, where grade 1 indicates an anxious, agitated, or restless state, grade 2 denotes a cooperative, oriented, and tranquil state, and grade 3 represents responsiveness to verbal commands only. Higher sedation levels include grade 4, where there is a quick response to a light glabellar tap or loud noise, grade 5, characterized by a delayed response to the same stimuli, and grade 6, indicating a complete lack of response.

Adverse Effects Monitoring: Patients were continuously monitored for adverse effects, including hypotension, defined as a $\geq 20\%$ decrease in systolic blood pressure (SBP) from baseline, bradycardia, characterized by a HR <60 beats/min, and nausea and vomiting, which were documented and managed according to standard protocols.

Ethical approval: This study was approved from The Medical Research Ethics Committee (IRB: 00013006), Faculty of Medicine, Sohag University). All participants provided written informed consents, and the trial was registered at Clinical Trials.gov (NCT06032624). The Helsinki Declaration was followed throughout the course of the investigation. $P \le 0.05$ deemed significant.

Statistical analysis

Data were analyzed with IBM SPSS (version 25). Qualitative data were presented as numbers and percentages, while quantitative data were summarized as mean. \pm SD for parametric distribution and median with interquartile range (IQR) for non-parametric distribution. Statistical analyses included the Chisquare test, unpaired Student's t-test, and the Mann-Whitney test. The p value is considered significant if \leq 0.05.



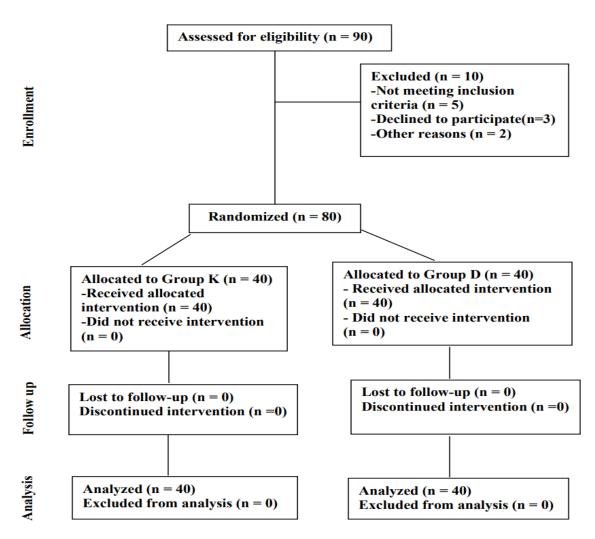


Figure (1): Consort Flow Diagram.

Eighty patients participated, evenly divided into group K and group D (40 each). Demographic characteristics (sex, age, BMI) were comparable between groups with no significance (Table 1).

		Group K (N=40)		Group D (N=40)		p-value
		Ν	%	Ν	%	
~	Male	19	47.5%	23	57.5%	0.050
Sex	Female	21	52.5%	17	42.5%	0.370
Age (years)	Median (IQR) Range		34.5- 58) 9- 70	44	4 (19- 74) 19- 74	0.973
BMI (Kg/m ²)	Mean± SD Range		42± 6.92 .7- 40.2		5.05± 6.57 3.7- 41.1	0.365

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Baseline ASA classification (Class I, II) also showed no notable differences (p = 0.431) (Table 2).

	Group K (N=40)	Group D (N=40)	Dualua
	No (%)	No (%)	– P-value
ASA classification			
– Class I	29(72.5%)	32(80%)	0.431
- Class II	11(27.5%)	8(20%)	
Duration of surgery (min)	65.5±22.2	58.3±19.1	0.124
Surgery site:			
– Knee	4 (10%)	6 (15%)	
– Tibia	16(40%)	14(35%)	0.144
– Ankle	8(20%)	12(30%)	
– Foot	12(30%)	8(20%)	

Table (2): American So	ciety of Anesthesiologists ((ASA) classification and surgical data	a

Data is presented as mean± SD, number (%)

Heart rate and MABP were assessed at multiple time points before and after the intervention. Both groups exhibited similar heart rate trends, with no notable differences observed throughout the study period. The baseline heart rate was 80 ± 10.88 bpm in group K and 78 ± 7.34 bpm in group D (p = 0.338). While, there were slight fluctuations during the study period, none of the time points showed notable differences among the groups (Table 3 & figure 2). Similarly, MABP showed no notable differences at any time point, with baseline measurements of 90 ± 15.36 mmHg for group K and 88 ± 11.65 mmHg for group D (p = 0.513) (Table 4 & figure 3).

Table (3): He	eart rate measurements	at different tim	e points
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	Group K (N=40)	Group D (N=40)	
	Mean ±SD	Mean ±SD	P-value
Baseline (0)	80.73 ±10.88	78.16 ± 7.34	0.338
5 min	85.15 ±19.25	77,2±17.5	0.055
10 min	83.48 ±22.26	72,81±28.31	0.057
15 min	80.52 ± 16.56	73.5±15.14	0.052
30 min	85.11 ±19.65	77.31±18.34	0.064
45 min	82.7 ±26.02	73.17±17.68	0.074
60 min	81.41 ± 18.09	74.22±18.93	0.095
90 min	83.39 ±22.87	73.6±19.35	0.061
Postoperative			
1 hr.	85.4 ± 25.98	74.35±23.64	0.051
2 hr.	82.37 ±20.61	74.18±17.68	0.066
4 hr.	85.62 ± 18.49	77.49±18.34	0.149
6 hr.	83.1 ±18.16	75.26±25.91	0.114
12 hr.	87.51 ±7.63	81.4±6.65	0.122
24 hr.	88.74 ±22.15	80.71±20.65	0.099

Data is presented as mean \pm SD.

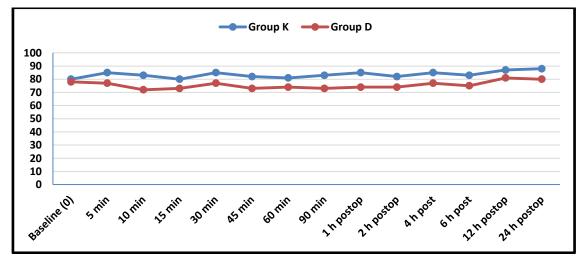


Figure (2): Comparison between the two groups regarding heart rate at different follow-up periods.

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	Group K	Group D	
	(N= 4 0)	(N=40)	P-value
	Mean ±SD	Mean ±SD	
Baseline(0)	90.11±15.36	88.3±11.65	0.513
5 min.	86.73±11.65	83.51±12.54	0.271
10 min.	88.2±12.6	83.47±11.65	0.069
15 min.	87.53±10.6	84.38±10.65	0.211
30 min.	85.66±11.38	82.21±12.65	0.268
45 min.	88.3±9.54	84.5±10.36	0.076
60 min.	84.11±9.26	80.26±9.35	0.086
90 min	89.76±14.35	83.42±16.64	0.088
Postoperative			
1 hr.	85.4±11.36	80.26±12.65	0.067
2 hr.	82.15±10.9	80.93±9.5	0.684
4 hr.	85.66±9.74	82.5±9.67	0.171
6 hr.	82.1±8.64	80.17±7.64	0.276
12 hr.	85.53±8.34	82.31±9.35	0.134
24 hr.	90.44±15.58	84.5±12.97	0.065

Table (4): Mean arterial blood pressure (MABP) at different time points

Data is presented as mean ±SD.

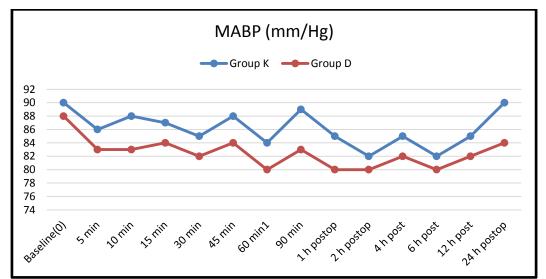


Figure (3): Comparison between the two groups regarding MABP at different follow-up period

The sensory block lasted significantly longer in the ketamine group than in the dexmedetomidine group $(14.81 \pm 0.35 \text{ vs.} 13.14 \pm 0.29 \text{ hours}, p = 0.003)$. However, motor block duration was similar between groups $(13.81 \pm 1.46 \text{ vs.} 13.3 \pm 0.9 \text{ hours}, p = 0.064)$, as were the onset times for both sensory and motor blocks (Table 5).

Table (5): Sensory and motor block characteristics

	Group K (N=40)	Group D (N=40)	P-value
	Mean ±SD	Mean ±SD	
Motor duration(hours)	13.81± 1.46	13.3 ± 0.9	0.064
Sensory duration (hours)	14.81±0.35	13.14±0.29	0.003*
Onset time of motor block (min)	19.52±4.32	18.56±4.15	0.314
Onset time of sensory block (min)	13.15±3.43	13.65±3.24	0.505

*p-value is significant

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VAS scores showed no notable differences at any time point. Also, total analgesic consumption was similar in the two groups. (Table 6).

	Group K (N=40)	Group D (N=40)	P-value
	Median (IQR)	Median (IQR)	
VAS 0	1(1-2)	1(0-2)	0.673
VAS 1hr.	1(1-2)	1 (0-2)	0.673
VAS 2hr.	1(1-2)	1(0-2)	0.673
VAS 4 hr.	2(1-2)	2(1-2)	0.690
VAS 6 hr.	2(1-2)	2(1-3)	0.591
VAS 12 hr.	2(1-3)	2(1-3)	0.861
VAS 24 hr.	3(2-4)	3(2-3)	0.245
Patients requested additional analgesia: N (%)	8(20%)	7(17.5%)	NS
Total analgesic consumption:			
Paracetamol (g)	0.2 ± 0.42	0.2±0.4	0.76
Morphine(mg)	$0.8{\pm}2.2$	0.9±2.3	0.87

Table (6): VAS Scores for Postoperative Pain Assessment and total analgesic consumption

Data is presented as median (IQR), Mean ±SD, N. (%)

Sedation levels were higher in group D across different time intervals. At 15 minutes, sedation was 2 ± 0.02 in group K vs. 2.5 ± 0.03 in group D (p < 0.001). This trend continued throughout the study, with group D, there was significantly higher sedation scores at all-time points, reaching p-values < 0.001 at all relevant times up to 6 hours. At 12 hours, however, the sedation scores were not notably different among both groups (Table 7 & figure 4).

Table (7): Sedation scores at different time Points

	Group K (N=40)	Group D (N=40)	P value
	Mean ±SD	Mean ±SD	
15 min	2.0±0.02	2.5±0.03	<0.001*
30 min	2.8±0.06	3.4±0.05	<0.001*
45 min	2.9±0.07	3.7±0.06	<0.001*
1 h	2.6±0.03	4.0±0.02	<0.001*
2 h	$2.4{\pm}0.09$	3.6±0.05	<0.001*
4 h	2.2 ± 0.04	3.0±0.06	<0.001*
6h	2.1±0.01	2.8±0.02	<0.001*
12h	2.0±0.01	2.0±0.05	1.00
24h	1.9±0.01	2.0±0.04	0.95

*p-value is significant.

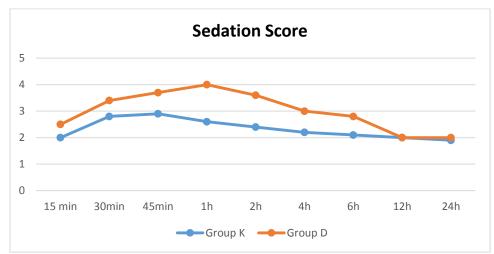


Figure (4): Comparison between the two groups regarding sedation score at different follow-up period.

As regards adverse events, bradycardia occurred significantly more often in group D (20%) versus group K (5%) (p = 0.043). Hypotension was reported in 20% of patients in group K and 30% in group D (p = 0.302), without notable differences. Other adverse effects, including vomiting, agitation, and sedation, were also recorded. The incidence of vomiting was 12.5% in group K and 5% in group D (p = 0.235). Agitation was seen in 10% of group K patients and 2.5% in Group D (p = 0.166) (Table 8).

Table (8): Incidence of adverse events in the two groups

	Group K	Group D	
	(N=40)	(N=40)	P-value
	No (%)	No (%)	
Bradycardia	2 (5%)	8 (20%)	0.043*
Hypotension	8 (20%)	12 (30%)	0.302
Vomiting	5 (12.5%)	2 (5%)	0.235
Agitation	4 (10%)	1 (2.5%)	0.166

*p-value is significant.

DISCUSSION

This study compared the effects of adding ketamine or dexmedetomidine to bupivacaine in ultrasound-guided femoral and sciatic nerve blocks for below-knee surgeries. Eighty ASA I–II patients were included, with no significant differences in age, gender, or BMI between groups. These findings are in the same line with **El Mourad** *et al.* ^[7] who also observed no notable differences in baseline characteristics, including gender and mean age, between their ketamine and dexmedetomidine groups.

Both heart rate and MABP remained stable across time points in our study, with no significant intergroup differences observed. These outcomes are similar to **Abdelhamid** *et al.* ^[8] who reported stable hemodynamic parameters with dexmedetomidine (p = 0.32).

The sensory block duration was significantly longer in the ketamine group compared to the dexmedetomidine group, indicating a potential advantage of ketamine in prolonging sensory analgesia. However, motor block duration did not differ significantly among the groups. Our findings are somewhat inconsistent with those of **Bailard** et al.^[9] who reported similar sensory and motor block durations between ketamine (7.5 \pm 1.3 hours) and dexmedetomidine (7.8 \pm 1.4 hours, p > 0.05). In contrast, **Prasad** *et al.* ^[10] found a slightly longer block duration with dexmedetomidine $(8.2 \pm 1.6 \text{ hours})$ compared to ketamine $(7.1 \pm 1.3 \text{ hours}, p = 0.034)$. This variation may be due to differences in dosages and administration techniques, or the type of regional block performed.

Regarding block onset times, our results showed no notable differences in the onset of sensory or motor blocks. **Chen et al.** ^[11] similarly found no notable difference in sensory block onset times (10.5 \pm 2.1 minutes for dexmedetomidine vs. 11.2 \pm 2.4 minutes for ketamine, p > 0.05). However, **Ibrahim** *et al.* ^[9] reported that dexmedetomidine resulted in faster sensory (8.3 ± 1.9 minutes) and motor block (12.5 ± 2.4 minutes) onset times compared to ketamine, suggesting potential variability in response based on administration protocols.

Postoperative pain intensity was evaluated using the VAS at multiple time points. In our study, there were no notable differences in VAS scores among both groups at any postoperative time point. Our findings indicated that both ketamine and dexmedetomidine provided comparable postoperative analgesia when used as adjuncts in regional anesthesia. These results are in line with Bailard et al. [9] who reported no notable differences in postoperative pain scores between dexmedetomidine and ketamine groups, which is in agreement with our study. Their study suggested that both drugs provided similar levels of postoperative analgesia when used in regional anesthesia, reinforcing the idea that both agents can serve as effective adjuncts for pain control. Prasad et al. [10] found that dexmedetomidine resulted in slightly lower pain scores compared to ketamine when used in peripheral nerve blocks without notable difference. This supports our finding that both agents provide comparable pain relief in the postoperative period. In contrast, Mohmed et al. reported that dexmedetomidine provided significantly better postoperative analgesia than ketamine, with lower VAS scores at 6 hours (1.9 ± 0.8) in the dexmedetomidine group vs. 2.7 ± 1.1 in the ketamine group, p = 0.01). Chen *et al.* ^[11] found that dexmedetomidine resulted in lower postoperative pain scores and reduced opioid consumption compared to ketamine in lower limb surgery patients. The reduced opioid requirement in the dexmedetomidine group suggests that it may enhance the quality of postoperative analgesia.

Sedation scores were significantly higher in the dexmedetomidine group at all-time points up to 6 hours postoperatively (p < 0.001). However, by 12 hours, the sedation scores had equalized between groups, suggesting that the sedative effect of dexmedetomidine diminishes over time. These findings are consistent with El Mourad et al.^[7] who similarly reported a significantly higher score of sedation in the dexmedetomidine group in the first few postoperative hours, with a gradual decline over time, reflecting dexmedetomidine' strong α_2 -adrenergic agonist effects that lead to dose-dependent sedation. A study by Mohamed et al. ^[13] demonstrated that patients receiving dexmedetomidine had significantly deeper and prolonged sedation compared to those receiving ketamine, with Ramsay sedation scores remaining elevated for up to 8 hours postoperatively. They also noted that dexmedetomidine's sedative effect allowed for better patient comfort and reduced the need for additional analgesics. Similarly, Kaye et al. [14] found that dexmedetomidine resulted in a higher level of intraoperative and postoperative sedation than

findings Their ketamine. showed that dexmedetomidine' patients had significantly higher sedation scores for up to 4-6 hours postoperatively, after which sedation levels between the two groups became comparable. However, Bailard et al. observed that while dexmedetomidine provided superior sedation, it also led to a higher incidence of delayed recovery in some patients, particularly those undergoing prolonged surgeries. This highlights the importance of considering patient-specific factors when choosing between ketamine and dexmedetomidine, particularly in cases where rapid postoperative recovery is a priority. Furthermore, Abdelhamid et al.^[8] noted that dexmedetomidine-induced sedation was associated with a decreased risk of postoperative agitation, which is a common concern with ketamine. In our study, although sedation scores were lower in the ketamine group, agitation was reported in 10% of group K patients compared to only 2.5% in group D (p = 0.166), supporting the observation that dexmedetomidine may provide a smoother recovery profile with reduced agitation-related adverse effects.

Bradycardia was significantly more common in group D (20%) than in group K (5%) (p = 0.043), which is aligning with El Mourad et al.^[7], who reported bradycardia in 35% of dexmedetomidine patients compared to 15% of ketamine patients (p = 0.01). Hypotension occurred more frequently in group D (30%) than in group K (20%), without a notable difference (p = 0.302). Other adverse events, including vomiting and agitation, showed no notable differences between groups. Vomiting was reported in 12.5% of group K patients and 5% of group D patients (p = 0.235), while agitation occurred in 10% of group K patients and 2.5% of group D patients (p = 0.166). These findings suggest that while both agents are generally well tolerated, dexmedetomidine is associated with a higher risk of bradycardia, warranting careful monitoring in at-risk patients.

Limitations: This study has some limitations including a relatively small sample size, which may limit the generalizability of the findings. We also did not assess opioid consumption or long-term analgesic effects, which could provide a more comprehensive evaluation of pain management. Future larger multicenter studies with extended follow-up are needed to confirm our findings.

CONCLUSION

Our study demonstrated that both agents effectively prolonged sensory and motor block durations, with ketamine providing a significantly longer sensory block. Postoperative pain scores were comparable, while dexmedetomidine induced deeper sedation but was associated with a higher incidence of bradycardia. Hemodynamic parameters remained stable in both groups, and adverse events were generally mild. These findings suggest that both agents are effective and safe, with the choice depending on clinical priorities such as the need for prolonged sensory blockade versus sedation.

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