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Comparative Study between the Effects of Intravenous or Intrathecal Dexmedetomidine on Characteristics of Bupivacaine Spinal Block in Lower Limb Orthopedic Surgeries

Mervat M Marzouk, Fahmy S Eskander, Eman M Abo-saif, Joseph S Halaka
Department of Anesthesia, Intensive Care and Pain Management, Faculty of Medicine, Ain-Shams University
Corresponding author: Joseph S Halaka; Mobile: 01224887768; **Email:** josephhalaka@yahoo.com

ABSTRACT

Background: The advantages of lower limb orthopedic procedures under spinal anesthetic are quick onset, preservation of spontaneous breathing, relaxation of the required muscles for the procedure, and affordability. It also has the benefit of not carrying the hazards associated with pulmonary aspiration and intubation.

Objective: This study aimed to compare the effects of intrathecal versus intravenous dexmedetomidine added to bupivacaine on characteristics of spinal blocks in patients undergoing lower limb orthopedic surgery.

Patients and methods: Sixty patients scheduled for lower limb orthopedic surgeries under spinal anesthesia were included in this prospective randomized comparative study. We evaluated the degree of sedation, the onset and duration of sensory and motor block, the quality of intra-operative anesthesia, postoperative analgesia, and adverse effects on patient hemodynamics.

Results: Administering dexmedetomidine intravenously or intrathecally shown to be a safe supplement to bupivacaine spinal anesthesia. Intrathecal dexmedetomidine was a better adjuvant. It offered less overall side effects, improved perioperative analgesia, increased augmentation to sensory and motor block, and more stable hemodynamics. During the intraoperative phase, a higher dose of sedation is provided via intravenous dexmedetomidine. In order to validate the outcomes of this work, more research with a greater number of patients is necessary.

Conclusion: Administration of dexmedetomidine intravenously or intrathecally shown to be a safe supplement to bupivacaine spinal anesthesia. When comparing intravenous dexmedetomidine to spinal bupivacaine, intrathecal dexmedetomidine was a better adjuvant.

Keywords: Dexmedetomidine, Bupivacaine spinal block, Lower limb, Orthopedic surgeries.

INTRODUCTION

Anesthesia can be administered locally, regionally (spinal or epidural), or generally for lower limb and abdominal procedures; nonetheless, neuraxial blocking is the recommended kind of anesthesia. Spinal block is still the favored technique due to its early onset, excellent blockage, low failure rates, reduced risk of infection from catheter in situ, and cost-effectiveness. Nevertheless, it has certain drawbacks, including no postoperative analgesia and a shorter block length. Spinal anesthetic also has the benefit of preserving spontaneous breathing and relaxing the muscles required for operation. Additionally, it has the benefit of not carrying the hazards of pulmonary aspiration or intubation [(1)].

Intracerebral adjuvants have become more widely used in recent years in an attempt to improve patient satisfaction, decrease resource consumption, lengthen the duration of the block, improve success rates, and speed recovery in comparison with general anesthetic. In order to enhance rehabilitation and expedite functional recovery, patients must receive proper pain management before they may return to their regular activities. Evidence has shown that the quality of spinal anesthesia can be improved by the addition of opioids (morphine, fentanyl, and sufentanil) and other medications as dextromethidine (DXM), clonidine, magnesium sulfate (Mg), neostigmine, ketamine, and midazolam. However, no medication can inhibit nociception without concurrently producing side effects [(2)].

In neuraxial anesthesia, bupivacaine, a medication with a long-lasting local anesthetic effect, offers a reliable and secure anesthetic [(3)].

Since they diminish the stress reactions to anesthesia and surgery as well as sympathetic tone, but also induce drowsiness and analgesia, alpha 2-adrenoceptor agonists have been utilized more frequently in critical care and anesthesia recently. They serve as adjuvants in regional anesthesia as well [(4)]. The most recent drug in this class to be licensed by the FDA for use in humans for sedation and analgesia was dexmedetomidine [(5)].

Dexmedetomidine was studied as an intrathecal adjuvant to bupivacaine spinal block in a variety of surgical procedures. These studies demonstrated that intrathecal dexmedetomidine added to bupivacaine increased postoperative analgesia, prolonged sensory block, and produced drowsiness without causing appreciable side effects during a range of surgical procedures [(6)]. Numerous studies also looked into the effects of intravenous dexmedetomidine as a spinal block adjuvant in a variety of surgical procedures. These studies showed that intravenous dexmedetomidine can prolong sensory and motor block durations as well as the time between the initial request for a spinal anesthetic and its start [(7)].

This study aimed to compare the effects of intrathecal versus intravenous dexmedetomidine added to

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bupivacaine on characteristics of spinal blocks in patients undergoing lower limb orthopedic surgery. These characteristics included the degree of sedation, the onset and duration of sensory and motor block, the quality of intra-operative anesthesia, postoperative analgesia, and adverse effects on patient hemodynamics.

PATIENTS AND METHODS

60 patients who were scheduled for lower limb orthopedic surgeries under spinal anesthesia were included in this prospective randomized comparative study after obtaining informed permission and clearance from our departmental ethical committee.

Inclusion criteria: Age 20-60 years. ASA physical status I-II. Lower limb orthopedic surgeries with duration about 90-120 minutes.

Exclusion criteria: Patient refusal. History of cardiac, hepatic or renal disease. Past history of allergy to any study-related medicines or amide-containing local anesthetics. The existence of any neurological conditions or reasons why regional anesthetic is not appropriate. Finally, failed or unsatisfactory spinal block.

Using a computer-generated random code, all patients were divided into three groups of 20 patients each:

Group I (I.T.): 20 patients received 15 mg in 3 ml hyperbaric bupivacaine intrathecally with 5 μg in 0.5 ml dexmedetomidine, followed by infusion of intravenous isotonic saline (10 ml) over 10 minutes and maintenance volume equivalent to the other patients groups throughout the period of surgery.

Group II (I.V.): 20 patients received 15 mg in 3 ml hyperbaric bupivacaine intrathecally with normal saline 0.5 ml, followed by intravenous bolus dose of dexmedetomidine 0.5 μg/kg diluted in 10 ml normal saline over 5 minutes, followed by intravenous infusion of maintenance volume of normal saline equivalent to other groups for the whole period of surgery.

Group III: 20 patients received 15 mg in 3 ml hyperbaric bupivacaine intrathecally with normal saline 0.5 ml, followed by intravenous isotonic normal saline 10 ml over 5 minutes and maintenance volume equivalent to other groups throughout the period of surgery.

Both patients and anesthesiologist were blinded to the drug and the evaluation was done by a separate investigator.

Methodology:

Preoperative day: Each patient had a standard preoperative assessment consisting of a clinical examination, laboratory investigations (coagulation profile, liver, kidney, and pancreas function tests and complete blood count), and full history. The patients were told about the trial protocol after giving their consent.

Operative day: Regular observation, including ECG, non-invasive blood pressure monitoring, and pulse oximetry were performed. Before the procedure began, baseline hemodynamic values were taken. Once IV access was achieved, infusion of 10 mL/kg of warmed crystalloid solution was started.

Anesthetic technique: The skin in the lumbar area was consistently treated with an antiseptic solution of 0.5% chlorhexidine alcohol, and the spinal block was performed while the patient was seated and under stringent aseptic guidelines.

- Complete aseptic procedures were followed, including skin sterilization, and 3-5 ml of 1% lidocaine were injected into the skin and subcutaneous regions to produce local anesthetic.
- A 25-gauge quincke needle was utilized to perform the spinal block at the L3-L4 or L4-L5 interspace level using a midline approach at first, and a paramedian technique when problems arose.
- To guarantee that the needle tip entered the subarachnoid space completely, a 360-degree rotation of the needle was performed following the removal of the trocar and the unobstructed flow of clear CSF.
- The injection took 10-15 seconds to administer.
- Patients were placed back into a supine posture after spinal anesthetic was administered, and during the surgery, they were given 4 L/min of oxygen using a facemask.

Assessment Parameters

1- Vital signs: Vital signs were monitored every three minutes during the first hour of surgery, every fifteen minutes until the procedure was completed, and every thirty minutes for the following three hours in the post-anesthesia care unit (PACU). Vital signs included heart rate (HR), systolic blood pressure (SBP), mean blood pressure (MAP), arterial oxygen saturation (SPO_2), and blood pressure. Hypotension was defined as a decrease in systolic blood pressure of greater than 30% of the baseline value or less than 90 mm Hg. Hypotension was treated with intravenous boluses of 10 mg ephedrine and crystalloid boluses of 250 ml fluid challenges spaced 10 minutes apart. Both were repeated in the event that the hypotension did not improve. Bradycardia was defined as a heart rate reduction of more than 30% from baseline or a heart rate less than 50 beats per minute, and it was treated with 0.5 mg of atropine. It was documented when and how much atropine, IV fluids, or ephedrine were needed.

2- Assessment of spinal block:

Assessment of sensory block: To evaluate the loss of pinprick feeling, a short, beveled, 25-gauge needle was inserted bilaterally along the mid-clavicular line once every minute. This allowed doctors to establish when the sensory block level reached T6, at which point surgery could begin. After then, the sensory level was

measured every three minutes to calculate the peak sensory level and the amount of time needed to reach it. The greatest block level for four tests in a row was considered the peak sensory level. Every 15 minutes for the first three hours, and then every 30 minutes after that, until the sensory level regressed to S1, sensory level testing was conducted. The spinal injection time served as time zero in all duration computations. In the event when the left and right sides' dermatomal levels disagree, the statistical analysis was performed using the greater level. The following details were observed: The period from zero injection time to the level of S1, the peak sensory level and its time, the maximum level of sensory block and its time, and the start of the sensory block (the time from zero injection time to the loss of pinprick at T6 level) are known as the regression time to S1.

Table (1): Assessment of motor block: Modified Bromage scale was used to assess motor block

Bromage 0	The hip, knee, and ankle can all be moved by the patient.
Bromage 1	The patient's ankle and knee can move, but not their hip.
Bromage 2	The patient can move their ankle, but not their hips or knees.
Bromage 3	The patient's ankle, knee, and hip are immobile.

The regression time to Bromage 0 was evaluated after surgery, and the time it took to reach the Bromage 3 motor block was measured before surgery. If the individual could not attain T6 or Bromage 3 following 20 minutes of spinal anesthesia, they were eliminated from the trial. This block was judged insufficient. After the patients' regression to the S1 dermatome and Bromage 0, they were discharged from the intensive care unit.

3- Assessment of pain: Throughout the course of surgery and the PACU, pain was measured hourly for 12 hours on the visual analogue pain scale (VAS), with 0 denoting no pain and 10 denoting the most severe pain. The patient was asked to point at a number to indicate the level of discomfort they were experiencing. The duration of complete analgesia was measured as the time from intrathecal injection to VAS score > 0. The duration of effective analgesia was measured using the time to VAS < 4. To achieve VAS < 4, the patient would then get an IV infusion of 1 gram of paracetamol and an intramuscular injection of 75 mg of diclofenac. The duration of the first analgesic request and the total number of analgesics taken throughout the course of a 12-hour period were recorded.

4- Assessment of sedation: Both in the PACU and after surgery, sedation was measured using the Ramsay sedation scale. During surgery, it was used every 15 minutes, and in the PACU, it was used every 30 minutes. A patient's rating on a scale of 1 to 6 is as follows:

Awake

1- Tense or fidgety or both
2- Calm, focused, and cooperative
3- Following instructions

A Sleep

4- Quick reaction to stimulus
5- Slow reaction to stimulus
6- No reaction to stimuli

5- Assessment of other side effects: Assessment of nausea, vomiting, headache, itching, shivering, and any other possible side effects as respiratory and cardiovascular events, were recorded. Nausea and vomiting were treated by rescue antiemetics IV metoclopramide 10 mg followed by ondansetron 4 mg IV if patient was not responsive to metoclopramide. Evaluating urinary retention involved timing the initial pee passage. Rubber catheters were inserted under stringent asepsis for patients who complained of urinary retention or were unable to pass pee in less than six hours. Meperidine hydrochloride 25 mg IV was used to treat shivering.

Ethical consideration: Ethical Committee of Faculty of Medicine, Ain Shams University provided its approval to the work. All participants gave informed consents after receiving a brief but comprehensive description of the study's goals, potential benefits, and assurances that there would be no costs to their health. For the duration of the research, the Helsinki Declaration was followed.

Statistical analysis

The data were analyzed using SPSS (Statistical Program for Social Science) version 20.0. The data were displayed statistically as mean ± standard deviation (SD). To express the qualitative data, percentage and frequency were utilized. The following tests were used: ANOVA in one direction is utilized when comparing more than two means, Post Hoc test for numerous comparisons between various variables and the Least Significant Difference (LSD) was employed. The Kruskall Wallis test was used for comparing groups in non-parametric data. A significance test (X^2) was employed to compare the proportions between two qualitative measures. The confidence interval was set at 95%, and the permitted margin of error at 5%. P-value ≤ 0.05 was considered significant. P-value ≤ 0.001 was considered as highly significant. P-value > 0.05 was considered insignificant.

RESULTS

Based on demographic data, the groupings in this table did not differ statistically from one another (Table 2).

Table (2): Comparison between groups according to demographic data

	Group I N=20	Group II N=20	Group III N=20	F/x2#	p-value
Age (year)					
Mean ± SD	48.65±12.19	48.42±11.48	49.39±11.70	0.682	0.381
Range	24-60	24-61	25-62		
Weight (kg)					
Mean ± SD	76.16±10.11	74.80±7.13	76.29±7.27	0.319	0.476
Range	61-97	66-92	68-94		
Height (cm)					
Mean ± SD	179.29±7.15	178.50±7.67	182.07±7.82	0.564	0.315
Range	165-190	166-192	170-196		
Sex					
Male	17 (85.0%)	17 (85.0%)	15 (75.0%)	0.490	0.274
Female	3 (15.0%)	3 (15.0%)	5 (25.0%)		
ASA score					
ASA I	7 (35.0%)	6 (30.0%)	4 (20.0%)	3.427	0.238
ASA II	13 (65.0%)	14 (70.0%)	16 (80.0%)		
Type of surgery					
Knee athroscope	11 (55.0%)	10 (50.0%)	10 (50.0%)	2.883	0.207
Inter locking nail tibia	4 (20.0%)	5 (25.0%)	5 (25.0%)		
Inter locking nail femur	4 (20.0%)	3 (15.0%)	4 (20.0%)		
Pott's fracture	1 (5.0%)	2 (10.0%)	1 (5.0%)		

F: ANOVA; X^2 Chi-square test

Based on baseline heart rate and MAP, the groups in this table did not differ statistically (Table 3).

Table (3): Comparison between groups according to baseline HR and MAP

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
Baseline HR (beat/min					
Mean ± SD	93.43±12.11	97.41±11.55	99.36±11.78	0.281	0.157
Range	70-114	77-112	78-114		
Baseline MAP(mmHg)					
Mean ± SD	99.35±8.00	98.94±6.61	100.92±6.74	0.244	0.137
Range	86-112	88-112	89-114		

HR: Heart rate MAP: Mean blood pressure

According to systolic blood pressure, table (4) displayed a statistically significant difference between the groups after 6 min to 90 min. Group [II (I.V.)] showed the most significant drop in SPB in the three groups. Also group [I (I.T.)] had lower SPB readings compared to group (III), which had the least significant SPB changes among the three groups.

Table (4): Comparison between groups according to systolic blood pressure (mmHg)

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
0 min.	136.80±20.95	140.66±17.35	139.59±21.37	1.4281	0.541
3 min.	130.96±20.31	128.15±17.95	133.63±20.73	2.548	0.181
6 min.	123.25±15.88	118.34±16.01	128.38±16.53	3.0574	0.017[a,b]
9 min.	116.14±6.50	113.76±14.96	120.98±6.78	3.0716	0.012[a,b]
12 min.	113.59±10.20	111.00±16.29	118.33±10.63	3.0231	0.028[a,b]
15 min.	109.44±18.27	106.06±20.45	114.00±19.03	3.0352	0.024[a,b]
20 min.	109.79±7.99	102.54±19.33	114.36±8.32	3.0999	0.003[a,b]
25 min.	111.77±13.26	108.01±13.98	116.42±13.82	3.0514	0.019[a,b]
30 min.	113.36±14.88	108.84±12.28	118.09±15.49	3.0756	0.011[a,b]
45 min.	117.17±10.80	114.22±15.07	122.05±11.25	3.0433	0.021[a,b]
60 min.	119.57±7.89	115.90±11.68	124.55±8.22	3.1039	0.002[a,b]
90 min.	119.84±7.79	118.13±10.89	123.54±8.03	3.0312	0.025[a,b]
2 hr	118.62±10.09	123.69±14.00	122.29±10.40	1.7596	0.434
3 hr	123.36±10.02	128.73±12.11	127.18±10.33	1.891	0.392
4 hr	124.59±8.48	129.76±13.78	128.45±8.75	1.7596	0.434
5 hr	126.45±10.35	133.06±14.41	130.36±10.68	2.2509	0.276
6 hr	128.01±10.34	133.34±14.01	131.97±10.67	1.7394	0.441

Min: minutes; hr: hours a: Significant difference between group (I) and group (II) b: Significant difference between group (II) and group (III)

Table (5) displayed statistically significant differences in mean arterial blood pressure between the groups after 9 min to 90 min. As in SPB chart, also MAP showed the most significant drop in group (II) then the two other groups. Group (I) showed more drop in MAP than group (III), which showed the least MAP changes among the three groups.

Table (5): Comparison between groups according to mean arterial blood pressure (mmHg)

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
0 min.	93.71±21.02	97.64±10.42	95.62±21.44	1.792	0.424
3 min.	92.34±18.32	95.11±9.76	94.23±18.70	1.450	0.534
6 min.	84.77±14.77	83.50±11.62	88.30±15.38	2.752	0.115
9 min.	83.09±6.22	80.12±10.43	86.56±6.48	3.092	0.006[a,b]
12 min.	81.48±3.88	78.28±8.32	84.87±4.04	3.096	0.005[a,b]
15 min.	80.15±6.15	75.42±5.42	83.50±6.40	3.092	0.006[a,b]
20 min.	78.28±10.41	74.91±8.27	81.54±10.85	3.082	0.009[a,b]
25 min.	80.60±9.34	76.59±11.13	83.96±9.74	3.086	0.008[a,b]
30 min.	79.83±10.70	77.27±9.94	83.15±11.14	3.023	0.028[a,b]
45 min.	80.51±10.15	78.78±4.71	83.86±10.57	3.059	0.016[a,b]
60 min.	81.55±8.86	78.61±7.32	84.94±9.23	3.096	0.005[a,b]
90 min.	82.10±10.59	78.78±7.43	84.64±10.92	3.061	0.016[a,b]
2 hr	83.38±9.31	85.01±6.90	85.95±9.61	1.752	0.437
3 hr	81.81±8.33	85.68±7.15	84.34±8.60	2.053	0.340
4 hr	83.35±8.37	86.02±8.89	85.92±8.64	1.159	0.627
5 hr	85.37±7.82	89.39±8.19	88.00±8.06	2.055	0.339
6 hr	86.54±8.73	90.57±6.29	89.21±9.00	2.075	0.333

min: minutes; hr: hours a: Significant difference between group (I) and group (II) b: Significant difference between group (II) and group (III)

When heart rate was compared across groups after 6 and 60 minutes, table (6) displayed statistically significant differences. Group (II) showed significant HR drop than the other two groups. In terms of HR changes, there was essentially no difference between groups I and III.

Table (6): Comparison between groups according to heart rate (Beat/min)

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
0 min.	92.49±17.21	91.23±20.58	90.64±16.87	1.487	0.522
3 min.	88.07±13.93	82.32±16.87	86.31±13.65	2.797	0.101
6 min.	85.85±15.31	77.94±14.52	82.42±14.70	3.019	0.029[a,b]
9 min.	88.58±19.48	77.60±17.18	85.03±18.71	3.061	0.016[a,b]
12 min.	86.18±13.91	77.44±16.62	82.74±13.35	3.033	0.025[a,b]
15 min.	84.97±12.75	77.54±13.64	81.57±12.24	3.027	0.027[a,b]
20 min.	85.07±14.20	76.51±15.05	81.67±13.64	3.041	0.022[a,b]
25 min.	88.68±21.06	77.27±12.97	85.13±20.22	3.072	0.012[a,b]
30 min.	86.53±22.78	76.08±6.24	83.06±21.87	3.061	0.016[a,b]
45 min.	86.32±16.11	76.43±14.44	82.87±15.46	3.070	0.013[a,b]
60 min.	85.75±13.54	76.43±12.69	82.32±13.00	3.088	0.007[a,b]
90 min.	84.77±16.42	79.62±13.83	82.22±15.93	2.692	0.135
2 hr	84.71±17.10	83.15±9.29	82.16±16.58	1.766	0.432
3 hr	83.05±16.52	87.03±9.81	80.56±16.03	2.556	0.178
4 hr	84.84±16.51	85.52±7.89	82.29±16.02	1.404	0.549
5 hr	85.72±17.13	84.00±11.49	83.14±16.61	1.796	0.423
6 hr	87.57±17.21	86.36±9.43	84.94±16.70	1.610	0.482

Min: minutes; hr: hours a: Significant difference between group (I) and group (II) b: Significant difference between group (II) and group (III)

Characteristics of spinal block:

Time to reach T6 dermatomal level (min):

Group (I) average time was 5 minutes (the fastest group to reach T6), while in groups (II) and (III) it took 6 and 6.5 minutes respectively. As can be seen in table (7), group I' time to achieve T6 dermatomal level was statistically substantially less than that of groups II and III (P value < 0.05).

Time to reach peak sensory level (min):

Once more, group (I) arrived at their destination the quickest, taking about 8.7 minutes, and group (II) took an average of 11.7 minutes. Group (III) arrived last, taking an average of 12.4 minutes to do so. The data presented in Table (7) indicated that group I reached peak sensory level much earlier than groups II and III (P value < 0.001).

Peak sensory level dermatome:

In this regard, peak sensory level dermatome was statistically not different amongst the three groups (Table 7).

Time to reach Bromage 3 (min):

Group (I) reached the fastest among the three groups after average of 8.1 minutes, followed by group (II) after 8.5 minutes, while group III was the last to reach Bromage 3 after average of 10.3 minutes. Table (7) showed statistical significance between groups in time to reach Bromage 3 (P value <0.05). The spinal block difference between the groups in this table was statistically significant, while the peak sensory level (thoracic dermatome) difference was not.

Table (7): Comparison between groups according to spinal block.

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
Time to T6 (min)					
Mean ± SD	5.10±1.37	6.05±1.42	6.32±1.35	3.682	0.028[a,b]
Range	3-8	4-9	4-9		
Time to peak sensory level (min)					
Mean ± SD	8.77±2.20	11.73±2.42	12.38±2.05	5.291	<0.001[a,b]
Range	5-12	9-15	9-16		
Peak sensory level (Thoracic dermatome)					
Mean ± SD	T6.10±1.22	T6.19±1.14	T6.26±1.13	1968	0.483
Range	T3-T8	T4-T8	T4-T8		
Time to Bromage 3 (min)					
Mean ± SD	8.16±2.35	8.47±2.11	10.29±2.18	3.231	0.027[a,b]
Range	6-12	6-12	6-12		

T6: 6th Thoracic dermatome Min: minutes; hr: hours a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III) c: Significant difference between group (II) and group (III)

There was a highly statistically significant difference between the groups in this table based on regression time to S1 level and regression to Bromage 0. After an average of 195 minutes, group (III) demonstrated the shortest time to S1 regression, with group (II) following suit after an average of 237 minutes. With the longest period, averaging 342 minutes, group (I) was the last to regress to the S1 level. Regarding regression to Bromage 0, group (I) showed the quickest regression at about 165 minutes, group (II) at 205 minutes on average, and group (III) at the end, which reached the target at 277 minutes on average (Table 8).

Table (8): Comparison between groups regarding regression time to S1 level and Bromage 0 (min)

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
Regression time to S1 level (min)					
Mean ± SD	342.21±22.27	237.66±26.37	195.25±24.41	6.991	**<0.001[a,b,c]**
Range	306-377	204-281	208-286		
Regression to Bromage 0 (min)					
Mean ± SD	277.10±25.88	205.70±20.85	164.65±20.58	4.331	**<0.001[a,b,c]**
Range	204-316	179-240	182-244		

a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III) c: Significant difference between group (II) and group (III)

The difference in the min of the time to the first analgesic request between the groups was highly statistically significant. After an average of 183 minutes, patients in group (III) were the first to request analgesia, but patients in group (II) did so after an average of 280 minutes. Group (I) patients were the last among other groups in asking for analgesia, after an average of 390 minutes (Table 9).

Table (9): Comparison between groups according to time to first analgesic request (min)

Time to first analgesic request (min)	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
Mean ± SD	392.70±90.24	279.48±27.95	183.84±22.98	3.997	**<0.001[a,b,c]**
Range	281-485	230-357	234-364		

a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III) c: Significant difference between group (II) and group (III).

Table (10) demonstrated that group (I) required more time than groups (II) and (III) to reach VAS ≥ 4, the analgesic trigger point.

Table (10): Comparison between groups according to visual analogue pain scale (VAS)

	Group I	Group II (N=20)	Group III (N=20)
After 1hr	0 (0)	0 (0)	0 (0)
After 2hr	1 (0)	1 (0)	1 (0)
After 3hr	2 (0)	2 (0)	2 (0)
After 4hr	3 (0)	4 (1)	4 (0)
After 5hr	3 (1)	4 (1)	3 (1)
After 6hr	4 (1)	4 (1)	3 (1)
After 7hr	4 (1)	3 (1)	3 (1)
After 8hr	3 (1)	3 (1)	3 (1)
After 9hr	3 (1)	3 (1)	3 (0)
After 10hr	3 (1)	4 (1)	3 (1)
After 11hr	3 (1)	4 (1)	3 (1)
After 12hr	4 (1)	4 (1)	3 (1)

Based on the mean VAS score, table (11) displayed a very statistically significant difference between the groups.

Table (1): Comparison between groups according to Mean VAS score

	Group I (N=20)	Group II (N=20)	Group III (N=20)	Kruskal Wallis	p-value
Median VAS score	3 (1)	3 (2)	4 (1)	5.911	**<0.001**[a,b,c]

a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III) c: Significant difference between group (II) and group (III)

The sedation score after 1hr and 2hr was displayed in table (12), which indicated statistically significant differences between the three groups.

Table (2): Comparison between groups according to sedation score.

Sedation score	Group I	Group II	Group III	ANOVA	p-value
After 1hr	2.3±0.5	3.0±0.6	2.1±0.4	2.954	0.024[a,b]
After 2hr	2.5±0.5	3.4±0.7	2.3±0.5	3.229	0.011[a,b]
After 3hr	2.3±0.5	2.4±0.5	2.2±0.4	0.965	0.347
After 4hr	2.1±0.4	2.2±0.4	2.1±0.4	1.167	0.755
After 5hr	2.0±0.4	2.0±0.4	2.0±0.4	0.361	0.296
After 6hr	2.0±0.4	2.0±0.4	2.0±0.4	0.213	0.119

hr: hours a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III)

Based on mean sedation score, table (13) displayed a very statistically significant difference between the groups. Group (II) showed the highest sedation score of 2.54, while group (I) score was 2.25. Group (I) showed the lowest score of 2.15.

Table (3): Comparison between groups according to mean sedation score

	Group I N=20	Group II N=20	Group III N=20	ANOVA	p-value
Mean sedation score	2.25±0.12	2.54±0.11	2.15±0.99	6.854	**<0.001**[a,b,c]

a: Significant difference between group (I) and group (II) b: Significant difference between group (I) and group (III) c: Significant difference between group (II) and group (III)

According to negative impacts, there was no statistically significant difference between the groups (Table 14).

Table (14): Comparison between groups according to adverse effects

	Group I (N=20)		Group II (N=20)		Group III (N=20)		Chi-square	p-value
	No.	%	No.	%	No.	%		
Hypotension	4	20.0%	5	25.0%	3	15.0%	1.626	0.542
Bradycardia	3	15.0%	5	25.0%	2	10.0%	1.557	0.519
Nausea	1	5.0%	1	5.0%	1	5.0%	0.000	1.000
Vomiting	0	0.0%	1	5.0%	0	0.0%	1.090	0.363
Urinary retention	0	0.0%	0	0.0%	0	0.0%	0.000	1.000
Shivering	0	0.0%	0	0.0%	2	10.0%	1.602	0.467
Pruritus	0	0.0%	0	0.0%	0	0.0%	0.000	1.000

DISCUSSION

Both regional and general anesthesia are options for lower limb procedures. The preservation of spontaneous breathing, low cost, lower risk of pulmonary aspiration, ease of surgery due to relaxed abdominal wall and intestines, elimination of the need for intubation, minimal disruption of blood chemistry, reduced surgical hemorrhage, and early restoration of intestinal motility are some advantages of spinal anesthesia. The disadvantages are that the block lasts less time and there is no postoperative analgesia [(8)].

Intrathecal adjuvants have become more and more popular in recent years because of their ability to lengthen the duration of a block, improve patient satisfaction, success rates, and lower resource utilization as compared to general anesthetic, as well as speed up recovery. Spinal anesthesia has been extended with a variety of additions, including vasoconstrictive drugs like clonidine, epinephrine, and phenylephrine. Additionally, substances including neostigmine and opioids had been utilized [(9)].

An effective α2-agonist that has been utilized intrathecally is clonidine. It extends both the period of spinal blockage and the duration of postoperative analgesia. Clonidine has also been demonstrated to prolong bupivacaine spinal anesthesia when administered intravenously with spinal block, all without adverse effects [(10)]. IV sedation is the main application for dexmedetomidine, a new selective α2 adrenoceptor agonist. Here is mounting evidence that the duration of anesthesia following single-injection neuraxial and peripheral nerve blocking is prolonged by the off-label use of dexmedetomidine as a local anesthetic adjuvant. Several central processes that suggest several routes of administration that may have similar effects have been postulated to explain this phenomena [(11)]. Numerous studies that looked at the effects of various intrathecal dexmedetomidine and bupivacaine dosages in spinal anesthesia demonstrated the intrathecal dexmedetomidine synergistic effects. The effects of 3μg dexmedetomidine + 12 mg bupivacaine in TURP procedures were investigated by **Patil *et al.* [(5)].** The effects of intrathecally administered 10 mg isobaric bupivacaine combined with 5 μg dexmedetomidine during gynecological procedures were assessed by **Aksu *et al.* [(12)].** In lower abdominal procedures, **Gupta *et al.* [(13)]** utilized a combination of 5μg dexmedetomidine and 12.5 mg hyperbaric bupivacaine. In lower limb procedures, **Kalbande *et al.* [(14)]** investigated the effects of intrathecal 12.5 mg bupivacaine + 5 μg dexmedetomidine. In lower abdominal procedures, **Jadon *et al.* [(1)]** investigated the combination of 10 μg dexmedetomidine and intrathecal 15 mg hyperbaric bupivacaine. According to all of these investigations, intrathecal dexmedetomidine was linked to a well-tolerated hemodynamic profile, a prolonged motor and sensory block, and a decreased need for rescue analgesics.

In patients undergoing major abdominal cancer surgery, intrathecal 5 μg dexmedetomidine increased both the quality and duration of post-operative analgesia, as well as having an analgesic sparing effect, as demonstrated by **Mohamed *et al.* [(15)].** Remarkably, they discovered that intrathecally administering 25 μg fentanyl in addition to dexmedetomidine had no significant clinical impact when compared to dexmedetomidine on its own. According to **Gupta *et al.* [(13)]**, intrathecal dexmedetomidine synergistic effects were also observed with ropivacaine. In lower limb procedures, they investigated the effects of 5 μg dexmedetomidine given to 3 ml 0.75% isobaric ropivacaine. They found that the duration of the motor and sensory block was extended when 5 μg of dexmedetomidine was added to intrathecaine. They came to the conclusion that dexmedetomidine appears to be a desirable substitute for spinal ropivacaine as an adjuvant during surgical procedures.

In a recent meta-analysis, **Abdallah and Brull [(16)]** investigated how perineural dexmedetomidine facilitates neuraxial block. Five trials that looked at dexmedetomidine as a component of spinal anesthesia assessed its effects when used as a local anesthetic adjuvant vs when used alone in neuraxial block. Intrathecal dexmedetomidine increased the average duration of sensory block by 150 minutes. The length of the motor block and the period until the first analgesic request increased. They found that when given intrathecally as part of spinal anesthesia, dexmedetomidine is a possible adjuvant that may show a facilitatory impact.

Interestingly, numerous investigations demonstrated that spinal anesthesia was improved by a single IV dosage of dexmedetomidine. In **Kaya *et al.* [(17)]** study, midazolam and a placebo were compared to a single preoperative dose of dexmedetomidine 0.5 μg/kg before bupivacaine 0.5% 15 mg was used for spinal anesthesia. **Reddy *et al.* [(18)]** investigated the effects of a single IV dosage of clonidine, dexmedetomidine, or placebo in patients undergoing lower limb surgery. **Hong *et al.* [(19)]** investigated the effects of a single IV dose of dexmedetomidine (1.0 μg/kg) on elderly patients undergoing TURP operations, and then low-dose bupivacaine spinal anesthesia. The outcomes of these investigations demonstrated that when combined with bupivacaine spinal anesthesia, intravenous dexmedetomidine was an improved adjuvant when compared to midazolam, clonidine, and placebo, respectively. It also produced more sedation and analgesia. The previously stated trials indicate that dexmedetomidine has been safely provided to patients having surgery under regional anesthesia. It has been shown that administering dexmedetomidine intravenously and intrathecally prolongs the duration of spinal anesthesia and enhances postoperative analgesia.

Our research aimed to ascertain which technique intravenous or intrathecal offers superior synergistic benefits in relation to bupivacaine spinal

anesthesia. We compared the effects of an intravenous 0.5 μg/kg of dexmedetomidine with bupivacaine 15 mg spinal block to a single intrathecal dosage of 5 μg dexmedetomidine in patients undergoing lower limb orthopedic procedures. When using intrathecal dexmedetomidine, one should take the safety profile into account. Numerous investigations carried out on rats, rabbits, and sheep revealed that intrathecal dexmedetomidine, administered at doses ranging from 2.5 to 100 μg, demonstrated minimal neurological impairment in a rat model of perinatal excitotoxic brain injury. Furthermore, it exhibited strong neuroprotective effects through the α2A-adrenoreceptors [(19)]. Humans exposed to 3–15 μg of dexmedetomidine showed a prolonged period of motor and sensory blockage without showing any obvious negative effects on the nervous system [(12)].

We chose to use a dose of 5 μg intrathecal dexmedetomidine patients in group (I) based on previous clonidine research. Dexmedetomidine has been shown to have a ten-fold greater affinity for α2 receptors than clonidine. Our choice of IV dosage in group (II) was based on earlier research. A moderate amount of analgesia was found in a study evaluating the analgesic effects of several intravenous dexmedetomidine doses (0.25, 0.5, and 1 μg/kg) on ischemic pain in healthy volunteers. The highest effect was seen at 0.5 μg/kg. **Bharti *et al.*** [(20)] suggest that the optimal range for dexmedetomidine dosage for intravenous premedication in minor surgery is between 0.33 and 0.67 μg/kg. **Jaakola *et al.*** [(21)] demonstrated significant analgesia with a ceiling effect at a dosage of 0.5 μg/kg. As a result, we carefully calculated a dosage of 0.5 μg/kg over the course of ten minutes in our experiment. Group III received intrathecal administration of 0.5 ml normal saline in addition to bupivacaine as a control group to enable a more precise comparison of the effects of dexmedetomidine on spinal block features.

Our findings showed that intrathecal dexmedetomidine outperformed bupivacaine as an adjuvant in spinal block. In contrast to groups II and III, group I showed reduced mean 12-hour VAS scale, a shorter time to first analgesic request, a higher peak sensory level, a longer time to first sensory onset to T6 dermatome, a longer sensory regression time to S1 dermatome, less total analgesic consumption, and fewer overall side effects. Group III needed more time to attain the Bromage 3 level of motor block than did groups I and II, which had comparable mean onset periods. The intrathecal group had a longer regression time to Bromage 0. Nevertheless, intravenous dexmedetomidine performed better in terms of delivering a higher amount of intraoperative sedation. The limited sedation in group (III) was intended to address the related hypotension.

In our investigation, intrathecal dexmedetomidine decreased the need for analgesics more than IV dexmedetomidine did, while also improving the anesthetic and analgesic qualities of bupivacaine. Neuraxial administration of dexmedetomidine appears to be the most effective way to administer it as an adjuvant because of its high lipophilicity, which enables quick absorption into the cerebrospinal fluid and binding to the α2-adrenoreceptor in the spinal cord. This is because α2 agonists primarily act at the spinal level to produce analgesia [(22)].

The topic of the analgesic effect of α2 agonists is complex. They can produce analgesia in three different places: The brain and brainstem, the spinal cord, and the peripheral tissues. α2 agonists inhibit substance P release at the dorsal root neuron level in the nociceptive pathway. There is substantial evidence to suggest that the stimulation of α2-receptors in the spinal cord causes analgesia [(23)]. Patients under the peculiar sedation caused by dexmedetomidine become calm, cooperative, and alert when aroused, but return to sleep when not stimulated. With dexmedetomidine, confusion has not been reported as a common side effect, despite other traditional sedatives being known to predominantly rely on activation of the gamma-aminobutyric acid pathway [(24)].

In contrast to intrathecal dexmedetomidine, intravenous (IV) dexmedetomidine was found to considerably lower heart rate, systolic and mean arterial pressures in our investigation. Intrathecal dexmedetomidine did not increase the blood pressure-lowering effects of bupivacaine. Hemodynamic effects were least pronounced in group (III). The mechanism via which local anesthetics impact blood pressure could provide an explanation for this. Local anesthetics work by lowering sympathetic output, which lowers blood pressure. Intrathecal dexmedetomidine did not lower blood pressure any more, most likely due to the almost maximal sympathetic blocking caused by bupivacaine.

Dextromethorphan stimulates the α2 inhibitory neurons in the brainstem's medullary vasomotor center, resulting in a reduction in norepinephrine release and sympathetic nerve outflow from the central nervous system to the peripheral tissues. Bradycardia is caused by central stimulation of parasympathetic outflow, which results in an increase in vagal tone and a decrease in sympathetic drive [(23)].

The two most often reported side effects of intrathecal α2 agonist use were bradycardia and hypotension. Based on our findings, bradycardia and hypotension were the most frequent adverse events. Both groups (I) and (II) experienced these side effects, however the intravenous group experienced them more frequently [(6)]. Dexmedetomidine prevented shivering in groups I and II of our investigation, as evidenced by the absence of shivering in both groups. **Maroof *et al.*** [(25)] discovered that the α2 adrenergic drugs have anti-shivering properties.

CONCLUSION

Administering dexmedetomidine intravenously or intrathecally showed to be a safe supplement to bupivacaine spinal anesthesia. When comparing intravenous dexmedetomidine to spinal bupivacaine, intrathecal dexmedetomidine was a better adjuvant. It offered less overall side effects, improved perioperative analgesia, increased augmentation to sensory and motor block, and more stable hemodynamics. During the intraoperative phase, a higher dose of sedation was provided via intravenous dexmedetomidine.

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