

COMPARISON OF SUBARACHNOID BLOCK IN MIXED VERSUS SEQUENTIAL ADMINISTRATION OF LEVOBUPIVACAINE AND DEXMEDETOMIDINE IN LOWER LIMB SURGERIES: A RANDOMIZED CLINICAL STUDY

Pooja N. Parmar¹, Kashmir Pander², Jyotsana Maliwad³

Received : 06/09/2026
Received in revised form : 05/10/2026
Accepted : 17/10/2026

Keywords:

Dexmedetomidine; levobupivacaine; spinal anaesthesia; subarachnoid block; sequential administration; lower limb surgery.

Corresponding Author:

Dr. Pooja N. Parmar,
Email: poojaparmar1112@gmail.com

DOI: 10.47009/jamp.2026.8.5.137

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (5); 862-868



¹Senior Resident, Department of Anaesthesiology, Government Medical College, Baroda, Gujarat, India.

^{2,3}Assistant Professor, Department of Anaesthesiology, Government Medical College, Baroda, Gujarat, India.

ABSTRACT

Background: Levobupivacaine is increasingly used for spinal anaesthesia because it provides reliable neural blockade with a comparatively favourable cardiovascular and neurological safety profile. Dexmedetomidine, a selective alpha-2 adrenergic agonist, is used as an intrathecal adjuvant to prolong sensory and motor blockade and improve postoperative analgesia. The technique of intrathecal administration may influence drug distribution and block characteristics. This study compared premixed and sequential intrathecal administration of hyperbaric levobupivacaine and dexmedetomidine in patients undergoing lower limb surgery. **Materials and Methods:** This prospective, randomized, double-blind clinical study included 58 patients aged 18–60 years with American Society of Anesthesiologists physical status I–III undergoing elective lower limb surgeries under spinal anaesthesia. Patients were randomly allocated into two groups of 29 each. Group M received 12.5 mg hyperbaric levobupivacaine combined with dexmedetomidine 10 µg in a single syringe. Group S received 12.5 mg hyperbaric levobupivacaine followed by dexmedetomidine 10 µg through a separate syringe. Sensory and motor block characteristics, haemodynamic parameters, sedation, duration of postoperative analgesia, rescue analgesic requirement, and adverse effects were evaluated. **Results:** Demographic characteristics, ASA physical status, type and duration of surgery, and baseline haemodynamic variables were comparable between groups. Group S demonstrated significantly faster onset of sensory block at L1, faster onset of motor block, earlier attainment of maximum sensory and motor block, and longer sensory and motor block duration than Group M. The duration of effective postoperative analgesia was significantly prolonged in Group S, while rescue analgesic consumption during the first 24 postoperative hours was lower. Haemodynamic parameters, oxygen saturation, and adverse-effect profiles were comparable between groups. **Conclusion:** Sequential intrathecal administration of dexmedetomidine after hyperbaric levobupivacaine provides faster onset and longer duration of sensory and motor blockade than premixed administration. It also prolongs postoperative analgesia and reduces rescue analgesic requirement without clinically significant haemodynamic instability.

INTRODUCTION

Spinal anaesthesia is commonly used for lower limb surgery because it is technically simple, provides rapid and reliable anaesthesia, avoids airway manipulation, and offers effective early postoperative analgesia. The technique is associated with reduced perioperative stress response, lower opioid

requirement, and improved postoperative recovery in appropriately selected patients. The quality of a subarachnoid block depends on several variables, including the characteristics and dose of the local anaesthetic, baricity of the injected solution, volume of cerebrospinal fluid, injection technique, patient position, and use of intrathecal adjuvants.^[1,2]

Bupivacaine has traditionally been the most widely used local anaesthetic for spinal anaesthesia. However, levobupivacaine, the pure S(-)-enantiomer of bupivacaine, has become an important alternative because of its lower potential for cardiotoxicity and neurotoxicity. Levobupivacaine produces adequate sensory and motor blockade for lower limb procedures, while maintaining a favourable clinical safety profile.^[2] Hyperbaric formulations permit more predictable intrathecal spread and facilitate the establishment of a reliable surgical block.

The addition of intrathecal adjuvants to local anaesthetics is a well-established strategy for improving the quality and duration of spinal anaesthesia. Dexmedetomidine is a highly selective alpha-2 adrenergic receptor agonist with sedative, analgesic, sympatholytic, and anaesthetic-sparing effects. Its intrathecal use has been associated with earlier onset and prolonged duration of sensory and motor blockade, improved postoperative analgesia, and lower rescue analgesic requirement.^[3-6] Dexmedetomidine exerts its spinal analgesic effect through activation of alpha-2 receptors in the dorsal horn of the spinal cord, where it suppresses nociceptive transmission and enhances the action of local anaesthetics.

Although dexmedetomidine is frequently added to intrathecal local anaesthetics, the method of drug administration may influence the resulting block. Intrathecal drugs can be administered as a premixed solution in a single syringe or sequentially through separate syringes. When solutions with different densities are mixed, the baricity of the final solution may change. This alteration may influence cephalad spread, onset, and duration of neural blockade.^[7] Hyperbaric levobupivacaine and dexmedetomidine differ in their physical properties; therefore, sequential administration may preserve the initial distribution of the hyperbaric local anaesthetic before the adjuvant is introduced.

Previous studies evaluating mixed and sequential administration of intrathecal local anaesthetics and adjuvants have reported variable findings. Some investigators have observed faster block onset and longer duration of anaesthesia with sequential administration, whereas others have found comparable block characteristics.^[8-10] However, evidence specifically comparing mixed and sequential administration of levobupivacaine with dexmedetomidine remains limited.

The present study was designed to compare the sensory and motor block characteristics of mixed and sequential intrathecal administration of hyperbaric levobupivacaine with dexmedetomidine in patients undergoing lower limb surgery. The secondary objectives were to evaluate intraoperative haemodynamic stability, sedation, postoperative analgesic duration, rescue analgesic requirement, and incidence of adverse effects.

MATERIALS AND METHODS

Study design and setting: This prospective, randomized, double-blind clinical study was conducted in the Department of Anaesthesiology at a tertiary-care teaching hospital between September 2024 and May 2025. The study was initiated after approval from the Institutional Ethics Committee. Written informed consent was obtained from all patients before enrolment.

Study population

A total of 58 patients of either sex, aged between 18 and 60 years, with American Society of Anesthesiologists physical status I, II, or III, scheduled for elective lower limb surgery under spinal anaesthesia were included. Surgical procedures with an anticipated duration of approximately 2–2.5 hours were considered eligible. Patients were excluded if they refused spinal anaesthesia or study participation; had contraindications to spinal anaesthesia, including coagulopathy, local infection at the puncture site, severe hypovolaemia, or raised intracranial pressure; had clinically significant cardiovascular, respiratory, hepatic, renal, or neurological disease; had known hypersensitivity to study drugs; had spinal deformity; were pregnant or lactating; or had a body mass index greater than 30 kg/m².

Sample size and randomization

The sample size was estimated on the basis of the difference in sensory regression time reported in previous studies comparing intrathecal administration techniques. With a confidence level of 99%, power of 80%, and allowance for possible exclusions, 58 patients were enrolled.

Patients were randomly allocated into two equal groups using a sealed-envelope randomization method. Allocation concealment was maintained by using sequentially numbered, opaque, sealed envelopes. A consultant anaesthesiologist not involved in patient monitoring or data collection prepared the study drugs. The anaesthesiologist administering spinal anaesthesia, the observer recording study variables, the surgeon, and the patient were blinded to group allocation.

Preoperative assessment and preparation

All patients underwent routine preanaesthetic evaluation, including medical history, physical examination, airway assessment, and relevant laboratory investigations. Patients were instructed to remain nil per oral according to institutional fasting guidelines. Oral ranitidine 150 mg was administered on the night before surgery.

On arrival in the operating room, an 18-gauge intravenous cannula was inserted and standard monitoring was applied, including electrocardiography, non-invasive blood pressure monitoring, and pulse oximetry. Baseline pulse rate, systolic blood pressure, diastolic blood pressure, and peripheral oxygen saturation were recorded. Patients were preloaded with Ringer's lactate at 10 mL/kg.

Glycopyrrolate 5 µg/kg and ondansetron 0.15 mg/kg were administered intravenously approximately 15 minutes before spinal anaesthesia. No sedative premedication was given.

Study groups

Patients were assigned to one of the following groups:

Group M (mixed group): Patients received 2.5 mL of 0.5% hyperbaric levobupivacaine containing 12.5 mg levobupivacaine combined with dexmedetomidine 10 µg in a single syringe. Sterile water was used to make the final volume 3 mL.

Group S (sequential group): Patients received 2.5 mL of 0.5% hyperbaric levobupivacaine containing 12.5 mg levobupivacaine, followed immediately by dexmedetomidine 10 µg administered from a separate syringe. The total injected volume was 3 mL.

Anaesthetic technique

Spinal anaesthesia was performed with the patient in the sitting position under strict aseptic precautions. The L3–L4 intervertebral space was identified, and a 23-gauge Quincke spinal needle was inserted through a midline approach. After confirmation of free and clear cerebrospinal fluid flow, the assigned intrathecal drug was injected over an appropriate period.

Patients were placed supine immediately after injection. Oxygen was administered only when clinically indicated. Surgery was initiated after adequate sensory and motor blockade had been achieved. Any patient requiring conversion to general anaesthesia because of failed or inadequate spinal blockade was excluded from the final analysis.

Assessment of sensory block

Sensory block was assessed bilaterally along the midclavicular line using loss of pinprick sensation. Assessment was performed every minute until achievement of the highest sensory level, then at predetermined intervals until regression of block. The following sensory-block variables were recorded:

- Time from intrathecal injection to sensory block at L1
- Maximum sensory level achieved
- Time to attain maximum sensory level
- Time to two-segment sensory regression from the highest level
- Total duration of sensory block, defined as time from intrathecal injection to regression of sensory block to S1

Assessment of motor block

Motor block was assessed using the modified Bromage scale:

- Grade 0: Full flexion of knees and feet
- Grade 1: Inability to raise extended leg; able to flex knees and feet
- Grade 2: Inability to flex knees; able to flex feet

- Grade 3: Inability to flex ankles, knees, or hips
- Onset of motor block was defined as time from intrathecal injection to Bromage grade 1. Time to maximum motor block was defined as time required to achieve Bromage grade 3. Duration of motor block was recorded from intrathecal injection until complete recovery to Bromage grade 0.

Haemodynamic monitoring and postoperative evaluation

Pulse rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation were recorded at baseline; 1, 3, 5, 10, 15, 20, 30, 45, and 60 minutes after spinal injection; and thereafter at 90, 120, and 150 minutes intraoperatively. Postoperative monitoring was continued at regular intervals for 24 hours.

Hypotension was defined as a systolic blood pressure below 90 mmHg or a decrease of more than 20% from baseline. It was managed with intravenous fluids and vasopressors as required. Bradycardia was defined as a heart rate below 60 beats/minute or a decrease of more than 20% from baseline and was treated with intravenous atropine when necessary.

Sedation was assessed using the Ramsay Sedation Scale. Postoperative pain was assessed using the visual analogue scale, ranging from 0 to 10. Effective analgesia duration was defined as the time between intrathecal injection and the first visual analogue scale score of 4 or greater. Intravenous paracetamol 1 g was administered as rescue analgesia.

Nausea, vomiting, shivering, urinary retention, respiratory depression, pruritus, bradycardia, hypotension, and hypersensitivity reactions were recorded.

Statistical analysis

Data were entered into a spreadsheet and analysed using appropriate statistical methods. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequency and percentage. Intergroup comparisons for continuous variables were performed using the unpaired Student's t-test. Categorical variables were analysed using the chi-square test or Fisher's exact test, as appropriate. Repeated haemodynamic measurements were assessed using analysis of variance. A p value of less than 0.05 was considered statistically significant.

RESULTS

All 58 enrolled patients completed the study and were included in the final analysis. There were 29 patients in Group M and 29 patients in Group S.

Demographic and surgical characteristics

The two groups were comparable with respect to age, sex distribution, ASA physical status, and duration of surgery. No statistically significant difference was observed in baseline demographic characteristics.

Table 1: Demographic and surgical characteristics

Characteristic	Group M (n=29)	Group S (n=29)	p value
Age, years	39 ± 13	40 ± 11	>0.05
Male:Female ratio	23:6	24:5	>0.05
ASA I/II/III, n	6/15/8	7/17/5	>0.05
Duration of surgery, min	109 ± 28	103 ± 31	>0.05

The spectrum of surgical procedures was similar in both groups. Procedures included arthroscopic anterior cruciate ligament repair, fracture fixation, below-knee amputation, debridement, incision and drainage, patellar tension-band wiring, and tibial procedures.

Baseline haemodynamic parameters

Baseline pulse rate, systolic blood pressure, diastolic blood pressure, and peripheral oxygen saturation were comparable between the two groups.

Table 2: Baseline haemodynamic variables

Variable	Group M	Group S	p value
Pulse rate, beats/min	85.58 ± 7.49	82.62 ± 6.37	>0.05
Systolic blood pressure, mmHg	128.20 ± 13.09	129.51 ± 10.51	>0.05
Diastolic blood pressure, mmHg	78.62 ± 8.97	76.41 ± 8.01	>0.05
Oxygen saturation, %	98.51 ± 0.63	98.31 ± 0.47	>0.05

Sensory block characteristics

The onset of sensory block at L1 was significantly faster in Group S than in Group M. Group S also achieved the maximum sensory level earlier. Time to two-segment regression and total duration of sensory blockade were significantly longer in Group S.

The highest sensory level was predominantly between T6 and T8 in both groups. Although a larger proportion of patients in Group M achieved a T6 level, the overall distribution of peak sensory level was clinically comparable.

Table 3: Sensory block characteristics

Parameter	Group M	Group S	p value
Onset of sensory block at L1, min	4.34 ± 0.58	2.94 ± 0.58	<0.001
Maximum sensory level T6, n (%)	18 (62.07)	13 (44.83)	—
Maximum sensory level T8, n (%)	11 (37.93)	16 (55.17)	—
Time to maximum sensory level, min	13.37 ± 1.34	11.82 ± 1.31	<0.001
Two-segment regression time, min	123.37 ± 6.67	136.82 ± 4.26	<0.001
Total sensory block duration, min	205.86 ± 16.15	233.79 ± 16.67	<0.001

Motor block characteristics

Motor block developed earlier in the sequential group. The time to attainment of complete motor

block was also significantly shorter in Group S. In addition, the duration of motor blockade was significantly longer with sequential administration.

Table 4: Motor block characteristics

Parameter	Group M	Group S	p value
Onset of motor block, min	5.18 ± 0.47	4.00 ± 0.58	<0.001
Time to maximum motor block, min	6.17 ± 0.50	4.91 ± 0.58	<0.001
Duration of motor block, min	171.03 ± 15.66	197.58 ± 14.55	<0.001

Haemodynamic profile

A decrease in pulse rate and blood pressure was observed after spinal anaesthesia in both groups. However, the changes were clinically acceptable and no statistically significant intergroup differences

were observed at any recorded time point. Oxygen saturation remained stable throughout the intraoperative and postoperative periods in both groups.

Table 5: Summary of haemodynamic outcomes

Outcome	Group M	Group S	Intergroup comparison
Pulse rate	Mild reduction after spinal block	Mild reduction after spinal block	p>0.05
Systolic blood pressure	Transient decrease	Transient decrease	p>0.05
Diastolic blood pressure	Stable with minor variation	Stable with minor variation	p>0.05
Oxygen saturation	Maintained near 98%	Maintained near 98%	p>0.05

Sedation and postoperative analgesia

Both groups demonstrated acceptable sedation levels. Ramsay Sedation Scale score 3 was more common in Group M, whereas Ramsay score 2 was more

frequent in Group S. No patient in either group developed deep sedation requiring intervention. The duration of effective postoperative analgesia was significantly greater in Group S. Patients receiving sequential administration also required fewer rescue

doses of paracetamol during the first 24 postoperative hours.

Table 6: Sedation and postoperative analgesia

Parameter	Group M	Group S	p value
Effective analgesia duration, min	812 ± 116	882 ± 88.1	<0.05
Rescue analgesic doses in 24 h	2.1 ± 0.7	1.6 ± 0.5	<0.01
Ramsay sedation score 2, n (%)	7 (24.13)	15 (51.72)	—
Ramsay sedation score 3, n (%)	18 (62.06)	13 (44.82)	—
Ramsay sedation score 4, n (%)	4 (13.79)	1 (3.44)	—

Adverse effects

No serious adverse event occurred in either group. Bradycardia, hypotension, and nausea/vomiting were infrequent. Although these events were numerically

more frequent in Group M, the difference was not clinically significant. No respiratory depression, shivering, urinary retention, or hypersensitivity reaction was observed.

Table 7: Adverse effects

Adverse effect	Group M, n (%)	Group S, n (%)
Bradycardia	2 (6.89)	0
Hypotension	3 (10.34)	2 (6.89)
Nausea/vomiting	2 (6.89)	1 (3.44)
Respiratory depression	0	0
Hypersensitivity reaction	0	0
Shivering	0	0
Urinary retention	0	0

DISCUSSION

The present randomized, double-blind study compared mixed and sequential intrathecal administration of hyperbaric levobupivacaine and dexmedetomidine in lower limb surgery. The principal findings were that sequential administration resulted in faster onset of sensory and motor block, earlier achievement of peak block, prolonged sensory and motor blockade, and longer postoperative analgesia. Sequential administration also reduced the need for rescue analgesics during the first postoperative day. These advantages were achieved without significant differences in haemodynamic stability, oxygen saturation, or clinically important adverse effects.

The onset of sensory blockade at L1 was significantly faster in Group S than in Group M. Similarly, Group S achieved maximum sensory level more rapidly. The onset of motor blockade and time to complete motor blockade were also shorter in the sequential group. These findings suggest that the sequence of intrathecal drug administration influences the early distribution and action of the injected local anaesthetic-adjuvant combination.

The physical characteristics of intrathecal solutions may explain the observed differences. Baricity is an important determinant of the spread of local anaesthetics in cerebrospinal fluid. Hyperbaric levobupivacaine has a density greater than cerebrospinal fluid, while dexmedetomidine solution has different physical properties. Premixing dexmedetomidine with hyperbaric levobupivacaine may reduce or alter the baricity of the final injectate. This may modify intrathecal spread and contribute to a slower onset of block. In contrast, sequential injection permits hyperbaric levobupivacaine to

begin its distribution before the dexmedetomidine solution is administered.^[7]

Chaudhry et al. compared premixed and sequential intrathecal dexmedetomidine administration with hyperbaric bupivacaine in lower limb surgery and reported faster onset of sensory and motor block with sequential administration.^[8] Their findings support the results of the present study. Similarly, studies evaluating sequential intrathecal administration of fentanyl or clonidine with local anaesthetics have shown that injection sequence can influence block onset and duration.^[9-11]

The duration of sensory block was significantly longer in Group S. The time to two-segment regression was prolonged by approximately 13 minutes, while the overall sensory-block duration was increased by nearly 28 minutes compared with Group M. Motor-block duration was also significantly prolonged in Group S. These findings are clinically relevant because a longer and denser block may provide improved surgical conditions in operations of moderate duration and delay the onset of postoperative pain.

Dexmedetomidine acts on presynaptic and postsynaptic alpha-2 adrenergic receptors in the spinal cord. Its analgesic action results from inhibition of release of nociceptive neurotransmitters and hyperpolarization of spinal interneurons. The drug may also prolong the effects of local anaesthetics by reducing neuronal firing and enhancing inhibition of pain transmission [3-6]. Since both groups received identical doses of levobupivacaine and dexmedetomidine, the differences observed in the present study are likely related to the technique of intrathecal administration rather than dose-related effects.

The duration of effective postoperative analgesia was significantly greater in Group S. Patients in the sequential group experienced a mean analgesic duration of 882 minutes compared with 812 minutes in the mixed group. The requirement for rescue analgesia was also lower in Group S. This prolonged analgesic effect is important because lower limb procedures may be associated with moderate postoperative pain, particularly after fracture fixation, arthroscopic reconstruction, and amputation procedures.

Studies investigating intrathecal dexmedetomidine with levobupivacaine or bupivacaine have consistently reported prolonged postoperative analgesia and decreased analgesic requirement.^[4-6,12-14]

Basuni and Ezz reported improved postoperative pain relief following the addition of dexmedetomidine to levobupivacaine spinal anaesthesia for knee arthroscopy.^[12] Al-Mustafa et al. also observed prolonged postoperative analgesia with intrathecal dexmedetomidine combined with bupivacaine in urological procedures.^[13]

Haemodynamic stability is a major safety consideration during spinal anaesthesia, especially when alpha-2 agonists are used. Dexmedetomidine can cause bradycardia and hypotension because of its sympatholytic effects. However, in the present study, the mean pulse rate and blood pressure showed comparable trends in both groups. Although a mild reduction in haemodynamic variables occurred after spinal anaesthesia, no statistically significant intergroup difference was demonstrated.

Bradycardia occurred in two patients in Group M and none in Group S. Hypotension occurred in three patients in Group M and two patients in Group S. All episodes were mild and managed successfully with standard treatment. No patient developed clinically significant respiratory depression, which is a beneficial feature of dexmedetomidine compared with intrathecal opioids. These findings are consistent with previous reports that low-dose intrathecal dexmedetomidine provides acceptable haemodynamic stability when used with appropriate monitoring.^[4,5,14]

Sedation was acceptable in both groups. Most patients had Ramsay sedation scores of 2 or 3, indicating a calm and cooperative state without excessive sedation. Although Group M had a greater proportion of patients with score 3 and score 4, no patient experienced deep sedation or respiratory compromise. The sedative effect of dexmedetomidine may improve patient comfort during surgery while preserving spontaneous respiration and responsiveness.

The present study has several limitations. First, the sample size was modest and may not have been adequate to identify rare adverse effects. Second, the study included only patients undergoing lower limb surgery, which limits generalization to obstetric, urological, abdominal, or high-risk surgical populations. Third, exact density and baricity measurements of the prepared intrathecal mixtures

were not performed. Such measurements could have directly confirmed the proposed mechanism underlying the differences between mixed and sequential administration. Finally, long-term neurological outcomes and patient satisfaction were not specifically evaluated.

Despite these limitations, the study provides clinically relevant evidence that sequential intrathecal administration of dexmedetomidine after hyperbaric levobupivacaine improves the onset and duration of spinal blockade without compromising safety. The technique is simple, does not require additional equipment, and may be readily adopted in routine lower limb surgical practice.

CONCLUSION

Sequential intrathecal administration of dexmedetomidine 10 µg after 0.5% hyperbaric levobupivacaine 12.5 mg produced faster onset of sensory and motor blockade, earlier attainment of maximum block, prolonged sensory and motor block duration, and longer postoperative analgesia compared with premixed administration. The sequential technique also reduced rescue analgesic requirement during the first 24 postoperative hours. Haemodynamic variables, oxygen saturation, sedation, and adverse-effect profiles were comparable between the two techniques. Sequential administration of levobupivacaine and dexmedetomidine may therefore be preferred for lower limb surgery performed under spinal anaesthesia.

REFERENCES

- Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: Current understanding and future trends. *World J Clin Cases.* 2017;5(8):307-323.
- Bajwa S, Kaur J. Clinical profile of levobupivacaine in regional anesthesia: A systematic review. *J Anaesthesiol Clin Pharmacol.* 2013; 29:530-539.
- Kataria AP, Jarewal V, Kumar R, Kashyap A. Comparison of levobupivacaine and levobupivacaine with dexmedetomidine in infraumbilical surgeries under spinal anesthesia. *Anesth Essays Res.* 2018; 12:251-255.
- Halder S, Das A, Mandal D, Chandra M, Ray S, Biswas MR, et al. Effect of different doses of dexmedetomidine as adjuvant in bupivacaine-induced subarachnoid block for traumatized lower limb orthopaedic surgery: A prospective, double-blinded and randomized controlled study. *J Clin Diagn Res.* 2014;8(11):GC01-GC06.
- Naaz S, Bandey J, Ozair E, Asghar A. Optimal dose of intrathecal dexmedetomidine in lower abdominal surgeries in average Indian adult. *J Clin Diagn Res.* 2016;10(4):UC09-UC13.
- Kapinegowda ST, Anandswamy TC, Narayanappa VH, Kumar S, Hatti P. To compare the effects of different doses of dexmedetomidine on intrathecal bupivacaine in infraumbilical surgeries: A prospective, randomized, double-blind clinical study. *Anesth Essays Res.* 2017;11:847-853.
- Imbelloni LE, Moreira AD, Gaspar FC, Gouveia MA, Cordeiro JA. Assessment of the densities of local anesthetics and their combination with adjuvants: An experimental study. *Rev Bras Anesthesiol.* 2009;59:154-165.
- Chaudhry G, Singla D, Dureja J, Bansal P, Ahuja K. Efficacy of premixed versus sequential administration of dexmedetomidine as an adjuvant to intrathecal hyperbaric

- bupivacaine in lower limb surgery. *South Afr J Anaesth Analg*. 2016;22(3):81-85.
9. Malhotra A, Singh U, Singh MR, Sood D, Grewal A, Mahajan A. Efficacy of premixed versus succedent administration of fentanyl and levobupivacaine in subarachnoid block for lower limb surgeries: A randomized control trial. *Indian J Anaesth*. 2020;64:175-179.
 10. Imam S, Vardhan H. Comparison of characteristics of mixed versus sequential administration of levobupivacaine and fentanyl in subarachnoid block for lower limb surgeries: A randomized control study. *Int J Sci Res*. 2023;12.
 11. Sachan P, Kumar N, Sharma JP. Intrathecal clonidine with hyperbaric bupivacaine administered as a mixture and sequentially in caesarean section: A randomized controlled study. *Indian J Anaesth*. 2014;58:287-292.
 12. Basuni AS, Ezz HAA. Dexmedetomidine as supplement to low-dose levobupivacaine spinal anesthesia for knee arthroscopy. *Egypt J Anaesth*. 2014;30:149-153.
 13. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. *Saudi Med J*. 2009;30(3):365-370.
 14. Esmaoğlu A, Türk S, Bayram A, Akın A, Uğur F, Ulgey A. The effects of dexmedetomidine added to spinal levobupivacaine for transurethral endoscopic surgery. *Balkan Med J*. 2013;30(2):186-190.