

A Comparative Study between Intrathecal Dexmedetomidine vs Ketamine with Intrathecal Bupivacaine in Orthopedic Lower Limb Surgeries

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ABSTRACT

Background: Many adjuvants have been used to increase the analgesic duration of intrathecal bupivacaine.

Objective: This work was aimed at comparing intrathecal ketamine vs dexmedetomidine for patients with lower limb surgery regarding advantages, efficacies, and hemodynamic stability.

Patients and methods: This prospective randomized double-blind study involved 100 individuals whose ages ranged from eighteen to fifty years, both sexes, who underwent orthopedic lower limb surgeries. All participants went through an even categorization into two groups: Group D: administering calculated dosage of intrathecal hyperbaric bupivacaine 0.5 % according to body weight and 5µg dexmedetomidine and Group K: administering calculated dosage of intrathecal hyperbaric bupivacaine 0.5 % according to body weight and 0.1 mg/kg of ketamine.

Results: Intraoperative HR as well as MAP measurements were significantly higher during 15 min, 30min, 45min and end of surgery within group K as opposed to group D (P value <0.05). Postoperative HR, MAP, SaO₂ as well as VAS measurements were significantly less during 30 min, 2h, 4h and 6h within group K as opposed to group D (P value <0.05). Time to first analgesic request was significantly delayed within group K as opposed to group D (P value <0.001). Complications (bradycardia as well as hypotension) were insignificantly varied among two groups. Respiratory depression occurrence was not present in both groups.

Conclusions: Ketamine produces better analgesic outcomes compared to dexmedetomidine in patients with lower limb surgery. However, it is associated with higher intraoperative HR and MAP and lower postoperative HR and MAP compared to dexmedetomidine with no difference in complications among them.

Keywords: Intrathecal Dexmedetomidine, Ketamine, Intrathecal Bupivacaine, Orthopedic Lower Limb Surgeries

INTRODUCTION

Proper pain management is of the highest value to anyone caring for patients going through surgeries. Monitoring pain relief has become a vital essential measure of postoperative quality, as it offers substantial physiological advantages. Postoperative pain management is aimed at minimizing or alleviating pain as well as discomfort while avoiding adverse events [1].

Numerous medications, involving opioid vs. nonopioid, with various administration routes such as oral, intravenous, neuraxial, as well as regional were introduced along with patient control approaches (patient controlled vs. "as needed"). Pain alleviation is proved to be a human right by both the WHO as well as the International Association for the study of pain [2]. Chronic pain that lowers quality of life is linked to uncontrolled acute pain development [3].

Managing pain properly exhibits benefits, involving reduced hospitalization, decreased expenses, as well as improving satisfaction. Therefore, postoperative pain control remains a more essential quality measure [4].

The need for greater effectiveness and shorter hospital stay has made anesthesia as well as acute post-surgical pain control more important for orthopedic surgeries. Orthopedic anesthesia as well as acute post-surgical control, two anesthesiology subspecialties, have got more credit for reducing hospital stays, promoting functional recovery and improving patient satisfaction [5].

Continuous nerve block methods have become more popular recently for treating postoperative pain. Regional procedures are frequently a component of a multimodal pain management strategy that also includes pharmacological and nonpharmacological methods [6].

This work was aimed at comparing intrathecal ketamine vs dexmedetomidine for those undergoing lower limb surgery regarding advantages, efficacies, and hemodynamic stability.

PATIENTS AND METHODS

This prospective randomized double-blind study included a total of 100 patients who underwent orthopedic lower limb surgeries under intrathecal anesthesia and ASA class I and II, attending at Department of Anesthesiology, Surgical Intensive Care and Pain Medicine, Sohag University Hospitals. This study was conducted between March 2023 to September 2023.

The patients were of both sexes, whose ages ranged between eighteen and fifty years.

Exclusion criteria: Patients having drug abuse, neurological, psychiatric, or neuromuscular disorders, chronic pain as well as prior allergies to study medications.

All participants went through an even categorization into two groups (50 participants in each) in a parallel manner by computer-generated numbers and their allocation code was kept in a closed opaque envelope: **Group D:** Patients were administered intrathecal hyperbaric bupivacaine dosage 0.5 % according to body weight and 5µg dexmedetomidine while **Group K:** they were administered calculated intrathecal hyperbaric bupivacaine dosage 0.5 % according to body weight in addition to ketamine dosage of 0.1 mg/kg. A non-participating anesthesiologist prepared the drug solutions. All participants and the anesthesiologist performing the intrathecal injection and observing the patients were blinded to the treatment group.

All participants underwent a comprehensive medical history, clinical assessments as well as routine laboratory testing. They underwent a fasting duration for eight hours before surgery. While admitting to the operating room, all participants underwent monitoring utilizing ECG, NIBP, pulse oximetry, as well as temperature probe. A 20-gauge IV cannula was applied to the nonoperative arm, and then a dosage of five ml/kg/h Ringer's lactate was administered.

Spinal anesthesia:

All participants were in supine positions. Under a well-established sterilized environment, spinal anesthesia administration was done at L4-L5 interspace level while sitting utilizing a midline or paramedian method with a 25G Quincke spinal needle. Anesthetic medication is administered for each patient according to their group allocation at a dosage of around two ml/sec. The study's participants underwent the operation under intrathecal anesthesia by 0.2 mg/ kg hyperbaric bupivacaine dosage 0.5 % as well as dosage of five µg dexmedetomidine within group D while 0.1 mg/kg dosage of ketamine for group K.

Assessing hemodynamic changes HR, MAP as well as SpO₂ was continuously done and documented: preoperative, after block, then every 15 minutes intraoperative. Following the surgical procedure, they were transferred to the PACU.

VAS scale was utilized for assessing postoperative pain. It has a scale from zero to ten. Zero exhibits pain absence while ten exhibits sever pain. VAS was assessed during 30 minutes as well as 2, 4, 6, 12, 18 and 24 hours post-surgically.

Patients with VAS score > 3 receive rescue analgesic in the form of ketorolac IV (0.5 mg/ kg maximum dose 120 mg) if VAS score is still > 3. Morphine IV shots at dosage of 0.1- 0.2 mg /kg was administered. Time for rescue analgesia requirement as well as total ketorolac and morphine intake among both groups were recorded. Postoperative hemodynamics changes were recorded at 30 minutes and then at 2, 4, 6, 12, 18 and 24 hours postoperative.

Any adverse effects in recovery room were monitored: Managing hypotension (decrease in basal MAP by 20%) was accomplished utilizing I.V. fluid. While IV dosage of 0.02 mg/kg atropine was administered to manage bradycardia (defined by reduced basal HR by 20%). Respiratory depression (the SpO₂ < 95% as well as required O₂ supplementation), disturbed conscious level, hallucinations, abnormal movement and nausea and vomiting were recorded. Our primary outcome was aimed at assessing the patients' number asking for rescue analgesia while secondary ones involved time for first request as well as total morphine consumption.

Sample Size Calculation:

Calculating sample size was accomplished utilizing G. power 3.1.9.2 (University Of Kiel,, Germany), based on patients' number requested rescue analgesia was (100%) with dexmedetomidine and (70%) with ketamine regarding a prior study [7]. Depending on the following considerations: 0.05 α error as well as 99% power of the study, allocation ration 1:1. Three individuals were incorporated to compensate for dropout. So, 50 patients will be assigned.

Ethical approval:

Sohag Medical Ethics Committee, the Sohag Faculty of Medicine gave its approval to this study. All participants gave written consent after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

Data went through a statistical analysis utilizing SPSS v26 (IBM Inc., Chicago, IL, USA). Shapiro-Wilks test as well as histograms were utilized for assessing the normality of the distribution of data. Quantitative parametric variables were displayed as mean and standard deviation (SD), a comparison between the two groups was accomplished utilizing unpaired Student's t- test. Quantitative non-parametric data were presented as median and interquartile range (IQR) and were analyzed by Mann Whitney-test. Qualitative variables were displayed as frequency and percentage (%). Analysis was accomplished utilizing the Chi-square test or Fisher's exact test when appropriate. A two tailed P value < 0.05 deemed to be statistically significant.

RESULTS

The current study involved 118 patients evaluated for eligibility, twelve of them did not match the inclusion criteria, while six disagreed to take part in the research. The rest underwent a random categorization into two equal groups (50 participants in each). They underwent a follow up period as well as statistical analysis. **Figure 1**

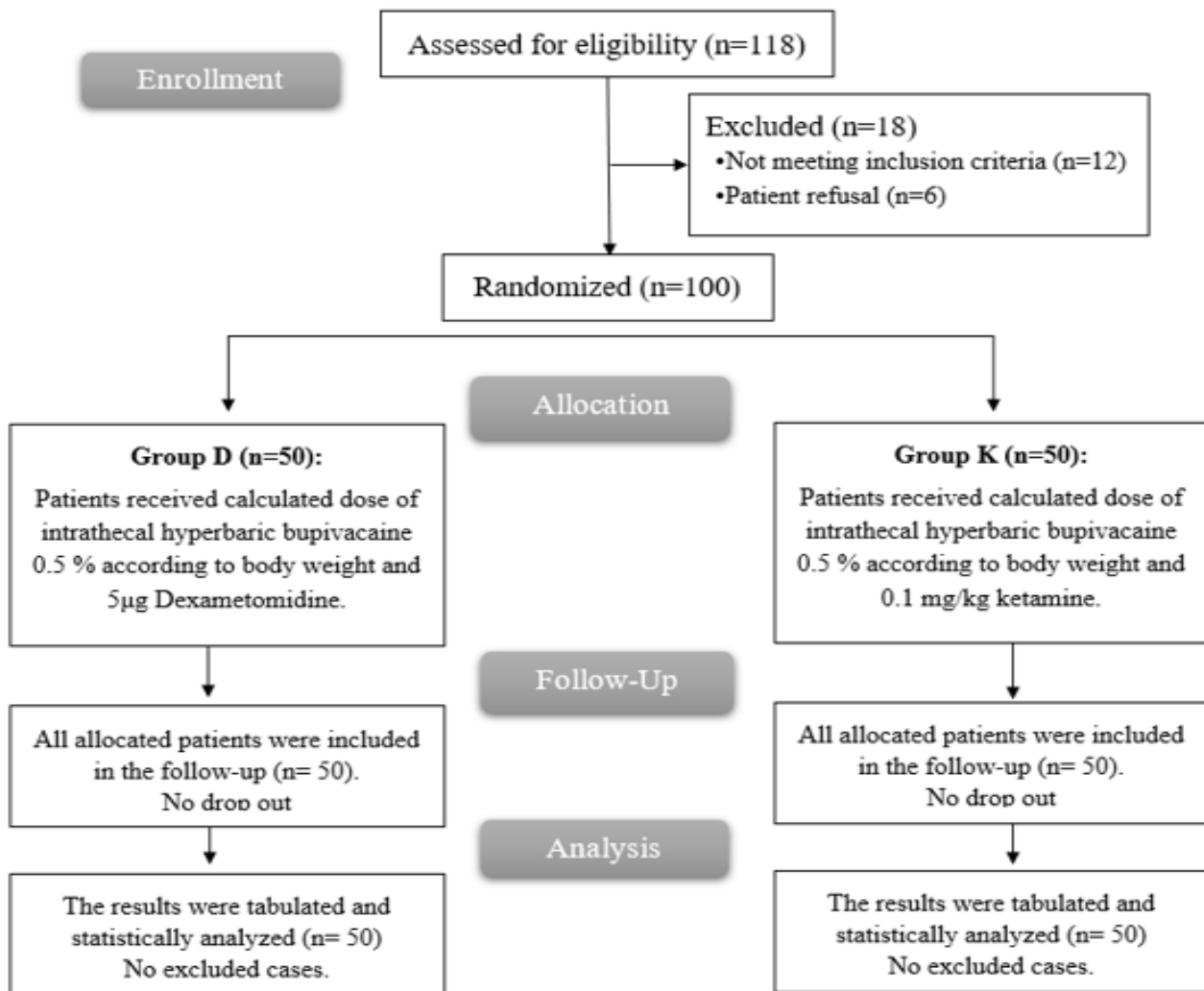


Figure (1): CONSORT flow diagram of the participants through each stage of the trial

Regarding patient characteristics as well as surgical duration, insignificant variations were documented among both groups. **Table 1**

Table (1): Demographic data as well as surgical duration among studied groups

		Group D (n=50)	Group K (n=50)	P
Age (years)		34.08 ± 8.13	33.78 ± 8.04	0.853
Weight (kg)		71.62 ± 7.18	73.32 ± 7.03	0.234
Height (m)		1.64 ± 0.06	1.63 ± 0.07	0.354
BMI (kg/m ²)		26.59 ± 3.11	27.73 ± 3.7	0.099
ASA	ASA I	27 (54%)	31 (62%)	0.418
	ASA II	23 (46%)	19 (38%)	
Duration of surgery (min)		89.1 ± 17.72	86.7 ± 17.75	0.500

Data are exhibited as mean ± SD or frequency (%). *Significant p value <0.05, BMI: Body mass index, ASA: American society of anesthesiologists.

Table 2 shows that A visual analogue scale (VAS) measurements were significantly lower at 30 min, 2h, 4h and 6h within group K as opposed to group D (P value <0.05) and were insignificantly different at 12h, 18h and 24h among two groups.

Table (2): VAS measurements of the studied groups

	Group D (n=50)	Group K (n=50)	P value
30 min	1 (0.25 - 1)	0 (0 - 1)	<0.001*
2h	2 (1 - 4.5)	1 (1 - 1)	<0.001*
4h	2 (1.25 - 5)	1 (1 - 2)	0.001*
6h	3 (2 - 3)	2 (2 - 3)	0.006*
12h	3 (2 - 5)	3 (2 - 4)	0.151
18h	4 (2 - 5)	4 (2 - 4)	0.585
24h	3 (2 - 5)	3 (2 - 4)	0.812

Data are exhibited as mean ± SD.*Significant p value <0.05.

Time to first analgesic request exhibited significant delays within group K as opposed to group D (P value<0.001). Complications (bradycardia as well as hypotension) were insignificantly varied among two groups. Respiratory depression occurrence was not present among two groups (**Table 3**).

Table (3): Total ketorolac dosage, time to first analgesic request, total morphine dosage as well as complications among studied groups

	Group D (n=50)	Group K (n=37)	P
Time to first analgesic request (h)	4.72 ± 2.18	8.11 ± 1.7	<0.001*
	Group D (n=50)	Group K(n=50)	
Total dose of ketorolac consumption in 1st 24h postoperative (mg)	85.2 ± 18.65	61.8 ± 27.53	<0.001*
Number of patients required morphine (%)	50 (100%)	37 (74%)	<0.001*
Total dose of morphine consumption in 1st 24h postoperative (mg)	14.6 ± 5.03	9.8 ± 7.42	<0.001*
Complications			
Bradycardia	3 (6%)	1 (2%)	0.307
Hypotension	4 (8%)	1 (2%)	0.169
Respiratory depression	0 (0%)	0 (0%)	---

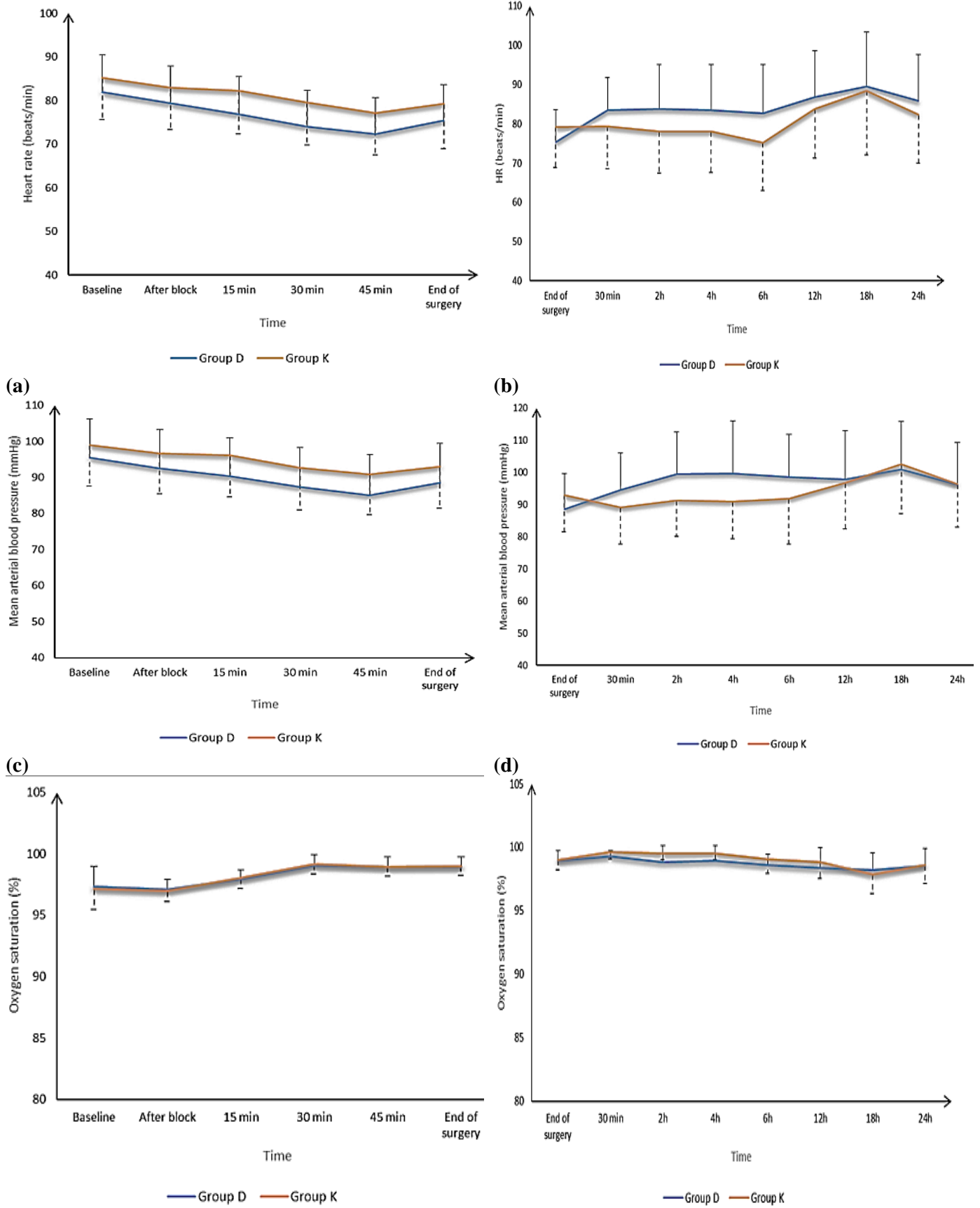
Data are exhibited as mean ± SD.*Significant p value <0.05.

Intraoperative HR and MAP, measurements at baseline and after block were insignificantly varied among both then were significantly higher at 15min, 30min, 45min and end of surgery within group K as opposed to group D (P value <0.05). Intraoperative SaO₂ measurements were insignificantly varied among two groups at all measurements times. Postoperative HR and MAP and SaO₂ measurements were significantly less at 30 min, 2h, 4h and 6h within group K as opposed to group D (P value <0.05) and were insignificantly different at 12h, 18h and 24h among two groups.

Figure 2

Intraoperative measurements

Postoperative measurements



(a) **(b)** **(c)** **(d)** **(e)** **(f)**
Figure (2): Intraoperative(a) HR, (b) MAP and (c) oxygen saturation and postoperative (d) HR, (e) MAP increases postoperative morbidity.

DISCUSSION

The control of perioperative pain is a significant challenge to anesthesiologists. Reduced perioperative morbidity and death may result from postoperative pain relief [5]. Optimizing postoperative analgesia enables to decrease postoperative problems, promote healing in the immediate postoperative period, and support early patient departure [5].

Ketamine remains the most efficient clinical N-methyl-D-aspartate receptor channel blocker utilized. When administered intrathecally, ketamine has local anesthetic effects in both people and animals [8]. Studies on humans showed that when ketamine was used as the sole anesthetic agent intrathecally at dosages of 0.7-0.95 mg/Kg, sensory and motor block were produced [9].

Regarding intraoperative hemodynamic parameters, our study addressed, intraoperative HR as well as MAP measurements were significantly higher at 15min, 30min, 45min and end of surgery in group K than group D. Intraoperative oxygen saturation (SaO₂) measurements exhibited insignificant variation among two groups at all measurements times.

Mohamed et al. [10] conducted a similar study to assess the intrathecal dexmedetomidine effectiveness as well as safety, and incorporating ketamine, or both into bupivacaine for postoperative analgesia while performing major abdominal cancer surgeries. Ninety participants went through a random categorization to be administered with either intrathecal dosage of ten mg hyperbaric bupivacaine 0.5% as well as five µg of dexmedetomidine (group I, n = 30), a dosage of ten mg hyperbaric bupivacaine 0.5 as well as a dosage of 0.1 mg/kg ketamine (group II, n = 30), or a dosage of ten mg hyperbaric bupivacaine 0.5% as well as a dosage of five µg of dexmedetomidine in addition to 0.1 mg/kg of ketamine (group III, n = 30). Hemodynamics, pain score, time for rescue analgesia need, total PCA morphine intake, sedation score, as well as adverse events during first 24 hours post-surgically were documented. Aligned with our results, **Mohamed et al.** [10] addressed a significant intra-operative pulse rate decrease within group I as opposed to groups II from a duration between 10 minutes and 180 minutes. Systolic blood pressure exhibited a significant decrease within group I from a duration between five min and 120 min as opposed to group II. The intra-operative diastolic blood pressure significantly reduced within group I from a duration between 5 min and 180 min, in comparison to group II.

Postoperative HR and MAP and SaO₂ measurements were significantly lower at 30 min, 2h, 4h and 6h within group K as opposed to group D (P value <0.05) exhibiting insignificantly differences at 12h, 18h and 24h between both groups. Different from our findings, **Mohamed et al.** [10] reported addressed a significant decrease regarding postoperative pulse rate within group I immediately postoperative till twelve hours when compared to groups II. no significant

differences among groups regarding postoperative systolic as well as diastolic blood pressure were documented (P > 0.05). In disagreement with the present results, **Peyyety et al.** [11] conducted a study for performing a comparison regarding the analgesic efficacy and ketamine, fentanyl hemodynamic effects as well as placebo, when administered along with hyperbaric bupivacaine intrathecally for individuals going through elective total knee replacement surgery. A prospective randomized double-blind placebo-controlled study involved ninety individuals who underwent a categorization into three groups of 30 each based on the intrathecal adjuvant utilized. Monitoring as well as standardized anesthetic approach for subarachnoid block (and epidural catheter placement) with a dosage of 3 mL of 0.5% hyperbaric bupivacaine was accomplished. Additionally, Group K (n = 30) were administered a dosage of 0.3 mg/kg of preservative free ketamine, Group F (n = 30) were administered a dosage of 25 µg (0.5 mL) of fentanyl while Group C (control group, placebo, n = 30) were administered 0.5 mL normal saline. Onset as well as duration of sensory and motor block and analgesia duration, hemodynamic parameters, sedation scores intra operatively and post-operatively and adverse events were documented and analyzed.

This study reported that the ketorolac total dosage intake in 1st 24h postoperative, number of patients required morphine and total dose of morphine intake at 1st 24h post-surgically were significantly less within group K as opposed to group D (P value <0.001). Time for first analgesic request was significantly prolonged within group K as opposed to group D (P value <0.001). Aligned with our study, **Mohamed et al.** [10] reported that the time for first rescue analgesic exhibited delays within group II as opposed to group I. In addition, total morphine intake for 24 hours post-surgically was greater within group I as opposed to group II. Additionally, all participants within group I requested rescue analgesia while only 70% of group II did. In disagreement with our results, **Radbin et al.** [12] reported that narcotic consumption during surgery and after surgery was statistically significant lower in dexmedetomidine compared to ketamine.

VAS measurements were significantly lower at 30 min, 2h, 4h and 6h within group K as opposed to group D (P value <0.05). Similarly, **Mohamed et al.** [10] reported that NRS score was less within group II at 4h, as well as 6h compared to group I with no difference at 18h and 24h. Different to our findings, NRS was lower in group II at 12 h as well. Different from our findings, **Radbin et al.** [12] reported that VAS score was statistically significant less within the dexmedetomidine group as opposed to ketamine group.

Complications (bradycardia as well as hypotension) were insignificantly varied among both groups. Respiratory depression occurrence was not present among both groups.

Aligned with these results, **Mohamed *et al.*** ^[10] addressed, regardless of sedation, no significant differences regarding occurrence of other side effects were documented among the 3 studied groups. Different from our findings, **Radbini *et al.*** ^[12] reported that shivering was greater within ketamine group as opposed to dexmedetomidine with no nausea and vomiting occurrence between both groups.

Limitations: A single-centered study, no comparison with placebo group, doses of the adjuvants were not investigated, and different local anesthetics were not investigated.

CONCLUSIONS

Ketamine produces better analgesic outcomes compared to dexmedetomidine in patients with lower limb surgery. However, it is linked to higher intraoperative HR and MAP as well as lower postoperative HR and MAP compared to dexmedetomidine with no difference in complications among them.

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Conflict of Interest: Nil

REFERENCES

1. **Lavand'homme P, Kehlet H, Rawal N *et al.* (2022):** Pain management after total knee arthroplasty: PROcedure SPECific Postoperative Pain Management recommendations. *Eur J Anaesthesiol.*, 39: 743-48.
2. **Mondardini M, Sperotto F, Daverio M *et al.* (2023):** Analgesia and sedation in critically ill pediatric patients: an update from the recent guidelines and point of view. *Eur J Anaesthesiol.*, 182:2013-26.
3. **Szatmary P, Grammatikopoulos T, Cai W *et al.* (2022):** Acute pancreatitis: Diagnosis and treatment. *Drugs*, 82:1251-76.
4. **Cheung C, Adeola J, Beutler S *et al.* (2022):** Postoperative Pain Management in Enhanced Recovery Pathways. *J Pain Res.*, 15:123-35.
5. **Kehlet H, Holte K (2001):** Effect of postoperative analgesia on surgical outcome. *Br J Anaesth.*, 87:62-72.
6. **Chitnis S, Tang R, Mariano E (2020):** The role of regional analgesia in personalized postoperative pain management. *Korean J Anesthesiol.*, 73:363-71.
7. **Mohamed S, El-Rahman A, Fares K (2016):** Intrathecal Dexmedetomidine, Ketamine, and their Combination Added to Bupivacaine for Postoperative Analgesia in Major Abdominal Cancer Surgery. *Pain Physician*, 19:829-39.
8. **Gebhardt B (1994):** Pharmacology and clinical results with peridural and intrathecal administration of ketamine. *Anaesthetist*, 43(2): 34-40.
9. **Hawksworth C, Serpell M (1998):** Intrathecal anesthesia with ketamine. *Reg Anesth Pain Med.*, 23: 283-8.
10. **Mohamed S, El-Rahman A, Fares K (2016):** Intrathecal Dexmedetomidine, Ketamine, and their Combination Added to Bupivacaine for Postoperative Analgesia in Major Abdominal Cancer Surgery. *Pain Physician*, 19: 829-39.
11. **Peyyety J, Reddyoglu D, Mukku K *et al.* (2021):** A comparative study of analgesic effects of ketamine, fentanyl and saline added to hyperbaric bupivacaine for central neuraxial blockade in total knee replacement surgery: A prospective, randomised, double-blind and placebo-controlled study. *J Clin sci Res.*, 10:55-60.
12. **Radbini T, Kamali A, Yazdi B *et al.* (2021):** Efficacy of dexmedetomidine and ketamine addition to bupivacaine 0.25% by epidural method in reducing postoperative pain in patients undergoing femur fracture surgery. *J Family Med Prim Care*, 10: 832-37.