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Comparison of Post-Operative Analgesic Effects of Intrathecal Dexmeditomidine Versus Intrathecal Ketamine Added to Bupivacaine in Total Knee Replacement Surgeries

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ABSTRACT

Objective: To compare the analgesic efficacy of Dexmedetomidine versus Ketamine when added to intrathecal Bupivacaine in patients undergoing unilateral total knee replacement surgery.

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Anesthesia, Combined Military Hospital, Rawalpindi, Pakistan, from May to Oct 2022.

Methodology: Our study enrolled a total of 80 patients, divided into Dexmedetomidine group (n=40) and Ketamine group (n=40) group using non-probability consecutive sampling. Patients in both groups received 2.5 ml of 0.5% Bupivacaine with Dexmedetomidine group receiving 5 mcg (0.5 ml) of the drug and Ketamine group 0.1 mg/kg of Ketamine in 0.5 ml to a total volume of 3 ml. Data analysis was performed using SPSS 26.0, with significance set at $p \leq 0.05$.

Results: Time of onset for sensory block in Dexmedetomidine group was delayed than Ketamine group with mean time of onset 4.34±0.14 minutes versus 3.38±0.10 minutes ($p<0.0001$). The duration of block was more for Ketamine group with mean time of 326.20±12.67 minutes versus 243.76±2.54 minutes ($p<0.0001$). When comparing motor blockade, the time of onset to successfully reach Bromage Score 3 was similarly delayed in Dexmedetomidine group with mean time of onset 3.33±0.12 minutes versus 2.36±0.09 minutes ($p<0.0001$). A similar trend was seen in duration of block with mean time 203.40±1.46 minutes versus 263.01±13.44 minutes ($p<0.0001$)

Conclusion: Ketamine provided superior analgesia, block onset and duration with less post-operative analgesia requirement.

Key Words: Bupivacaine, Dexmedetomidine, Intrathecal, Ketamine, Total knee replacement.

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INTRODUCTION

Total knee replacement is a critical curative procedure in orthopedic surgery. With the burden of osteoarthritis exceeding 16% in South Asian patients above 50 years of age,[1,2] the prevalence of total knee replacement has also increased from 1.2% in the 2000s to 4.2%,[3] at present, with this burden expected to increase ten-fold in the next 25 years. While total knee replacement offers excellent post-operative results, with respect to improvement in quality of life and patient satisfaction, it is a major surgery resulting in considerable patient debility. One of the major hurdles in early mobilization and subsequent re-habilitation is post- procedure pain,[4] as without effective analgesia this pain can reach up to a scale of 7-8 on the Visual Analog Scale,[5] Ketamine, an NMDA receptor antagonist,[6] is as an intravenous anesthetic agent, however, in recent years, it has also been used as an intrathecal adjunct, resulting in reduction of block onset, prolonging total block time along with providing sedation and anxiolysis,[7] however, its dissociation effects on the nervous system prevent it from being universally accepted for administration among all patients.[8] Dexmedetomidine, a selective α_2 agonist, exerts its effects on the spinal cord by stimulation of α_2 receptors at the substantia gelatinosa of the dorsal horn leading to inhibition of the release of substance P.[9] Dexmedetomidine is also being used as an excellent adjunct, but its adverse effects of hypotension and bradycardia cause considerable patient discomfort.[10] Thus, the aim of this study was to compare the superiority and efficacy of both drugs with intrathecal Bupivacaine, in patients undergoing unilateral total knee replacement while also comparing their adverse effect profile.

METHODOLOGY

This quasi-experimental study was carried out at the Department of Anesthesiology, Combined Military Hospital (CMH), Rawalpindi, Pakistan, from May to October 2022. Approval from the Ethics Review Board was sought and granted vide Letter no. 247, dated 30

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Apr 2022. A minimum sample size of 62 patients was found after calculating sample size using World Health Organization (WHO) calculator, keeping the confidence interval at 95%, margin of error at 5% and using the population prevalence of unilateral total knee replacement at 4.2%, as reported in literature.[3]

Inclusion Criteria: All American Society of Anesthesiologists (ASA) physical status classification Class I, II and III patients, between ages of 50 to 75 years, presenting for scheduled unilateral total knee replacement under spinal anesthesia were included.

Exclusion Criteria: Patients unwilling for spinal anesthesia, with allergy to either Ketamine, Dexmedetomidine and Bupivacaine, deranged coagulation profile, previous history of major heart or respiratory disease or BMI > 45 kg/m^2.

We enrolled 80 patients, using non-probability consecutive sampling via lottery method, who were then divided into the Dexmedetomidine group (n=40) and the Ketamine group (n=40). As this was a double-blind study, the anesthetist on duty in the operating room was unaware of the study protocol and received sealed envelopes with the two adjuvant vials labelled 1 and 2. Patients in both groups received 2.5 ml of 0.5% of hyperbaric Bupivacaine with the Dexmedetomidine group receiving 5 mcg (0.5 ml) of the drug and the Ketamine group receiving 0.1 mg/kg in 0.5 ml to a total volume of 3 ml. The study solutions were given in both groups in the L2-L3 or L3-L4 space. Bradycardia was defined as a heart rate of <60 beats per minute,[11] and hypotension as Mean Arterial Pressure (MAP) <50 mm Hg[12] and was treated with 5 mg Ephedrine and 600 mcg of Glycopyrrolate where needed. Post-operation, first rescue analgesia for pain through an epidural top-up of 5 ml 0.25% Bupivacaine was given once the pain on VAS reached.[5] Sensory blockade till the T12 dermatome level was confirmed by loss of sensation to cold ethyl chloride spray in the mid-line bilaterally below umbilicus while motor blockade with Bromage score of 313 was considered successful. Total duration of block was calculated when sensory level was at S1 dermatome and Bromage score was 0. Primary variables measured were time to complete sensory and motor block, total duration of the block, time to first rescue analgesia after block regression and 24- hour total dose of epidural analgesia needed while secondary variables observed were hypotension, nausea, vomiting, dissociation, shivering and respiratory depression. Demographic data were statistically described in terms of Mean±SD, frequencies, and percentages and a *p*-value of ≤0.05 was considered statistically significant. All data was analysed using Statistical Package for the Social Sciences (SPSS) ver 26.0.

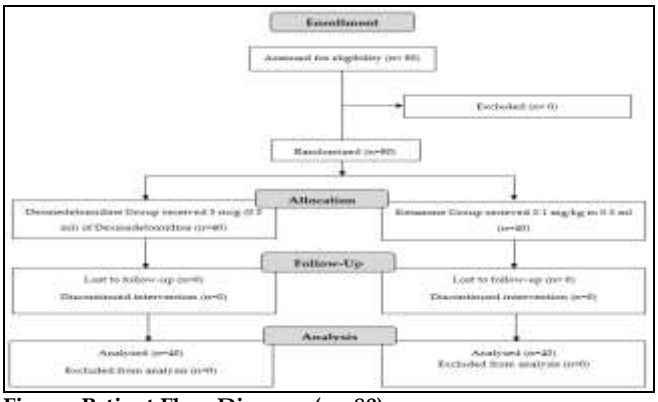

Figure: Patient Flow Diagram (n= 80)

RESULTS

A total of 80 patients were divided into the Dexmedetomidine group (n=40) and Ketamine group (n=40) with mean age of patients in the Dexmedetomidine group being 66.45±4.19 years versus 66.50±4.01 years in the Ketamine group while mean weight of patients was 73.80±4.91 kg for Dexmedetomidine group and 74.92±5.21 kg for the Ketamine group. These findings are listed in Table-I.

Table-I: Age and Weight Characteristics of Participants (n=80)

Variable	Dexmedetomidine Group (n=40)	Ketamine Group (n=40)
Mean Age (years)	66.45±4.19	66.50±4.01
Mean Weight (kg)	73.80±4.91	74.92±5.21

Time of onset for sensory block in the Dexmedetomidine group was more delayed than the Ketamine group with mean time of onset being 4.34±0.14 minutes versus 3.38±0.10 minutes (p<0.0001) and duration of block was found to be more for the Ketamine group, with mean time of 326.20±12.67 minutes versus 243.76±2.54 minutes (p<0.0001) in the comparison group. For motor blockade, the time of onset to reach Bromage Score 3 was similarly delayed in the Dexmedetomidine group, with mean time of onset being 3.33±0.12 minutes versus 2.36±0.09 minutes (p<0.0001) in the Ketamine group. A similar trend was seen in duration of block between both drugs with mean time 203.40±1.46 minutes versus 263.01±13.44 minutes (p<0.0001). These findings are listed in Table-II.

Table-II: Comparison of Block Onset, Block Regression and Rescue Analgesia (n=80)

Variable	Dexmedetomidine Group (n=40)	Ketamine Group (n=40)	*p*-value (≤0.05)
Sensory Block			
Mean Time for Onset of Block (T12) (min)	4.34±0.14	3.38±0.10	<0.001
Mean Time for Block Regression (S1) (min)	243.76±2.54	326.20±12.67	<0.001
Motor block			
Mean Time for Onset of Block (Bromage Score= 3) (min)	3.33±0.12	2.36±0.09	<0.001
Mean Time for Block Regression (Bromage Score = 0) (min)	203.40±1.46	263.01±13.44	<0.001
Mean Time to First Dose Rescue Analgesia (hrs)	3.45±0.27	5.2±0.24	<0.001
Mean Vol of Analgesia Given in ICU (mg/24 hr)	54.30±4.28	41.85±5.17	<0.001
Mean ICU Stay (days)	2.21±0.16	1.39±0.12	<0.001

We found that time to first rescue analgesia after cessation of sensory block in both groups showed that mean time for patient requiring epidural analgesia, once reaching VAS score of 5, was 3.45±0.27 hours in the Dexmedetomidine group versus 5.2±0.24 hours in the Ketamine group (p<0.0001). Mean length of ICU stay was 2.21±0.16 days versus 1.39±0.12 days (p<0.0001). The frequency of hypotension was 7(17.5%) patients in the Dexmedetomidine group with no patients experiencing hypotension in the Ketamine group and 4(10%) patients had nausea and vomiting in the Dexmedetomidine group similar to 4(10%) in the Ketamine group while shivering was seen in 5(12.5%) patients versus 2(5%) patients between both groups. Notably, dissociation post-surgery was seen in 5(12.5%) patients in only the Ketamine group. These findings have been tabulated in Table-III.

Table-III: Frequency of Side Effects (n=80)

Variable	Dexmedetomidine Group n(%)	Ketamine Group n (%)
Hypotension	7(17.5%)	0(0%)
Nausea/vomiting	4(10%)	4(10%)
Dissociation	0(0%)	5(12.5%)
Shivering	5(12.5%)	2(5%)
Respiratory Depression	2(5%)	0(0%)

DISCUSSSION

The aim of this study was to assess the effectiveness of the sensory and motor block of both drugs as well as their role in reducing the overall analgesia required 24 hours post-operatively. One study demonstrated that Ketamine proved to be an excellent adjunct even when used with regional blocks to increase the sensory block duration.[14] When compared with opioids, including nalbuphine given intrathecally, it was effective in increasing the block duration with early onset.[15] This was consistent with our findings even though the block onset and total duration also increased with Dexmedetomidine, Ketamine remained the superior choice as demonstrated by another study.[16] It was reported by an author[17] that the total dose, as well as the frequency of rescue analgesia, both by IV and epidural route, decreased considerably when Ketamine was used as a spinal adjunct, however, the IV route was associated with considerable dissociation in patients and could not be recommended in geriatric patients with acute pain.[18] Local studies on the subject have also revealed similar results, with the adjuvant groups offering better analgesia[1], superior patient satisfaction and less hospital stay[2] especially for mean ICU stay, where Ketamine provided better per-operative analgesia with increased duration, resulting in considerably less analgesia top-up by the epidural route, resulting in early mobilization and patient being shifted to the ward or HDU, which is beneficial in our local hospitals due to heavy patient load and limited ICU bed availability. The adverse effect profile showed a higher frequency of dissociation; however, it was considerably less when compared to IV route administration, therefore, this route can prove beneficial in decreasing the adverse effects,[19] especially when compared with Dexmedetomidine, the occurrence of hypotension and respiratory depression, makes Ketamine a comparatively better choice.

LIMITATIONS OF STUDY

Several important limitations of this study warrant consideration. Primarily, this investigation was conducted at a single center, which inherently constrains the generalizability of our findings. A multi-center approach would have provided access to a more diverse patient population across different geographic and demographic contexts, potentially yielding more robust and generalizable results. The single-center design may have introduced selection bias due to the specific patient demographics, local clinical practices, and institutional protocols unique to our facility. Additionally, regional variations in disease presentation, treatment approaches, and healthcare delivery systems were not captured in our analysis.

CONCLUSION

Ketamine demonstrates superior analgesic efficacy, characterized by faster block onset, prolonged block duration, and a reduced need for post-operative analgesia

compared to alternative agents. These findings suggest that Ketamine could be a valuable component of multimodal analgesia strategies, offering enhanced pain control and potentially improving patient satisfaction and recovery outcomes.

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Authors' Contribution

The following authors have made substantial contributions to the manuscript as under:

FH & MS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SQAS & MMR: Conception, data analysis, drafting the manuscript, approval of the final version to be published.

WK & MHS: Data acquisition, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Sun X, Zhen X, Hu X, Li Y, Gu S, Gu Y, et al. Osteoarthritis in the middle-aged and elderly in China: prevalence and influencing factors. Int J Environ Res Public Health 2019; 16(23): 4701. https://doi.org/10.3390/ijerph16234701
2. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine 2020; 29: 100587. https://doi.org/10.1016/j.eclinm.2020.100587
3. Kremers HM, Larson DR, Crowson CS, Kremers WK, Washington RE, Steiner CA, et al. Prevalence of total hip and knee replacement in the United States. J Bone Joint Surg Am 2015; 97(17): 1386. https://doi.org/10.2106/JBJS.N.01141
4. Li CY, Chung KJNC, Ali OM, Chung ND, Li CH. Literature review of the causes of pain following total knee replacement surgery: prosthesis, inflammation and arthrofibrosis. EFORT Open Rev 2020; 5(9): 534-43. https://doi.org/10.1302/2058-5241.5.200033
5. Danoff JR, Goel R, Sutton R, Maltenfort MG, Austin MS. How much pain is significant? Defining the minimal clinically important difference for the visual analog scale for pain after total joint arthroplasty. J Arthroplasty 2018; 33(7): S71-S5. e2. https://doi.org/10.1016/j.arth.2018.02.029
6. Sial OK, Parise EM, Parise LF, Gnecco T, Bolaños-Guzmán CA. Ketamine: The final frontier or another depressing end? Behav Brain Res 2020; 383: 112508. https://doi.org/10.1016/j.bbr.2020.112508
7. Sohnen S, Dowling O, Shore-Lesserson L. Single dose perioperative intrathecal Ketamine as an adjuvant to intrathecal Bupivacaine: A systematic review and meta-analysis of adult human randomized controlled trials. J Clin Anesth 2021; 73: 110331. https://doi.org/10.1016/j.jclinane.2021.110331
8. Meshkat S, Rodrigues NB, Di Vincenzo JD, Ceban F, Jaberi S, McIntyre RS, et al. Pharmacogenomics of Ketamine: A systematic review. J Psychiatr Res 2022; 145: 27-34. https://doi.org/10.1016/j.jpsychires.2021.12.034
9. Sekar EB, Vijayaraghavan U, Sadiqbasha AM. Effect of Intravenous Dexmedetomidine on Spinal Anesthesia. Cureus 2021; 13(6): e16066. https://doi.org/10.7759/cureus.16066
10. Bhirud PH, Chellam S, Mote MN, Toal PV. Effects of intravenous Dexmedetomidine on spinal anesthesia and sedation–A comparison of two different maintenance infusions. J Anaesthesiol Clin Pharmacol 2020; 36(1): 78. https://doi.org/10.4103/joacp.JOACP_32_19
11. Sidhu S, Marine JE. Evaluating and managing bradycardia. Trends Cardiovasc Med 2020; 30(5): 265-272. https://doi.org/10.1016/j.tcm.2019.09.005
12. Yu Q, Qi J, Wang Y. Intraoperative hypotension and neurological outcomes. Curr Opin Anesthesiol 2020; 33(5): 646-650. https://doi.org/10.1097/ACO.0000000000000895
13. Craig D, Carli F. Bromage motor blockade score–a score that has lasted more than a lifetime. Can J Anesth 2018; 65(7): 837-838. https://doi.org/10.1007/s12630-018-1126-0
14. EL-Soudy EM, Atia AMA, Ali WM, Abdel Sabour AI. The effect of Ketamine as adjuvant in ultrasonic guided Supraclavicular brachial plexus block. Egypt J Hosp Med 2019; 76(7): 4643-4648. https://doi.org/10.21608/ejhm.2019.53248
15. Kataria AP, Singh H, Mohan B, Thakur M, Jarewal V, Khan S. Intrathecal nalbuphine versus Ketamine with hyperbaric Bupivacaine in lower abdominal surgeries. Anesth Essays Res 2018; 12(2): 366. https://doi.org/10.4103/aer.AER_17_18
16. Panigrahi S, Mhatre A. Comparative study between Ketamine and Bupivacaine intrathecally in lower abdomen and lower limb surgery. Int J Res Pharm Sci 2018; 8(3): 1-7.
17. Imani F, Varrassi G. Ketamine as adjuvant for acute pain management. Anesthesiol Pain Med 2019; 9(6): e96528. https://doi.org/10.5812/aapm.96528
18. Kitch BB. Out-of-hospital Ketamine: review of a growing trend in patient care. J Am Coll Emerg Physicians Open 2020; 1(3): 183-189. https://doi.org/10.1002/emp2.12041
19. Natoli S. The multiple faces of Ketamine in anaesthesia and analgesia. Drugs Context 2021; 10: 1-13. https://doi.org/10.7573/dic.2021-3-5
20. Nazir W, Khan AW. Use of Dexmedetomidine for Anesthesia and Pain Management. Anaesth Pain Intensive Care 2022; 26(5): 702-709. https://doi.org/10.35975/apic.v26i5.2044
21. Kapadia R, Kapdi M, Prajapati A. Comparison of analgesic efficacy of caudal Dexmedetomidine versus caudal tramadol with Bupivacaine 0.25% in pediatric infra-umbilical surgeries. Serbian J Anesth Intensive Ther 2022; 44(7-8): 99-111. https://doi.org/10.5937/sjait2208099K