e-ISSN: 0975-1556, p-ISSN:2820-2643
Available online on www.ijpcr.com
International Journal of Pharmaceutical and Clinical Research 2024; 16(2); 1773-1778

Original Research Article

Randomized Double-Blind Study: Evaluating Dexmedetomidine, Clonidine, and Nalbuphine as Adjuvants to Hyperbaric Ropivacaine 0.5% in Bilateral Total Knee Replacement under Combined Spinal-Epidural Anesthesia

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Received: 25-12-2023 / Revised: 23-01-2024 / Accepted: 20-02-2024
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Conflict of interest: Nil

Abstract:

Background: Successful postoperative outcomes require effective pain management in patients undergoing bilateral total knee replacement (TKR). Combined spinal-epidural anesthesia (CSEA) with ropivacaine reduces pain, and various adjuvants like dexmedetomidine, clonidine, and nalbuphine have been studied to improve it.

Methods: Dexmedetomidine, clonidine, and nalbuphine were added to hyperbaric ropivacaine 0.5% in bilateral TKR under CSEA in this randomized double-blind trial. Eighty patients were randomized into three groups and analyzed for intraoperative anesthesia, hemodynamic stability, postoperative analgesia, patient satisfaction, and adverse events.

Results: When compared with clonidine and nalbuphine, dexmedetomidine had faster onset of sensory block, better postoperative analgesia, lower heart rates, and improved patient satisfaction. Adverse occurrences were similar between groups.

Conclusion: Dexmedetomidine added to hyperbaric ropivacaine 0.5% in CSEA for bilateral TKR improved analgesia and patient satisfaction over clonidine and nalbuphine with acceptable safety.

Recommendation: Dexmedetomidine should be considered as a preferred adjuvant in CSEA for bilateral TKR to optimize pain management and patient outcomes.

Keywords: Total knee replacement, Combined spinal-epidural anesthesia, Dexmedetomidine, Clonidine, Nalbuphine.

Introduction

The management of postoperative pain in patients undergoing bilateral total knee replacement (TKR) surgeries is a pivotal factor that significantly impacts their recovery trajectory, overall satisfaction with the surgical experience, and the ultimate success of the procedure [1]. In this context, combined spinal-epidural anesthesia (CSEA) has gained prominence as a preferred anesthetic technique. CSEA offers the dual advantages of spinal and epidural anesthesia, combining the rapid onset and potent pain control provided by the former with the flexibility and prolonged duration of analgesia characteristic of the latter. Among the various local anesthetics employed in CSEA, ropivacaine stands out for its favorable safety profile, notably its reduced potential for cardiotoxicity and neurotoxicity compared to other agents in its class, making it a go-to choose for many practitioners [2].

Given the continuous quest for enhancing the analgesic efficacy and extending the duration of pain relief provided by ropivacaine, the role of adjuvants has come under scrutiny. Dexmedetomidine, clonidine, and nalbuphine emerge as significant adjuvants in this regard, each contributing uniquely to the analgesic regimen [3]. Dexmedetomidine, known for its selectivity as an α2-adrenergic agonist, not only prolongs the duration of spinal anesthesia but also offers the added benefit of sedation without compromising respiratory function. This characteristic makes it an invaluable addition to the anesthetic regimen, potentially improving the quality and duration of analgesia when combined with local anesthetics [4].

Clonidine, although less selective than dexmedetomidine as an α2-adrenergic agonist, is recognized for its capacity to extend the effects of

spinal anesthesia. However, its use requires careful consideration due to potential cardiovascular effects [5]. On the other hand, nalbuphine stands out among opioids for its unique profile as a combined κ-opioid receptor agonist and μ-opioid receptor antagonist, offering effective analgesia with a markedly reduced risk of respiratory depression. The incorporation of these adjuvants into the ropivacaine regimen is aimed not just at prolonging analgesia but also at elevating the quality of postoperative pain management, thereby minimizing the necessity for systemic analgesics and mitigating their associated adverse effects [6].

The core objective of this research is to meticulously compare the impacts of integrating dexmedetomidine, clonidine, and nalbuphine with hyperbaric ropivacaine 0.5% during CSEA in the context of bilateral TKR. Through a randomized double-blind trial, this study seeks to discern the most efficacious adjuvant by scrutinizing various critical parameters, including the onset and duration of analgesia, hemodynamic stability, patient satisfaction, and the incidence of side effects. The insights gleaned from this research endeavour will significantly contribute to refining pain management protocols for patients undergoing bilateral TKR, ultimately enhancing patient outcomes and satisfaction with the surgical experience.

Material and Methodology

Study Design: This study utilized a randomized, double-blind design to evaluate the impact of different aduvants when added to hyperbaric ropivacaine 0.5% in patients undergoing bilateral total knee replacement (TKR) under combined spinal-epidural anesthesia.

Study Setting: The study was conducted over two years at Civil Hospital, Badal.

Participants: A total of ninety patients were selected to participate in the study, all of whom were scheduled to undergo bilateral total knee replacement surgery under combined spinal-epidural anesthesia. The inclusion criteria consisted of adult patients who were 18 years of age or older and had an American Society of Anesthesiologists (ASA) physical status classification of I-III.

Exclusion Criteria:

1. Known allergy to study drugs.
2. Severe hepatic or renal impairment.
3. History of significant cardiovascular disease.

Bias: Efforts were made to reduce bias by using randomization and double-blinding techniques. Measures were taken to ensure that the allocation was concealed to prevent any biases in participant selection. Additionally, both the participants and researchers were blinded to minimize any potential biases in observation.

Variables: The main focus was on the intraoperative anesthesia parameters, such as the time it took for the sensory and motor block to take effect and how long it lasted. Additionally, postoperative analgesia was measured by assessing pain scores and the number of epidural top ups given. Hemodynamic stability, including blood pressure and heart rate, was also monitored. Lastly, patient satisfaction was evaluated as well. Secondary variables encompassed any adverse events or problems associated with the study interventions.

Data Collection: Data collection was conducted by well-trained research personnel. Before the surgery, various assessments were conducted to gather information about the patient's background, past medical records, and initial characteristics. Real-time recordings were made of the anaesthesia variables and hemodynamic variables during the surgery. After the surgery, we conducted evaluations to measure the level of pain experienced by the patients at specific time intervals. We also tracked the amount of pain medication they consumed and gathered feedback from the patients themselves. Any negative occurrences or problems were also recorded.

Procedure: Participants were assigned at random to one of three groups: the dexmedetomidine group (Group A), the clonidine group (Group B) or the nalbuphine group (Group C). The research protocol and drugs were made by an impartial investigator to ensure the integrity of the study.

Anaesthesia Technique: All patients received standard premedication according to the hospital protocol.

Anaesthesia was administered in all patients in sitting position.

Epidural Insertion: L3-L4 space was identified and local infiltration with 2 ml of 2% lignocaine was given. Epidural space was identified using 18 G Tuohy's needle and loss of resistance to saline. Epidural catheter was inserted and test dose with 3 ml of lignocaine with adrenaline was given in all patients. Catheter was fixed according to depth of needle and further procedure was done only if test dose comes out negative.

Sub-arachnoid block was given using a 25-gauge Quincke needle in L4-L5 interspace.

Patients received hyperbaric ropivacaine (0.5%) 3 ml along with either dexmedetomidine, nalbuphine or clonidine depending on group allocation making the total amount of drug given in subarachnoid block to 3.2 ml.

- In the dexmedetomidine (A) group, dexmedetomidine 20 micrograms was added to hyperbaric ropivacaine 0.5%.
- In the clonidine (B) group, clonidine 20 micrograms was added to hyperbaric ropivacaine 0.5%.
- In the nalbuphine (C) group, nalbuphine 20 micrograms was added to hyperbaric ropivacaine 0.5%.

After completion of surgery, all patients were monitored in PACU for first 24 hours. Epidural top-ups(rescue analgesia) was given using 8 ml of 0.025% of ropivacaine and pain scores were noted using VAS. Consistent protocols for anaesthesia, surgery, and postoperative care were adhered to for all patients.

Statistical Analysis: Descriptive statistics were employed to present the clinical and demographic details of the participants. Mean ± standard deviation were used to express continuous variables, while frequencies and percentages were used for categorical variables. Statistical tests such as ANOVA and chi-square test were utilized for contrasting variables among the three groups, as necessary. A p-value below 0.05 was deemed to have statistical significance.

Results

In a comprehensive study aimed at optimizing pain management in bilateral total knee replacement surgery, ninety patients were methodically assigned into three groups to assess the efficacy and safety of different adjuvants used with hyperbaric ropivacaine 0.5% under combined spinal-epidural anesthesia. The groups were distinguished based on the adjuvant administered: dexmedetomidine (30 patients), clonidine (30 patients), and nalbuphine (30 patients). This careful division ensured a robust comparison across the study, with each participant successfully completing the study procedure, allowing for a complete and thorough analysis of the results.

An initial assessment revealed no significant demographic or baseline characteristic differences among the groups, including age, gender distribution, body mass index (BMI), ASA (American Society of Anesthesiologists) physical status categorization, and duration of surgery. (Table 1) This parity ensured that the outcomes could be attributed with greater certainty to the pharmacological interventions rather than underlying patient differences.

Table 1: Characteristics of Study Participants

Variable	Group A (n=30)	Group B (n=30)	Group C (n=30)	P-value*
Age (years)	62.4 ± 6.8	63.1 ± 7.2	61.8 ± 6.5	0.562
Gender (male/female)	17/13	16/14	18/12	0.826
BMI	28.3 ± 3.1	27.9 ± 2.9	28.6 ± 3.2	0.691
ASA Physical Status (I/II/III)	10/12/8	10/11/9	9/13/8	0.914
Duration of surgery (mins)	118±2.6	117.6±2.8	118.2±3.0	0.680

Surgical Considerations and Outcomes:

Sensory Block: The patients in group A experienced a significantly faster onset of sensory block compared to the B and C groups, indicating a more efficient initiation of analgesia. However, the duration of the sensory block was consistent across all groups, suggesting that while dexmedetomidine accelerates the onset, it does not extend the overall length of sensory analgesia. (Table 2)

Table 2: Characteristics of Sensory Block

	Sensory Block			
	Onset (Mins)	P Value	Duration (Mins)	P Value
Group A	7.36±3.09	0.002	207.72±18.04	0.562
Group B	9.36±2.56	0.602	205.8±25.64	0.826
Group C	9.40±2.80	0.588	208.8±25.64	0.691

Motor Block: Analysis of the motor block onset and duration revealed no significant differences among the groups, underscoring the specificity of dexmedetomidine's benefits to sensory analgesia without impacting motor function adversely.

Table 3: Characteristics of Motor Block

	Motor Block			
	ONSET (Mins)	P value	DURATION (Mins)	P value
Group A	10.36±4.29	0.660	230.72±0.43	0.691
Group B	11.36±3.86	0.662	225.8±0.64	0.914
Group C	10.40±4.30	0.678	228.8±0.54	0.680

Postoperative Analgesia

Patients in group A reported significantly lower pain scores post-surgery at various time intervals, demonstrating its superior analgesic effect. Additionally, the need for rescue analgesics was notably lower in group A, highlighting its prolonged analgesic benefits and potential to reduce the reliance on additional pain medication. (Table 4 and Fig 1)

Table 4: Rescue analgesia

	Group A	Group B	Group C	P value
Time for first dose (after surgery)	148.19±13.86	128.20±11.86	126.18±10.66	<0.005
Total no. of doses in 24 hours	3	5	6	<0.005

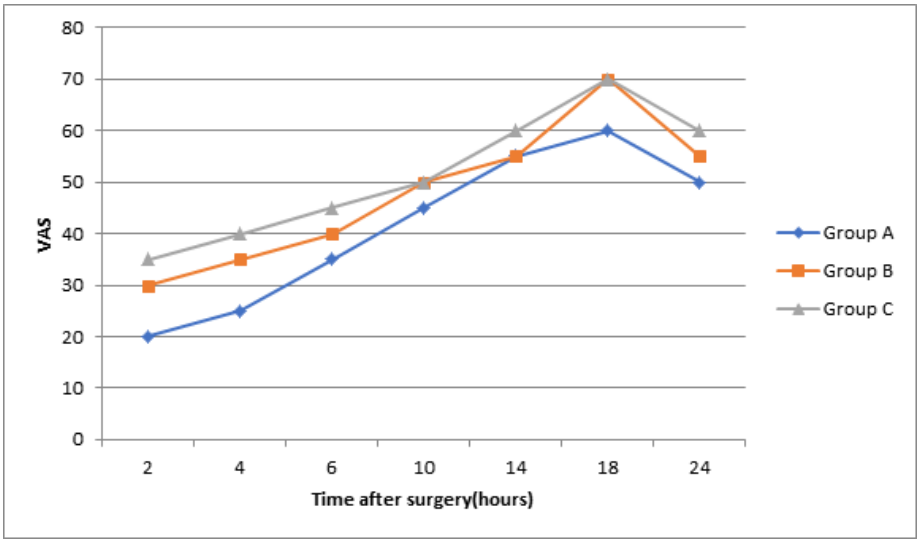

Figure 1: Post op Pain Scores

Hemodynamic Stability: The study closely monitored hemodynamic stability, finding no significant differences in intraoperative and postoperative blood pressure among the groups. However, dexmedetomidine recipients exhibited significantly lower heart rates during and immediately following surgery, suggesting an enhanced ability to maintain a more stable and favorable hemodynamic profile.

Patient Satisfaction and Recovery Experience

Overall Satisfaction: Patients in the group A reported higher satisfaction scores, indicating a better overall experience and outcome from the surgery and anesthesia.

Recovery Experience: These patients also described a quicker and smoother recovery process compared to those receiving clonidine and nalbuphine, further endorsing dexmedetomidine's role in facilitating a more comfortable postoperative period.

Unfavorable Incidents

The study meticulously recorded adverse events, noting that the incidence of nausea and vomiting was comparable across all groups, ensuring that the advantages of dexmedetomidine did not come at the cost of increased nausea or vomiting. Sedation levels were higher in the group A but remained within safe and acceptable limits, with no adverse outcomes reported.(Table 5)

Table 5: Adverse Events

	Group A	Group B	Group C
Hypotension (>20%fall in BP)	3	2	1
Bradycardia (>20% decrease in heart rate)	2	2	0
Nausea	2	1	1
Vomiting	0	0	0
Sedation	3	1	1
Dry Mouth	0	0	0
Urinary retention	1	0	0
Shivering	1	0	0

The integration of dexmedetomidine with hyperbaric ropivacaine 0.5% for patients undergoing bilateral total knee replacement under combined spinal-epidural anesthesia provided significant benefits, including accelerated onset of sensory block, enhanced postoperative pain relief, improved hemodynamic stability, and elevated patient satisfaction compared to clonidine and nalbuphine. The study's findings substantiate the effectiveness and safety of dexmedetomidine as a valuable adjuvant in clinical practice for this patient demographic, suggesting a pivotal role in advancing postoperative care and recovery.

Discussion

In recent years, a comprehensive study involving 90 patients undergoing bilateral total knee replacement surgery under combined spinal-epidural anesthesia has provided insightful data on the efficacy of adjunctive pharmacological treatments in enhancing surgical outcomes. These patients were meticulously divided into three groups, each receiving one of three drugs: dexmedetomidine, clonidine, or nalbuphine. This randomized allocation ensured an unbiased comparison across the groups, with demographic and baseline variables showing no significant differences, indicating a well-balanced study design [7].

The study revealed that the onset of sensory block was notably quicker in patients administered dexmedetomidine as compared to those receiving clonidine and nalbuphine. This faster onset did not compromise the duration of the sensory or motor block, which remained consistent across all groups. A significant reduction in postoperative pain scores and a decreased need for rescue analgesics were observed in the dexmedetomidine group, suggesting its superior analgesic efficacy. Moreover, these patients exhibited lower heart rates during and post-surgery, indicating a potential for enhanced hemodynamic stability, although blood pressure variations were minimal across the groups. Patient satisfaction, a critical measure of surgical recovery quality, was significantly higher in the dexmedetomidine group. This enhanced satisfaction could be attributed to the improved pain management and possibly the more stable hemodynamic profile offered by dexmedetomidine. The incidence of common side effects such as nausea, vomiting, and sedation was similar among the groups, demonstrating that the superior outcomes associated with dexmedetomidine did not come at the cost of increased adverse effects. The utilization of dexmedetomidine alongside hyperbaric ropivacaine 0.5% showcased a promising synergy, resulting in improved sensory block onset, postoperative pain relief, stable blood pressure, and overall patient satisfaction. This suggests dexmedetomidine's potential to significantly enhance the outcomes of bilateral total knee replacement surgeries performed under combined spinal-epidural anesthesia. Further investigations conducted in India have echoed these findings, highlighting the effectiveness and safety of using adjuvant agents like clonidine and dexmedetomidine with ropivacaine in anesthesia for surgical procedures, especially total knee replacements. These studies underscore the potential benefits of adjunctive treatments in surgical anesthesia, contributing to a broader understanding and adoption of these practices. One particular study explored the effects of different doses of dexmedetomidine combined with 0.2% ropivacaine in the Adductor Canal Block (ACB) for knee arthroscopic surgeries. Ninety patients were divided into three groups, with the third group receiving the highest dosage of dexmedetomidine and showing the longest duration of pain relief, minimal need for additional pain medications, and the highest levels of patient satisfaction. These outcomes not only facilitated earlier patient mobilization but also underscored the absence of negative side effects, highlighting the precise dosage of dexmedetomidine as a critical factor in optimizing postoperative recovery. Additional research focusing on cervical epidural anesthesia for modified radical mastectomy found that adding 2dexmedetomidine to a minimal dose of ropivacaine resulted in a quicker onset and longer duration of pain relief compared to adding clonidine. This study contributes valuable insights into the nuanced effects of these medications on the anesthesia process, reinforcing the importance of adjunctive treatments in enhancing surgical patient outcomes [8,9,10,11].

Collectively, these studies signify a shift in anesthesia practices in India, emphasizing the benefits of integrating medications like dexmedetomidine and clonidine with ropivacaine to improve pain management and patient satisfaction in surgical settings. This body of research advocates for a refined approach to anesthesia, where the addition of specific pharmacological agents can significantly enhance the quality of patient care and recovery.

Conclusion

This study offered valuable insights into optimizing postoperative pain management in patients going through bilateral total knee replacement under combined spinal-epidural anesthesia. It compared the effects of different adjuvants to hyperbaric ropivacaine 0.5%. In comparative studies, Dexmedetomidine has been shown to outperform clonidine and nalbuphine in various aspects. It provides a quicker onset of sensory block, better postoperative pain relief, reduced heart rates, and increased patient satisfaction. These findings indicate that dexmedetomidine can be a valuable

addition in this context, potentially decreasing the reliance on general pain relievers and enhancing the overall well-being and contentment of patients. Additional investigation and careful evaluation are necessary to fully incorporate dexmedetomidine into pain management strategies for bilateral total knee replacement under combined spinal-epidural anesthesia (CSEA), intending to improve patient outcomes and surgical effectiveness.

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