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Evaluating Dexmedetomidine and Ketamine for Control of Post-Operative Pain in Lower Segment Caesarean Section Surgeries

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ABSTRACT

Background: Effective control for postoperative pain that follows lower-segment cesarean section (LSCS) remains a clinical challenge, with the opioid-related side effects prompting the use of multimodal analgesia. Dexmedetomidine and ketamine have shown synergistic analgesic effects, but optimal dosing of dexmedetomidine in this combination is not well established. To compare the analgesic efficacy and safety of three different doses of dexmedetomidine combined with a fixed dose of ketamine for postoperative pain control after LSCS.

Methods: In this randomized controlled trial **RCT Registered (NCT07022821)**, 90 participants undergoing elective LSCS under spinal anesthesia were assigned to one of three groups (n=30 each) from March to May 2025 at Department of Anesthesia FMH Lahore. A random sampling technique was used for sample size distribution. All received ketamine 0.25 mg/kg/hr, with Group A receiving dexmedetomidine 0.02 µg/kg/hr, Group B 0.3 µg/kg/hr, and Group C 0.4 µg/kg/hr. Infusions continued for 24 hours postoperatively. Pain was assessed using the Visual Analog Scale (VAS) at multiple intervals. Secondary outcomes included opioid consumption, time to rescue analgesia, and adverse effects. Data were analyzed using SPSS v25. $p < 0.05$ was considered significant.

Results: Group C consistently exhibited the lowest VAS scores across all time points ($p < 0.001$), significantly lower opioid use (4.1 ± 1.3 mg nalbuphine), and the longest time to first rescue analgesia (8.3 ± 2.3 hrs). Mild sedation was more frequent in Group C, but it was not clinically significant.

Conclusion: A dexmedetomidine dose of 0.4 µg/kg/hr combined with ketamine provides superior postoperative analgesia after LSCS, with reduced opioid requirements and acceptable safety. This regimen may enhance the recovery and comfort of patients in obstetric anesthesia.

Keywords: Cesarean Section, Postoperative Pain, Dexmedetomidine, Ketamine, Analgesia, Patient-Controlled, Randomized Controlled Trial.

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INTRODUCTION

Postoperative pain after lower-segment caesarean section (LSCS) is a major clinical challenge. Most women report moderate to severe pain, which impairs early ambulation, maternal-infant bonding, and initiation of breastfeeding[1]. Poorly managed pain may also hinder recovery, lower maternal satisfaction, and contribute to post-surgical pain[2]. Although cesarean deliveries are common worldwide, the linked pain is often underestimated and minimally treated because of apprehension from the side effects of analgesics to the mother and the neonate[3,4].

Opioids are used regularly as an analgesic agent but contain unpleasant effects, including: nausea, vomiting, sedation, and respiratory depression[5,6]. These risks have encouraged the uptake of multimodal analgesia, where agents with different mechanisms of action are used to maximize analgesia while minimizing requirements for opioid drugs[7,8]. Among them, dexmedetomidine, a selective a2-adrenergic receptor agonist, and ketamine, a noncompetitive NMDA receptor antagonist, have demonstrated promising synergistic action[9]. Ketamine also acts as an analgesic agent and prevents central sensitization, while dexmedetomidine helps sedate and analgesize without causing significant respiratory depression[10].

Although these agents have been studied both individually and in combination, optimal dosing, particularly for dexmedetomidine, in a cesarean section is poorly explored. Previous studies reported the dose-dependent benefits, while others have observed the limited hemodynamic improvement and increased sedation. Therefore, a study was needed to compare the efficacy of different dose treatments.

Therefore, this study was conducted to compare the analgesic efficacy and safety of three different doses of dexmedetomidine combined with a fixed dose of ketamine for postoperative pain control after LSCS.

METHODS

This randomized controlled trial was conducted in the Department of Anesthesia at Fatima Memorial Hospital, Lahore, Pakistan from March to May 2025, following ethical approval (CPSP-ANS-060-2754 and FMH-27/03/25-1636) and RCT Registration (NCT07022821). Ninety pregnant females aged 18–50 years (ASA I–II) were scheduled for elective lower-segment Caesarean section under spinal anesthesia were enrolled via non-probability consecutive sampling. Inclusion criteria were age 18–50 years, ASA physical status I–II, elective LSCS under spinal anesthesia, and ability to provide informed consent. Exclusion criteria included known allergy to study drugs (dexmedetomidine, ketamine, bupivacaine, nalbuphine, paracetamol), major comorbidities (e.g., significant cardiac disease, epilepsy, uncontrolled hypertension), chronic opioid use or dependence, psychiatric illness affecting pain reporting or consent, emergency surgery, or inability to follow up.

Participants were randomly allocated (1:1:1) into three groups (n=30 each) using a computer-generated sequence and opaque envelope concealment; outcome assessors were blinded to group assignment, while care providers and patients were not. Sample size (n = 0) was calculated in OpenEpi 3.0.0 based on an expected effect size of 1.0, power 80%, a = 0.05, with no allowance for attrition. All patients received 2 mL of 0.75% hyperbaric bupivacaine intrathecally and intraoperative nalbuphine 0.1 mg/kg IV; postoperative paracetamol 1 g IV was given every eight hours, and rescue nalbuphine 0.1 mg/kg IV was administered for VAS > 5. Group A received dexmedetomidine 0.02 µg/kg/hr + ketamine 0.25 mg/kg/hr, Group B 0.3 µg/kg/hr + 0.25 mg/kg/hr, and Group C 0.4 µg/kg/hr + 0.25 mg/kg/hr via infusion for 24 hours. Pain (VAS) was measured at 0, 2, 4, 6, 8, 12, 16, 20, and 24 hours.

Baseline variables such as BMI, ASA class, and age were compared across groups using the ANOVA or the Kruskal Wallis test, considering appropriateness. Data were analyzed per protocol in SPSS v25: quantitative variables as mean ± SD via ANOVA with Bonferroni correction for repeated measures; categorical variables as frequencies via Chi-square test; $p < 0.05$ denoted significance. Missing data were not imputed.

RESULTS

Table 1. Demographic Characteristics of Study Participants

Variable	Group A	Group B	Group C	p-value
Age (years)	28.4 ± 4.1	27.9 ± 3.8	28.7 ± 4.0	0.594
BMI (kg/m²)	26.1 ± 2.5	25.8 ± 2.8	26.3 ± 2.6	0.690
ASA I/II (%)	18 (60%) / 12 (40%)	19 (63%) / 11 (37%)	18 (60%) / 12 (40%)	0.913

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A total of 90 patients were enrolled and randomized equally into three groups (n = 30 each). Baseline characteristics such as age, BMI, and ASA classification were comparable across the groups, ensuring homogeneity and minimizing confounding factors. Results are shown in **Table 1**.

Table 2. Mean Pain Scores (VAS) at Various Time Points

Time (hours)	Group A	Group B	Group C	F-value	p-value
2	4.9 ± 1.1	3.5 ± 1.0	2.6 ± 0.8	34.6	<0.001
6	5.1 ± 1.0	3.9 ± 0.9	2.9 ± 0.7	40.2	<0.001
12	4.3 ± 0.9	3.2 ± 0.7	2.2 ± 0.6	45.8	<0.001
24	3.0 ± 0.8	2.4 ± 0.6	1.5 ± 0.5	36.7	<0.001

The primary outcome, postoperative pain scores, was measured at nine different time intervals using the Visual Analog Scale (VAS). Group C consistently showed significantly lower pain scores than Groups A and B at all time points. Group B demonstrated intermediate results, and Group A had the highest pain scores. Mean pain Scores can be seen in **Table 2.**

Table 3. Opioid Use and Rescue Analgesia

Group	Total Nalbuphine (mg)	Time to First Rescue (hrs)	Sedation Incidence (%)
Group A	9.6 ± 2.5	3.2 ± 1.4	6%
Group B	6.8 ± 2.0	5.6 ± 1.9	10%
Group C	4.1 ± 1.3	8.3 ± 2.3	15%
p-value	**<0.001**	**<0.001**	**0.336**

Group C (0.4 µg/kg/hr dexmedetomidine) exhibited the lowest mean VAS scores throughout the 24-hour observation period, with statistically significant differences ($p < 0.001$) at each measured interval. Group B (0.3 µg/kg/hr) also showed better pain control than Group A (0.02 µg/kg/hr), suggesting a dose-dependent improvement in analgesia.

Secondary outcomes included total opioid (nalbuphine) consumption, time to first rescue analgesia, and incidence of sedation. These findings further supported the primary outcome, with Group C showing superior performance. The results of these are shown in **Table 3**.

Patients in Group C required significantly less rescue opioid and had a prolonged time to first analgesic request, indicating more sustained analgesia. Although mild sedation was more frequent in Group C, no serious adverse events were reported, and no patient required pharmacologic reversal or ICU transfer.

The study showed a distinct and statistically significant advantage of administering higher doses of dexmedetomidine (0.4 µg/kg/hr) with ketamine (0.25 mg/kg/hr) to provide post-operation analgesia in LSCS. The most effective pain control was achieved using this regimen, and it minimized opioid usage and longer periods of being pain-free without endangering the patient.

DISCUSSION

The present study offered comparative information on the efficacy of various doses of dexmedetomidine, administered with a fixed dose of ketamine, on the management of postoperative pain after LSCS. The results showed that higher doses yielded better relief from pain in a dose-dependent manner. Unlike some studies from the past, which utilized only one dose, this study compared multiple doses, which allowed clearer insight into better titration [11,12].

The analgesic synergy between ketamine and dexmedetomidine is probably caused by their complementary action: NMDA receptor antagonism in the case of ketamine and a 2-adrenoceptor agonism in the case of dexmedetomidine, respectively [13,14]. In preclinical studies, ketamine has been shown to reduce central sensitization, whereas dexmedetomidine has been shown to increase descending inhibitory pathways, causing prolonged analgesia and suppressed hyperalgesia responses [15,16]. In contrast to some studies that involved the same protocol, this study demonstrated that controlled infusion rate could lead to better tolerability[17,18]. Also, retrospective data from tertiary centers demonstrate lower incidences of opioid related side effects based on dexmedetomidine-ketamine protocols [19].

An intriguing finding was that Group C experienced a significantly longer time to first rescue analgesia, indicating a longer-lasting effect and, consequently, fewer disruptions to rest and early

ambulation [20]. Mobilization within hours is an essential element of the enhanced recovery after surgery (ERAS) protocols that correlate with shorter hospitalization and aid in mother–infant bonding [21,22]. The decreased demand for opioids also reduces their risks of side effects such as: sedation, nausea, and respiratory depression [23].

Studies showed that with these analgesics, hemodynamic stability persisted without becoming clinically evident hypotension or bradycardia [24]. Although mild sedation was more common in Group C, patient safety was not jeopardized, and discharge was delayed. These observations confirmed the safety profile of dexmedetomidine, even in enhanced dosages, if given under close supervision and standardized procedures [25].

Clinical limitations include one-center layout and a short (24-hour) follow-up period that does not allow assessing any chronic pain development. Also, the study was excluding emergency LSCS cases, so findings are not generalizable to all obstetric populations.

To our knowledge, this study is one of the first to apply randomization while examining three ways of administering dexmedetomidine along with ketamine for LSCS. The 0.4 µg/kg/hr dose seemed to provide enhanced antinociceptive and opioid-sparing effects with minimal safety concerns, therefore, a strong contender for daily use in multimodal analgesia approaches for LSCS. Future research could be done on whether this regime played a role in better breastfeeding or reduced postpartum depression among participants or not.

CONCLUSION

The association between dexmedetomidine and ketamine provided additive opioid-sparing analgesia for patients with lower-segment cesarean sections. Combining a dexmedetomidine dose of 0.4 µg/kg/hr and a ketamine dose of 0.25 mg/kg/hr outperformed the other two regimens in terms of significant analgesic benefit with minimal side effects. These findings substantiated the integration of this combination into the routine multimodal postoperative analgesia protocols, improving recovery and maternal comfort after cesarean delivery. Future studies should incorporate multicenter studies with longer follow-up for the generalizability of results.

LIST OF ABBREVIATIONS

LSCS Lower Segment Caesarean Section
VAS Visual Analog Scale
ASA American Society of Anesthesiologists
ERAS Enhanced Recovery After Surgery
IV Intravenous
µg/kg/hr Micrograms per kilogram per hour
mg/kg/hr Milligrams per kilogram per hour
RCT Randomized Controlled Trial
CPSP College of Physicians and Surgeons Pakistan

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CONFLICT OF INTEREST

None

ETHICAL APPROVAL

This randomized controlled trial was conducted in the Department of Anesthesia at Fatima Memorial Hospital, Lahore, Pakistan from March to May 2025, following ethical approval (CPSP-ANS-060-2754 and FMH-27/03/25-1636).

AUTHORS' CONTRIBUTIONS

Equal Contribution as per ICMJE.

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