"Low-Dose Ketamine For Postoperative Analgesia In Maxillofacial Surgery: A Randomized Controlled Trial"

Dr. kasturi M Patel[1] , Dr. P B Jamale[2] , Ajay Kshirsagar[3] , Dr. Girish C Joglekar[4]

[1](Resident, Department of Anaesthesiology Krishna institute of medical sciences Deemed to be University,karad)
[2](Professor,Department of anaesthesiology Krishna institute of medical sciences Deemed to be university,karad)
[3](Resident, Department of Anaesthesiology krishna institute of medical sciences Deemed to be University,karad)
[4](Resident, Department of Anaesthesiology krishna institute of medical sciences Deemed to be University,karad)
Corresponding Author-
Dr. Kasturi M Patel - Resident Department of Anaesthesiology Krishna institute of medical sciences Deemed to be University,karad

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Abstract

Background: Effective postoperative pain control is essential for recovery, yet reliance on opioids poses public health concerns due to dependence and adverse effects. This study investigates the efficacy of low-dose intravenous ketamine as an adjunct for postoperative analgesia in patients undergoing maxillofacial surgery.
Methods: A randomized, double-blind, placebo-controlled trial was conducted among 60 patients (ASA I and II) scheduled for elective maxillofacial surgery. Participants were randomly assigned to receive either low-dose ketamine (0.5 mg/kg bolus, followed by 5 mcg/kg/min infusion) or normal saline as placebo. Pain scores were assessed using the Visual Analogue Scale (VAS) at multiple postoperative intervals, along with total opioid consumption.
Results: Patients in the ketamine group experienced significantly lower VAS scores at 30 minutes, 1 hour, 2 hours, and 6 hours postoperatively ($p < 0.05$). Total opioid consumption in the first 24 hours was also significantly reduced ($p < 0.01$). No severe adverse effects were observed.
Conclusion: Low-dose ketamine effectively reduces postoperative pain and opioid requirement following maxillofacial surgery. Its incorporation into perioperative protocols may enhance patient outcomes and reduce opioid burden, which has wider public health benefits in Southeastern Europe.

Introduction

Postoperative pain remains a significant concern in surgical care, particularly in maxillofacial procedures, which often involve manipulation of highly innervated structures such as the mandible, maxilla, temporomandibular joint, and associated soft tissues. These surgeries, whether performed for trauma, tumors, or reconstructive purposes, frequently result in moderate to severe pain in the immediate postoperative period, which, if not managed adequately, can adversely affect patient outcomes, recovery time, and overall satisfaction with care[1].

Effective postoperative analgesia is essential not only for humanitarian reasons but also for physiological recovery. Poor pain control has been associated with delayed wound healing, impaired respiratory function, increased risk of thromboembolic events due to immobility, and higher chances of developing chronic post-

surgical pain syndromes[2]. Traditionally, opioids have been the cornerstone of postoperative pain management, but their side effect profile—which includes nausea, vomiting, constipation, respiratory depression, sedation, and dependence—has prompted the need for alternative or adjunct analgesic strategies[3].

Ketamine, a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist, has emerged as a promising agent in the realm of multimodal analgesia. Initially introduced as an anesthetic, ketamine at subanesthetic doses has demonstrated analgesic, anti-hyperalgesic, and opioid-sparing properties in various surgical settings[4]. Its mechanism involves inhibition of central sensitization and prevention of "wind-up" phenomena in the spinal cord, which are pivotal in the pathogenesis of postoperative and chronic pain[5]. Additionally, ketamine modulates opioid receptors and reduces the need for higher opioid doses, thereby minimizing opioid-related side effects[6].

Clinical trials and systematic reviews have increasingly supported the efficacy of perioperative low-dose ketamine infusion in reducing pain scores and opioid requirements, particularly in surgeries with high pain burden such as orthopedic and abdominal procedure[7,8]. However, despite the growing evidence, its application in maxillofacial surgery remains under-researched, particularly in low- and middle-income countries where both opioid access and public health infrastructure may be limited[9].

In the context of Southeastern Europe and similar regions where healthcare systems are often under economic strain and face regulatory restrictions on opioid use, the incorporation of low-dose ketamine in perioperative pain management protocols offers a cost-effective, accessible, and potentially safer alternative[10]. Furthermore, enhancing recovery through improved pain management aligns with the principles of Enhanced Recovery After Surgery (ERAS), which is increasingly being adopted across surgical disciplines[11].

This study was designed to investigate the effectiveness of perioperative low-dose ketamine infusion in reducing postoperative pain and opioid consumption in patients undergoing maxillofacial surgery. By evaluating pain scores, rescue analgesia requirements, and side effect profiles, we aim to provide evidence that may inform clinical practice and public health policy in Southeastern European and comparable healthcare settings.

Methods

Study Design and Setting

A prospective, randomized, double-blind, placebo-controlled study was conducted at the Department of Oral and Maxillofacial Surgery in a tertiary hospital setting over six months.

Inclusion and Exclusion Criteria

Patients aged 18–60 years, classified as ASA I or II, and scheduled for elective maxillofacial surgery under general anesthesia were enrolled. Exclusion criteria included known hypersensitivity to ketamine, history of psychiatric illness, chronic analgesic use, pregnancy, and elevated intraocular or intracranial pressure.

Randomization and Blinding

Sixty patients were randomly allocated into two groups (n=30 each):

- **Group K (Ketamine):** Received 0.5 mg/kg ketamine IV bolus followed by 5 mcg/kg/min infusion during surgery.
- **Group S (Saline):** Received an equal volume of normal saline.

Randomization was achieved using computer-generated numbers and concealed in opaque envelopes. Both patients and assessors were blinded to group assignments.

Pain Assessment and Outcomes

Pain was assessed using the 10-point Visual Analogue Scale (VAS) at 30 min, 1 hr, 2 hrs, 6 hrs, and 24 hrs postoperatively. Additional outcomes included total opioid consumption (measured in mg of tramadol), time to first rescue analgesia, sedation levels (Ramsay scale), and adverse events.

Statistical Analysis

Data was analyzed using SPSS software. Categorical variables were assessed with the chi-square test, while continuous variables were analyzed using t-tests or Mann-Whitney U-tests were appropriate. A p-value of <0.05 was considered statistically significant.

Results

Demographic and Baseline Characteristics

A total of 60 adult patients undergoing elective maxillofacial surgery were enrolled and randomized equally into two groups (Group K – ketamine; Group S – saline), each consisting of 30 participants. Demographic characteristics were comparable across groups. In Group K, the majority of patients were aged 50 years or older (30.0%), whereas Group S had a slightly larger proportion of participants under 30 years of age (33.3%) (Table 1).

Table 1. Age Distribution by Treatment Group

Age Group	Group K (n = 30)	Group S (n = 30)
<30 years	6 (20.0%)	10 (33.3%)
30–39	7 (23.3%)	8 (26.7%)
40–49	8 (26.7%)	6 (20.0%)
≥50	9 (30.0%)	6 (20.0%)

The American Society of Anesthesiologists (ASA) physical status distribution indicated most patients were ASA Grade I in both groups, with a slightly higher proportion in Group S (66.7%) (Table 2).

Table 2. ASA Physical Status Classification

ASA Grade	Group K (n = 30)	Group S (n = 30)
I	17 (56.7%)	20 (66.7%)
II	13 (43.3%)	10 (33.3%)

Surgical procedures were varied but evenly distributed across both groups. TMJ ankylosis, facial trauma, and mandibular fractures were the most common indications for surgery (Table 3).

Table 3. Distribution of Surgeries by Treatment Group

Surgery Type	Group K (n = 30)	Group S (n = 30)
Facial Trauma	9 (30.0%)	7 (23.3%)
TMJ Ankylosis	8 (26.7%)	9 (30.0%)
Mandibular Fracture	5 (16.7%)	9 (30.0%)
Maxillary Cyst	6 (20.0%)	4 (13.3%)
Zygomatic Fracture	2 (6.7%)	1 (3.3%)

Postoperative Pain Scores

Pain levels assessed using the Visual Analogue Scale (VAS) revealed that patients in the ketamine group experienced significantly lower pain scores at 30 minutes, 1 hour, 2 hours, and 6 hours postoperatively

compared to the control group ($p < 0.05$). At 24 hours, the difference narrowed and was not statistically significant (Table 4).

Table 4. Mean Postoperative VAS Pain Scores

Time Post-Op	Group K (Mean ± SD)	Group S (Mean ± SD)
30 minutes	2.5	4.2
1 hour	2.8	4.5
2 hours	3.0	4.8
6 hours	3.2	5.1
24 hours	3.4	4.9

Analgesic Requirements

Ketamine infusion significantly reduced the requirement for postoperative opioids. The average tramadol requirement in Group K was 72 mg over 24 hours, compared to 122 mg in Group S ($p < 0.01$). Additionally, fewer patients in Group K required any rescue analgesia (12 vs. 26 patients in Group S) (Table 5).

Table 5. Postoperative Analgesic Consumption and Rescue Analgesia

Group	Mean Tramadol Use (mg)	Patients Requiring Rescue Analgesia
Group K	72	12
Group S	122	26

Side Effects

The incidence of side effects was low in both groups. Nausea and vomiting were the most commonly reported symptoms, with no significant intergroup difference. Notably, there were no reports of hallucinations or other psychotomimetic effects in either group (Table 6).

Table 6. Postoperative Side Effects Comparison

Side Effect	Group K (n = 30)	Group S (n = 30)
Nausea	4	5
Vomiting	2	3
Dizziness	1	2
Hallucination	0	0

Patient Satisfaction

Patient satisfaction was measured using a four-level ordinal scale. A greater proportion of patients in the ketamine group reported being "very satisfied" (53.3%) compared to the saline group (26.7%). Conversely, dissatisfaction was higher in Group S (13.3%) than in Group K (3.3%) (Table 7).

Table 7. Patient Satisfaction Ratings

Satisfaction Level	Group K (n = 30)	Group S (n = 30)
Very Satisfied	16	8
Satisfied	10	10
Neutral	3	8
Dissatisfied	1	4

Discussion

The findings of this randomized controlled study support the hypothesis that perioperative low-dose ketamine infusion is a safe and effective adjunct for managing postoperative pain in patients undergoing maxillofacial surgery. Compared to the control group, patients who received ketamine exhibited significantly lower pain scores in the early postoperative period (30 minutes to 6 hours), required substantially less opioid analgesia, and reported higher levels of satisfaction with their pain control. Importantly, these benefits were achieved without a corresponding increase in adverse events, including the psychotomimetic side effects often associated with ketamine.

Our results demonstrate that the ketamine group had lower mean VAS scores at all time points up to 24 hours postoperatively, with statistically significant reductions observed in the first six hours. This suggests that ketamine's NMDA receptor antagonism is particularly effective in mitigating acute nociceptive and central sensitization mechanisms that dominate early postoperative pain responses. Additionally, the opioid-sparing effect was marked, with a 41% reduction in total tramadol consumption in the ketamine group. This is clinically significant, considering the side effect burden and dependence potential of opioids, especially in resource-limited settings where careful opioid stewardship is essential.

Our findings align with several earlier studies across various surgical domains. A systematic review by Jouguelet-Lacoste et al. concluded that intravenous low-dose ketamine consistently reduces postoperative opioid consumption and, to a lesser extent, pain scores, without major side effects when used for up to 48 hours postoperatively [6]. Similarly, Brinck et al. reported that patients undergoing laparoscopic cholecystectomy who received ketamine intraoperatively had reduced postoperative opioid requirements and delayed first analgesic request, echoing the outcomes in our cohort[5].

In maxillofacial and head-and-neck surgeries specifically, data are more limited. However, Sarvjeet Kaur et al. observed that intraoperative low-dose ketamine significantly reduced postoperative morphine consumption and pain scores in patients undergoing open cholecystectomy [9], which aligns with our findings despite the differences in surgical type. Notably, our study expands this evidence base by demonstrating ketamine's analgesic efficacy in maxillofacial procedures—a domain characterized by complex sensory innervation and high variability in pain perception.

Furthermore, our patient satisfaction results correlate with findings from Subramaniam et al., who reported enhanced patient-reported outcomes, including satisfaction and comfort, when ketamine was used adjunctively with opioids[11]. This suggests that even moderate reductions in pain and opioid-related side effects can meaningfully influence the patient's subjective surgical experience.

One of the key strengths of this study is its robust randomized, double-blind, placebo-controlled design, which reduces potential bias and enhances the reliability of findings. Moreover, the standardization of anesthesia and surgical protocols minimize confounding variables that could influence pain outcomes. The inclusion of diverse maxillofacial procedures also increases the external validity of the study and reflects real-world clinical practice.

Additionally, our use of multiple outcome measures—including VAS scores, rescue analgesia needs, side effects, and satisfaction levels—provides a comprehensive assessment of ketamine's analgesic value. The 48-hour monitoring window, aligned with current enhanced recovery after surgery (ERAS) protocols, also ensures clinical relevance in modern perioperative care.

Despite its strengths, several limitations should be acknowledged. First, the sample size (n=60) may be underpowered to detect rare adverse events, such as psychotomimetic effects or delayed postoperative complications. Second, the study was conducted at a single center, which may limit the generalizability of results to different patient populations or healthcare settings. Additionally, while we assessed pain and opioid consumption for 24 hours postoperatively, the longer-term impact of ketamine on chronic postoperative pain, functional recovery, and quality of life was not explored.

Finally, our study relied on subjective measures of pain and satisfaction, which may be influenced by cultural, psychological, and individual expectations. However, such tools are widely accepted in clinical research and remain essential in evaluating patient-centered outcomes.

Given the global movement toward opioid stewardship and multimodal analgesia, the integration of low-dose ketamine into postoperative protocols offers a compelling, evidence-based strategy to enhance

surgical recovery, especially in regions with constrained healthcare resources like parts of Southeastern Europe. Our findings support the use of ketamine as a viable option to reduce opioid reliance and improve patient satisfaction, without compromising safety.

Conclusion

This randomized controlled trial demonstrates that perioperative low-dose ketamine infusion is a safe, effective, and well-tolerated adjunct for postoperative pain management in patients undergoing maxillofacial surgery. By significantly reducing pain intensity and opioid requirements in the early postoperative period, ketamine contributes to improved patient comfort and satisfaction without increasing the incidence of adverse effects. These findings support the integration of ketamine into multimodal analgesia protocols, particularly in regions facing opioid-related challenges or limited access to advanced pain management resources. Broader implementation of this strategy may enhance surgical outcomes and align with public health goals of reducing opioid dependence while improving the quality of perioperative care. Future multicentric studies with larger sample sizes and longer follow-up periods are recommended to explore the long-term benefits and applicability across other surgical disciplines.

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