

Research Article

Low-dose Ketamine Infusion for Prevention of Chronic Post-surgical Pain

Liaquat Ali¹, Qammar Yaqub², Aiman Ikram³, Muhammad Aslam⁴

¹Assistant Professor ENT, Mohi ud Din Islamic Medical College, Mirpur AJK

²Senior Registrar ENT, Mohi ud Din Teaching Hospital Mirpur, AJK

³Senior Registrar General Surgery, Mohi-ud-Din Islamic Medical College, Mirpur AJK

⁴Associate Professor of Anaesthesia, Mohi-ud-Din Islamic Medical College, Mirpur AJK

Corresponding author: Muhammad Aslam, Associate Professor of Anaesthesia, Mohi-ud-Din Islamic Medical College, Mirpur AJK, **Email:** draslam201@hotmail.com

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ABSTRACT

Background: Chronic post-surgical pain is among the dominant issues of post-surgery complications that may persist after a period of several months and impact the daily functioning, sleep patterns, and quality of life negatively. The clinical problem is linked to the guard of the transition relationship between acute postoperative pain and chronic pain despite the efforts to develop better methods of managing the former. Ketamine at low dosage with its anti-hyperalgesic and opioid-sparing effect has become a promising adjunctive agent that could improve the results of postoperative pain.

Objective: To assess the role of low-dose ketamine infusion in the prevention of chronic post-surgical pain among patients undergoing elective surgical procedures.

Methodology: It was a retrospective comparative cohort study that was conducted at Mohi ud Din Teaching Hospital Mirpur, AJK between February 2025 and July 2025. The sample size was 72 patients who were divided into two groups (those who received a low dose of ketamine infusion during perioperation n=36) and those who did not receive ketamine (n=36). Data were obtained using medical records, anesthesia charts, post-operative records and follow-up records. The baseline parameters, perioperative parameters, post-operative pain outcomes, opioid use, and 1 and 3 months chronic post-operative pain outcomes were observed. Data comparison was done with the assistance of SPSS 26 and the p-value value of 0.05 was considered.

Results: Patients who received low-dose ketamine infusion showed lower intraoperative opioid consumption and reduced postoperative pain scores compared with the control group. The ketamine group also had a longer time to first rescue analgesia and lower postoperative opioid requirement. Persistent pain at 1 month and 3 months was less frequent in the ketamine group. In addition, pain-related interference with daily activities and sleep disturbance were less common among patients who received ketamine. Adverse effects were generally mild, and no serious complication was observed.

Conclusion: Low-dose ketamine infusion was associated with improved perioperative pain control, reduced opioid requirement, and a lower frequency of chronic post-surgical pain. These findings suggest that ketamine may be a useful adjunct in multimodal analgesic strategies aimed at preventing long-term postoperative pain.

Keywords: Ketamine, chronic post-surgical pain, postoperative analgesia, opioid-sparing effect, perioperative pain management

INTRODUCTION

Post-surgical pain is a normal clinical phenomenon that in certain patients fails to resolve with the standard tissue healing, and instead was prolonged to weeks or months, causing chronic post-surgical pain. This type of pain has been becoming clinically more significantly important due to its possible

impact on mobility, functional capacity, sleep disturbance, as well as negatively affect emotional well-being and quality of life. The chronic post-surgical pain is additional to healthcare use and extends the recovery beyond the acute post-surgery period. Consequently, the prevention of the occurrence of persistent postoperative pain

has become the subject of contemporary perioperative care [1-3].

Chronic post-surgical pain is a multifactorial problem and affects preoperative, intraoperative, and postoperative factors. Central sensitization and prolonged presence of pain are caused by severe acute postoperative pain, nerve damage and inflammatory reactions, type of surgery and repetitive nociceptive input. Poorly managed early pain is also a factor of special concern, as it can tend to lead to the development of acute pain into a chronic pain condition. Consequently, the interventions with the ability to decrease the level of pain during and right after the surgery can also be used to restrain the subsequent pain chronicity [4-7].

Ketamine is a famous N-methyl -D-aspartate (NMDA) receptor antagonist that has the analgesic, anti-hyperalgesic and opioid-sparing properties. Ketamine has also been adopted as a complement to the traditional analgesic routine in low doses at the perioperative stage. The advantage it proposes is that it will reduce central sensitization, postoperative analgesic need, and enhance pain management without significant respiratory depression. These characteristics render ketamine a potentially useful agent in preventing the process of the progression of acute postoperative pain to chronic post-surgical pain, particularly among patients undergoing the procedures that are characterized by moderate to severe post-surgical pain [8-10].

Despite multiple researches investigating the use of ketamine as acute postoperative analgesia, the research on the issue of its efficiency in preventing chronic post-surgery pain is inconsistent, and more information gathered in clinical contexts is still requested. The current research paper was thus developed to determine how low-dose ketamine infusion would help to reduce the occurrence of chronic post-surgical pain in patients subjected to elective surgical operations. The study also evaluated its effect on perioperative opioid requirement, postoperative pain scores, and related adverse effects.

METHODOLOGY

This study was carried out as a retrospective comparative cohort study at Mohi ud Din Teaching Hospital Mirpur, AJK over a study

period from February 2025 to July 2025. The objective was to assess the role of low-dose ketamine infusion in reducing the development of chronic post-surgical pain among patients undergoing elective surgical procedures. A total of 72 patients were included in the study. Based on perioperative analgesic management documented in medical records, the patients were divided into two groups: those who had received low-dose ketamine infusion during the perioperative period and those who had not received ketamine and served as the control group. Each group comprised 36 patients.

The study reviewed the records of adult patients of both genders who had surgery under general anesthesia within the study period. The inclusion criteria were having full perioperative and follow up data in the hospital record. The patients who had a chronic pain disorder history, were using opioids chronically, and had major psychiatric illness, had significant hepatic or renal dysfunction, were known to be allergic to ketamine, or had only incomplete records were excluded during the analysis. The information on patient files, anesthesia charts, postoperative notes, and follow-up records were gathered with the help of a structured data extraction form.

Baseline variables that were collected on each patient consisted of age, gender, body mass index, ASA status, type of surgery and preoperative pain status where possible. Perioperative measures were period of operation, period of anesthesia, intraoperative opioid use, use of other analgesics, and the administration of low dose ketamine infusion. There were also records of early postoperative pain as pain scores in the first 48 hours, overall postoperative opioid need, time to first rescue analgesia, and additional analgesic medication need.

In the evaluation of chronic post-surgical pain, the follow-up data was taken in the outpatient records or measured during the postoperative reviews. Pain was measured 1 month and 3 months postoperative. The most significant finding was the frequency of persistent post-operative pain at the 3-month. Where pain severity was reported, some of the secondary outcomes were pain severity, interference with daily activities, sleep disturbance by pain and patient satisfaction with pain management. The medical record was also used to extract

adverse effects like nausea, vomiting, dizziness, hallucinations, sedation, hypotension, and bradycardia.

Data entry and analysis were performed on SPSS version 26. The mean age, body mass index, duration of surgery, pain scores, and opioid use were reported as mean with a standard deviation whereas qualitative variables, including gender, ASA class, type of surgery, chronic pain status, and adverse effects were presented as frequency and percentage. The independent sample t-test was utilized with continuous variables and the chi-square test employed with categorical variables to compare the two groups. The p-value of 0.05 and below was regarded as statistically significant.

RESULTS

The study involved 72 patients, and they were split into two groups: the ketamine group (36 participants) and the control group

(36 participants). The analysis compared baseline profile, perioperative characteristics, early postoperative pain outcomes, chronic post-surgical pain outcomes, and adverse effects between the two groups. The ketamine group demonstrated better pain-related outcomes, particularly in relation to postoperative analgesic requirement and the frequency of chronic post-surgical pain at follow-up.

Table 1 describes demographics and baseline clinical characteristics of the study participants. The two groups were similar in terms of age, sex ratio, body mass index, ASA, and type of surgery showing a proper match at baseline. There was no statistically significant difference between the two groups at baseline on any variable and this indicated that there were reduced chances of later differences in pain outcomes being caused by preoperative imbalance.

Table 1: Overview of demographic and clinical features of the participants included in the study (n = 72)

Variable	Ketamine Group (n=36)	Control Group (n=36)	p-value
Age (years), mean $\pm$ SD	41.8 $\pm$ 10.6	43.1 $\pm$ 9.8	0.591
Male, n (%)	20 (55.6)	18 (50.0)	0.637
Female, n (%)	16 (44.4)	18 (50.0)	0.637
BMI (kg/m ²), mean $\pm$ SD	26.1 $\pm$ 3.4	25.7 $\pm$ 3.7	0.648
ASA I, n (%)	19 (52.8)	17 (47.2)	0.635
ASA II, n (%)	17 (47.2)	19 (52.8)	0.635
Preoperative pain score (VAS 0–10), mean $\pm$ SD	2.3 $\pm$ 1.1	2.4 $\pm$ 1.0	0.712
Abdominal surgery, n (%)	15 (41.7)	14 (38.9)	0.808
Orthopedic surgery, n (%)	12 (33.3)	13 (36.1)	0.803
Thoracic surgery, n (%)	9 (25.0)	9 (25.0)	1.000

Table 2 summarizes the intraoperative and immediate perioperative characteristics of both study groups. The duration of surgery and anesthesia was similar in the two groups, while intraoperative opioid

consumption was lower in the ketamine group. This finding suggests that low-dose ketamine infusion contributed to an opioid-sparing effect during the operative period.

Table 2. Intraoperative characteristics and analgesic exposure

Variable	Ketamine Group (n=36)	Control Group (n=36)	p-value
Duration of surgery (minutes), mean $\pm$ SD	96.4 $\pm$ 21.5	99.2 $\pm$ 24.1	0.607
Duration of anesthesia (minutes), mean $\pm$ SD	118.7 $\pm$ 26.2	121.5 $\pm$ 28.0	0.664
Intraoperative fentanyl consumption (mcg), mean $\pm$ SD	118.5 $\pm$ 24.7	144.2 $\pm$ 31.6	0.001
Additional intraoperative analgesic required, n (%)	8 (22.2)	17 (47.2)	0.026
Hemodynamic instability, n (%)	3 (8.3)	5 (13.9)	0.455

Table 3 represents the results of early postoperative pain during the first 48 hours

after operation. The pain scores at 6, 12, 24, and 48 hours were always lower in the ketamine group and the time to first rescue

analgesia was higher in comparison with the control group. Better acute pain control was also reflected in less opioid usage by the

patient during postoperative care as they received ketamine infusion.

Table 3. Early postoperative pain and analgesic outcomes

Variable	Ketamine Group (n=36)	Control Group (n=36)	p-value
VAS at 6 hours, mean $\pm$ SD	3.4 $\pm$ 1.1	4.8 $\pm$ 1.3	<0.001
VAS at 12 hours, mean $\pm$ SD	3.0 $\pm$ 1.0	4.2 $\pm$ 1.2	<0.001
VAS at 24 hours, mean $\pm$ SD	2.5 $\pm$ 0.9	3.6 $\pm$ 1.1	<0.001
VAS at 48 hours, mean $\pm$ SD	2.0 $\pm$ 0.8	2.9 $\pm$ 0.9	<0.001
Time to first rescue analgesia (hours), mean $\pm$ SD	6.8 $\pm$ 2.1	3.9 $\pm$ 1.6	<0.001
Total postoperative morphine equivalent (mg), mean $\pm$ SD	12.6 $\pm$ 4.3	19.1 $\pm$ 5.0	<0.001
Rescue analgesia required, n (%)	14 (38.9)	26 (72.2)	0.004
Length of hospital stay (days), mean $\pm$ SD	3.1 $\pm$ 0.8	3.5 $\pm$ 0.9	0.052

Table 4 shows the follow-up results involving chronic post-surgery pain. Persistent pain was less frequent in the ketamine group both at 1 month and 3 months, but the difference gained increased clinical significance at 3 months. The level of pain, sleep disturbance and disturbance related to pain and interference in normal functioning of patients who received ketamine infusion were minimized.

Table 4: Chronic post-surgical pain outcomes at follow-up

Variable	Ketamine Group (n=36)	Control Group (n=36)	p-value
Persistent pain at 1 month, n (%)	11 (30.6)	20 (55.6)	0.032
Persistent pain at 3 months, n (%)	6 (16.7)	15 (41.7)	0.020
VAS pain score at 1 month, mean $\pm$ SD	1.8 $\pm$ 1.0	3.0 $\pm$ 1.4	<0.001
VAS pain score at 3 months, mean $\pm$ SD	1.1 $\pm$ 0.8	2.4 $\pm$ 1.2	<0.001
Pain interfering with daily activity at 3 months, n (%)	5 (13.9)	13 (36.1)	0.029
Sleep disturbance due to pain at 3 months, n (%)	4 (11.1)	12 (33.3)	0.024
Patient satisfaction with pain control, n (%)	30 (83.3)	21 (58.3)	0.019

Table 5 compares the frequency of adverse effects in the two groups. There was a minor decrease in nausea and vomiting with ketamine, and a few ketamine treated patients were experiencing mild cases of

dizziness and temporary hallucinations. All in all, infusion of ketamine in low doses was very well tolerated and no drug related complication was documented.

Table 5. Overview of side effects and safety observations during the study

Adverse effect	Ketamine Group (n=36)	Control Group (n=36)	p-value
Nausea, n (%)	6 (16.7)	9 (25.0)	0.388
Vomiting, n (%)	4 (11.1)	7 (19.4)	0.331
Dizziness, n (%)	5 (13.9)	3 (8.3)	0.455
Hallucinations, n (%)	2 (5.6)	0 (0.0)	0.153
Sedation, n (%)	3 (8.3)	2 (5.6)	0.643
Hypotension, n (%)	2 (5.6)	4 (11.1)	0.393
Bradycardia, n (%)	1 (2.8)	2 (5.6)	0.554
Serious adverse event, n (%)	0 (0.0)	0 (0.0)	—

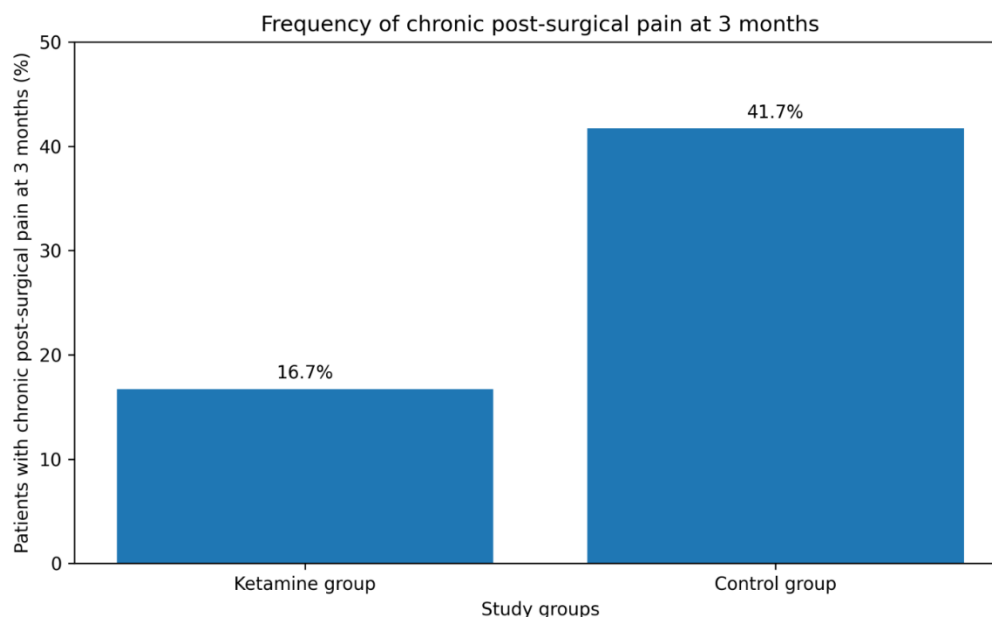


Figure 1: Frequency of chronic post-surgical pain at 3 months among patients receiving low-dose ketamine infusion and controls. The proportion of patients with persistent post-surgical pain at 3 months was lower in the ketamine group (16.7%) compared with the control group (41.7%), suggesting a beneficial effect of low-dose ketamine infusion in reducing chronic post-surgical pain.

DISCUSSION

The present retrospective comparative cohort study evaluated the association between low-dose ketamine infusion and the prevention of chronic post-surgical pain among patients undergoing elective surgery. The results indicated that the patients receiving low-dose ketamine during perioperative had lower opioid use intraoperative, better postoperative pain rating, a delayed time to rescue analgesia, and a decreased incidence of persistent pain at follow-up in comparison to the control group. These observations indicate that ketamine can play a positive role in constraining the process of acute postoperative pain to chronic postoperative pain [11-13].

The enhanced management of acute postoperative pain was among the significant results of the research in the ketamine group. The pain rate during the first 48 hours also proved to be lower in those patients who were receiving ketamine infusion and the need to receive post-surgical opioids was also lower. Such a pattern is important clinically, as the incorrectly treated acute postoperative pain is one of the factors that determine the further appearance of the painful chronic post-surgical one. The low dose ketamine may be useful in pain control in the early phase and opioid dependence during the initial surgical hours because of

the reduction in central sensitization and the amplification of nociceptive effects in the perioperative period [14, 15].

The second significant observation was the decreased percentage of patients with persistent pain at 1 month and 3 months in the ketamine group. Chronic post-operative pain is a significant issue to observe due to the fact that it has adverse impacts on physical activities, sleep, emotional status, and quality of life. Besides the frequency of persistent pain decreased in the current study, the interference of the pain with daily activities and sleep disturbance were also less frequent in patients who received ketamine. The results of this research reinforce the perception that perioperative ketamine does not only offer the advantage of short-term pain but also may contribute to the decreased long-term morbidity of post-surgery pain [16, 17].

The opioid-sparing effect witnessed in this study is worth mentioning too. The intraoperative use of fentanyl and morphine equivalent use after surgery were lesser in the ketamine group with longer time to first rescue analgesia. The practical significance of this finding is that an exposure to opioids could be reduced to minimize adverse effects associated with opioids and enhance overall recovery postoperative. Reduced opioid use and analgesia measures are highly regarded in the contemporary perioperative pain

management. The current results thus confirm the use of ketamine as a helpful adjunct in the multimodal analgesic regimen [18].

The stability of low rate ketamine infusion was usually safe. As compared to mild dizziness and temporal hallucinations which were observed in few patients, there was no dramatic episode which was reported. Ketamine group did not raise the incidence of nausea and vomiting and hemodynamic complications in either of the groups were low. It means that ketamine is safe in the low doses and under the appropriate supervision in the perioperative setting. This can be potentially applicable to the selected surgical patients because of the trade-off between the improved results of pain management and the limited adverse effects [19, 20].

This research however has its limitations. Incomplete documentation and residual confounding cannot be excluded since the study was a retrospective study. The sample was also limited, and the sample of patients of other types of surgery was utilized, which might have contributed to a certain level of fluctuation to the pain experience and analgesic demand. In addition, the following outcomes were founded on the accessible records which may not have been as precise in capturing all aspects of chronic pain. Despite these weaknesses, the study provides viable practical evidence that low-dose ketamine infusion is potentially associated with a reduction in acute postoperative pain as well as reduction of chronic post-surgical pain.

CONCLUSION

Low-dose ketamine infusion was associated with better perioperative pain control, lower opioid requirement, and a reduced frequency of chronic post-surgical pain at follow-up among patients undergoing elective surgery. Patients receiving ketamine also experienced less pain-related interference with daily activities and sleep, while the adverse effects remained mild and manageable. These findings suggest that low-dose ketamine infusion may serve as a beneficial adjunct in perioperative analgesic management for the prevention of chronic post-surgical pain.

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