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Original Article

Effect of Low Dose Ketamine on Post Operative Analgesic Requirements in Patients Receiving General Anaesthesia for Major Surgeries

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ABSTRACT

Background: Postoperative pain remains a significant clinical concern despite advances in anaesthesia and analgesic techniques. Low-dose ketamine has been increasingly used as an adjuvant in multimodal analgesia because of its analgesic and opioid-sparing properties.
Aim: To assess whether intraoperative low-dose ketamine reduces postoperative analgesic requirement in patients undergoing major surgery under general anaesthesia.
Methods: This prospective observational study included 100 adult patients undergoing major surgery under general anaesthesia. Patients were divided into two groups: control group (n=50) and ketamine group (n=50). The ketamine group received low-dose intravenous ketamine intraoperatively. Postoperative analgesic requirement, pain intensity at predefined intervals, adverse effects, and overall tolerability were compared between the groups. Pain scores were assessed in the post-anaesthesia care unit and at 2, 6, 12, and 24 hours postoperatively.
Results: Patients receiving ketamine had a significantly longer time to first rescue analgesia and required fewer rescue analgesic doses during the first 24 hours. Total postoperative opioid and diclofenac consumption were significantly lower in the ketamine group. Pain scores were also significantly lower in the ketamine group in the immediate postoperative period and at 2 and 6 hours, although differences at 12 and 24 hours were not statistically significant. Hallucinations and sedation were more frequent in the ketamine group, while postoperative nausea and vomiting were less frequent. Overall tolerability was significantly better in the ketamine group.
Conclusion: Intraoperative low-dose ketamine reduced postoperative analgesic requirement and improved early postoperative pain control in patients undergoing major surgery under general anaesthesia, supporting its role as a useful component of multimodal postoperative analgesia.

Keywords*: ketamine, postoperative pain, multimodal analgesia, general anaesthesia, opioid-sparing.*

INTRODUCTION

Postoperative pain remains a major clinical problem despite advances in anaesthetic and analgesic techniques. Inadequately controlled acute postoperative pain is associated with delayed ambulation, impaired respiratory function, prolonged hospital stay, patient dissatisfaction, and an increased risk of persistent postsurgical pain.[1] Effective postoperative pain management is therefore a key component of perioperative care and enhanced recovery.

Current clinical practice guidelines recommend a multimodal analgesic approach for postoperative pain, combining agents and techniques with different mechanisms of action in order to improve analgesia while reducing opioid consumption and opioid-related adverse effects.[2,3] Within this framework, interest has grown in the use of ketamine as an adjuvant analgesic, particularly in patients undergoing major surgery where postoperative pain intensity and analgesic requirements are expected to be high.

Ketamine is a phencyclidine derivative that, at subanaesthetic doses, produces analgesia primarily through antagonism of the N-methyl-D-aspartate receptor. By modulating central sensitization and reducing wind-up phenomena, ketamine may attenuate postoperative hyperalgesia and decrease subsequent analgesic requirement.[4] These properties have made it an attractive adjunct in perioperative pain management, especially as part of opioid-sparing strategies.

Previous studies have shown that perioperative ketamine may reduce postoperative pain scores and opioid consumption, although the magnitude and consistency of benefit have varied across studies.[5,6] Systematic reviews suggest that ketamine is most likely to be beneficial when used in subanaesthetic doses in procedures associated with moderate to severe postoperative pain.[5,7] Consensus guidelines also support the use of intravenous subanaesthetic ketamine as an adjunct for acute pain management in selected perioperative settings, while emphasizing the need to balance analgesic benefit against psychotomimetic and sedative adverse effects.[8]

Despite growing evidence, uncertainty remains regarding the extent of benefit of intraoperative low-dose ketamine in routine major surgical practice, particularly with respect to total postoperative analgesic requirement, temporal trends in pain intensity, and overall tolerability. The present study was therefore undertaken to assess whether intraoperative low-dose ketamine reduces postoperative analgesic requirement in patients receiving general anaesthesia for major surgeries, and to compare postoperative pain intensity, ketamine-related adverse effects, and tolerability between study groups.

AIM

To assess whether intraoperative low-dose ketamine reduces postoperative analgesic requirement in patients receiving general anaesthesia for major surgeries.

OBJECTIVES

1. To compare total postoperative analgesic requirement in the study groups.
2. To compare postoperative pain intensity at predefined time intervals.
3. To assess ketamine-related adverse effects and overall tolerability.

MATERIALS AND METHODS

This prospective observational study was conducted in 100 adult patients undergoing major surgery under general anaesthesia. Patients were divided into two groups according to the intraoperative analgesic regimen received: a control group (n=50) and a low-dose ketamine group (n=50). Postoperative analgesic requirement, postoperative pain intensity at predefined intervals, adverse effects, and overall tolerability were evaluated and compared between the two groups.

Study population

Patients aged 18 to 65 years, of either sex, belonging to American Society of Anesthesiologists (ASA) physical status I–III, and scheduled for elective major surgery under general anaesthesia were considered eligible for inclusion. The types of surgery included gynecologic major surgery, laparoscopic abdominal surgery, open abdominal surgery, orthopedic major surgery, and urologic major surgery.

Inclusion criteria

Patients fulfilling all of the following criteria were included in the study:

1. Age between 18 and 65 years
2. Either sex
3. ASA physical status I, II, or III
4. Scheduled for elective major surgery under general anaesthesia
5. Expected postoperative observation for at least 24 hours
6. Ability to understand the pain assessment scale and provide informed consent

Exclusion criteria

Patients were excluded if they had any of the following:

1. Refusal to participate in the study
2. Known allergy, hypersensitivity, or contraindication to ketamine
3. History of major psychiatric illness, psychosis, hallucinations, or other severe behavioural disorder
4. Chronic opioid use, opioid dependence, or long-term analgesic abuse
5. Preoperative use of ketamine or other centrally acting analgesic adjuvants that could influence postoperative pain assessment
6. Severe hepatic, renal, cardiovascular, or neurological disease
7. Uncontrolled hypertension or ischemic heart disease
8. Raised intracranial pressure or seizure disorder
9. Pregnancy or lactation
10. Emergency surgery

11. Inability to communicate reliably or assess pain postoperatively

Ketamine dose and timing
Patients in the ketamine group received intravenous ketamine at a dose of 0.5 mg/kg as a slow bolus after induction of anaesthesia and before surgical incision, followed by a continuous intraoperative infusion at 0.1 mg/kg/hour until completion of surgery or skin closure. Patients in the control group did not receive ketamine.

Anaesthetic management
All patients received general anaesthesia according to institutional protocol. Standard intraoperative monitoring was used in all cases. Apart from administration of ketamine in the study group, the remaining anaesthetic management was carried out as per routine clinical practice and at the discretion of the attending anaesthesiologist.

Postoperative analgesic assessment
Postoperative pain was assessed at predefined time intervals in the post-anaesthesia care unit (PACU), and at 2, 6, 12, and 24 hours after surgery. Time to first rescue analgesic was recorded. Total postoperative analgesic requirement during the first 24 hours was assessed in terms of number of rescue analgesic doses, total opioid consumption expressed as morphine equivalent, paracetamol consumption, and diclofenac consumption.

Adverse effects and tolerability
Patients were observed for ketamine-related and postoperative adverse effects, including nausea and vomiting, hallucinations, dizziness, nightmares, transient hypertension, and sedation. Overall tolerability was also assessed and categorized as excellent, good, fair, or poor.

Outcome measures
The primary outcome measure was total postoperative analgesic requirement during the first 24 hours. Secondary outcome measures included postoperative pain scores at predefined intervals, time to first rescue analgesia, incidence of adverse effects, and overall tolerability.

Statistical analysis
Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as number and percentage. Continuous variables between the two groups were compared using the independent samples t-test, and categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Changes in postoperative pain scores over time within each group were analysed using the Friedman test. A p value of less than 0.05 was considered statistically significant.

RESULTS
A total of 100 patients were included in the analysis, with 50 patients in the control group and 50 patients in the low-dose ketamine group. Postoperative analgesic requirement, pain intensity at predefined time intervals, adverse effects, and overall tolerability were compared between the two groups.

Baseline characteristics
The two groups were broadly comparable with respect to age, sex distribution, body mass index, ASA physical status, and type of surgery (Table 1). A statistically significant difference was noted in duration of surgery, which was longer in the ketamine group than in the control group (164.72 ± 31.64 min vs 147.96 ± 33.63 min, p = 0.012).

Table 1. Baseline characteristics of the study groups.

Characteristic	Control (n=50)	Ketamine (n=50)	p value
Age (years)	48.82 ± 11.25	45.98 ± 12.19	0.229
BMI (kg/m²)	25.61 ± 4.96	23.89 ± 4.40	0.069
Duration of surgery (min)	147.96 ± 33.63	164.72 ± 31.64	0.012
Sex: Male	24 (48.0)	27 (54.0)	0.689
Sex: Female	26 (52.0)	23 (46.0)	
ASA grade I	15 (30.0)	14 (28.0)	0.406
ASA grade II	22 (44.0)	17 (34.0)	
ASA grade III	13 (26.0)	19 (38.0)	
Gynecologic major surgery	8 (16.0)	9 (18.0)	0.473
Laparoscopic abdominal surgery	11 (22.0)	6 (12.0)	
Open abdominal surgery	11 (22.0)	14 (28.0)	
Orthopedic major surgery	16 (32.0)	13 (26.0)	
Urologic major surgery	4 (8.0)	8 (16.0)	

Postoperative analgesic requirement

Patients receiving low-dose ketamine required less postoperative analgesia than those in the control group (Table 2). The ketamine group had a significantly longer time to first rescue analgesia (216.14 ± 64.55 min vs 151.20 ± 54.97 min, $p < 0.001$), fewer rescue analgesic doses in the first 24 hours (2.56 ± 0.99 vs 3.78 ± 1.11, $p < 0.001$), lower total opioid requirement (11.96 ± 5.96 mg vs 16.38 ± 4.40 mg morphine equivalent, $p < 0.001$), and lower diclofenac consumption (93.84 ± 30.55 mg vs 113.52 ± 25.27 mg, $p < 0.001$). Paracetamol consumption was lower in the ketamine group, but the between-group difference was not statistically significant ($p = 0.081$).

Table 2. Comparison of postoperative analgesic requirement between the study groups.

Outcome	Control (n=50)	Ketamine (n=50)	p value
Time to first rescue analgesic (min)	151.20 ± 54.97	216.14 ± 64.55	<0.001
Rescue analgesic doses in 24 h	3.78 ± 1.11	2.56 ± 0.99	<0.001
Total opioid requirement in 24 h (mg morphine equivalent)	16.38 ± 4.40	11.96 ± 5.96	<0.001
Paracetamol consumption in 24 h (g)	3.46 ± 0.49	3.29 ± 0.45	0.081
Diclofenac consumption in 24 h (mg)	113.52 ± 25.27	93.84 ± 30.55	<0.001

Postoperative pain intensity at predefined time intervals

Postoperative pain scores were lower in the ketamine group during the early postoperative period (Table 3). Mean pain intensity in the ketamine group was significantly lower in the post-anesthesia care unit (4.98 ± 1.48 vs 5.98 ± 1.32, $p = 0.001$), at 2 hours (4.32 ± 1.00 vs 5.52 ± 1.18, $p < 0.001$), and at 6 hours (3.64 ± 1.22 vs 4.58 ± 0.99, $p < 0.001$). By 12 hours and 24 hours, pain scores remained numerically lower in the ketamine group, but the between-group differences were not statistically significant ($p = 0.068$ and $p = 0.263$, respectively) as shown in figure1.

Table 3. Comparison of postoperative pain scores at predefined time intervals.

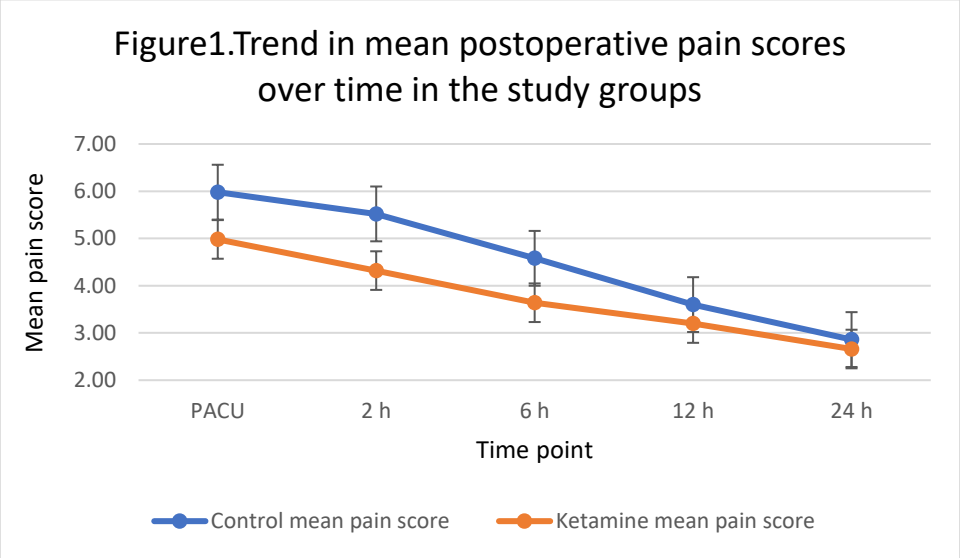
Time point	Control (n=50)	Ketamine (n=50)	p value
PACU	5.98 ± 1.32	4.98 ± 1.48	0.001
2 h	5.52 ± 1.18	4.32 ± 1.00	<0.001
6 h	4.58 ± 0.99	3.64 ± 1.22	<0.001
12 h	3.60 ± 1.01	3.20 ± 1.11	0.068
24 h	2.86 ± 0.88	2.66 ± 0.96	0.263

Within-group postoperative pain trend

Pain scores decreased significantly over time within both groups (Table 4). In the control group, the mean pain score declined from 5.98 ± 1.32 in the immediate postoperative period to 2.86 ± 0.88 at 24 hours (Friedman test, $p < 0.001$). In the ketamine group, the corresponding decline was from 4.98 ± 1.48 to 2.66 ± 0.96 (Friedman test, $p < 0.001$). These findings indicate progressive postoperative pain relief in both groups, with lower early pain intensity in patients who received ketamine.

Table 4. Within-group change in postoperative pain scores over time.

Group	PACU mean ± SD	24 h mean ± SD	Within-group p value (Friedman)
Control	5.98 ± 1.32	2.86 ± 0.88	<0.001
Ketamine	4.98 ± 1.48	2.66 ± 0.96	<0.001



Adverse effects and tolerability

Adverse effects were generally infrequent and mostly mild (Table 5). Postoperative nausea and vomiting occurred less often in the ketamine group than in the control group (14.0% vs 28.0%), although this difference did not reach statistical significance (p = 0.140). Hallucinations were observed only in the ketamine group (14.0%), and this difference was statistically significant (p = 0.012). Sedation scores were also higher in the ketamine group (median [IQR], 1.0 [1.0–2.0] vs 0.0 [0.0–1.0], p = 0.001). No significant between-group differences were found for dizziness or transient hypertension.

Table 5. Comparison of postoperative adverse effects between the study groups.

Adverse effect / tolerability	Control (n=50)	Ketamine (n=50)	p value
Postoperative nausea/vomiting	14 (28.0)	7 (14.0)	0.14
Hallucinations	0 (0.0)	7 (14.0)	0.012
Dizziness	3 (6.0)	5 (10.0)	0.715
Nightmares	0 (0.0)	0 (0.0)	
Transient hypertension	3 (6.0)	7 (14.0)	0.318
Sedation score (median [IQR])	0.0 [0.0-1.0]	1.0 [1.0-2.0]	0.001

Overall tolerability distribution differed significantly between the groups (Table 6). The ketamine group had a higher proportion of patients rated as having good tolerability (60.0% vs 38.0%) and a lower proportion rated as fair (12.0% vs 36.0%), although the proportion rated as poor was similar in both groups (10.0% vs 8.0%). The overall difference in tolerability categories was statistically significant (p = 0.035).

Table 6. Overall tolerability in the study groups.

Overall tolerability	Control (n=50)	Ketamine (n=50)	p value
Excellent	9 (18.0)	9 (18.0)	0.035
Good	19 (38.0)	30 (60.0)	
Fair	18 (36.0)	6 (12.0)	
Poor	4 (8.0)	5 (10.0)	

DISCUSSION

In this prospective observational study, intraoperative low-dose ketamine was associated with reduced postoperative analgesic requirement in patients undergoing major surgery under general anaesthesia. Patients who received ketamine had a significantly longer time to first rescue analgesia, required fewer rescue analgesic doses during the first 24 hours, and consumed lower amounts of opioids and diclofenac postoperatively. Pain scores were also significantly lower in the ketamine group in the immediate postoperative period and at 2 and 6 hours, although this benefit was not sustained at 12 and 24 hours. Hallucinations and sedation were more frequent with ketamine; however, overall tolerability was better in the ketamine group.

The findings are in agreement with previous studies showing that low-dose ketamine is an effective adjunct for acute postoperative pain management.[9,10] Ketamine, through N-methyl-D-aspartate receptor antagonism, is believed to reduce central sensitization and thereby attenuate postoperative pain amplification. This mechanism likely explains the opioid-sparing effect observed in the present study. Similar reductions in postoperative analgesic consumption have been reported in earlier clinical studies and later supported by systematic reviews and meta-analyses.[11,13,16]

A notable finding in the present study was that the benefit of ketamine was most pronounced in the early postoperative period. Pain scores were significantly lower in the PACU and at 2 and 6 hours, but not at 12 and 24 hours. This temporal pattern is consistent with previous reports suggesting that intraoperative low-dose ketamine improves immediate postoperative analgesia more than late postoperative pain outcomes.[12,15,18] The significantly prolonged time to first rescue analgesia in the ketamine group further supports a meaningful early analgesic effect. From a clinical perspective, improved pain control during this period is particularly important, as inadequate early postoperative analgesia may adversely affect patient comfort, respiratory effort, and early recovery.

In addition to reduced opioid use, patients in the ketamine group also required less diclofenac. This suggests that ketamine reduced overall postoperative analgesic burden rather than merely decreasing opioid exposure alone. Such a finding is relevant in the context of multimodal analgesia, where the goal is to improve pain control while minimizing the cumulative requirement for rescue medications.[11,13,14] The absence of a significant difference in paracetamol consumption may reflect its routine and relatively fixed use in both groups.

The adverse-effect profile observed in this study is also consistent with the known clinical effects of ketamine. Hallucinations were seen only in the ketamine group, and sedation scores were significantly higher. These findings are in keeping with previous literature showing that, although low-dose ketamine is generally well tolerated, psychotomimetic effects remain a relevant concern.[16-18] At the same time, postoperative nausea and vomiting were numerically lower in

the ketamine group, although the difference was not statistically significant. Importantly, despite the higher incidence of hallucinations and sedation, overall tolerability was superior in the ketamine group. This may indicate that the analgesic benefit of ketamine outweighed these largely transient adverse effects in many patients.

An important consideration in interpreting the present results is the significantly longer duration of surgery in the ketamine group. Since longer operations may be associated with greater surgical trauma and higher postoperative analgesic requirement, this imbalance would ordinarily be expected to favor the control group. The observation of better analgesic outcomes in the ketamine group despite longer procedures may therefore support the presence of a true beneficial effect. Nevertheless, as this was an observational study, the possibility of residual confounding cannot be excluded.

LIMITATIONS

The observational design limits causal inference compared with a randomized controlled trial. Also the inclusion of different categories of major surgery may have introduced heterogeneity in postoperative pain severity and analgesic requirements. The difference in duration of surgery between groups may have influenced postoperative outcomes. Finally, follow-up was limited to 24 hours, and longer-term outcomes such as recovery quality, duration of hospital stay, and persistent postoperative pain were not evaluated.

CONCLUSION

Intraoperative low-dose ketamine was associated with reduced postoperative analgesic requirement and lower early postoperative pain scores in patients undergoing major surgery under general anaesthesia. The analgesic benefit was most evident in the immediate postoperative period and was accompanied by reduced opioid and diclofenac consumption. Although hallucinations and sedation were more frequent, overall tolerability remained favorable. These findings support the use of low-dose ketamine as a useful component of multimodal analgesia for major surgery, while highlighting the need for appropriate patient selection and monitoring for psychotomimetic adverse effects.

REFERENCES

1. Gan TJ, Habib AS, Miller TE, White W, Apfelbaum JL. Poorly controlled postoperative pain: prevalence, consequences, and prevention. *J Pain Res.* 2017;10:2287-2298.
2. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain.* 2016;17(2):131-157.
3. Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesth Analg.* 1993;77(5):1048-1056.
4. Radvansky BM, Shah K, Parikh A, Sifonios AN, Le V, Eloy JD. Role of ketamine in acute postoperative pain management: a narrative review. *Biomed Res Int.* 2015;2015:749837.
5. Elia N, Tramèr MR. Ketamine and postoperative pain: a quantitative systematic review of randomised trials. *Pain.* 2005;113(1-2):61-70.
6. Bell RF, Dahl JB, Moore RA, Kalso E. Peri-operative ketamine for acute post-operative pain: a quantitative and qualitative systematic review. *Acta Anaesthesiol Scand.* 2005;49(10):1405-1428.
7. Bell RF, Dahl JB, Moore RA, Kalso EA. Perioperative ketamine for acute postoperative pain. *Cochrane Database Syst Rev.* 2006;(1):CD004603.
8. Schwenk ES, Viscusi ER, Buvanendran A, et al. Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. *Reg Anesth Pain Med.* 2018;43(5):456-466.
9. Roytblat L, Korotkoruchko A, Katz J, et al. *Postoperative pain: the effect of low-dose ketamine in addition to general anesthesia.* Anesth Analg. 1993;77(6):1161-1165.
10. Fu ES, Miguel R, Scharf JE. *Preemptive ketamine decreases postoperative narcotic requirements in patients undergoing abdominal surgery.* Anesth Analg. 1997;84(5):1086-1090.
11. Subramaniam K, Subramaniam B, Steinbrook RA. *Ketamine as adjuvant analgesic to opioids: a quantitative and qualitative systematic review.* Anesth Analg. 2004;99(2):482-495.
12. Argiriadou H, Himmelseher S, Papagiannopoulou P, et al. *Improvement of pain treatment after major abdominal surgery by intravenous S(+)-ketamine.* Anesth Analg. 2004;98:1413-1418.
13. Laskowski K, Stirling A, McKay WP, Lim HJ. *A systematic review of intravenous ketamine for postoperative analgesia.* Can J Anaesth. 2011;58(10):911-923.
14. Jouguelet-Lacoste J, La Colla L, Schilling D, Chelly JE. *The use of intravenous infusion or single dose of low-dose ketamine for postoperative analgesia: a review of the current literature.* Pain Med. 2015;16(2):383-403.
15. Kaur S, Saroa R, Aggarwal S. *Effect of intraoperative infusion of low-dose ketamine on management of postoperative analgesia.* J Nat Sci Biol Med. 2015;6(2):378-382.

16. Brinck ECV, Tiippana E, Heesen M, et al. *Perioperative intravenous ketamine for acute postoperative pain in adults.* Cochrane Database Syst Rev. 2018.
17. Schwenk ES, Viscusi ER, Buvanendran A, et al. *Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists.* Reg Anesth Pain Med. 2018;43(5):456-466.
18. Wang X, Lin C, Lan L, Liu J. *Perioperative intravenous S-ketamine for acute postoperative pain in adults: a systematic review and meta-analysis.* J Clin Anesth. 2021;68:110071.