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LOW DOSE KETAMINE AT INDUCTION OF ANESTHESIA CAN HAVE OPIOID SPARING EFFECTS IN IMMEDIATE POST-OPERATIVE PERIOD FOLLOWING LAPAROSCOPIC CHOLECYSTECTOMY

Dr. Ana Akbar*[1], Lt cdr Raja Ahmed[2], Major Muhammad Umair Khan[3], Col Muhammad Asif Saleem[4], Dr Ali Aftab[5], Major Syed Muhammad Shah[6]

*[1]*Combined Military Hospital, Lahore*
[2]*Senior Registrar Anaesthesia PNS Shifa Karachi*
[3] *Senior Registrar Anesthesia, Bahria University of Health and Sciences Karachi*
[4] *Assistant Professor Anesthesia, Bahria University of Health and Sciences Karachi*
[5]*Assistant Professor in Anesthesiology Bahria University of Health and Sciences Karachi*
[6]*PGR Anaesthesia PNS Shifa Karachi*

*[1]ana_anu03@hotmail.com, [2]drpanhwer2006@gmail.com, [3]redberet.uk@gmail.com, [4]drasif910@gmail.com, [5]alijiwani316@gmail.com, [6]syedmuhammadshah2853@gmail.com

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Corresponding Author: *

Abstract

Introduction: *Laparoscopic Cholecystectomy (LC), a minimally invasive surgical procedure, has gained widespread use in recent decades. Although these operations are less invasive, they need postoperative analgesia. In this context, Ketamine may decrease postoperative pain and opioid use.*

Due to the considerable variability in studies regarding the efficacy of ketamine for pain management across various surgical procedures, anesthetic techniques, and administration methods and dosages, this study sought to examine the preemptive application of low-dose ketamine in patients undergoing laparoscopic cholecystectomy, with the potential to diminish opioid consumption and associated side effects during the recovery phase.

Aims & Objectives: *To compare the mean pain score in a group receiving low-dose bolus of ketamine (0.1mg/kg) (K group) to a control group receiving normal saline (C group), in patients undergoing laparoscopic cholecystectomy.*

Material & Methods: *This was a randomized controlled trial conducted at the Department of Anesthesiology at Combined Military Hospital (CMH), Lahore. A total of 72 patients were equally distributed into two groups of 36 patients each (Group K and Group C) using non-probability consecutive technique.*

Results: *In this study the mean age of the cases in Group K was 36.14 ± 6.66 years while in Group C was 39.56 ± 5.09. There were 19 (52.8%) males found in Group K while 17 (47.2%) in Group C. The mean of VAS score at 1st hour was 6.89 ± 1.19 in Group K and 6.50 ± 1.73 in Group C with insignificant p-value 0.271. Similarly, the mean of VAS score at 6th and 24th hour was 4.72 ± 0.51 and 4.64 ± 1.27 in Group K and 5.58 ± 1.18 and 6.06 ± 2.14 in Group C with significant p-value < 0.01.*

Conclusion: *Low-dose ketamine (0.1 mg/kg) was found to be effective in reducing pain scores at 6th and 24th hour post-operatively.*

INTRODUCTION

Laparoscopic cholecystectomy has become the standard procedure for gallbladder removal, offering advantages over open techniques, including reduced blood loss, pain, mortality, and hospital stay [1-3]. Effective post-operative pain management is crucial, as poor management can lead to prolonged hospital stays, increased complications, and decreased patient satisfaction [4]. Various pain relief modalities are used, including opioids, but their side effects, such as respiratory depression, addiction, and dependence, are concerns [5-6]. Ketamine, with its analgesic, amnesic, antidepressant, and anesthetic properties, offers a promising alternative [8-9]. Its analgesic properties have been established worldwide, and it's being used in various settings, including perioperative and postoperative periods, minor surgical procedures, intensive care units, chronic pain syndrome, and cancer pain management [10-12]. The preemptive use of ketamine is a relatively new concept, and multiple studies are exploring its benefits [13]. In addition to reducing opioid-related complications, ketamine administration during surgery has been shown to alleviate postoperative nausea and vomiting [14–15]. Overall, the evidence was moderate, according to a meta-analysis conducted by Riddle et al., which comprised 20 researches. Both overall opioid usage and VAS score are considerably reduced by ketamine. For the objective, the standardized mean difference (SMD) was -0.82 [-1.24, -0.40], p=0.0001, and for the visual analog scale (VAS), it was -0.53 [-0.91, -0.15], p=0.006, and for the subjective assessment, it was -0.60 [-1.05, -0.16], p=0.008) [16]. According to a 2010 Cochrane review by Bell et al., 27 out of 37 studies showed that ketamine decreased analgesic demand and/or VAS in adult surgical patients who took it during the operation as opposed to a placebo. [17] The use of perioperative ketamine was linked to a statistically significant decrease in postoperative pain levels, according to a 2005 systematic analysis by Elia and Tramèr, who examined 53 randomized studies including both adults and children. In 850 individuals, sixteen trials examined the efficacy of preventative intravenous ketamine (0.4 mg/kg, range: 0.1-1.6). At 6, 12, 24, and 48 hours after surgery, the weighted mean difference (WMD) for pain intensity (0-10 cm visual analogue scale) was -0.89 cm, -0.42, -0.35, and -0.27, respectively. [18]

A study conducted by Adam in 2005 showed mean pain score of 15.03 ± 7.67 in ketamine group while 21.55 ± 9.04 in control group. [19] Similarly, Cengiz [20] in 2014 found mean pain score of 47 ± 15.3 in ketamine group while 85.2 ± 8 in control group

This study aimed to investigate the preemptive use of low-dose ketamine in patients undergoing laparoscopic cholecystectomy, potentially reducing opioid use and side effects in the recovery period.

Material & Methods

This was a randomized controlled trial conducted at the Department of Anesthesiology at Combined Military Hospital (CMH), Lahore over the period of 6 months from 15 December, 2024 to 15 June, 2025. A total of 72 patients were equally distributed into two groups of 36 patients each (Group K and Group C) using non-probability consecutive technique. Sample size calculations were performed using a two-sample mean comparison formula. Mean pain score of 15.03 ± 7.67 in ketamine group while 21.55 ± 9.04 in control group. [19]

Inclusion criteria:

Patients of either gender, 18-50 years of age and undergoing laparoscopic cholecystectomy declared as ASA class I and II. **Exclusion criteria:** ASA III, IV and V patients having history of chronic pain, opioids self-administration and psychiatric disorders.

Operational definition:

Low dose ketamine:

Low dose, ketamine means 0.1 mg per kg of ideal body weight.

Post-operative pain:

Post-operative pain was assessed after 1, 6 and 24 hours in the recovery room. VAS Range 0 – 10 "0" was considered as no pain and "10" was considered as worst pain.

All patients received the same general anesthetic technique. Patients received midazolam 0.05 mg/kg and ondansetron 4 mg IV as premedication. Induction was done using nalbuphine 0.1mg/kg IV, propofol 2mg/kg, and atracurium 0.5mg/kg IV, followed by intubation. Group K received 0.1mg/kg of ketamine at induction, while Group C received normal saline in the same volume via a similar syringe. Maintenance of anesthesia was achieved by isoflurane 1.2% in oxygen and air mixture. Atracurium 0.125mg/kg was given as required.

Data analysis:

We used IBM SPSS Statistics 29 to analyze the data. The two groups' means were compared using an independent sample t-test. It was deemed statistically significant if the P-Value was less than 0.05.

Results

Table 1: Demographics and clinical parameters

Demographics and clinical parameters				
		Group K	Group C	P-Value
Age (Mean ± S.D)		36.14 ± 6.66	39.56 ± 5.09	0.017
Gender	Male	19 (52.8%)	17 (47.2%)	0.814
	Female	17 (47.2%)	19 (52.8%)	
Weight (Kg)	(Mean ± S.D)	76.44 ± 15.59	75.58 ± 11.53	0.791
BMI (Mean ± S.D)		29.26 ± 7.91	27.55 ± 4.15	0.254
ASA Classification	ASA I	4 (11.1%)	6 (16.7%)	0.496
	ASA II	32 (88.9%)	30 (83.3%)	

In this study the mean age of the cases in Group K was 36.14 ± 6.66 years while in Group C was 39.56 ± 5.09. There were 19 (52.8%) males found in Group K while 17 (47.2%) in Group C. The mean weight and BMI in Group K was 76.44 ± 15.59 and 29.26 ± 7.91 respectively while in Group C 75.58 ± 11.53 and 27.55 ± 4.15. There were 4 (11.1%) patients found with ASA I and 32 (88.9%) with ASA II in Group K while 6 (16.7%) with ASA I and 30 (83.3%) with ASA II in Group C. **(Table 1)**

Table 2: Comparison of VAS score at 1st, 6th and 24th hour post-operatively

Comparison of VAS score			
	Group K	Group C	P-Value
VAS at 1st hour	6.89 ± 1.19	6.50 ± 1.73	0.271
VAS at 6th hour	4.72 ± 0.51	5.58 ± 1.18	< 0.01
VAS at 24th hour	4.64 ± 1.27	6.06 ± 2.14	< 0.01

The mean of VAS score at 1st hour was 6.89 ± 1.19 in Group K and 6.50 ± 1.73 in Group C with insignificant p-value 0.271. Similarly, the mean of VAS score at 6th and 24th hour was 4.72 ± 0.51 and 4.64 ± 1.27 in Group K and 5.58 ± 1.18 and 6.06 ± 2.14 in Group C with significant p-value < 0.01**. (Table 2)**

Discussions

Opioids are traditionally used in balanced anesthesia; nevertheless, the supply of narcotics poses a challenge in less wealthy nations for numerous reasons. Consequently, there is a need to investigate alternative approaches or strategies that minimize narcotic usage. A potent analgesic, ketamine blocks "wind-up," the process by which neurons in the spinal cord become hypersensitive to pain signals; it is therefore an alternate analgesic of choice in areas where drugs are scarce. [21] Its safety profile is excellent.

The fear of hemodynamic instability and side effects from the induction dose of ketamine has been a major barrier to its usage. Research has shown that administering modest doses of ketamine does not substantially change hemodynamic status. In a trial carried out by Bilgin et al. [22], the dosing of ketamine was described as an intravenous bolus of 0.5 mg/kg followed by an infusion of 600 μg/kg/h. Postoperatively this dosage was associated with better hemodynamic stability, less morphine usage, and significantly lower VAS pain ratings. Our VAS score values at 6 and 24 hours were in agreement with their results.

A further trial involving patients having laparoscopic gynecological operations indicated that ketamine at a dosage of 0.15 mg/kg exhibited no significant differences across groups for hemodynamic characteristics or adverse effects. [23]

Improving morphine-induced analgesia without significantly affecting phase I recovery has been shown by intravenous administration of low-dose ketamine at 50-100 μg/kg. [24] Combining these little doses with additional anesthetics in a well-rounded regimen, including fentanyl at 1 μg/kg, significantly reduced the associated side effects. Postoperative settings have been the primary locations of studies with low-dose ketamine. Patients suffering from pain after surgery were studied by Weinbroum [25] to determine the effect of administering 0.25 mg/kg of morphine and ketamine together postoperatively on the intensity of pain. Whereas just 3.5% of patients given 0.03 mg/kg of morphine alone had satisfactory analgesia, 68% of patients given this dose reported similar results.

Numerous side effects have been linked to the use of ketamine anesthesia. Approximately one-third of patients have disturbing dreams or symptoms similar to acute psychosis, which might or could not include hallucinations in emergency situations, when administered anesthetic levels of ketamine (i.e., 1-3 mg/kg). Research has shown that benzodiazepine premedication may effectively reduce psychotomimetic symptoms both before and after ketamine anesthesia. Hallucinations occurred in 15% of patients, which is much lower than the rates seen with greater quantities. [26]

Some studies have shown that a dose of 0.3 mg/kg of ketamine, given 24 hours after surgery, causes increased sleepiness in the ketamine-treated group, which is consistent with the drowsiness that has been reported with this medication. [27]

According to a thorough examination by Elia and Tramèr [28] ketamine at a dose of 0.4 mg/kg (range: 0.1-1.6) was not able to reduce morphine-related discomfort. When benzodiazepine was not included in the ketamine regimen, the risk of hallucinations was highest in both awake and sedated participants.

Conclusion

Low-dose ketamine (0.1 mg/kg) was found to be effective in reducing pain scores at 6th and 24th hour post-operatively.

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