International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

Comparative Analysis of Use of Intravenous Low-Dose Ketamine in Addition to Systemic Analgesia Against Systemic Analgesia Alone for Post-Operative Pain Management Following Laparotomies

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ABSTRACT

Background: Postoperative pain is one of the most undesirable experiences for a patient undergoing surgery. The present study was done to compare Intravenous low-dose ketamine in addition to systemic analgesia versus systemic analgesia alone for post-operative pain management in laparotomies.

Materials and Methods: The study comprised of 100 subjects. The subjects were divided into 2 groups. Ten minutes prior to the incision, subjects in group 1 (ketamine group: group 1) obtained an IV bolus of 0.15 mg/kg of ketamine from the "Bolus" syringe. This was followed by an infusion pump that started twenty-four hours postoperatively and administered 2 mg/kg/min (or 0.12 mg/kg/hr) of ketamine. Ten minutes prior to the incision, subjects in group 2 (control group: group 2) underwent an IV bolus of normal saline.

Results: Over the course of 24 hours, the Ketamine group's Ramsay Sedation Score (RSS) at zero, five, ten, as well as sixty minutes was substantially higher than that of the Control group. Similar RSS was observed in both groups from 90 minutes to 24 hours after surgery.

Conclusion: Preventive low-dose IV Ketamine is an excellent addition to systemic analgesia in abdominal procedures.

Keywords: Ketamine, Anaesthesia, Laparotomy.

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Article History:

Received: 17-06-2019, **Revised:** 03-07-2019, **Accepted:** 27-07-2019

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2019.5.4.084	

INTRODUCTION

Postoperative pain is one of the most undesirable experiences for a patient undergoing surgery. Deliberate action should be taken to prophylactically treat the pain. If postoperative pain does develop, it should be managed early and aggressively, because severe pain not only induces a delay in discharge and poorer patient satisfaction, but also can create a hyperalgesic condition known as persistent postoperative pain (PPP). This strains not only the patient, but also the healthcare system as a whole. Recent studies show that PPP has an incidence as high as 40%. Furthermore, 18.3% of patients report that this pain is moderate to severe.[1] Therefore, it is in the anesthesiologist's best interest to be aware of the severity of this problem and of all the pharmacological agents used to prevent and treat postoperative pain. To date, the mainstay of treatment has been the administration of exogenous opioids such as morphine or fentanyl. However, pain is not always fully relieved by such agents, and often patients develop tolerance to them. The ever-increasing doses of opioids are clearly not without their adverse effects. In addition to that, many patients and even some clinicians wrongly believe that addiction can be inevitable after administration of opioids.[2]

Many preoperative, intraoperative, and postoperative interventions and management strategies are available and continue to evolve for reducing and managing postoperative pain. The American Pain Society (APS), with input from the American Society of Anesthesiologists (ASA), commissioned a guideline on management of postoperative pain to promote evidence-based, effective, and safer postoperative pain management in children and adults, addressing areas that include preoperative education, perioperative pain management planning, use of different pharmacological and nonpharmacological modalities, organizational policies and procedures, and transition to outpatient care. The ASA published a practice guideline for acute pain

management in the perioperative setting in 2012; the APS has not previously published guidelines on management of postoperative pain. After completion, the guideline was also reviewed for approval by the American Society of Regional Anesthesia and Pain Medicine.[3, 4] The present study was done to compare Intravenous low-dose ketamine in addition to systemic analgesia versus systemic analgesia alone for post-operative pain management in laparotomies.

MATERIAL AND METHODS

A prospective, randomized controlled trial was conducted on 100 subjects. Patients between the ages of 18 to 70 who were having laparotomies under general anesthesia, ASA grades 1-3, BMI ≤ 30 kg/m^2, and willingness to take part in the research comprised the inclusion criteria. Those having uncontrolled hypertension, elevated intracranial tension, elevated intraocular pressure, globe injuries, history of psychosis, and hepatic dysfunction had been excluded from the study. The subjects had been divided into 2 groups. Ten minutes prior to the incision, subjects in group 1 (ketamine group) obtained an IV bolus of 0.15 mg/kg of ketamine from the "Bolus" syringe. This was followed by an infusion pump that started twenty-four hours postoperatively and administered 2 mg/kg/min (or 0.12 mg/kg/hr) of ketamine. Ten minutes prior to the incision, subjects in group 2 (control group) underwent an IV bolus of normal saline. They then got systemic analgesia solely as well as an IV infusion of normal saline for twenty-four hours following surgery. An infusion as well as saline bolus were administered at the study group's comparable volume/rate. The individuals were brought into the operating room, where balanced general anesthesia was used for all procedures. Monitors for SPO2, ECG, ETCO2, as well as NIBP had been attached. Approximately thirty minutes before the completion of the surgical operation, 1 g of intravenous paracetamol was administered to each participant. Following surgery, subjects were monitored in the post-anaesthesia care unit (PACU) for a full day, while infusions kept going in accordance with their group allocation. After surgery, 1g of paracetamol was administered every eight hours for twenty-four hours.

Table 1: Comparison of baseline demographic characteristics of two groups

Baseline characteristics	Group 1 (Ketamine) (n=50)	Group 2 (Control) (n=50)
Age	42.57±12.25	43.63±11.4
Gender		
Males	40	39
Females	10	11
Weight	55.74 ± 9.67	60.28±11.88
BMI	18.47±2.96	18.84 ± 2.95
ASA		
Grade 1	30	35
Grade 2	10	15
Grade 3	05	00

Table 2: Comparison of relevant indices of two groups

Parameters	Group 1	Group 2
Time for first rescue	16.29 ± 7.8 mins	4.3 ± 4.69 mins
Mean total analgesia	78.69 ± 23.55	201 ± 21.55
Ramsay sedation scores	2.8±0.96	1.69±0.89

RESULTS

Age, gender, weight, BMI, as well as ASA grade data were gathered, analysed, as well as it was discovered that the groups had been equivalent. The research group 1's first rescue analgesia (TFA) time was substantially longer than the Control group's (6.2 ± 4.27 mins), at 18.79 ± 7.6 mins. Compared to group 2, (204 ± 29.64), Group K required considerably less Tramadol (mg) for mean total rescue analgesia (74.61±21.65) (p=0.0001). For the most of the 24-hour period, the Ketamine group's mean NRS was substantially lower than the Control group's, with a p value of 0.0001, with the exception of minutes 20, 25, 30, as well as 45, when the difference in NRS was statistically not substantial. Over the course of 24 hours, the Ketamine group's Ramsay Sedation Score (RSS) at zero, five, ten, as well as sixty minutes was substantially higher (p value>0.05) than that of the Control group. Similar RSS was observed in both groups from 90 minutes to 24 hours after surgery.

DISCUSSION

Preoperative patient evaluation and planning is vital to successful postoperative pain management. Recommended preoperative evaluation includes a directed pain history, a directed physical exam and a pain control plan; however, the literature is insufficient in regards to efficacy.[3] Likewise patient preparation should include adjustments of preoperative medications to avoid withdrawals effect, treatment to reduce preoperative pain/anxiety, and preoperative initiation of treatment as part of a multimodal pain management plan. There is some support that preoperative pain levels may predict levels of postsurgical pain.[4,5] Certain preoperative variables such as age, anxiety levels, and depression may have an effect on levels of postoperative pain.[6] Higher postoperative pain levels can be associated with lower quality of care.[7] Ketamine is in clinical use since 1970.[8] It is a unique intravenous (IV) anaesthetic that produces a wide spectrum of pharmacological effects including sedation, catalepsy, somatic analgesia, bronchodilation, and sympathetic nervous

system stimulation.[9] The availability of newer drugs, the disturbing emergence reactions of ketamine, its stigma as a "vet medicine" and gaining popularity as a drug with abuse potential are factors, which would discourage its use by present day anesthesiologists.[10,11] However, ketamine because of its unique properties and newly found clinical properties has stood the test of time.[12,13] It has a wide range of clinical applications even today. Most of the modern anesthesiologists receive minimal training with ketamine.[14] Hence, this study was done to compare Intravenous low-dose ketamine in addition to systemic analgesia versus systemic analgesia alone for post-operative pain management in laparotomies.

In this study, the research group 1's first rescue analgesia (TFA) time was substantially longer than the Control group's (6.2 ± 4.27 mins), at 18.79 ± 7.6 mins. Compared to group 2, (204 ± 29.64), Group K required considerably less Tramadol (mg) for mean total rescue analgesia. For the most of the 24-hour period, the Ketamine group's mean NRS was substantially lower than the Control group's, with a p value of 0.0001, with the exception of minutes 20, 25, 30, as well as 45, when the difference in NRS was statistically not substantial. Over the course of 24 hours, the Ketamine group's Ramsay Sedation Score (RSS) at zero, five, ten, as well as sixty minutes was substantially higher (p value>0.05) than that of the Control group. Similar RSS was observed in both groups from 90 minutes to 24 hours after surgery. Brinck EC et al[15] evaluated the efficacy and safety of perioperative intravenous ketamine in adult patients when used for the treatment or prevention of acute pain following general anaesthesia. Studies compared ketamine with placebo, or compared ketamine plus a basic analgesic, such as morphine or non-steroidal anti-inflammatory drug (NSAID), with a basic analgesic alone. Ketamine was given to 4588 participants and 3753 participants served as controls. Types of surgery included ear, nose or throat surgery, wisdom tooth extraction, thoracotomy, lumbar fusion surgery, microdiscectomy, hip joint replacement surgery, knee joint replacement surgery, anterior cruciate ligament repair, knee arthroscopy, mastectomy, haemorrhoidectomy, abdominal surgery, radical prostatectomy, thyroid surgery, elective caesarean section, and laparoscopic surgery. Racemic ketamine bolus doses were predominantly 0.25 mg to 1 mg, and infusions 2 to 5 µg/kg/minute; 10 studies used only S-ketamine and one only R-ketamine. Risk of bias was generally low or uncertain, except for study size; most had fewer than 50 participants per treatment arm, resulting in high heterogeneity, as expected, for most analyses. They did not stratify the main analysis by type of surgery or any other factor, such as dose or timing of ketamine administration, and used a non-stratified analysis. Perioperative intravenous ketamine reduced postoperative opioid consumption over 24 hours by 8 mg morphine equivalents. Over 48 hours, opioid consumption was 13 mg lower (95% CI 10 to 15; 19% from 67 mg with placebo, moderate-quality evidence; 37 studies, 2449 participants). Perioperative intravenous ketamine reduced pain at rest at 24 hours by 5/100 mm on a visual analogue scale, and at 48 hours by 5/100 mm. Pain during movement was reduced at 24 hours, and 48 hours. Results for primary outcomes were consistent when analysed by pain at rest or on movement, operation type, and timing of administration, or sensitivity to study size and pain intensity. No analysis by dose was possible. There was no difference when nitrous oxide was used. We downgraded the quality of the evidence once if numbers of participants were large but small-study effects were present, or twice if numbers were small and small-study effects likely but testing not possible. Ketamine reduced postoperative nausea and vomiting from 27% with placebo to 23% with ketamine (RR 0.88, 95% CI 0.81 to 0.96; the number needed to treat to prevent one episode of postoperative nausea and vomiting with perioperative intravenous ketamine administration was 24. Sumihisa Aida, M.D et al[16] conducted a study where gastrectomy patients were given preemptive analgesia consisting of epidural morphine, intravenous low-dose ketamine, and combinations of these in a randomized, double-blind manner. Postsurgical pain intensity was rated by a visual analog scale, a categoric pain evaluation, and cumulative morphine consumption. Preemptive analgesia by epidural morphine and by intravenous low-dose ketamine were significantly effective but not definitive. With epidural morphine, a significant reduction in visual analog scale scores at rest was observed at 24 and 48 h, and morphine consumption was significantly lower at 6 and 12 h, compared with control values. With intravenous ketamine, visual analog scale scores at rest and morphine consumption were significantly lower at 6, 12, 24, and 48 h than those in control subjects. The combination of epidural morphine and intravenous ketamine provided definitive preemptive analgesia: Visual analog scale scores at rest and morphine consumption were significantly the lowest at 6, 12, 24, and 48 h, and the visual analog scale score during movement and the categoric pain score also were significantly the lowest among the groups. The results suggested that for definitive preemptive analgesia, blockade of opioid and N-methyl-d-aspartate receptors is necessary for upper abdominal surgery such as gastrectomy; singly, either treatment provided significant, but not definitive, postsurgical pain relief. Epidural morphine may affect the spinal cord segmentally, whereas intravenous ketamine may block brain stem sensitization via the vagus nerve during upper abdominal surgery.

CONCLUSION

Preventive low-dose IV Ketamine considerably extends the time to first rescue analgesia (TFA), lowers mean total analgesic demand, and lowers pain scores (NRS) in the post-operative period with minimal side effects, making it an excellent addition to systemic analgesia in abdominal procedures.

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Source of Support: Nil.

Conflict of Interest: None Declared.

Cite this article as: Kumar SS, G. Johnson Devasahaya Raj. Comparative Analysis of Use of Intravenous Low-Dose Ketamine in Addition to Systemic Analgesia Against Systemic Analgesia Alone for Post-Operative Pain Management Following Laparotomies. Int J Med Res Prof. 2019 July; 5(4): 331-34. DOI:10.21276/ijmrp.2019.5.4.084