Original Article

Comparison of Intravenous Ketamine Dosages for Postoperative Analgesia: Efficacy and Adverse Reactions in Abdominal Hysterectomy

Ritu Pauranik, Kiran Girwal, Aseem Sharma, Kishore Kumar Arora

Department of Anaesthesiology, M.G.M. Medical College and M.Y. Hospital, Indore, Madhya Pradesh, India

Abstract

Introduction: Following an abdominal hysterectomy, preemptive analgesia with two intravenous ketamine injections has been used as multimodal analgesia for postoperative pain. Ketamine's ideal dosage for postoperative analgesia that has the least amount of adverse reactions is still up for discussion. **Materials and Methods:** This investigation was conducted at M.G.M. Medical College and M.Y. Hospital, Indore. The study included a total of 90 participants, classified as the American Society of Anesthesiologists classes 1 and 2, within the age range of 18–65 years. There were three groups made after dividing the patients with the help of the chit method so that no preference could be done. Group A was given an intravenous ketamine injection of 0.3 mg/kg, Group B was given an intravenous ketamine injection of 0.2 mg/kg, and Group C then got an intravenous ketamine injection of 0.1 mg/kg. In addition, all groups received subsequent 0.1 mg/kg ketamine injections every 30 min until the completion of the surgery. Various parameters were recorded for 24 h following the procedure, including the time to the first dosage, combined dose of rescue analgesia, combined number of doses of rescue analgesia, and incidence of adverse reactions. **Results:** The demographic profiles of all three groups were found to be comparable. The average time to request the first dosage of rescue analgesia was 316.33 ±66.345, 230± 44.721 & 89 ±26.698 minutes and 89 min, respectively, in Groups A, B, and C. Group A exhibited a significantly longer duration compared to Groups B and C. Postoperatively, at the 24-h mark, Group A displayed the lowest mean pain score (Visual Analog Scale) compared to Group B and Group C, with a statistically significant difference observed at $P = 0.05$. However, the frequency of nausea and vomiting between Groups A and B, as well as C, was not significant. **Conclusion:** Patients undergoing abdominal hysterectomy under spinal anesthesia experience reduced postoperative discomfort when administered intravenous ketamine at a dosage of 0.3 mg/kg, as opposed to lower doses. These results emphasize the potential benefits of higher dosage administration in enhancing postoperative analgesia in such procedures.

Keywords: Postoperative pain, preemptive analgesia, rescue analgesia

Introduction

Preemptive analgesia, which refers to the administration of analgesic therapy before surgery, reduces the development of anomalous processing of sensory input, thereby reducing the magnitude of postoperative pain. Among the various medications investigated for their preemptive analgesic effects, N-methyl D-aspartate (NMDA) receptor antagonists have garnered significant attention due to their involvement in central sensitization and neural regulation.[1]

The most prevalent problem following any surgical procedure is postoperative pain, which calls for the proper analgesia. In the first 24 h following an abdominal hysterectomy, patients experience severe acute pain as the effects of spinal anesthesia start to fade away.[2] There are several medications and methods for reducing postoperative pain; systemic analgesics or local methods are frequently used. Abdominal hysterectomy has

Address for correspondence: Dr. Aseem Sharma, Department of Anaesthesiology, M.G.M. Medical College and M.Y. Hospital, Indore - 452 001, Madhya Pradesh, India.
E-mail: aseem4224@gmail.com

Submitted: 30-Jun-2023 **Revised:** 28-Jul-2023
Accepted: 31-Oct-2023 **Published:** 22-Dec-2023

Access this article online

Quick Response Code:

Website: www.actamedicainternational.com

DOI: 10.4103/amit.amit_46_23

How to cite this article: Pauranik R, Girwal K, Sharma A, Arora KK. Comparison of intravenous ketamine dosages for postoperative analgesia: Efficacy and adverse reactions in abdominal hysterectomy. Acta Med Int 2023;10:121-6.

been managed with a variety of medications, including alpha-2 receptor agonists, nonsteroidal anti-inflammatory medicines, acetaminophen, opioids, tramadol, and local anesthetics.[3-5]

Nonsteroidal anti-inflammatory drugs are ineffective analgesics for abdominal hysterectomy incisions, and systemic opioids have the potential to cause respiratory distress.[6]

To mitigate side effects such as nausea, vomiting, pruritus, and respiratory depression, the utilization of opioid-free analgesia is encouraged throughout the perioperative period.[7] Epidural analgesia serves as an alternative method for alleviating discomfort during abdominal hysterectomy. However, technical challenges associated with its insertion can potentially give rise to life-threatening side effects, including spinal hemorrhage, epidural abscess, and paraplegia.[8,9]

The NMDA receptor antagonist ketamine noncompetitively occupies the phencyclidine binding site of the NMDA receptor. By blocking the NMDA receptor-mediated enhancement of pain, ketamine exerts its effect through an allosteric mechanism.[10] It is believed that the suppression of spinal cord central sensitization underlies the sustained analgesic action of ketamine, despite its short half-life and subanesthetic dosages. Moreover, ketamine hinders the internalization of opioid receptors and activates the monoaminergic descending inhibitory pathway at supraspinal sites, thereby preventing the development of acute tolerance to opioids, hyperalgesia, and hyperreflexia. Subanesthetic dosages (0.3 mg/kg) offer analgesic benefits with reduced overt adverse effects.[7]

The need for postoperative analgesics can be alleviated by the administration of a small dosage range of 0.1–0.3 mg/kg of ketamine. However, the determination of an ideal ketamine dosage that effectively relieves postoperative pain while minimizing significant adverse effects remains a subject of ongoing debate. Despite the existence of numerous trials examining the analgesic efficacy of low-dose ketamine, there is a scarcity of research comparing different intravenous ketamine dosages specifically for postoperative analgesia. Thus, we investigated the analgesic effectiveness of three distinct ketamine dosages in patients scheduled for abdominal hysterectomy.

The primary objective was to assess the duration of postoperative analgesia among patients who received three different subanesthetic intravenous ketamine dosages. Secondary objectives included the comparison of the combined amount of rescue analgesia administered, the combined number of doses administered, the monitoring of hemodynamic changes, and the evaluation of the frequency of side events within each group in the 24 h following surgery.

Materials and Methods

On receiving approval from the Institutional Ethics Committee (EC/MGM/July-21/47), a comparative research study employing a randomized, double-blind design was conducted at M.G.M. Medical College and M.Y. Hospital, Indore. The study cohort consisted of 90 patients scheduled for spinal abdominal hysterectomy, classified as the American Society of Anesthesiologists (ASA) physical status Grades 1 or 2 [Figure 1]. During a preoperative examination which was conducted one day prior to the surgery. The patient's consent and a detailed discussion of the research protocol, was conducted. In the preoperative room, detailed instructions were provided to patients regarding the comprehension of the Visual Analog Scale (VAS) score. Patients were designated randomly to one of the three groups utilizing chits.

An 18-gauge cannula was inserted for intravenous administration, following which the patients received a preload of 10 ml/kg of lactated Ringer's solution half an hour before the administration of spinal anesthesia. The patient's pulse, blood pressure (BP), and oxygen saturation (SpO_2) were monitored at the commencement of the surgical procedure. Spinal anesthesia was induced by injecting 3.2cc of 0.5% bupivacaine heavy into the L3–L4 interspinous region using a 25-gauge spinal needle while the patient was in a seated position. Subsequently, the patient was positioned supine immediately after the spinal anesthesia block.

Pin-prick tests were performed in the midclavicular line on both sides at 1-min intervals to evaluate the sensory block, and surgery was only permitted when the block height approached T6. The medication in the research was given intravenously 5 min before the incision was made.

Each group received an initial dose of ketamine intravenously (0.3 mg/kg in Group A, 0.2 mg/kg in Group B, and 0.1 mg/kg in Group C), followed by a 0.1 mg/kg injection intravenously every half an hour until the completion of the operation.

All participants received 1 mg of intravenous midazolam injection before receiving the study medication. A simple face mask was used to deliver 4 L/min of oxygen. After the spinal anesthetic was administered, continuous monitoring of the pulse rate, BP (systolic, diastolic, and mean arterial pressure [MAP]), and peripheral SpO_2 was set up.

In cases of hypotension ("a decrease in MAP of 20% or more from the preanesthetic baseline value"), a 100 ml IV fluid bolus and intravenous injection of 5 mg of ephedrine were administered. A heart rate of <50 beats/min was considered bradycardia, and an intravenous dose of atropine (0.6 mg) was used to treat it. The Ramsay Sedation Score was used to track the level of sedation during and after surgery.

Injection of diclofenac sodium 1 mg/kg intravenously for 30 min was administered as rescue analgesia when the VAS score was more than 4 at 0, 2, 6, 10, 14, 18, and 24 h after surgery. The duration of analgesia was defined as "the time that passed between the initial request for rescue analgesia and the injection of the study medication." In the first 24 h, the number and kind of analgesic dosages taken were documented.

For the first 24 h, every patient was closely monitored for adverse reactions. Ondansetron, in a dose of 4 mg, was injected

intravenously to combat postoperative sickness. At regular intervals after surgery, the patient's BP, pulse rate, SpO_2, VAS score, and sedation score were recorded.

Statistical analysis

Using an analysis of variance with three groups and a large effect size of 0.4, the sample size was determined with the help of G*Power, version 3.1.9.2. The estimated total number of participants was 87. According to the consort diagram, we divided our 90 patients into two groups of 30 each.

Results

The demographics of the three groups were compared in this study. Age (in years) showed no significant difference among the groups ($P = 0.730$). Weight (in kilograms) also did not differ significantly between the groups ($P = 0.103$). The distribution of ASA grades (Grade 1 or Grade 2) was similar across all groups ($P = 0.629$).

Table 1 compares the time taken for the first dose of rescue analgesia among the groups. Group A had the longest duration for the first dose of rescue analgesia, followed by Group B, and then Group C. The analysis revealed a significant difference in the time of the first dose of rescue analgesia between the groups ($P = 0.02$).

The results in Table 2 indicate that patients in Group A and Group B required significantly less rescue analgesic within 24 h after surgery compared to Group C, despite Group C having the highest mean total dosage.

In Table 3, the combined number of rescue analgesia dosages within a 24-h period was compared among groups. The statistical analysis by Pearson's Chi-square test indicated a significant difference in the combined number of rescue analgesia dosages among the three groups ($P = 0.02$). Group A had a higher proportion of patients requiring a single dosage, while Group B had a higher proportion requiring two dosages. Group C had the highest proportion of patients requiring three dosages.

Significant differences were observed [Table 4] between the groups at several time points. Immediately after surgery (0 h), Group C had the highest mean VAS score (0.9 ± 0.31) compared to Group A (0.2 ± 0.5) and Group B (0.4 ± 0.41) ($P = 0.023$). Throughout the postoperative period, Group C consistently had higher mean VAS scores compared to the other groups. This trend was particularly notable at 2 h (Group C: 4.9 ± 3.26), 4 h (Group C: 4.4 ± 3.25), 5 h (Group C: 1.7 ± 2.14), and 6 h (Group C: 6 ± 2.57) ($P < 0.05$). Furthermore, Group C had significantly higher mean VAS scores than Group A and Group B at 12 h ($P = 0.003$) and 24 h ($P = 0.02$) postsurgery.

Table 5 presents the comparison of adverse effects among the three groups: Group A, Group B, and Group C. No cases of hallucination, vivid dreams, or nystagmus were reported in any of the study groups. For nausea/vomiting, Group A had six cases, Group B had four cases, and Group C had three cases. However, there was no statistically significant difference in the number of cases of nausea/vomiting between Group A and both Group B and Group C.

Table 1: Comparison of time of the first dosage of rescue analgesia among the three groups

Group	Mean duration – first dose of rescue analgesia (min)	*P*
Group A	316.33±66.345	0.02
Group B	230±44.721	
Group C	89±26.698	

Table 2: Comparison of the combined dosage of rescue analgesia between the groups

	Mean combined dosage of rescue analgesia (mg)	*P*
Group A	95±33.733	0.01
Group B	140±38.056	
Group C	255±103.474	

Table 3: Comparison of the combined number of dosage of rescue analgesia among the three groups

Combined number of rescue analgesia in 24-h	Group A	Group B	Group C	Total
1	22	6	0	28
2	8	24	6	38
3	0	0	24	24
Pearson's Chi-square		91.083		
P		0.02		

Table 4: Comparison of the mean Visual Analog Scale score between the three groups in the postoperative period

Time (h)	Group A	Group B	Group C	*P*
0	0.2±0.5	0.4±0.41	0.9±0.31	0.02
1	1±0.0	1±0.0	2.8±2.8	0.014
2	1.13±0.35	1.47±1.78	4.9±3.26	0.021
3	1±0.0	1.33±0.8	1.53±1.78	0.185
4	1±0.0	1.93±2.24	4.4±3.25	0.031
5	1±0.0	1±0.37	1.7±2.14	0.049
6	2.79±0.5	5.73±2.82	6±2.57	0.003
12	2.89±2.96	3.73±3.41	5.67±2.82	0.003
24	1.07±0.0	2.07±0.45	5.4±2.95	0.02

Table 5: Comparison of adverse effects

Adverse effect	Group A	Group B	Group C	Total
Nausea/vomiting	6	4	3	13
Hallucination	0	0	0	0
Vivid dream	0	0	0	0
Nystagmus	0	0	0	0
Pearson's Chi-square		1.259		
P		0.533		

Discussion

A comparative analysis of age, body mass index (BMI), and ASA physical statuses among the three groups was conducted, as presented in Table 6. The findings revealed no noticeable differences, indicating that the patient populations in the groups were comparable. Table 1 examined the duration to the first rescue analgesic dosage. Notably, patients in Group A took significantly longer in both Group B and Group C before requesting a rescue analgesic. A higher intravenous ketamine dose (0.3 mg/kg) resulted in delayed pain alleviation and reduced the need for additional analgesics in Group A. In Table 2, the mean combined dosages of rescue analgesia were compared among the three groups. Group A exhibited substantially lower mean combined doses compared to Groups B and C. In Group C, the mean combined dose was greater, indicating a greater need for additional pain relief. Table 3 focused on the number of rescue analgesia doses administered within a 24-h period. Group A had significantly fewer rescue analgesia doses compared to Groups B and C. These findings suggest that pain management was more effective in Group A, as patients required fewer combined analgesic doses. The VAS scores, as presented in Table 4, provided insights into the pain levels experienced by the three groups over time. Group A consistently exhibited the lowest average VAS scores, indicating superior pain management compared to Groups B and C. However, at the 24-h mark, Group C had the highest mean VAS score, indicating suboptimal pain management in that group. Finally, Table 5 compares the occurrence of adverse effects among the groups. There was no statistically significant difference in the number of cases of nausea/vomiting between Group A and both Group B and Group C. Episodes of nystagmus, vivid dreams, or hallucinations were not complained of or noticed.

Table 6: Comparison of demographics

Characteristics	Mean±SD			*P*
	Group A	Group B	Group C	
Age (years)	55.66±4.92	56.13±3.98	56.50±3.25	0.730
Weight (kg)	55.60±5.09	53.58±5.85	54.06±5.76	0.103
ASA grade (1/2)	20/10	18/12	20/10	0.629

SD: Standard deviation, ASA: American Society of Anesthesiologists

Significant postoperative discomfort is common after abdominal hysterectomy, which contributes to a higher rate of morbidity for these patients. A prolonged hospital stay, atelectasis, hypoxemia, sputum retention from decreased coughing, and an increased risk of developing a deep-vein thrombosis have all been linked to postoperative discomfort that is too intense for the patient to tolerate. Chronic pain can be alleviated with subanesthetic dosages of ketamine due to its analgesic properties. Anesthesia using ketamine has been shown in many clinical trials to lower postoperative pain medication need for opioids.[11]

Participants across all three groups in this study were similar in terms of age, BMI, and ASA classification. In a comparative analysis of the three groups (Groups A, B, and C), it was found that Group A had a longer time to request the first rescue analgesic medication postoperatively, with a mean time of 316 min, compared to Group B (230 min) and Group C (89 min). Similarly, in another study conducted by Bhiwal *et al*.,[12] a high-dose intravenous ketamine group (0.3 mg/kg) waited on average 6.18 ± 1.61 h longer than the low-dose ketamine group (0.15 mg/kg) and the control group (receiving saline) before requesting rescue analgesia.

Menkiti *et al*. conducted a study on African parturients undergoing cesarean birth under spinal anesthesia and found that intravenous ketamine (0.15 mg/kg) provided long-lasting postoperative analgesia than the control group. The ketamine group (Group BK) experienced significantly longer analgesia duration (20,914.7 min) than Group B (16,414.1 min, $P < 0.001$).[13] Similarly, Sen *et al*. conducted a trial involving 90 participants undergoing cesarean delivery with spinal anesthesia.

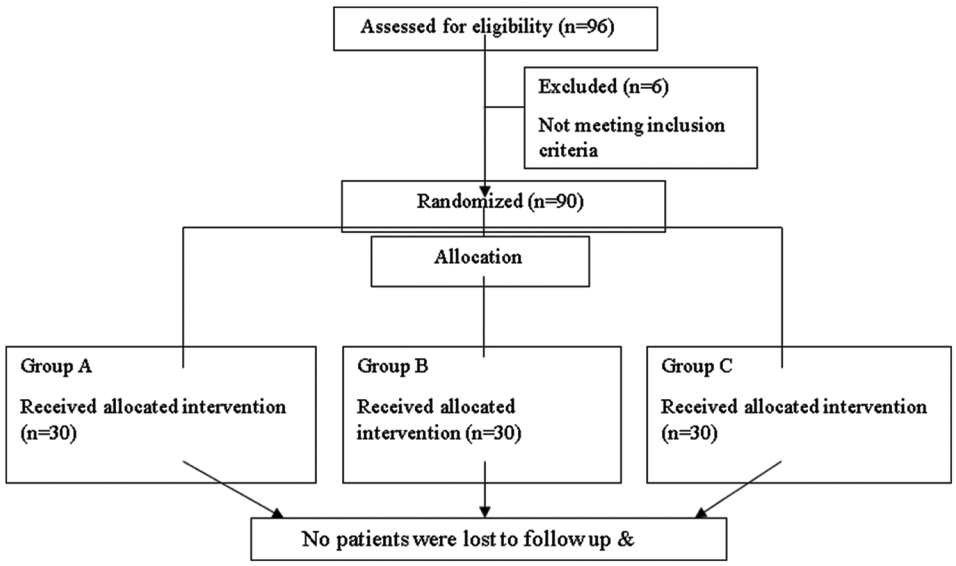

Figure 1: Consort diagram

They found that both the ketamine group (0.15 mg/kg) and the fentanyl group required a significantly longer time compared to the control group (144 min) before requesting analgesia for the first time.[14] In another randomized clinical trial, it was observed that intravenous ketamine (0.25 mg/kg) reduced the need for postoperative analgesics and had fewer side effects compared to opioids in recovering from cesarean section.[15] These studies demonstrate that higher doses of intravenous ketamine result in delayed pain relief and decreased need for rescue analgesics, while lower doses can provide long-lasting analgesia. However, it is important to note that the specific dosages used varied. Postoperative pain is caused by cerebral and peripheral sensitization, according to research. Several mechanisms have been proposed to explain how low-dose ketamine can be analgesic, based on clinical trials. These include the activation of monoaminergic descending inhibitory pathways at supraspinal sites, the prevention of acute opioid tolerance, and the suppression of central sensitization. The ketamine used in our trial was administered intravenously at a low dosage, which may have helped lessen discomfort and slowed the development of central sensitization. Ketamine's antagonism of spinal NMDA receptor sites may be responsible for this action, although it also acts on many opioid and cholinergic receptors. It appears that total blockage of the nociceptive input and NMDA receptor activation may be required for a final analgesic response since better postoperative analgesia is seen with greater subanesthetic dosages of intravenous ketamine. When the plasma concentration of ketamine is more than 100 ng/ml, it has a direct analgesic effect.[14,15]

At 0, 0.5, 1, 2, 3.4, 6, 12, and 24 h after surgery, patients in Group C reported substantially higher VAS ratings compared to patients in Groups A and B ($P < 0.05$). In Groups A and B, patients reported much less pain immediately following surgery than those in Group C, where the mean VAS score was 5.4 ± 2.95 compared to 1.07 ± 00 and 2.07 ± 0.45, respectively. In line with previous research, Rahmanian *et al*.[16] demonstrated that the control group had higher VAS scores at multiple postoperative time points (1, 2, 6, and 12 h). In a study conducted by Menkiti ID *et al*., it was observed that the control group exhibited elevated postoperative Visual Analog Scale (VAS) scores up to 150 minutes after the procedure, Similarly, Sen S *et al*. also reported increased VAS scores in the control group at 90 minutes, 150 minutes, and 180 minutes post-surgery.[13,14]

In contrast, Bauchat *et al*. found no significant differences in the Numeric Rating Scale scores between the groups within the first 24 h after surgery.[17] This lack of significant difference may be caused by the implementation of a multimodal analgesic approach, which included the administration of fentanyl (15 μg) and morphine (150 μg) intrathecally in addition to 12 mg hyperbaric bupivacaine during spinal anesthesia, as well as the provision of a standardized postoperative analgesic regimen.

Regarding sedation levels, all patients in Group A achieved a Ramsay Sedation Score of 1 immediately after the surgical procedure, indicating an alert and responsive state. Only one patient in Group A required light sedation (Ramsay Sedation Score 2). None of the patients in any of the three groups exhibited higher sedation scores postoperatively. Menkiti *et al*. also reported similar findings of moderate sedation.[13] Ebong *et al*. observed a maximum Ramsay Sedation Score of 2 in the ketamine group, likely resulting from the central nervous system depressant effect of ketamine, while Sen *et al*. observed mild drowsiness in only two individuals (6.6%).[14,18]

The current investigation, along with previous studies conducted by Rahmanian *et al*., Bauchat *et al*., and Haliloglu *et al*., suggests that there were no notable discrepancies in the incidence of postoperative nausea and vomiting among the three groups.[16,17,19] In addition, none of the participants in any group exhibited hallucinations, abnormal dreaming, or nystagmus. Moreover, the intraoperative hemodynamic profiles were comparable across all groups.

The limitations of our investigation were significant. There was no placebo group present. The study's pain evaluation method is subjective, which may introduce bias into patients' reports. Patients receiving only one specific operation were included in the research. Our findings need to be confirmed by larger, multicenter studies.

Women undergoing spinal anesthesia for abdominal hysterectomy had longer durations of postoperative analgesia and lower combined analgesic requirements in the first 24 h after receiving 0.3 mg/kg of intravenous ketamine compared to 0.2 mg/kg and 0.1 mg/kg.

Conclusion

This study provides evidence that administering a greater dose of intravenous ketamine (0.3 mg/kg) has a substantial positive impact on the treatment of postoperative pain in women who have abdominal hysterectomy while under spinal anesthesia. Patients administered with this dosage revealed a postponed initiation of pain, necessitated a reduced amount of supplementary pain relievers, and reported diminished pain levels, as evidenced by VAS ratings. The results, together with a positive safety record, highlight the promise of ketamine in improving techniques for managing postoperative pain.

Acknowledgment

We would like to extend our gratitude to those who have helped me in the completion of this research paper. Special thanks to Dr. Ritu Pauranik, Dr. Kiran Girwal, and Dr. K.K. Arora.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Singh H, Kundra S, Singh RM, Grewal A, Kaul TK, Sood D. Preemptive analgesia with ketamine for laparoscopic cholecystectomy.

J Anaesthesiol Clin Pharmacol 2013;29:478-84.
2. Raja SN, Carr DB, Cohen M, Finnerup NB, Flor H, Gibson S, *et al.* The revised international association for the study of pain definition of pain: Concepts, challenges, and compromises. Pain 2020;161:1976-82.
3. Sherman M, Sethi S, Hindle AK, Chanza T. Multimodal pain management in the perioperative setting. Open J Anesthesiol 2020;10:47-71.
4. McEvoy MD, Scott MJ, Gordon DB, Grant SA, Thacker JK, Wu CL, *et al.* American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) joint consensus statement on optimal analgesia within an enhanced recovery pathway for colorectal surgery: Part 1-from the preoperative period to PACU. Perioper Med (Lond) 2017;6:8.
5. Kashefi P. The benefits of intraoperative small-dose ketamine on postoperative pain after cesarean section. Anesthesiology 2006;104:27.
6. Vadivelu N, Mitra S, Schermer E, Kodumudi V, Kaye AD, Urman RD. Preventive analgesia for postoperative pain control: A broader concept. Local Reg Anesth 2014;7:17-22.
7. Kwok RF, Lim J, Chan MT, Gin T, Chiu WK. Preoperative ketamine improves postoperative analgesia after gynecologic laparoscopic surgery. Anesth Analg 2004;98:1044-9.
8. Kararmaz A, Kaya S, Karaman H, Turhanoglu S, Ozyilmaz MA. Intraoperative intravenous ketamine in combination with epidural analgesia: Postoperative analgesia after renal surgery. Anesth Analg 2003;97:1092-6.
9. Subramaniam K, Subramaniam B, Pawar DK, Kumar L. Evaluation of the safety and efficacy of epidural ketamine combined with morphine for postoperative analgesia after major upper abdominal surgery. J Clin Anesth 2001;13:339-44.
10. Aroni F, Iacovidou N, Dontas I, Pourzitaki C, Xanthos T. Pharmacological aspects and potential new clinical applications of ketamine: Reevaluation of an old drug. J Clin Pharmacol 2009;49:957-64.
11. Behdad S, Hajiesmaeili MR, Abbasi HR, Ayatollahi V, Khadiv Z, Sedaghat A. Analgesic effects of intravenous ketamine during spinal anesthesia in pregnant women undergone caesarean section; a randomized clinical trial. Anesth Pain Med 2013;3:230-3.
12. Bhiwal AK, Sharma V, Sharma K, Tripathi A, Gupta S. Sub-anaesthetic bolus dose of intravenous ketamine for postoperative pain following caesarean section. J Obstet Anaesth Crit Care 2019;9:88-93.
13. Menkiti ID, Desalu I, Kushimo OT. Low-dose intravenous ketamine improves postoperative analgesia after caesarean delivery with spinal bupivacaine in African parturients. Int J Obstet Anesth 2012;21:217-21.
14. Sen S, Ozmert G, Aydin ON, Baran N, Caliskan E. The persisting analgesic effect of low-dose intravenous ketamine after spinal anaesthesia for caesarean section. Eur J Anaesthesiol 2005;22:518-23.
15. Samuel H, Aweke S, Tuni J. Effect of low-dose intravenous ketamine on postoperative pain following cesarean section under spinal anesthesia: A prospective cohort study, Ethiopia. Ann Med Surg (Lond) 2022;77:103570.
16. Rahmanian M, Leysi M, Hemmati AA, Mirmohammadkhani M. The effect of low-dose intravenous ketamine on postoperative pain following cesarean section with spinal anesthesia: A randomized clinical trial. Oman Med J 2015;30:11-6.
17. Bauchat JR, Higgins N, Wojciechowski KG, McCarthy RJ, Toledo P, Wong CA. Low-dose ketamine with multimodal postcesarean delivery analgesia: A randomized controlled trial. Int J Obstet Anesth 2011;20:3-9.
18. Ebong EJ, Mato CN, Fyneface-Ogan S. Pre-incisional intravenous low-dose ketamine does not cause pre-emptive analgesic effect following caesarean section under spinal anaesthesia. J Anaesth Clin Res 2011;2:138.
19. Haliloglu M, Ozdemir M, Uzture N, Cenksoy PO, Bakan N. Perioperative low-dose ketamine improves postoperative analgesia following cesarean delivery with general anesthesia. J Matern Fetal Neonatal Med 2016;29:962-6.