Journal of Midwifery & Reproductive Health

JMRH.mums.ac.ir

The Effect of Intravenous Ketamine on Analgesic Requirement after Spinal Anesthesia in Women Undergoing Caesarean Section: a Randomized Clinical Trial

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ARTICLE INFO

Article type:
Original article

Article History:
Received: 27-Jul-2023
Accepted: 04-Sep-2023

Keywords:
Ketamine
Midazolam
Pain
Cesarean Section
Spinal Anesthesia

ABSTRACT

Background & aim: The use of opioids for pain relief after cesarean section (C/S) can result in adverse maternal and neonatal outcomes. Therefore, it is important to consider non-opioid analgesics as an alternative. This study examined the effect of intravenous ketamine on analgesic requirement after spinal anesthesia in women undergoing C/S.

Methods: This double-blind randomized clinical trial included 80 pregnant women under spinal anesthesia during a planned C/S, who were recruited from trainig hospitals of Mashhad, Iran between February and August 2022. The participants were selected using convenience sampling and assigned to two intervention (40) and control (40) groups through random allocation. The intervention group received intravenous ketamine (0.5 mg/kg) and midazolam (0.02 mg/kg) immediately after umbilical cord clamping, while the control group received midazolam alone (0.02 mg/kg). Pain scores were recorded at baseline, 6th, 12th, and 24th hours after elective C/S using the Visual Analog Scale(VAS), along with the amount of requiremen to analgesics. Data analysis was performed by SPSS software (version 16) using Chi-square, T-test and repeated measure ANOVA test.

Results: A significant difference was seen in pain scores between the two groups at different hours and over time (P=0.009). The intervention group reported significantly lower levels of pain than the control group (P=0.002) and a significantly lower need for painkillers during the first hour (P=0.04).

Conclusion: Administration of intravenous ketamine in elective C/S with spinal anesthesia in the first hour has a significant effect on pain relief Therefore, it can be considered the drug of choice for alleviating pain.

► *Please cite this paper as*:

Samedi M, Tabari M, Bakhtiari E, Abolbashari S, Asghari S. The Effect of Intravenous Ketamine on Analgesic Requirement after Spinal Anesthesia in Women Undergoing Cesarean Section: A Randomized Clinical Trial. Journal of Midwifery and Reproductive Health. 2025; 13(1): 4633-4641. DOI: 10.22038/JMRH.2023.74012.2160

Introduction

Postoperative pain is a common problem following surgery and can significantly affect patient satisfaction during the post-surgery period (1). Managing postoperative pain is one of the major challenges in clinical medicine (2), particularly after a cesarean section (C/S), where pain management is crucial for successful breastfeeding and maternal-infant bonding. Two primary groups of analgesics opioids and non-opioids, are used to control pain after a C/S (3). While opioids are typically the first choice for controlling severe and acute pain, they can have adverse side effects on both mothers and infants, depending on the dose and administration method. Therefore, finding an effective solution with minimal side effects and drug consumption to manage acute and chronic postoperative pain has become a research priority in this field (4). Ketamine, a fast-acting, non-barbiturate anesthetic with a high safety margin, is effective in treating various types of pain, including chronic and persistent pain, neuropathy, depression, postoperative pain, and shivering (5). Ketamine functions as a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors, which play a crucial role in processing pain input data (6). However, the use of ketamine can cause psychomimetic side effects and hallucinations (7). Despite experimental

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research on animals, its use in humans has produced variable results (8). Several studies have reported the benefits of intravenous ketamine for reducing postoperative pain, but others have not shown any clinical advantages (9-10). In contrast, midazolam, one of the most common benzodiazepines used in anesthesia, affects the transmission of pain signals in the spinal cord by modulating Gamma-Aminobutyric Acid (GABA) receptors (11). The analgesic effects of intrathecal midazolam have been investigated in several patient populations and conditions (12), but few studies have examined its intravenous effects on acute pain after C/S (13). Furthermore, it is unclear whether combining ketamine and midazolam would be more effective in reducing painkiller requirements after a C/S. This study aimed to examine the effect of intravenous ketamine on analgesic requirement after spinal anesthesia in women undergoing C/S.

Materials and Methods

This randomized, double-blind, two-parallel-arms clinical trial was conducted among pregnant women admitted for cesarean surgery in educational hospitals affiliated with Mashhad University of Medical Sciences, Mashhad, Iran between February and August 2022 (registered as IRCT20211013052753N1 at IRCT.ir).

A total of 80 pregnant women, who were candidates for elective C/S according to the criteria of American Society of Anesthesiologists (ASA) class I, were involved in this study (Figure 1). Inclusion criteria included pregnant women over 18 years of age who were candidates for C/S, consented to participate in the study, did not have drug allergies or experienced incidents during the C/S such as severe bleeding that required blood transfusion, no contraindications for spinal anesthesia, no head trauma history, no addiction, no use of psychiatric drugs and painkillers, no hallucinations, no delirium, no history of seizure, hypertension, intracranial bleeding, and no sensitivity to ketamine. Unwillingness to continue the study was the exclusion criterion.

A sample size of 40 participants in each group was calculated according to the mean difference in painkiller dose used in pregnant women receiving ketamine compared with controls (54.17±12.86 and 74.44±33.82, respectively) according to the study by Behdad et al. (14) using α=0.05 and β=0.1 and 10% drop out. The participants were selected using convenience sampling and assigned to two intervention (40) and control (40) groups through random allocation.

In this double-blind randomized clinical trial, both participants and outcome assessors were blinded. Block randomization was performed using a computer-generated sequence, and allocation concealment was achieved through sealed envelopes. The intervention group underwent an intravenous injection of 0.5 mg/kg ketamine (Rotexmadica; Germany) along with 0.02 mg/kg midazolam (Aburaihan Pharmaceutical Co., Tehran, Iran) in a 2 ml syringe, while the control group received only 0.02 mg/kg midazolam in the same syringes. During the C/S, the anesthesiologist administered midazolam with or without ketamine to the participants after umbilical cord clamping based on random numbers generated by a table. To perform spinal anesthesia, bupivacaine 0.5% (Mylan S.A.S., France) was injected in either midline or paramedian orientation at the L2-L3 or L3-L4 intervertebral spaces using spinal needles while the participant was in a sitting position. Standard anesthesia monitoring was performed for all participants throughout the operation. The tools used in the research include the demographic information form, which includes nine questions, and the Visual Analogue Scale (VAS). Pain scores were measured using the VAS at 0, 6, 12, and 24 hours after delivery, with the VAS being a 10-cm line where 0 indicates "no pain" and 10 indicates "worst possible pain". The validity and reliability of VAS were documented in previous studies (15). Throughout the study, the interviewer consistently employed a standardized set of instructions to assess and score VAS. Apgar scores for newborns were measured in the first and fifth minutes after birth.

Data was analyzed using SPSS version 16 (SPSS Inc., Chicago, Illinois, United States). Mean± standard deviation (SD) was used to present quantitative variables, while qualitative variables were expressed in percentage form. The association of qualitative variables was

assessed by the Fisher exact test, or Chi-square. Quantitative variables were compared via an independent-sample T-test. The pain score at different time points was compared using a repeated measure ANOVA test. A p-value lower than 0.05 was considered statistically significant.

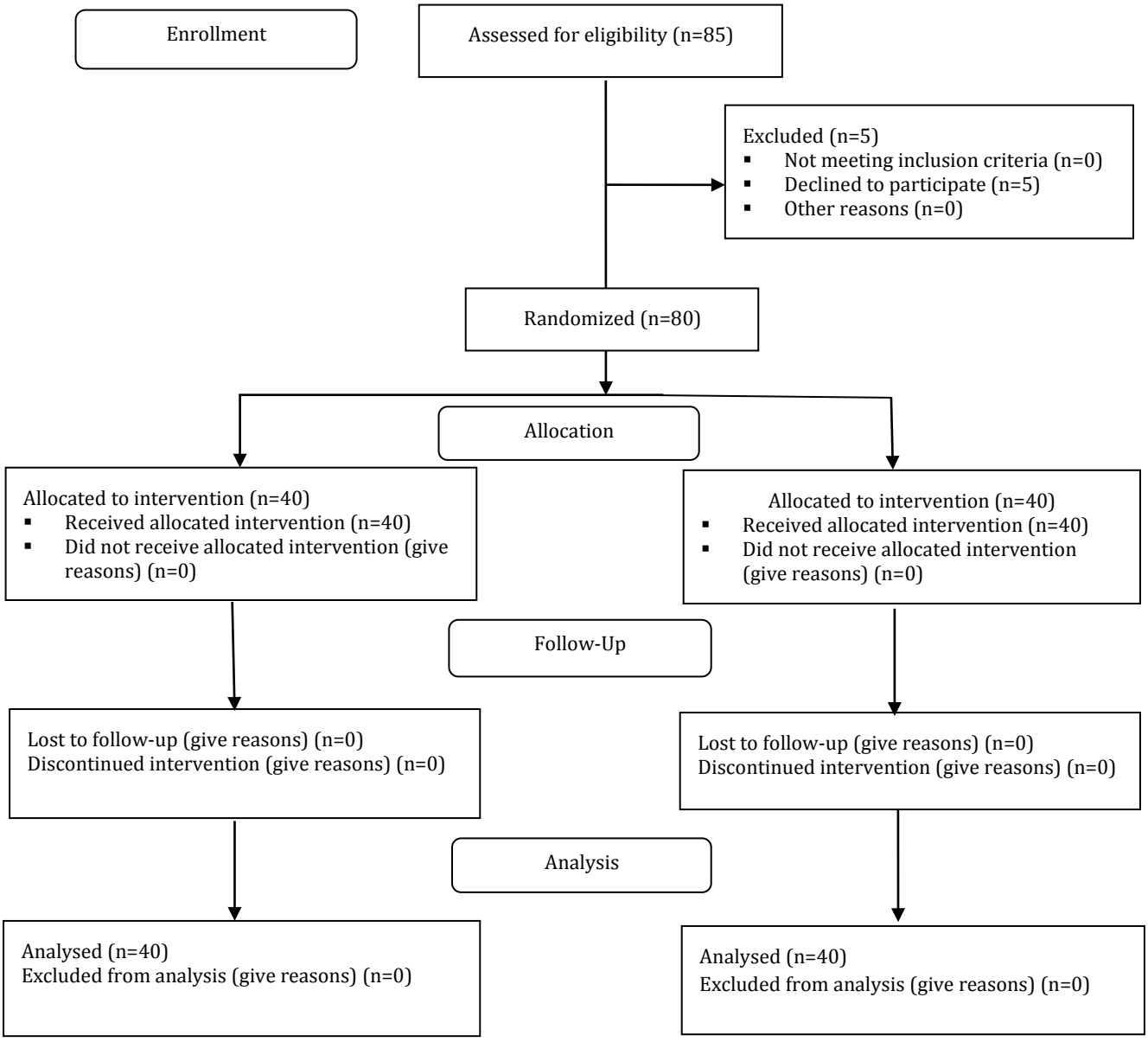

Figure 1. The CONSORT flow diagram of participants' selection in the two groups

Results

In this study, 80 pregnant women who were candidates for elective C/S were included. Based on the data presented in Table 1, the average age of the participants in the control and intervention groups was 28.63±7.71 and 28.6±48.75 years, respectively (P=0.92). Furthermore, the two groups did not differ in terms of weight (P=0.78) and height (P=0.14)(Table 1).

Table 1. Comparison of age, weight, and height in two intervention and control groups

Variable	Control	Intervention	P-Value*
Age (years)	28.63±7.71	28.48±6.75	0.92
Weight (kilograms)	74.38±8.02	73.88±8.03	0.78
Height (centimeters)	160.35±4.67	158.88±4.28	0.14
Delivery details			
Gravidity (number)	2.85±1.49	2.38±1.35	0.14
Living children (number)	1.40±1.03	1.20±1.06	0.39

*independent sample t-test

The most common underlying disease among the groups was Gestational diabetes mellitus (GDM). Levothyroxine was the most commonly used drug among the participants (6.25%), and there was a statistically significant difference in the prevalence of the drug used between the intervention and control groups (P=0.01). Most of the participants in both groups had no history of previous transfusions. The data are presented in Table 2.

Table 2. Comparison of individual characteristics in two intervention and control groups

Variable	Control (%)	Intervention (%)	P-Value#
Underlying disease			
GDM	6 (60)	3 (30)	0.07
*Low platelet	1 (10)	0 (0)	
Asthma	1 (10)	1 (10)	
Minor thalassemia	2 (20)	0 (0)	
Hypothyroid	0 (0)	5 (50)	
HBV	0 (0)	1 (10)	
History of transfusion			
No	39 (97.5)	40 (100)	0.14
Yes	1 (2.5)	0 (0)	
Sex of children			
Male	18 (45)	16 (40)	0.65
Female	22 (55)	24 (60)	

* A platelet count of less than 150,000 is considered thrombocytopenia in this study. # Chi-square or Fisher exact test
GDM: Gestational Diabetes Mellitus, HBV: Hepatitis B Virus

Based on the data presented in Table 3, it was found that during the first hour after the operation, 5% of participants in the intervention group required painkillers, compared to 20% in the control group. The difference in the percentage of participants who needed painkillers between the two groups during this time was statistically significant (P=0.04). However, no significant differences were observed in the need for painkillers between the two groups during the other investigated hours (P=0.39, p=0.36 and P>0.99 for 6, 12 and 24 hours after the operation, respectively). In terms of the type of painkiller used at 0, 6, and 12 hours after the operation, there was no statistically significant difference between the two groups (P=0.467, p=0.634 and p=174 respectively). At 24 hours after the operation, diclofenac was found to be the most commonly used painkiller and a statistically significant difference was observed between the two groups (P=0.001).

Table 3. The frequency of need for painkillers in intervention and control groups

Need to painkillers(hour)	Control (%)	Intervention (%)	P-Value*
0			
No	32 (80)	38 (95)	0.04
Yes	8 (20)	2 (5)	
6			
No	2 (5)	4 (10)	0.39
Yes	38 (95)	36 (90)	
12			
No	5 (12.5)	8 (20)	0.36
Yes	35 (87.5)	32 (80)	
24			
No	24 (60)	23 (57.5)	>0.99
Yes	16 (40)	17 (42.5)	

*Chi-square test, a p-value less than 0.05 was considered as significant

Table 4. Comparison of pain scores at different hours in two intervention and control groups

Pain (hour)	Control	Intervention	P-Value*
0	1.95±1.64	0.95±1.13	0.00
6	6.08±1.50	5. 43±1.56	0.06
12	5.30±1.47	5.05±1.78	0.49
24	2.73±1.08	2.58±1.25	0.57

*Independent T-test, a p-value less than 0.05 was considered as significant

The overall pain score measured at different times showed a significant difference between the intervention and control groups (P=0.009). However, there was no statistically significant difference in the pain score between the two groups at 6, 12, and 24 hours after the operation (P=0.06, p=0.49 and P=0.57 respectively). The difference was only significant in the first hour after the operation (P=0.002). The data are presented in Table 4. Furthermore, the results showed a significant difference between the two groups with the pain score over time, with participants in the intervention group experiencing less pain than those in the control group (P=0.03).

Figure 2 shows the changes in the pain level in the groups. Based on the statistical analysis of the pain level in the two groups, there was a significant difference over time.

In the intra-group examination, in terms of pain level and based on the Repeated Measure ANOVA test, the pain level in the first hour after the operation and at 6, 12, and 24 hours after the operation had a statistically significant difference in the intervention group (P<0.001). Also, in this group, the amount of pain at 6 hours was statistically significantly different from the amount of pain at 24 hours (P<0.001). Also, the amount of pain at 12 hours and 24 hours had a statistically significant difference (P<0.001).

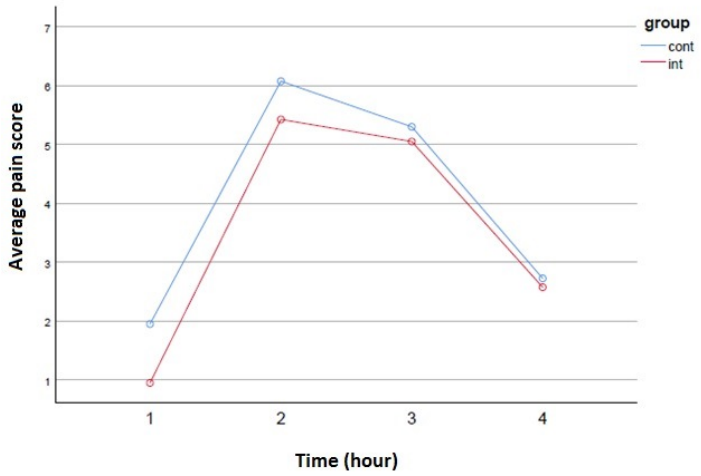

Figure 2. Comparison of average pain scores at different hours in two intervention and control groups

Discussion

The study aimed to evaluate the effect of intravenous ketamine on analgesic requirement after spinal anesthesia in women undergoing C/S. The results showed that the use of ketamine significantly reduced pain levels and the need for painkillers in the first hour following surgery, but there was an insignificant difference in pain reduction between the two groups at 6, 12, and 24 hours post-surgery. Other parameters such as type and dose of painkillers used, history of transfusion, frequency of underlying diseases, and drugs used by patients were not significantly different between the two groups. Therefore, it can be concluded that ketamine has a beneficial effect on reducing pain levels and the need for painkillers in the early hours after surgery in elective C/S.

Improper pain control after surgery causes short-term and long-term complications. Therefore, the use of appropriate painkillers after surgery leads to earlier activity by the mother, better care of the baby (including breast milk feeding and mother-baby communication), and prevention of post-surgery morbidities. The use of ketamine as an antagonist of NMDA receptors is effective in postoperative analgesia and the prevention of neuropathic pain (16). In a randomized, double-blind clinical trial study led by Milani et al. (2014), 60 women who underwent C/S entered the study and were randomly divided into two groups: the case group received ketamine with a dose of 0.2 mg/kg, and the control group received normal saline with an equal volume before the operation. The results of this study did not report any significant statistical difference in the mean VAS between the two groups (P=0.70), neither in terms of the mean number of diclofenac suppositories consumed (P=0.87) nor in the meantime to start the first dose (P=0.76). Furthermore, no use of pethidine was reported in the case group, while in the control group, 20% of patients needed pethidine (P=0.02). The results of this study stated that the use of ketamine prophylaxis before the operation can be effective in reducing the consumption of painkillers after the operation. This finding is consistent with our study (17).

In a study conducted by Sen et al. (2005) in Turkey, 90 cesarean patients were involved in the study, who were randomly assigned to one of three groups: the control group received normal saline, the second group received ketamine (0.15 mg/kg), and the third group received fentanyl (10 mg). The study results revealed that the ketamine group had a significantly longer time of need for analgesia (197 minutes) compared to the fentanyl group (165 minutes) and the control group (144 minutes) (18).

In previous studies, ketamine has been found to play a significant role in controlling postoperative pain when compared to placebo. Most studies have reported the usefulness of

ketamine in analgesia after a C/S. However, in the majority of these studies, the dose of ketamine used was between 0.3 mg/kg IM and up to 2 mg orally. Similar results to our study have been stated in the studies by Han SY et al. and Qazi Saeed et al. (19). In these studies, researchers stated that using a low dose of ketamine (0.2 mg/kg) caused a statistically significant difference in the VAS scale (P<0.001).

In the present study, ketamine was used as a preemptive analgesia. The results of the mentioned studies also reported that the use of ketamine reduces the request for consumption of painkillers after surgery in comparison to the control group, which was also reported in our study (20).

It is known that in neuropathic pain, the activity of glutaminergic pathway neurons increases significantly through NMDA receptors, and finally, PKC activity and proto-oncogene expression cause an increase in pain sensitivity. Therefore, the block of these receptors causes pain relief. As a non-competitive antagonist of NMDA receptors, ketamine prevents the transmission of pain to the central nervous system by blocking these receptors in the postsynaptic membrane of the posterior horn of the spinal cord. In our study, in addition to ketamine, we used intravenous midazolam at a dose of 1 mg, and no difference in terms of analgesia was reported in this group compared to the ketamine group. GABA is the most significant inhibitory neurotransmitter in the central nervous system, and the main site of action of benzodiazepines such as midazolam is the presynaptic GABA receptors in the posterior branch of the spinal cord, so probably the intraspinal method before surgery can increase the effectiveness of the analgesic property of midazolam (21). Also, in a study conducted by Jabarzadeh et al. (2020) in Urmia, Iran, 126 pregnant women entered the study and were randomly allocated to intervention and control groups. In group A, ketamine was injected at a rate of 0.2 mg/kg, and in group B, 1 mg of midazolam was injected intravenously after the operation. In the control group (C), the same volume of normal saline was injected, and then variables related to pain were recorded every 1, 2, 6, and 12 hours after the operation. The researchers found that the use of these two drugs in the control of pain after C/S is not significantly different from each other, but in the use of painkillers after the operation in the ketamine group compared to the other two groups, a statistically significant difference was reported. According to the results of this study, the use of low-dose intravenous ketamine after a C/S can reduce the request for the consumption of painkillers after the operation (22). In our study, unlike this study, ketamine caused a significant reduction in pain in the first hour after surgery, while in this study, ketamine had no effect on reducing postoperative pain and only reduced the need for painkillers after surgery. Also, in another clinical trial study conducted by Behdad et al. (2013), 60 pregnant women with spinal anesthesia undergoing C/S were randomly allocated into intervention and control groups. The intervention group received ketamine (30 mg) and midazolam (1 mg), and the control group received 1 mg of midazolam after spinal anesthesia. The pain level was measured one, two, and three hours after the operation. Results showed that in the intervention group, the patients had a substantial improvement in pain one hour after the operation compared to the control group. The amount of meperidine used in the ketamine group was significantly lower than in the control group. The side effects caused were not significantly different between the two groups. It was concluded that a low dose of intravenous ketamine combined with midazolam has a greater effect on reducing postoperative pain. Similar to our study, the pain level in the first hour after the operation in the ketamine group was significantly reduced. The need for painkillers after the operation was significantly reduced in the ketamine group; this finding was also consistent with our study (14).

One of the strengths of this study is that an available and relatively inexpensive medication has been used which can reduce patients' pain. The variation in the surgical abilities of the gynecologists who performed the C/S is one potential limitation of this study, which may have had an impact on the severity of postoperative pain the patients experienced.

For future investigations, studies in the form of clinical trials using a larger sample size can be done. Also, due to the rapid effect of ketamine in preventing the transformation of acute pain into

chronic pain, examining patients in terms of the effect of ketamine in controlling chronic pain after surgery in the future can bring interesting results. Administration of different pain control protocols is also suggested in future studies.

Conclusion

Considering the results obtained from this study, ketamine reduces pain after surgery in patients who are candidates for elective C/S with spinal anesthesia and also reduces the need for painkillers after such surgeries. According to the conditions of pregnant women, specialists can use ketamine to reduce postoperative pain in those patients undertaking elective C/S with spinal anesthesia.

Declarations

Acknowledgements

The current study is a result of an anesthesiology residency thesis that Mashhad University of Medical Sciences in Mashhad, Iran, granted (grant number: 992264). The authors would like to express their gratitude to all the pregnant mothers participating in this study.

Conflicts of interest

The authors declared no conflicts of interest.

Ethical considerations

All participants provided informed consent before their inclusion in the study. They were informed that their participation in the study is entirely voluntary and they could withdraw from the study at any time without any prejudice. The confidentiality of all data obtained was guaranteed.

Code of Ethics

The study procedure was approved by the Ethics Committee of Mashhad University of Medical Sciences (ethical code: IR.MUMS.MEDICAL.REC.1400.119).

Funding

This study was financially supported by Vice Chancellors for Research, Mashhad University of Medical Sciences, Mashhad, Iran with grant number of 992264.

Authors' contributions

MS and MT contributed substantially in the conception and design of the study. MS and SA carried out the data collection. EB and SA analysed and interpreted the data. MS drafted the manuscript. MT reviewed the manuscript critically for important intellectual content. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the study.

References

1. Arroyo-Novoa CM, Figueroa-Ramos MI, Miaskowski C, Padilla G, Paul SM, Rodriguez-Ortiz P, et al. Efficacy of small doses of ketamine with morphine to decrease procedural pain responses during open wound care. The Clinical Journal of Pain. 2011; 27(7): 561-566.
2. Rakic AM, Golembiewski J. Low-dose ketamine infusion for postoperative pain management. Journal of Perianesthesia Nursing. 2009; 24(4): 254-257.
3. Madineh H, Rajaei EM, Ghaherei H, Akhlaghi M, Gangi F. The effect of intravenous low dose ketamine on postoperative pain. Journal of Shahrekord University of Medical Sciences. 2005; 7(2): 29-34.
4. Ribeiro I, Nunes F, Ghira M. Evaluation of analgesia after cesarean section. Acta médica portuguesa. 2001; 14(4): 395-398.
5. Argiriadou H, Himmelseher S, Papagiannopoulou P, Georgiou M, Kanakoudis F, Giala M, et al. Improvement of pain treatment after major abdominal surgery by intravenous S+-ketamine. Anesthesia and analgesia. 2004; 98(5): 1413-1418.
6. Menkiti ID, Desalu I, Kushimo OT. Low-dose intravenous ketamine improves postoperative analgesia after caesarean delivery with spinal bupivacaine in African parturients. International journal of obstetric anesthesia. 2012; 21(3): 217-221.
7. Powers AR 3rd, Gancsos MG, Finn ES, Morgan PT, Corlett PR. Ketamine-Induced Hallucinations. Psychopathology. 2015; 48(6): 376-385.
8. Minville V, Fourcade O, Girolami JP, Tack I. Opioid-induced hyperalgesia in a mice model of orthopaedic pain: preventive effect of ketamine. British journal of anaesthesia. 2010; 104(2): 231-238.
9. Abate SM, Belihu AE. Efficacy of low dose

bupivacaine with intrathecal fentanyl for cesarean section on maternal hemodynamic: Systemic review and meta-analysis. Saudi Journal of Anaesthesia. 2019; 13(4): 340-351.
10. Bilgen S, Koner O, Ture H, Menda F, Ficicioglu C, Aykac B. Effect of three different doses of ketamine prior to general anaesthesia on postoperative pain following Caesarean delivery: a prospective randomized study. Minerva anestesiologica. 2012; 78(4): 442-449.
11. Kuriyama K, Yoneda Y. Morphine induced alterations of gamma-aminobutyric acid and taurine contents and L-glutamate decarboxylase activity in rat spinal cord and thalamus: possible correlates with analgesic action of morphine. Brain Research. 1978; 148(1): 163-179.
12. Bharti N, Madan R, Mohanty PR, Kaul HL. Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia. Acta anaesthesiologica Scandinavica. 2003; 47(9): 1101-1105.
13. Ho KM, Ismail H. Use of intrathecal midazolam to improve perioperative analgesia: a meta-analysis. Anaesthesia and Intensive Care. 2008; 36(3): 365-373.
14. 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. Anesthesiology and Pain Medicine. 2013; 3(2): 230.
15. Bijur PE, Silver W, Gallagher EJ. Reliability of the visual analog scale for measurement of acute pain. Academic emergency medicine : official journal of the Society for Academic Emergency Medicine. 2001; 8(12): 1153-1157.
16. Pan W, Zhang G-F, Li H-H, Ji M-H, Zhou Z-Q, Li K-Y, et al. Ketamine differentially restores diverse alterations of neuroligins in brain regions in a rat model of neuropathic pain-induced depression. Neuroreport. 2018; 29(10): 863.
17. Milani F, Haryalchi K, Sharami SH, Faraji R, Asgharnia M, Salamat F, et al. The effect of low‐dose ketamine (preemptive dose) on postcesarean section pain relief. Journal of Basic and Clinical Reproductive Sciences. 2014; 3(2): 97-100.
18. Sen S, Ozmert G, Aydin ON, Baran N, Calıskan E. The persisting analgesic effect of low-dose intravenous ketamine after spinal anaesthesia for caesarean section. European Journal of Anaesthesiology. 2005; 22(7): 518-523.
19. Han SY, Jin HC, Yang WD, Lee JH, Cho SH, Chae WS, et al. The effect of low-dose ketamine on post-caesarean delivery analgesia after spinal anesthesia. The Korean Journal of Pain. 2013; 26(3): 270-276.
20. Ghazi Saidi K , Hajipour A. Effects of preemptive Ketamine on post-cesarean analgesic requirement. Acta Medica Iranica. 2002; 40(2): 100-103.
21. Tucker AP, Mezzatesta J, Nadeson R, Goodchild CS. Intrathecal midazolam II: combination with intrathecal fentanyl for labor pain. Anesthesia & Analgesia. 2004; 98(6): 1521-1527.
22. Jabarzade S, Abdollahzade Fard A, Norozi L, oshnouei S. The effect of ketamine and midazolam in reducing use of sedatives following spinal anesthesia in elective cesarean. Studies in Medical Sciences. 2020; 30(12): 941-949.