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Original Research Article

LOW-DOSE KETAMINE AS POSTOPERATIVE ANALGESIA IN CESAREAN SECTIONS IN REMOTE AREAS WITH LIMITED MEDICAL SUPPLIES

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ABSTRACT

Introduction: Cesarean section is the most common surgical procedure performed in the world and its postoperative pain is still a major issue in several countries. In a low-resource setting, this management poses a challenge for anesthesiologists. Ketamine is the most used anesthetic drug in the world due to its easy access and proven benefits. **Objective**: This research aims to analyze the effectiveness of low-dose ketamine as postoperative analgesia in cesarean sections conducted in areas with limited medical supplies. **Methods**: A Randomized Controlled Trial (RCT) was done from August 2020 to January 2021 with consenting pregnant patients who had undergone cesarean section. The sampled population was randomized to receive either ketamine intravenously or a placebo before the Subarachnoid Block (SAB). Low dose ketamine was divided into three groups 0.15 mg/kg, 0.25 mg/kg, and 0.5 mg/kg. The outcome was divided into primary outcome (pain score after 1-hour post-operation, 2 hours post-operation, 24 hours post-operation, and 48 hours post-operation) and secondary outcome (Apgar Score in the first minute and 5 minutes, hypotension after SAB, sedative effect during operation, postoperative nausea vomiting, time to receive opioid postoperative as rescue analgesia and total opioid uses). **Results**: This study screened 105 patients and recruited 90 patients that were randomized into two groups consisting of 45 patients that received either low-dose ketamine or a placebo. The groups administered ketamine showed a lower pain score in 1 hour (p-value = 0.0037) and 2 hours post-operation (p-value = 0.0037). They also showed that it could prolong the administration of fentanyl (p-value = 0.0003) and lower total fentanyl used (p-value = 0.0008). The groups administered ketamine showed that there was a sedation effect (p-value = 0.0001) that depended on the dosage used. **Conclusion**: Intravenous ketamine with low doses can reduce pain scores at 1 hour to 2 hours post-operation and shows the need to reduce opioid requirements.

Keywords: Analgesia; Caesarean Section; Ketamine Low dose; Maternal Health; Postoperative Pain; Subarachnoid Block

ABSTRAK

Pendahuluan: *Sectio Caesaria* (SC) merupakan operasi yang sering dilakukan di dunia dan nyeri pascaoperasi masih menjadi masalah di beberapa negara. Manajemen nyeri pascaoperasi di rumah sakit dengan sumber terbatas merupakan tantangan yang tersendiri untuk dokter anestesi yang bekerja di tempat tersebut. Ketamin merupakan obat anestesi yang sering dipakai yang mudah didapat serta terbukti memiliki keuntungan. **Tujuan:** Tujuan dari penelitian ini adalah untuk menganalisis keefektifan dari penggunaan Ketamin dosis rendah sebagai analgesik pascaoperasi pada opersi SC dengan kondisi persediaan alat dan bahan medis yang terbatas. **Metode:** Penelitian ini merupakan *Randomized Controlled Trial* (RCT) yang dilakukan selama agustus 2020 hingga januari 2021, dilakukan pada ibu hamil yang akan dilakukan SC yang secara acak dibagi mendapatkan perlakuan pemberian ketamin intravena atau placebo sebelum dilakukan *Sub-Arachnoid Block* (SAB). Pembagian dosis rendah ketamin dibagi menjadi dosis 0,15mg/kg, 0,25mg/kg dan 0,5 mg/kg. Outcome penelitian ini dibagi menjadi keluaran primer (skor nyeri setelah 1 jam pascaoperasi, 2 jam pascaoperasi, 24 jam pasca operasi dan 48 pascaoperasi) dan keluaran sekunder (APGAR pada menit pertama dan 5 menit, hipotensi setelah SAB,efek sedasi selama operasi, kejadian mual-muntah setelah operasi,waktu menerima opioid sebagai analgesi pascaoperasi dan total opioid selama perawatan). **Hasil:** Studi ini memeriksa 105 pasien dan mendapatkan 90 pasien sebagai subjek

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penelitian yang dibagi secara random menjadi dua kelompok dengan 45 pasien pada masing masing kelompok. Kelompok ketamine menunjukkan skor nyeri yang lebih rendah pada 1 jam (nilai p 0,037) dan 2 jam pascaoperasi (nilai p 0,037), waktu yang lebih lama untuk pemberian fentanyl pertama pascaoperasi (nilai p 0,003) serta total penggunaan fentanyl (nilai p 0,008). Kelompok ketamin juga menunjukkan adanya efek sedasi selama operasi (nilai p 0,001) dan tergantung pada dosis yang digunakan. **Kesimpulan:** Ketamin intravena dengan dosis rendah dapat menurunkan skor nyeri pada 1 jam hingga 2 jam pascaoperasi serta kebutuhan menurunkan kebutuhan opioid.

Kata kunci: Analgetik; *Sectio Caesaria*; Ketamine Dosis Rendah; Kesehatan Ibu; Nyeri Pasca Operasi; *Subarachnoid Block*

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INTRODUCTION

Cesarean section is one of the most frequently performed operations in the world, more than 1 million cesarean sections are performed in America in one year. The prevalence in different countries varies with a ratio of about 10 to 30% in one year (1). Postpartum pain after cesarean section is often unreported, causing it to be negligible. However, postpartum pain is a serious issue because it can impact the mother and the baby if not handled properly. Postoperative pain will create stress for the mother, so the interaction between the baby and the mother will be delayed, hindering the healing of the mother and causing postpartum depression (2).

A study reported that pain after a cesarean section was ranked ninth on the first day after surgery and had a mean NRS of 6 (IQR 4.5–8.0) which corresponds to trauma/orthopedic patients. Moreover, pain during mobilization has the highest intensity compared to other gynecological operations (3).

Postoperative pain management of cesarean sections can be done by providing multimodal analgesics. Administration of NSAIDs in combination with Paracetamol is the recommended combination by ERAS, but in some patients, this combination is insufficient. Interventions at the time of surgery such as long-term opioids (morphine) in intrathecal and Transverse Abdominis Plane (TAP) blocks can provide good analgesics. However, these techniques are difficult to conduct in places with limited resources. Another thing that needs to be considered is the mother's need to breastfeed, so drugs and techniques need to be safe for breastfeeding mothers (4,5).

In a developing country such as Indonesia where the conditions of numerous regions have limited or lack resources, postoperative pain management is a challenge. The difficulties that may arise are lack of awareness from patients (causing them to rarely report their pain to health workers), low nurse-patient ratio (causing difficulties to assess pain and monitor side effects of interventions performed by anesthesiologists), and the limited availability of drugs and supporting equipment (6). Therefore, the administration of drugs or interventions to reduce pain in patients after cesarean sections requires a safe and effective method.

The management of post-operative pain is ideally done by providing multi-modal therapy. However, as there are difficulties in procuring medical and pharmaceutical supplies in distant and remote areas, other alternatives must be considered.

Ketamine is an antagonist of the N-Methyl-D-Aspartate (NMDA) receptor which is often used as an anesthetic agent. NMDA receptor antagonists can provide an analgesic effect by desensitizing NMDA receptors,

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therefore inhibiting pain transmission in the central nervous system (7). Greater attention should be paid to this drug because it has been proven to be effective in relieving pain and is relatively available in remote areas (8).

Furthermore, ketamine is also able to inhibit the tolerance of opioids hence reducing the need for it. A meta-analysis from Cochrane showed that the administration of ketamine at subanesthetic doses reduced pain intensity and the need for opioids and produced minimal side effects (9). Ketamine is also safe for the fetus as well as for nursing mothers because although it can cross the placenta, its administration of less than 1 mg/kg will not cause fetal depression. Moreover, although the level of ketamine in breast milk has never been measured, some data has shown that it has not caused any effects on the baby or the lactation process (10,11).

Ketamine at subanesthetic doses has shown varying analgesic effects in several studies. It is believed to have a preemptive analgesic effect so that it can provide long-term analgesic effects (7–9,12). In another study, the preemptive analgesic effect of ketamine was not proven (5,13,14). A meta-analysis study also stated that the administration of preoperative ketamine could reduce morphine consumption and prolong postoperative analgesic requirements. This study also mentioned that there is a difference in pain scores at 1 to 12 hours postoperatively, but this is not statistically significant (15).

Furthermore, a study stated that the effectiveness of ketamine as preemptive analgesia depends on the intensity of the noxious stimulus, the dose of ketamine used, and the additional drug administered (16). The doses of ketamine used in several studies were 0.15 mg/kg (12,15), 0.25 mg/kg (5,8,9,15), and 0.5 mg/kg (13,15,16). These three doses have been proven to be safe for pregnant women and have not shown any significant side effects on the fetus (5,8,12,16).

In conclusion, previous studies have shown an analgesic effect in postoperative cesarean sections, but different anesthetic techniques and doses of ketamine give varying results (5,8,12,16). This study conducted an RCT to demonstrate the postoperative analgesic effect of low-dose intravenous ketamine in patients undergoing cesarean sections with Sub-Arachnoid Blocks (SAB). The hypothesis is that there was a difference in the postoperative analgesic effect of low-dose intravenous ketamine versus the placebo based on data from previous studies.

METHODS

This study implemented an RCT and was conducted from August 2020 to January 2021 at the Kuala Pembuang Hospital, Seruyan - Central Kalimantan. Patients undergoing Cesarean Section with SAB would be included as subjects if they agreed to participate by signing the informed consent form. The inclusion criteria in this study were patients with the American Society of Anesthesiology (ASA) Scores I and II. The exclusion criteria are patients with a history of hypertension, patients with preeclampsia - eclampsia, patients with a history of hypersensitivity to ketamine, psychological disorders, and patients with a history of SAB procedure and are at risk for General Anesthesia (GA). This study used a total sampling technique on patients who underwent SC from August 2020 to January 2021. The Simple Random Sampling technique was conducted by the pharmacist who prepared the drug. The patients were divided into two groups (the ketamine group and the control group), and the ketamine group was further divided into three sub-groups (0.15 mg/kg; 0.25 mg/kg; 0.5 mg/kg).

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This was a double-blind study as all of the subjects and data takers do not know the type of drug administered. Only the anesthesiologist was aware of the type of drug being administered. This was done for the safety of the patient and due to the limited manpower. The blind process was conducted on the anesthetic records during surgery.

Research Procedure

The patients arrived in the operating room and were measured for their hemodynamics (Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and pulse rate) using a non-invasive monitor before they were given the intervention (the administration of low-dose intravenous ketamine).

Five minutes later, the patients were re-evaluated, and if there were no disturbances, the patient was positioned for left lateral decubitus for SAB. The SAB drug given was hyperbaric bupivacaine 5% 12.5 mg with adrenaline 1:200,000. The block level targeted was sensory T6. If the target level has been reached, the patient would be disinfected in preparation for the cesarean section.

The patients were then given dexamethasone 10 mg intravenously and ketorolac 30 mg intravenously before the incision. Hypotension in this study was a decrease in MAP of more than 20% basal MAP. This was then treated with ephedrine 5-10 mg intravenously according to the anesthesiologist performing the SAB. Sedation during surgery in this study was measured using the Ramsey Sedation Score (RSS) with patients deemed sedated when an RSS score of 2 or more was recorded during anesthesia. Five minutes before the end of the operation the patients were given pethidine 1 mg/kg intravenously. Post-operation, the patients were brought to the Recovery Room (RR) for monitoring and evaluation. In the RR, if the patient was experiencing nausea/vomiting after surgery, 8 mg of ondansetron and 50 mg of ranitidine were administered intravenously.

This study used the Wong-Baker Face Scale (WBFS) as the pain score, with the diagnosis of postoperative pain determined by WBFS > 2. Postoperative pain was treated with fentanyl (rescue analgesia) 0.5-2 mcg/kg. Patients would also be returned to the ward with a Bromage score of IV and an Alderette score of > 9.

In the ward, if the patient experienced pain (WBFS > 2), the nurse would report to the anesthesiologist on duty and the patient would be treated using a fentanyl bolus or with a syringe pump. The data taken in this study were divided into two, namely primary results (consisting of WBFS 1 hour, 2 hours, 24 hours, and 48 hours post-operation) and secondary results (consisting of APGAR scores at 1 minute and 5 minutes). Hypotension after SAB, sedation during surgery, postoperative nausea/vomiting, the timing of the first postoperative rescue analgesia (fentanyl), and total rescue analgesia (fentanyl) administered during treatment) were entered in the Data Collection Sheet (LPD).

Statistical Analysis

The statistical analysis in this study was done using SPSS 23. The data in this study were age (years), body weight (kg), ASA Score, SBP (mmHg), DBP (mmHg), MAP (mmHg), pulse (times/minute), the urgency of the surgery, as well as primary and secondary results. This study used the Kolmogorov-Smirnov test to determine the distribution of the data. If the data distribution was normal, a parametric test would be used (Pearson, univariate one-way ANOVA, univariate two-way ANOVA) and if the data distribution was not normal, a non-parametric test would be

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used (Spearman, x2, Mann-Whitney test, x2 with K sample).

RESULTS AND DISCUSSION

This study screened 105 patients, but 15 patients met the exclusion criteria, hence 90 patients were eligible as this study's subjects. The subjects were divided into 2 groups, the control group and the ketamine group. Demographic data can be seen in table 1.

The primary outcome of this study showed there was a significant difference between WBFS 1-hour post-operation and WBFS 2 hours post-operation in the control group and the ketamine group. The mean one-hour postoperative WBFS was 0.44 ± 1.25 vs 0.98 ± 1.72 and 2-hour postoperative WBFS was 0.24 ± 0.82 vs 0.91 ± 1.57 with the ketamine group results being lower compared to the control group. The WBFS 24 hours post-operation and WBFS 48 hours post-operation between the ketamine and control groups showed a difference, but it was not statistically significant (the p-value of WBFS 24 hours post-operation was 0.299 and the p-value of WBFS 48 hours post-operation was 0.097). The complete data can be seen in table 2.

The secondary outcome of this study was that there was a significant difference in the incidence of sedation during surgery, time of first fentanyl administration, and total fentanyl administered. Fentanyl as the first rescue analgesia in the ketamine group was administered on average 52 minutes (±10.61) post-operation with an average total administration of fentanyl being 3.33 mcg (±22.36), while the control group was administered fentanyl on average at 44 minutes (±17.66) post-operation with a total mean of 38.33 mcg of fentanyl (±90.07). The post-spinal hypotensive effect in the control group was higher than in the ketamine group (20% vs 11%), but this was not statistically significant. Sedation was also common in 22% of patients given ketamine.

Table 1. Demographic Data

Variables	Ketamine Group Mean ± SD / N (%)	Control Group Mean ± SD / N (%)	p-Values
Age (years)	27 (±5.51)	27 (±6.31)	0.986*
Weight (kg)	60 (±10.14)	64 (±12.75)	0.080*
ASA Score			
I	32 (71 %)	29 (64%)	0.504**
II	13 (29%)	16 (36%)	
Preop SBP (mmHg)	108 (±10.95)	109 (±12.45)	0.948**
Preop DBP (mmHg)	63 (±8.31)	65 (±8.11)	0.485**
Preop MAP (mmHg)	80 (±7.77)	78 (±8.33)	0.168**
Preop Pulse (times/minutes)	72 (±8.57)	71 (±8.78)	0.699*
Surgery Urgency			
Elective	14 (31%)	10 (22%)	0.238***
Emergency	31 (69%)	35 (78%)	

* *Chi-square* (X^2) ***Mann-Whitney Test*

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Table 2. Primary Outcomes

Variables	Ketamine Group Mean ± SD	Control Group Mean ± SD	p-Values
1-hour postoperative WBFS	**0.44 (±1.25)**	**0.98 (±1.72)**	**0.037***
2-hour postoperative WBFS	**0.24 (±0.82)**	**0.91 (±1.57)**	**0.037***
24-hour postoperative WBFS	0.24 (±0.74)	0.76 (±1.74)	0.299*
48-hour postoperative WBFS	0.07 (±0.25)	0.24 (±0.57)	0.097*

* *Mann-Whitney Test*

Table 3. Secondary Outcomes

Variables	Ketamine Group (n:45)	Control Group (n:45)	p-Values
Hypotension after SAB	5 (11%)	9 (20%)	0.245*
Sedation during surgery	**10 (22%)**	**0**	**0.001***
1-minute Apgar score	7 (± 0.89)	7 (±1.47)	0.929**
5 minutes Apgar score	9 (±1.48)	9 (±1.48)	0.732**
Postoperative nausea/vomiting	6 (13%)	6 (13%)	1.000*
Timing of the first postoperative fentanyl (minutes)	**52 (±10.61)**	**44 (±17.66)**	**0.003****
Total fentanyl administered (mcg)	**3.33 (±22.36)**	**38.33 (±90.07)**	**0.008****

* Chi-square (X2) **Mann-Whitney Test

This study demonstrated that administering low-dose intravenous ketamine before SAB in cesarean sections can provide postoperative analgesia. This can be seen from the lower WBFS levels at 1 hour and 2 hours post-operation. The results in our study are in line with other studies (12,17) which found that the patients that were administered ketamine experienced a lower pain scale at 60 to 150 minutes after a cesarean section.

Ketamine can provide postoperative analgesia effects through several mechanisms, such as through the effect of preemptive analgesia due to its effect on central sensitization. The operation will cause tissue damage that will form a central pain pathway sensitization by releasing glutamate which causes a higher pain sensation due to the activation of NMDA receptors in the postsynaptic spinal cord (7,15,17).

Our study found a significant difference in early postoperative WBFS (ketamine group 0-1 vs control group 0-3) with a p-value of less than 0.05. This may be because ketamine can also reduce the occurrence of hypersensitization. After all, NMDA receptors are also found in pre-synaptic pain pathways in the dorsal horn (17). This study also showed a decrease in pain scale at 24 hours and 48 hours post-operation (WBFS range 0 - 1) with the use of ketamine, but there was no difference between the ketamine group and the control group (with a p-value of more than 0.05). This was also shown in several studies where the administration of low doses of ketamine (0.5-1.0 mg/kg) did not show a significant difference on the postoperative pain scale (0 to 24 hours) (13,14,16).

The preemptive effect of ketamine is influenced by the intensity of the pain stimulus produced (type of surgery) and the use of other drugs (16).

Our study also found that administering ketamine prolonged the patients' need to be administered rescue analgesia (fentanyl) than the control group (52[41-63] vs 44[27-62]) with a p-value of less than 0.05 (p-value 0.008). Similar results were found in several studies, where administration of low doses of ketamine was able to prolong the administration of

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additional postoperative analgesics (both cesarean or not cesarean) (5,7,8,12,15,17).

Several studies have also shown that the administration of low-dose ketamine in cesarean sections can delay the administration of the first additional analgesia to more than 2 hours (190 – 210 minutes) (5,7,12,17). In our study, the first rescue analgesia (fentanyl) was administered in approximately 52 minutes (41 – 63) with a p-value of less than 0.05 (p-value 0.003). The longer delay of rescue analgesia is due to the preemptive analgesic effect of ketamine. However, good perioperative pain management can suppress the activation of NMDA receptors so the administration of ketamine in these cases is insignificant. This was evidenced in a study of low-dose ketamine administration in patients undergoing cesarean section under general anesthesia, where the use of ketamine did not significantly reduce pain scale, and the consumption of morphine did not differ from 2 to 24 hours postoperatively (16).

Postoperative pain management in post-cesarean section patients has its challenges because improper pain management will cause morbidity for the patients and their babies. Inadequate pain management, especially during the first 24 hours will interfere with the bonding process between the baby and the mother. The use of analgesics also has to be done cautiously due to the patient's breastfeeding needs after giving birth (6,18). Thus, the administration of NSAIDs is the main choice for the management of postoperative cesarean section pain, but NSAIDs alone cannot treat moderate to severe pain. Opioids are still often the main choice in the management of acute pain, but their use in postoperative cesarean section (in breastfeeding) should be limited to 2 to 3 days, and the drugs selected should also not harm the fetus (16,19).

Our study chose fentanyl as rescue analgesia due to its minimal excretion into breast milk, therefore it is safer to use in postoperative cesarean section mothers who are planning to breastfeed (20). This study also showed a significant difference in the total consumption of fentanyl in patients who received ketamine. This is similar to other studies that showed how low-dose intravenous ketamine can reduce fentanyl consumption (21). Similar results were also seen in another study with other classes of opioids such as meperidine (8). In addition, the use of other classes of analgesics such as diclofenac was also lower (about 30-40%) 24 hours after cesarean section. This is because ketamine has several analgesic mechanisms that can trigger this phenomenon.

Ketamine is known to act on several receptor systems (such as opioidergic and cholinergic systems) and activate the supraspinal monoaminergic descending inhibitory pathway, resulting in anti-nociceptive effects (12). The use of low-dose ketamine in this study did not show a significant difference in the incidence of postoperative nausea and vomiting as 13% of patients in each group experienced nausea and vomiting. Several other studies also showed that there was no significant difference in the incidence of postoperative nausea and vomiting in the use of low-dose ketamine in patients who underwent cesarean section under anesthesia SAB (5,12,17). The analgesic effect of ketamine can also be triggered by the pre-synaptic and post-synaptic blockade of NMDA receptors causing a decrease in efferent transmission, thus reducing the "wind-up" and central sensitization phenomenon (17).

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Table 4. Comparison of Ketamine Doses to The Primary and Secondary Outcome

Variables	0.15mg/kg	0.25mg/kg	0.5mg/kg	p-value
1-hour postoperative WBFS	1.30 (±2.05)	0.87 (±1.55)	0.73 (±1.58)	0.617*
2-hour postoperative WBFS	0.40 (±1.29)	0.20 (±0.41)	0,27 (±0.45)	0.799*
24-hour postoperative WBFS	0.47 (±1.06)	0.27 (±0.70)	0	0.230*
48-hour postoperative WBFS	0.13 (±0.35)	0.07 (±0.25)	0	0.359*
Post SAB Hypotension	3 (20%)	1 (6%)	1 (6%)	0.254**
Nausea and Vomiting	2 (13%)	2 (13%)	2 (13%)	1.000**
1-minute Apgar Score	8 (±0.67)	7 (±1.04)	8 (±0.88)	0.238*
5 minutes Apgar Score	9 (±0.64)	9 (±1.22)	9 (±0.86)	0.500*
Sedation Effect	**0**	**2 (7%)**	**8 (53%)**	**0.000****
First Fentanyl Administration (minutes)	4 (±15.49)	0	0	0.376*
Total fentanyl use (mcg)	10.00 (±38.73)	0.00	0.00	0.376*

The secondary effect that was seen to be significantly different in this study was the presence of a sedative effect on the use of ketamine. The incidence of sedation during the administration of ketamine in this study was 22%. Ketamine can provide an analgesic effect at plasma concentrations of 100-160 ng/ml and will last about 1 to 2 hours. The ED50 for the narcotic effect of ketamine is at a dose of 0.4-0.7 mg/kg (22). This also occurred in another study where the administration of 30 mg of ketamine in patients who underwent cesarean sections under SAB caused hallucinations during surgery (8).

The sedative effect of ketamine use is believed to affect the dose of ketamine used. In another study using lower doses of ketamine (0.15 mg/kg), there was no hallucinatory effect but 10% of patients experienced sedation (but it was not statistically significant) (17). Another study using a ketamine dose of 0.25mg/kg also showed the same result where during the initial 30 minutes of surgery the patient was sedated with RSS (23).

The use of low-dose ketamine in this study did not show a significant difference in the incidence of postoperative nausea and vomiting. In this study, 13% of patients in each group experienced nausea and vomiting. Several other studies also showed that there was no significant difference in the incidence of postoperative nausea and vomiting in the use of low-dose ketamine in patients who underwent cesarean section under SAB (5,12,17).

This study also used ketamine at three different doses, in accordance with several other studies (0.15 mg/kg (12,17); 0.25 mg/kg (5); 0.5 mg/kg (21)). A comparison of the primary and secondary outcomes can be seen in Table 4. This study showed no significant difference in WBFS on 1 hour, 2 hours, 24 hours, and 48 hours post-operation. Much like the incidence of postoperative nausea and vomiting and post-SAB hypotension, there was no statistically significant difference. However, the incidence of post-SAB hypotension with a dose of ≥ 0.25 mg/kg was lower (6% vs 20%).

A significant difference was found in the sedative effect during surgery, the administration of ketamine at 0.5 mg/kg gave a higher possibility of a sedative effect than a dose of 0.25 mg/kg (53% vs 7%) and there was no sedation effect at a dose of 0.15 mg/kg. Furthermore, this study found that no rescue analgesia (fentanyl) was administered to patients who were given a ketamine dose of 0.25 mg/kg, but based on our statistical analysis there was no significant difference between the

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firsttime fentanyl was given and the total administration of fentanyl at the three other doses.

Ketamine at low doses (less than 1 mg/kg) can provide analgesic effects and is often used in the management of acute and chronic pain (24). Moreover, different doses of ketamine in cesarean sections are safe for infants with different analgesic efficacy (5,12,16,17,21). Effects other than analgesia can also be found with higher ketamine doses. Ketamine 0.5-1 mg/kg is often used for diagnostic sedation in children or adults. This study found that the use of 0.5 mg/kg caused sedation in 53% of patients whereas a dose of 0.25 mg/kg provided sedation in 7% of patients. An article review stated that a plasma concentration of 70 ng/ml ketamine can alter memory and a dose of 200ng/ml can cause an anesthetic effect (22).

This study showed that there was no significant difference in the postoperative pain scale with the use of three different doses of ketamine. The analgesic efficacy of ketamine can also be affected by additional drugs given during surgery. This study used dexamethasone and an NSAID (ketorolac) before incision as preemptive analgesia, which may influence the outcome of the postoperative pain scale. A study of the preemptive analgesic effect of ketorolac in ankle fracture surgery showed that administering ketorolac before a tourniquet could reduce postoperative pain (25). Dexamethasone can also reduce the intensity of postoperative cholecystectomy pain as well as the consumption of meperidine (23).

CONCLUSION

Administration of low-dose ketamine in patients undergoing cesarean section with SAB can provide a better analgesic effect 1 to 2 hours post-operation and delay the postoperative administration of fentanyl and total fentanyl use. Additionally, administration of 0.25 mg/kg can provide the same analgesic effect as a higher dose (0.5 mg/kg) with a lower sedative effect.

Limitations

Observation bias is the main limitation of this study as the non-blind test on the anesthetic operator may confuse the results of this study and the reasons for not selecting single blinding have been described previously. Thus, a more objective examination of the analgesic efficacy of low-dose ketamine in cesarean sections under SAB is needed.

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Conflict of Interest

No conflict of interest in this study.

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Authors' Contributors

All authors have contributed to all process in this research.

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