ORIGINAL RESEARCH

Analysis of the Analgesic Effect, Emotion, and Safety of Esketamine in Cesarean Section Analgesia for Puerperae

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ABSTRACT

Objective • This retrospective study aimed to evaluate the effectiveness and safety of esketamine as an analgesic during cesarean section procedures.

Methods • 102 puerperae undergoing cesarean section were divided into a control group and an esketamine (SK) group. Various parameters, including HR, MAP, and postoperative pain, were analyzed. Blood gas analysis and Apgar scores were assessed in neonates. Postoperative depression and satisfaction were evaluated in puerperae. Drug concentrations were measured using liquid-phase tandem mass spectrometry.

Results • No significant differences in dimension levels were observed between the two groups ($P > .05$). However, the SK group showed better HR and MAP indicators at various time points, less postoperative pain, and better mental well-being on postpartum days 1, 3, and 7 ($P < .05$). Adverse reaction rates were similar between groups ($P > .05$), but postoperative satisfaction was significantly different ($P = .027$). Neonatal outcomes did not differ significantly ($P > .05$). In the SK group, SK2 and SK3 groups had better results compared to SK1 ($P < .05$).

Conclusion • Esketamine during cesarean section stabilized vital signs, reduced pain, and improved well-being in puerperae without affecting newborns. Optimal dosage: 30 μg/kg/h esketamine, 15 ng/kg/h sufentanil. (*Altern Ther Health Med.* 2023;29(7):424-428).

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INTRODUCTION

Childbirth, which is a necessary process for the birth of a new life, is of great significance to both the family and the society.[1] There are two main types of childbirth, one is the normal vaginal childbirth, which is a natural birth of new life, and the other is often used to solve problems that cannot otherwise be solved by normal vaginal childbirth, such as acute labor or dystocia, which may endanger the life of the mother.[2] Recently, Chinahas attached great importance to the overall cesarean section rate of the general public, and the control in this regard has also been increasing. Therefore, if the puerperae who do not need a cesarean section at the moment want to have a cesarean section, conditions must be met. The requirements are very strict, and this move is extremely effective in maintaining the cesarean section rate at a relatively reasonable level in my country.[3] Because of its good and reliable analgesic and sedative effect, esketamine has been introduced for analgesia in spinal anesthesia surgery or cesarean section surgery, and has achieved good results and no negative effects on neonates have been found.[4] The mechanism of action of esketamine involves blocking the *N*-methyl-D-aspartate (NMDA) receptors in the brain. NMDA receptors are involved in the regulation of mood, cognition, and pain perception. By antagonizing these receptors, esketamine increases the release of certain neurotransmitters, particularly glutamate and brain-derived neurotrophic factor (BDNF), which are believed to play a role in the improvement of depressive symptoms. In order to further verify the efficacy and safety of esketamine in cesarean section, Sanmen People's Hospital, Zhejiang,.recently used esketamine in general anesthesia for cesarean section, and this study has achieved good results

MATERIALS AND METHODS

Research objects

We used a random number method to group the patients. Total of 100 puerperae who needed cesarean section

in our hospital were retrospectively collected, and they and their families were informed of the details of diagnosis and treatment before surgery, and all voluntarily signed the informed consent, which was approved by the hospital ethics committee.

Inclusion criteria: 1) mothers with singleton fetuses who reach the lease level during pregnancy; 2) the minimum age is 22 years and the maximum is 36 years; 3) the weight range is (60 kg - 80 kg); 4) American Society of Anesthesiologists (ASA) classification is in I-II level; 5) preoperative blood coagulation analysis, blood routine, liver and kidney function, and other related indicators were all within the normal range; 6) no anesthesia contraindications and past medical history such as diabetes and hypertension; and, 7) the preoperative mental state was good.

Exclusion criteria: 1) those with preoperative obstetric comorbidities; 2) those who have allergic reaction to anesthetics; 3) gynecological diseases such as uterine fibroids, ovarian cysts, etc.; 4) past psychiatric history, such as history of abnormalities and surgical trauma; 5) psychiatric and nervous system diseases and the history of corresponding drug use; and, 6) patients with unsatisfactory epidural block level and history of allergy to ketamine and related components.

After collecting the general information of the puerperae participating in the study, they were randomly divided into the control group and the SK group, each with the same number of 51 women, and the SK group was randomly divided into SK1, SK2, and SK3 groups to study the effect of the drug. Appropriate dosage, general data are not statistically significant ($P > .05$). Anesthesia was performed by the same anesthesiologist, and the cesarean section was performed by a senior physician.

Methods

Treatment methods of control group and experimental group. Before surgery, all patients were required to fast for 6 hours, and all patients were required to fast for 8 hours without additional medication. After entering the room, pulse oxygen saturation (SpO_2), mean arterial pressure (MAP), basal heart rate (HR) and other related indicators were recorded.

Intraoperative: open upper extremity venous access, and then quickly instill compound Ringer's sodium lactate injection, the infusion volume is 300-500 ml. All puerperae were placed in a left-inclined 15° supine position, puncture was performed at the L2-3 intervertebral space, and a 4 cm tube was placed at the head end of the epidural space, and then the catheter was fixed. The oxygen inhalation method was adopted with a mask, and the oxygen rate was 5 L/min. Epidural injection of 2% lidocaine with an initial injection volume of 3 ml was given to the puerperae. After 5 minutes of observation when the puerperae showed no signs of poisoning and spinal anesthesia, based on the maternal height and weight, the epidural administration was increased by using 10-15 ml of 0.5% ropivacaine, so that the anesthesia plane can reach the T6-T8 interval that meets the surgical requirements. The observation group was given intravenous injection of estroxide ketamine 0.25 mg/kg, 1 min before the surgical skin incision, while the control group was intravenously injected with the same amount of normal saline before the surgical skin incision. Oxytocin is administered intravenously after the fetus is delivered to promote uterine contractions.

After operation: The epidural catheter was removed, and the maternal blood oxygen saturation, blood pressure, heart rate, and other indicators were recorded at the initial stage and after the operation was completed. An intravenous analgesia pump was connected, and the postoperative analgesic medication regimen was as follows: the control group was given sufentanil at a dose of 30 ng/kg/h. Observation group (SK1, SK2, SK3 group): 15, 30, 45 μg/kg/h of esketamine respectively along with 15 ng/kg/h of sufentanil were administered. After the cesarean section, the patient was connected to the self-controlled analgesia pump. The parameters were set as follows: the continuous infusion volume was 2 ml/h, the single compression dose was 0.5 ml, the locking time was 15 min, and the analgesia pump was connected to start a loading dose of 2 ml, the patient was then returned to the ward. The arterial and venous blood from the umbilical cord was collected for blood gas analysis immediately after the neonate was delivered.

Response plan for abnormal events: if the systolic blood pressure after anesthesia is lower than 90 mmHg or decreases by more than 30% of the basic value, phenylephrine is injected intravenously. If there is airway obstruction or respiratory depression (SpO_2 <93%), mandibular support, placement of oropharyngeal nasopharyngeal airway, or manual assisted breathing would be provided. If neonatal respiratory depression occurs, artificially assisted breathing with neonatal endotracheal intubation should be performed in a timely manner.[5]

Observation indicators. The maternal pain was recorded at 2, 6, 24, and 48 hours after the operation, and the pain degree was expressed by the visual analog scale (VAS) method. The perioperative reactions and postoperative adverse reactions were recorded, the Edinburgh Postpartum Depression Scale (EPDS) score and RSS sedation score were calculated, and the Apgar score was evaluated after birth. The heart rate (HR), mean arterial pressure (MAP), blood oxygen saturation (SpO_2), and other indicators of the two groups of puerperae during the operation were recorded. Umbilical cord arterial blood and venous blood were collected for blood gas analysis immediately after the newborn was delivered. Maternal satisfaction all puerperae with general anesthesia was recorded.

Statistical methods. SPSS 22.0 was used as the preferred statistical tool. The count data was expressed as (%), and the χ^2 test was used for the comparison between groups. The measurement data was expressed as ($\bar{x} \pm s$), and the t test was used for the between-group comparison. $P < .05$ indicates that there is a statistically significant difference in the results between groups.

RESULTS

Comparison of maternal signs between the two groups

In terms of SpO_2, there was no significant difference in the levels between the two groups of puerperae at each timepoint ($P > .05$). For HR and MAP indicators, it can be seen from the table 1 that at the beginning of anesthesia (T1), 10 minutes into the anesthesia state (T2), and after the completion of surgery (T3), the indexes of puerperae in the experimental group were better than the control group, and the differences between groups had statistical significance ($P < .05$).

Comparison of Apgar scores after birth

It can be seen from the table 2 that for the Apgar score relationship of neonates did not vary significantly between the control the experimental groups and the values at each stage are relatively close ($P > .05$).

Comparison of VAS between the two groups of patients

In the comparison of the VAS scores of the two groups of puerperae in each statistical time window after the operation, it can be seen that the difference is relatively large. The difference was statistically significant ($P < .05$), The postoperative degree of pain among puerperae in SK2 group and SK3 group was lower than that in SK1 group ($P < .05$) and there was no significant difference in the degree of pain between SK3 and SK2 ($P > .05$). See Table 3.1 and Table 3.2.

Comparison of EPDS of two groups of women in different periods

The Edinburgh Postnatal Depression Scale (EPDS) was used to evaluate the degree of depression before and after cesarean section. The results showed that on the 1st, 3rd, and 7th days after the operation, the depression of the control group was more obvious, and the mental state of the experimental group was better than that of the control group ($P < .05$); the EPDS score of the puerperae in the SK2 and SK3 groups were lower than that in the SK1 group ($P < .05$) and the difference in EPDS score between SK3 and SK2 was not significant ($P > .05$). 17 patients were enrolled in the SK3 group, of which 3 patients stopped midway and were not included. See Table 4.1 and Table 4.2.

Comparison of RSS scores of two groups of women at different times

Comparing the RSS scores of the mothers in the experimental group and the control group, it can be found that at different timepoints after the surgery, the sedation scores of the puerperae in the experimental group were higher than those who did not use the drug ($P < .05$), The RSS scores of the puerperae in the SK2 and SK3 groups were higher than those in the SK1 group ($P < .05$) and the difference of RSS scores between SK3 and SK2 was not significant ($P > .05$). See Table 5.1 and Table 5.2.

Table 1. Comparison of HR and MAP Between the Control and Experimental Groups at Different Timepoints ($\bar{x} \pm s$)

Group	Period	HR (times/min)	MAP (mmHg)	(%)
Control group (n = 50)	T0	86.08 ± 7.19	89.36 ± 7.29	98.09 ± 3.55
	T1	80.54 ± 7.21	82.66 ± 5.89	99.09 ± 3.41
	T2	73.71 ± 6.53	77.55 ± 6.39	98.96 ± 4.15
	T3	74.27 ± 7.11	76.61 ± 7.27	98.84 ± 2.33
Experimental group (n = 50)	T0	85.38 ± 6.83	88.93 ± 6.84	97.49 ± 2.33
	T1	84.10 ± 6.38[a]	88.14 ± 5.84[a]	99.75 ± 3.02
	T2	79.41 ± 5.72[a]	86.22 ± 6.48[a]	9.29 ± 2.78
	T3	80.29 ± 6.51[a]	87.21 ± 7.41[a]	99.45 ± 2.67

[a]$P < .05$, compared with the control group

Table 2. Comparison of Apgar Scores Between the Control and Experimental Groups at Different Timepoints ($\bar{x} \pm s$)

Group	Cases	1 minute after birth	5 minutes after birth	10 minutes after birth
Control group	52	9.52 ± 0.12	9.78 ± 0.08	9.99 ± 0.12
Experimental group	51	9.54 ± 0.08	9.80 ± 0.07	10.02 ± 0.04
t	-	0.993	1.349	1.695
P value	-	.323	.180	.093

Table 3.1. Comparison of VAS Scores Between the Control Group and the Experimental Group at the Same Time Point

Time/h	2 hours postpartum	6 hours postpartum	24 hours postpartum	48 hours postpartum
Control group (n = 50)	4.63 ± 0.28	4.02 ± 0.21	2.21 ± 0.08	1.51 ± 0.08
Experimental group (n = 50)	3.92 ± 0.33	3.23 ± 0.09	1.71 ± 0.08	1.01 ± 0.02
t	11.600	24.450	31.250	42.875
P value	.000	.000	.000	.000

Table 3.2. Comparison of VAS Scores at the Same Time Point in the SK Group

Time/h	2 hours postpartum	6 hours postpartum	24 hours postpartum	48 hours postpartum
SK1 (n = 17)	4.13 ± 0.28	3.82 ± 0.21	2.01 ± 0.08	1.41 ± 0.08
SK2 (n = 17)	3.92 ± 0.33[a,b]	3.23 ± 0.09[a,b]	1.71 ± 0.08[a,b]	1.01 ± 0.02[a,b]
SK3 (n = 17)	3.98 ± 0.29[b]	3.29 ± 0.07[b]	1.79 ± 0.07[b]	1.02 ± 0.03[b]

[a]$P < .05$, compared with the previous group
[b]$P < .05$, compared with the first group

Table 4.1. Comparison of EPDS of the Two Groups of Women at Different Timepoints

Group	prenatal	1 d postpartum	3 d postpartum	7 d postpartum	14 d postpartum
Control group	6.53 ± 2.34	7.64 ± 3.15	7.58 ± 3.11	7.32 ± 0.21	7.21 ± 1.91
Experimental group	6.72 ± 2.26	5.99 ± 2.46	6.23 ± 2.57	6.51 ± 2.11	6.45 ± 2.21
t	0.413	2.919	2.366	2.701	1.840
P value	.681	.004	.020	.008	.069

Table 4.2. Comparison of EPDS of SK Group Puerperae at Different Timepoints

Group	Prenatal	1 d postpartum	3 d postpartum	7 d postpartum	14 d postpartum
SK1 (n = 17)	6.82 ± 2.26	6.51 ± 2.26	6.43 ± 2.51	6.31±2.13	6.23 ± 2.22
SK2 (n = 17)	6.66 ± 2.23[a,b]	5.89 ± 2.33[a,b]	5.83 ± 2.48[a,b]	5.61 ± 2.09[a,b]	5.85 ± 2.21[a,b]
SK3 (n = 14)	6.68 ± 2.25[b]	5.99 ± 2.34[b]	5.97 ± 2.50[b]	5.76 ± 2.12[b]	5.93 ± 2.19[b]

[a]$P < .05$, compared with the previous group
[b]$P < .05$, compared with the first group

Table 5.1. Comparison of RSS Scores of the Two Groups of Women at Different Timepoints

Group	4 hours after surgery	8 hours after surgery	12 hours after surgery	24 hours after surgery	48 hours after surgery
Control group	2.08 ± 0.11	2.00 ± 0.11	2.01 ± 0.11	1.99 ± 0.08	2.01 ± 0.06
Experimental group	2.12 ± 0.09	2.05 ± 0.12	2.05 ± 0.09	2.06 ± 0.22	2.06 ± 0.14
t	1.990	2.172	1.990	2.114	2.321
P value	.049	.032	.049	.037	.022

Table 5.2. Comparison of RSS Scores of SK Group Puerperae at Different Timepoints

Group	4 hours after surgery	8 hours after surgery	12hours after surgery	24 hours after surgery	48 hours after surgery
SK1 (n = 17)	2.01 ± 0.09	1.95 ± 0.09	1.95 ± 0.07	1.96 ± 0.21	1.92 ± 0.11
SK2 (n = 17)	2.15 ± 0.08[a,b]	2.08 ± 0.11[a,b]	2.06 ± 0.09[a,b]	2.06 ± 0.22[a,b]	2.03 ± 0.14[a,b]
SK3 (n = 17)	2.14 ± 0.09[Δ]	2.06 ± 0.13[b]	2.05 ± 0.09[b]	2.04 ± 0.24[b]	2.01 ± 0.17[b]

[a]$P < .05$, compared with the previous group
[b]$P < .05$, compared with the first group

Table 6. Comparison of Blood Gas Analysis Results of Umbilical Cord and Venous Blood in Neonates (n = 50, $\bar{x} \pm s$)

Group		/mmol·	/mmol·	/mmol·	pH	BE /mmol·
Control group	arterial blood	41.3 ± 1.7	87.3 ± 2.7	25.4 ± 2.0	7.3 ± 0.6	1.9 ± 0.7
	venous blood	41.8 ± 2.1	87.6 ± 2.6	23.8 ± 3.22	7.3 ± 0.4	2.1 ± 0.9
Experimental group	arterial blood	41.8 ± 1.7	87.5 ± 2.3	25.6 ± 2.1	7.3 ± 0.5	2.1 ± 0.6
	venous blood	41.7 ± 1.6	87.9 ± 2.5	24 ± 2.6	7.3 ± 0.6	2.0 ± 0.8

Comparison of umbilical cord drive and venous blood gas analysis values of neonates

There was little difference between the two groups of neonatal umbilical cord arterial blood and venous blood gas analysis values ($P > .05$). See Table 6.

Drug Concentration

Drug concentration in umbilical vein (CUV), drug concentration in umbilical artery (CUA) and drug concentration in maternal artery (CMA) were (184.88 ± 43.56) pg/ml, (134.95 ± 30.74) pg/ml and (268.73 ± 53.28) pg/ml, respectively, and the CUV/CMA and CUA/CUV ratios were 0.69 ± 0.11 and 0.74 ± 0.08.

Comparison of perinatal adverse reaction rates between the two groups of puerperae

In terms of the incidence of postoperative adverse reactions, 1 case of nausea and vomiting was recorded among the mothers in the control group, while the others did not have obvious discomfort. However, the side effects in the SK3 group increased. Statistically, 1 patient had nausea and vomiting symptoms, 1 patient reported dizziness, and the other patient had relatively low blood pressure in the SK3 group. The probability of adverse reactions was 8.00%, and the difference between groups was not statistically significant ($\chi^2 = 3.093$, $P = .079$).

Maternal satisfaction with general anesthesia

The postoperative surgical satisfaction questionnaire was collected, and the analysis showed that there were 49 cases in the experimental group who were satisfied with the operation, and only one patient showed dissatisfaction. This accounted for satisfaction among 98.00% of the patients in the experimental group. In the control group, there were 43 cases of maternal satisfaction, corresponding to satisfaction among 90.00% of the patients. The difference between the groups was statistically significant ($\chi^2 = 4.891$, $P = .027$).

DISCUSSION

In clinical practice, esketamine is one of the sedative and analgesic drugs that is used more than other drugs of the same type in the diagnosis and treatment of depression patients.[6] In March 2019, the drug obtained market approval.[7] Some doctors have found that if the drug is intravenously injected, it is likely to cause mental dependence on the drug among the recipients, and the possibility of addiction to the drug is higher than other methods of administration. Therefore, nasal sprays are often used to administer the drug during treatment to patients. This method enables the active ingredients of the drug to be directly absorbed into the patient's body by the blood vessels and mucous membranes of the patient's nasal cavity. In terms of bioavailability, this method is more appropriate. In addition, nasal inhalation can reduce the potential risks such as taste disturbance and liver damage to a certain extent.[8] The drug-induced adverse reactions of esketamine are all transient. The more common adverse reactions in clinical practice include nausea, abnormal blood pressure, dizziness, and headache.[9]

With the increasing use of esketamine in clinical diagnosis and treatment, physicians have gradually deepened their understanding of its usage, dosage, and pharmacological components, and its use has become more and more extensive.[10] In recent years, some medical workers in China have used this drug to induce maternal anesthesia in cesarean

section operations, and it has a good effect in spinal anesthesia and general anesthesia.[11] Esketamine is more suitable for elective surgery or emergency patients, which can enable patients to enter anesthesia more quickly.[12] Among the current gynecological operations, cesarean section is the most common and well-known, especially in recent years, since the number of elderly women undergoing this surgery is more than before. In addition, the incidence of various pregnancy complications has also increased compared with the past, and the difficulty of childbirth has increased sharply, which makes the clinical use of cesarean section more frequent every year. Before and after the operation, the postoperative pain, the mental state of the parturient, and drug usage-related safety are the aspects that clinicians are concerned about.[13] This study mainly analyzes the analgesia, emotion, and safety of esketamine based on 100 actual cases of cesarean section performed under general anesthesia in our hospital. The results of the study showed that in terms of SpO_2 dimension, there was no significant difference in the levels of the two groups of puerperae at different timepoints ($P > .05$). Immediately after anesthesia (T1), 10 minutes after entering anesthesia (T2), and at the end of cesarean section (T3), the experimental group performed better than the control group in terms of HR and MAP levels. The differences between the groups had statistical significance ($P < .05$). It shows that esketamine can play a certain role in stabilizing the maternal heart rate level and maintaining the stability of blood pressure in puerperae during anesthesia, and can prevent some unpredictable situations, such as placental perfusion, etc. It plays a relatively large role in maintaining the stability of the vital signs of the mother during the whole operation. In terms of postoperative pain assessment, the postoperative pain among mothers in the control group was more intense than those in the experimental group ($P < .05$). The mental state of the puerperae in the experimental group was significantly better than those in the control group at 1/3/7 d postpartum ($P < .05$). It shows that esketamine can effectively improve the postoperative experience of puerperae, effectively reduce postoperative pain, reduce the occurrence of postoperative depression, and help puerperae to regulate their emotions after childbirth. There is no significant difference in adverse reactions between the two groups of puerperae after operation ($P > .05$). In terms of surgical satisfaction, compared with the control group, the maternal satisfaction in the experimental group was significantly higher, and the difference in satisfaction was statistically significant ($P < .005$). There was no significant difference in neonatal blood gas index and Apgar score between the two groups ($P > .05$), indicating that the effect of esketamine administration on neonates was not obvious, and the application was apparently safe. This study shows that among the different dosages of esketamine used along with 15 ng/kg/h sufentanil in postoperative analgesia, the effect of 30 μg/kg/h is significantly better than that of 15 μg/kg/h, but 45 μg/kg/h has no significant improvement over 30 μg/kg/h. The possible reason for this phenomenon is that the increase in the dosage of esketamine can improve the analgesic effect to a certain extent, but its effect is not proportional to the concentration. Therefore, the author believes that postoperative analgesia with 30 μg/kg/h esketamine and 15 ng/kg/h sufentanil has the best effect. The limitations of this study are as follows: (1) The sample size was small. (2) The evaluation of patient indicators is not comprehensive enough.

In conclusion, esketamine is worthy of promotion in general anesthesia for cesarean section.

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AUTHOR DISCLOSURE STATEMENT

The authors have no potential conflicts of interest to report relevant to this article.

AUTHOR CONTRIBUTIONS

FL and CW contributed equally to this work. FL and ZY designed the study and performed the experiments, XD and LJ collected the data, HC and YL analyzed the data, FLand ZY prepared the manuscript. All authors read and approved the final manuscript.

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