Original Article

Effect of low-dose esketamine on pain control and postpartum depression after cesarean section: a retrospective cohort study

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Background: Esketamine is used to control postoperative pain and reduce postoperative depression in surgical patients. This study was performed to determine the effects of esketamine on pain control as well as postpartum depression (PPD) in pregnant women who underwent cesarean section (CS).

Methods: Pregnant women who underwent CS between March 2018 and February 2020 at our hospital were retrospectively reviewed. Parturients in the control group received 50 μg sufentanil citrate and 0.25 mg palonosetron hydrochloride, while those in the experimental group received additional 0.2–0.5 mg/kg esketamine. The primary outcomes included postoperative pain control according to the numeric rating scale (NRS) and the incidence of PPD according to the Edinburgh postnatal depression scale (EPDS). Multivariable linear regression analysis was performed to determine the relationship between the use of esketamine, pain control, and the incidence of PPD after CS.

Results: There were 132 parturients in the control group and 108 parturients in the esketamine group in this study. All NRS scores at rest at any time point were much lower in the esketamine group than those in the control group. Besides, NRS scores when coughing were also lower in the esketamine group within 24 hours. EPDS scores were lower in the esketamine group than those in the control group within 3 months postpartum. Esketamine acted as a protector of pain control and was confirmed to improve the incidence of PPD using multivariable linear regression. Parturients had dramatically better sleep quality within 1 week postpartum (P=0.044), and morphine consumption within 24 hours postpartum was lower in the esketamine group than in the control group (P<0.001). The quality of recovery within 3 months postpartum was also better in the esketamine group (P=0.001). A subgroup analysis of 2 subgroups divided according to the dose of esketamine was then performed, indicating no significant difference between the low-dose group and high-dose group in most included outcomes.

Conclusions: This study confirmed the effects of esketamine on pain control and the incidence of PPD in pregnant women who underwent CS. Considering the potential adverse events, low-dose esketamine may be more suitable for pregnant women who have undergone CS.

Keywords: Esketamine; pain control; postpartum depression (PPD); cesarean section (CS); retrospective cohort study

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Introduction

Elective or emergency cesarean section (CS) is one of the most common operations, accounting for approximately 25% to 45% of all births in China (1-4). Although a large number of pregnant women undergo CS, which provides significant management experience, the postoperative nursing of these pregnant women is still a challenge. The most important problem is postoperative pain control after CS, including pain caused by surgical incision and uterine contraction (5). Persistent postoperative pain can lead to maternal inability to discharge respiratory secretions, intestinal obstruction, and venous thrombosis caused by long-term bed rest (6). In addition, postoperative pain will also affect the secretion of milk, delay the milk feeding of newborns, and reduce the intimate communication between mothers and infants (7). More seriously, long-term chronic pain may lead to postpartum depression (PPD). A previous study indicated that postoperative pain was correlated with the early onset of PPD after CS (8). PPD is present in 10–20% of pregnant women, mostly within 1 year after delivery (9-11). PPD significantly affects the mother's quality of recovery, and can delay the baby's growth and development due to the deterioration of the mother-infant relationship. In the most serious cases, PPD can lead to maternal suicide. It has been reported that PPD is associated with about 20% of maternal postoperative deaths (12). Therefore, the proper management of postoperative pain should be further explored to improve the quality of recovery of pregnant women undergoing CS.

The standard treatment of postoperative pain after CS is the use of opioids, which can exert a rapid analgesic effect for a long time, but may also lead to some adverse reactions (13). Nowadays, many drugs are used in combination to reduce the use of opioids, maintain effective analgesia, and reduce the incidence of adverse reactions. Esketamine, an enantiomer of ketamine, acts as a non-selective N-methyl-D-aspartic acid (NMDA) receptor inhibitor. Esketamine was initially used as a psychotropic drug for treatment-resistant depression, which was reported to improve the functional outcomes of patients (14). In recent years, some studies have also begun to use esketamine to control postoperative pain and reduce the use of opioids. Nielsen *et al.* reported that intraoperative esketamine could reduce postoperative pain and opioid use in patients undergoing spinal surgery (15). Furthermore, Liu *et al.* reported that esketamine was effective for reducing postoperative depression in breast cancer patients without increasing the incidence of adverse events (16). However, no study to date has been performed to determine the effects of esketamine on pain control as well as PPD in pregnant women undergoing CS. This retrospective cohort study was conducted in a single center to explore the effects of esketamine by comparing postoperative pain and PPD after CS between pregnant women receiving esketamine and those not receiving esketamine. Meanwhile, subgroup analysis was also performed to compare the effects of different doses of esketamine. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3343/rc).

Methods

Study design

This study was performed in Wuxi No. 9 People's Hospital Affiliated to Soochow University. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Wuxi No. 9 People's Hospital Affiliated to Soochow University (No. 0021022). Individual consent for this retrospective analysis was waived.

Patient selection

Pregnant women who had undergone CS between March 2018 and February 2020 at our hospital were retrospectively reviewed by 2 independent investigators. The following pregnant women were included in this study: (I) those older than 18 years; (II) those with American Society of Anesthesiologists class II; (III) those who received spinal anesthesia; (IV) those who underwent elective or emergency CS; and (V) those who received patient controlled intravenous analgesia (PCIA) using the combination of sufentanil citrate and palonosetron hydrochloride with/without esketamine after CS. The following pregnant women were excluded from this study: (I) those with a psychotic disorder; (II) those allergic to esketamine; (III) those who did not receive PCIA including sufentanil citrate and palonosetron hydrochloride; (IV) those who received combined spinal-epidural anesthesia; (V) those with life-threatening chronic comorbid diseases; and (VI) those who participated in other clinical studies. After including pregnant women, the following demographic and clinical

data were collected: age, pre-pregnancy body mass index (BMI), gestational weeks (full term, preterm, and post term), pregnancy complications (gestational diabetes, gestational hypertension, acute fatty liver of pregnancy, placenta previa, and placental abruption), gravidity, parity, prior history of CS, marital status, educational level, employment, pressure during pregnancy, type of CS (elective or emergency), operation time, anesthesia time, volume of blood loss, blood transfusion, fetus, and dose of esketamine. The pressure during pregnancy was classified as high, moderate, and low according to a previous study (17). These data were also collected and discussed by 2 independent investigators.

Procedures

Spinal anesthesia was performed using 12 mg bupivacaine hydrochloride in L2-L3 or L3-L4 subarachnoid spaces before the CS procedure. The anesthesia block level was controlled below T6, and vital signs of parturients were routinely monitored. PCIA was attached to all parturients after CS. The PCIA protocol in the control group consisted of sufentanil citrate 50 μg and palonosetron hydrochloride 0.25 mg in 200 mL saline, while the PCIA protocol in the experimental group consisted of sufentanil citrate 50 μg, palonosetron hydrochloride 0.25 mg, and esketamine 0.2–0.5 mg/kg in 200 mL saline. The infusion rate was 4 mL/h, the bolus dose was 4 mL, and the lockout time was 30 min. All parturients were taught to use PCIA properly in wards, and it was recommended that PCIA be used at least 24 hours after CS. A subgroup analysis was then performed to divide parturients receiving esketamine into a high-dose group (>0.3 mg/kg) and low-dose group (≤0.3 mg/kg) and determine the effects of different doses of esketamine on pain control and PPD.

Outcomes

All parturients were followed up for 3 months and those who were lost to follow-up were excluded from this study. The primary outcomes in this study included postoperative pain control and the incidence of PPD. Pain control was assessed using the numeric rating scale (NRS), which ranged from 0 (painless) to 10 points (most severely painful). PPD was assessed by the Edinburgh postnatal depression scale (EPDS) at 4–6 weeks postpartum and at 3 months postpartum. The EPDS contained 10 questions, with a total score of 30. A total score higher than 9 indicated the existence of PPD in the parturient and timely comprehensive interventions were needed. The secondary outcomes included analgesia-related adverse events (nausea and vomiting, dizziness, and pruritus), sleep quality, cumulative morphine consumption, postpartum anxiety, and quality of recovery. Postpartum anxiety was assessed by the generalized anxiety disorder-7 (GAD-7) scale, with total scores of 21 and higher indicating the existence of postpartum anxiety. The quality of recovery was assessed by a 15-item quality of recovery questionnaire (QoR-15), and higher scores indicated better quality of recovery.

Statistical analysis

Statistical analysis in this study was performed using SPSS 20.0 (IBM Corp., NY, USA). Continuous data were expressed using mean with standard deviation and compared between 2 groups using Student's *t*-test. Categorical data were expressed using number with percentage and compared between 2 groups using the chi-square test. Multivariable linear regression analysis was performed to further determine the relationship between the use of esketamine, pain control, and the incidence of PPD after CS. P values less than 0.05 were considered as statistically different.

Results

According to the medical record system of our hospital, 1,138 pregnant women who underwent CS were included in this study and 806 patients were excluded based on the exclusion criteria. Then, 92 out of 332 parturients were excluded because of loss to follow-up. Finally, there were 240 parturients included in this study, with 132 parturients in the control group and 108 parturients in the esketamine group, as shown in *Figure 1*.

The preoperative data of the included pregnant women are shown in *Table 1*. The mean age of parturients was 29.6±4.6 years old and the mean pre-pregnancy BMI was 23.6±3.1 kg/m^2 in the control group, as shown in *Table 1*. A total of 107 parturients (81.1%) were full term and more than half of parturients were not primiparas. A total of 63 parturients (47.7%) had a prior history of CS. Most parturients (97.0%) had been married and 33 parturients (25.0%) were unemployed. Fourteen parturients (10.6%) had high pressure during pregnancy and 44 parturients (33.3%) had moderate pressure. Twelve parturients (9.1%) were diagnosed with gestational diabetes and 21 parturients were diagnosed with gestational hypertension. Additionally,

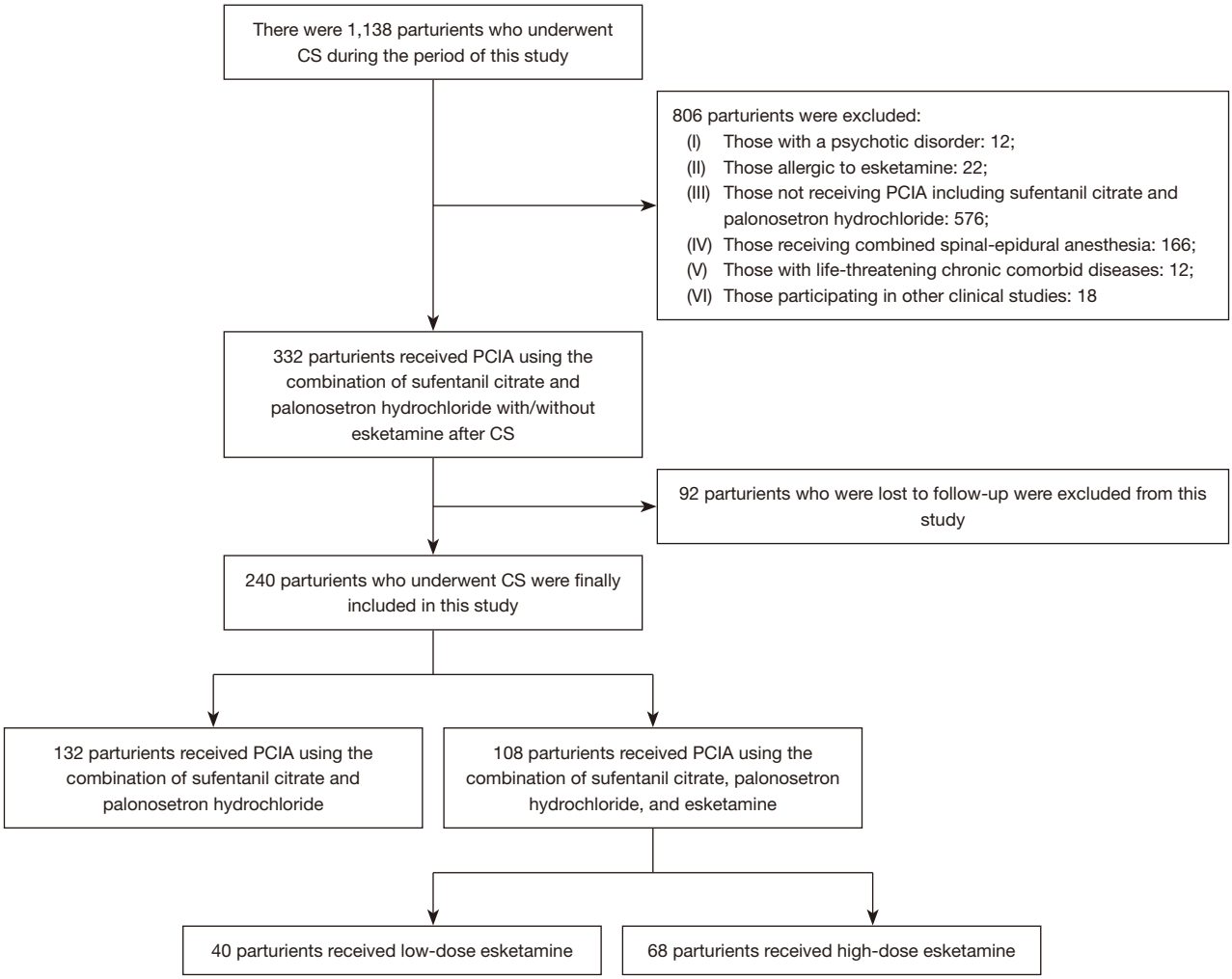

Figure 1 Flow chart. CS, cesarean section; PCIA, patient controlled intravenous analgesia.

34 parturients (25.8%) were diagnosed with placenta previa. On the other hand, the mean age of parturients was 29.5±4.0 years old and the mean pre-pregnancy BMI was 24.1±3.5 kg/m^2 in the esketamine group. There were 41 parturients diagnosed with placenta previa, significantly more than in the control group (P=0.042), and much fewer parturients were unemployed before pregnancy (P=0.019).

The intraoperative data of the included pregnant women are shown in *Table 2*, and there was no significant difference between the control group and esketamine group. More than 80% of parturients received elective CS. The mean operation time was 41.5±12.4 minutes in the control group and 43.3±16.5 minutes in the esketamine group. The volume of blood loss was 508.6±285.8 mL in the control group and 520.1±272.0 mL in the esketamine group. Less than 5% of parturients received blood transfusions. The mean dose of esketamine in the esketamine group was 0.35±0.11 mg/kg.

The comparisons of the 2 primary outcomes, namely pain control according to the NRS score and PPD according to the EPDS score, are shown in *Figure 2*. The NRS scores at rest or when coughing at 2, 4, 8, 24, and 48 hours postpartum were compared between the 2 groups. It was found that all NRS scores at rest at any time point were much lower in the esketamine group than those in the control group. Furthermore, NRS scores when coughing were similar between the 2 groups within 2 hours, and they were much lower in the esketamine group at other time points. There was no significant difference in the EPDS scores at antenatal day 1 between the 2 groups. EPDS

Table 1 Preoperative data of the included pregnant women

Variables	Control group	Esketamine group	P value
Number	132	108	–
Age (year), mean ± SD	29.6±4.6	29.5±4.0	0.839
Pre-pregnancy BMI (kg/m^2), mean ± SD	23.6±3.1	24.1±3.5	0.291
Gestational weeks, n (%)			0.822
Full term	107 (81.1)	88 (81.5)	
Preterm	18 (13.6)	16 (14.8)	
Post term	7 (5.3)	4 (3.7)	
Pregnancy complications, n (%)			
Gestational diabetes	12 (9.1)	10 (9.3)	0.964
Gestational hypertension	21 (15.9)	17 (15.7)	0.972
Acute fatty liver of pregnancy	8 (6.1)	7 (6.5)	0.893
Placenta previa	34 (25.8)	41 (38.0)	0.042
Placental abruption	4 (3.0)	5 (4.6)	0.516
Gravidity, n (%)			0.667
0	50 (37.9)	38 (35.2)	
≥1	82 (62.1)	70 (64.8)	
Parity, n (%)			0.483
0	60 (45.5)	54 (50.0)	
≥1	72 (54.5)	54 (50.0)	
Prior history of CS, n (%)	63 (47.7)	52 (48.1)	0.948
Marital status, n (%)			0.644
Married	128 (97.0)	105 (97.2)	
Unmarried	3 (2.3)	3 (2.8)	
Divorced	1 (0.8)	0 (0)	
Educational level, n (%)			0.729
Master or above	118 (89.4)	98 (90.7)	
Bachelor or below	14 (10.6)	10 (9.3)	
Employment, n (%)			0.019
Employed	99 (75.0)	94 (87.0)	
Unemployed	33 (25.0)	14 (13.0)	
Pressure during pregnancy, n (%)			0.742
High	14 (10.6)	12 (11.1)	
Moderate	44 (33.3)	31 (28.7)	
Low	74 (56.1)	65 (60.2)	

SD, standard deviation; BMI, body mass index; CS, cesarean section.

Table 2 Intraoperative data of the included pregnant women

Variables	Control group	Esketamine group	P value
Type of CS, n (%)			0.245
Elective	109 (82.6)	95 (88.0)	
Emergency	23 (17.4)	13 (12.0)	
Operation time (minute), mean ± SD	41.5±12.4	43.3±16.5	0.041
Anesthesia time (minute), mean ± SD	75.6±29.1	78.2±31.9	0.509
Volume of blood loss (mL), mean ± SD	508.6±285.8	520.1±272.0	0.752
Blood transfusion, n (%)	6 (4.5)	4 (3.7)	0.745
Fetus, n (%)			0.588
1	121 (91.7)	101 (93.5)	
≥2	11 (8.3)	7 (6.5)	
Dose of esketamine (mg/kg), mean ± SD	–	0.35±0.11	–

CS, cesarean section; SD, standard deviation.

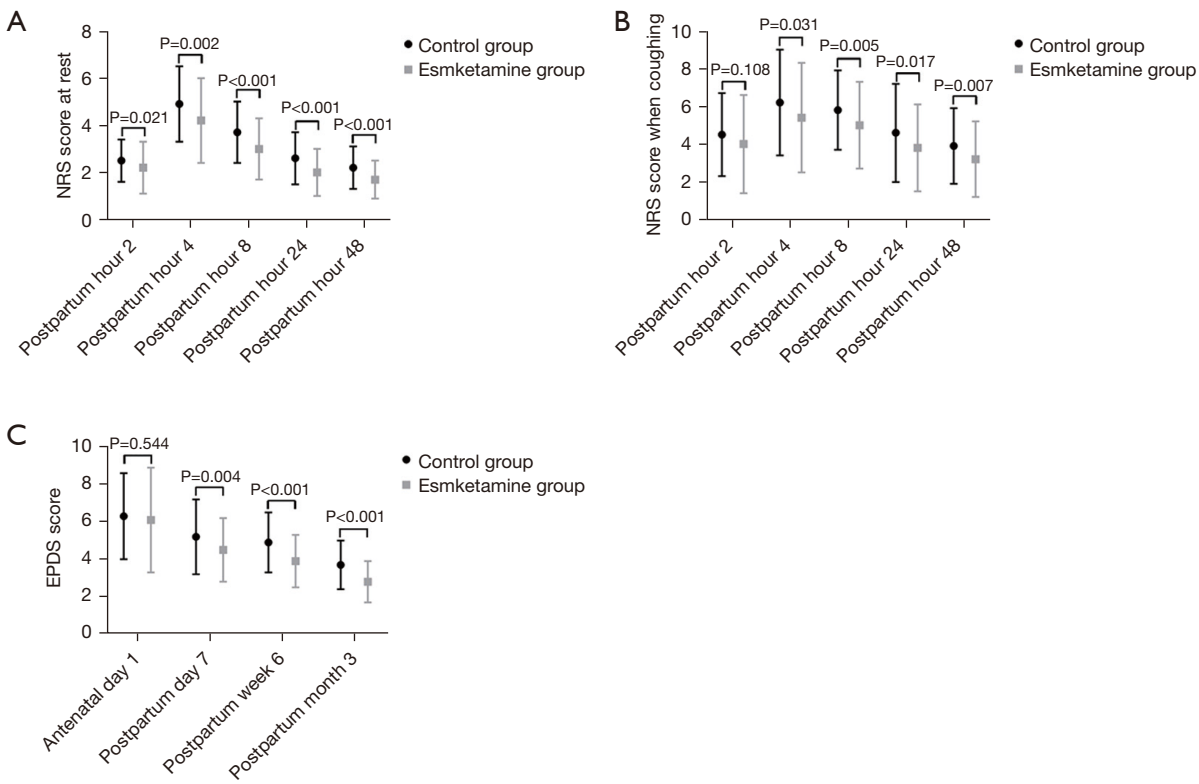

Figure 2 Numeric rating scale (NRS) scores at rest (A) and when coughing (B) at 2, 4, 8, 24, and 48 hours postpartum, and Edinburgh postnatal depression scale (EPDS) scores (C) at antenatal day 1, 7 days postpartum, 6 weeks postpartum, and 3 months postpartum were compared between the control group and esketamine group.

Table 3 Risk factors and predictors of pain control at rest within 24 hours and PPD within 3 months in the included parturients based on multivariable linear regression analysis

Characteristics	Multivariable analysis		
	β	95% CI	P value
Pain control based on NRS score			
Esketamine	−0.687	−0.962, −0.412	<0.001
Emergency CS	0.793	0.413, 1.174	<0.001
Longer operation time	0.024	0.001, 0.046	0.039
PPD based on EPDS score			
Esketamine	−0.404	−0.655, −0.153	0.002
Primiparas	0.250	0.006, 0.495	0.045
High pressure during pregnancy	0.716	0.539, 0.894	<0.001
High NRS score within 48 hours	0.144	0.064, 0.224	0.023

PPD, postpartum depression; CI, confidence interval; NRS, numeric rating scale; CS, cesarean section; EPDS, Edinburgh postnatal depression scale.

scores were much lower in the esketamine group than those in the control group within 3 months postpartum. Due to the retrospective design of this study, the risk factors and predictors of pain control and PPD were then analyzed using multivariable linear regression as shown in *Table 3*. Emergency CS and longer operation time were identified as risk factors of poor pain control, and esketamine acted as a protector of pain control in these parturients who underwent CS. Similarly, esketamine was confirmed to improve the incidence of PPD, and primiparas, high pressure during pregnancy, and high NRS score within 48 hours contributed to the increase of PPD.

Secondary outcomes are also shown in *Table 4*. The incidence of analgesia-related adverse events was slightly higher in the esketamine group than that in the control group, showing no significant difference. Parturients in the esketamine group had dramatically better sleep quality within 1 week postpartum (P=0.044). In addition, morphine consumption within 24 hours postpartum was lower in the esketamine group than in the control group (P<0.001). The GAD-7 score, indicating postpartum anxiety within 1 week postpartum, was lower in the esketamine group (P<0.001), and the quality of recovery within 3 months postpartum according to the QoR-15 score was also better in the esketamine group (P=0.001).

A subgroup analysis was then performed and parturients in the esketamine group were divided into 2 subgroups according to the dose of esketamine. Comparing the perioperative data of included parturients as shown in *Table 5*, the mean pre-pregnancy BMI was much lower in the high-dose group than that in the low-dose group, and the mean dose of esketamine was 0.25±0.05 mg/kg in the low-dose group, which was lower than 0.42±0.08 mg/kg in the high-dose group. No significant difference was found in other data between the 2 subgroups. NRS scores and EPDS scores in the 2 subgroups are shown in *Figure 3*. NRS scores at rest at 24 and 48 hours postpartum in the high-dose group were much lower than those in the low-dose group (P<0.001 and P=0.011, respectively). Also, the NRS score when coughing at 24 hours postpartum was lower in the high-dose group compared with the low-dose group. However, no significant difference was found between the 2 subgroups in postpartum EPDS scores. Secondary outcomes of the 2 subgroups were compared as shown in *Table 6*. The incidence of analgesia-related adverse events was slightly higher in the high-dose group, however, there was no significant difference compared with the low-dose group. Similarly, no significant difference was found between the 2 subgroups in other secondary outcomes.

Discussion

Very few studies have been performed to investigate the effects of esketamine on pain control and the incidence of PPD in pregnant women who have undergone CS. This

Table 4 Secondary outcomes of the included parturients

Variables	Control group	Esketamine group	P value
Analgesia-related adverse events, n (%)			
Nausea and vomiting	26 (19.7)	27 (25.0)	0.324
Dizziness	37 (28.0)	42 (38.9)	0.075
Pruritus	9 (6.8)	11 (10.2)	0.348
Sleep quality within 1 week postpartum, n (%)			0.044
Good	24 (18.2)	31 (28.7)	
Moderate	30 (22.7)	30 (27.8)	
Poor	78 (59.1)	47 (43.5)	
Morphine consumption within 24 hours postpartum (mg), mean ± SD	32.3±12.3	24.1±11.3	<0.001
Postpartum anxiety within 1 week postpartum, mean ± SD	7.2±2.1	6.2±2.2	<0.001
Quality of recovery within 3 months postpartum, mean ± SD	114.8±19.0	124.7±25.9	0.001

SD, standard deviation.

study retrospectively collected some perioperative data and analyzed data using multivariable linear regression, which found that the use of esketamine was beneficial for both pain control and improving PPD. It was also found that the effects of low-dose esketamine on the prognosis of parturients were similar to those of high-dose esketamine.

Many previous studies have investigated the effects of other potential drugs on pain control or the incidence of PPD. Dexmedetomidine was reported by Yu *et al.* to be useful for alleviating PPD following CS (18). Tramadol was also reported by Wu *et al.* to ameliorate PPD in high-risk woman after CS (12). On the other hand, inhalation of chamomile oil was reported to relieve CS pain in primiparous women (19). Shahraki *et al.* also reported that both oral methadone and intramuscular pethidine provided similar analgesic effects after CS (20). However, most of the above drugs can only relieve postoperative pain or reduce depressive symptoms alone, but drugs that can relieve both pain and PPD are rare. Esketamine is an NMDA receptor agonist and has a higher affinity for NMDA receptors than ketamine. NMDA receptor subunits have complex physiological functions, which can regulate the survival of neurons, the development of dendrites and axons and synaptic plasticity, and affect the formation of neurons and the process of learning and memory (21,22). As an agonist of NMDA receptors, esketamine was reported to be useful for the treatment of depressive disorder (23,24). Furthermore, esketamine was confirmed to be useful for pain control in surgical patients (15,16). Suppa *et al.* reported in 2012 that low-dose esketamine could effectively control postoperative pain in 56 pregnant women who underwent CS (25). Our study further reported the beneficial effects of esketamine on pain control and the incidence of PPD in pregnant women who underwent CS. Also, the consumption of morphine could be reduced by the use of esketamine, which was similar to a previous study (15).

Some other risk factors of poor pain control and PPD were also identified in this study. Emergency CS and longer operation time were related to poor pain control, while primiparas, high pressure during pregnancy, and high NRS score within 48 hours contributed to the incidence of PPD. Shen *et al.* reported previously that primiparas, emergency surgery, and NRS score of more than 1 point were related to the incidence of PPD in parturients who underwent CS (8). Yu *et al.* reported that domestic violence and life stress events also contributed to the incidence of PPD (18). However, the data of domestic violence and life stress events could not be obtained due to the retrospective design of this study.

The dose of esketamine used in parturients has not yet been determined. Generally, the dose of esketamine is 0.25 or 0.5 mg/kg (25,26). In cervical carcinoma patients, both 0.5 and 0.25 mg/kg esketamine improved short-term depression and pain after surgery, showing no difference between the 2 groups (27). In contrast, esketamine was reported to reduce the consumption of an opioid in a dose-dependent manner in patients who underwent major lumbar fusion surgery (28). Our study found that NRS scores

Table 5 Subgroup analysis of perioperative data of pregnant women receiving different doses of esketamine

Variables	Low-dose group	High-dose group	P value
Number	40	68	–
Age (year), mean ± SD	28.9±3.2	29.8±4.4	0.248
Pre-pregnancy BMI (kg/m^2), mean ± SD	26.7±1.7	23.0±2.4	<0.001
Gestational weeks, n (%)			0.056
Full term	28 (70.0)	60 (88.2)	
Preterm	10 (25.0)	6 (8.8)	
Post term	2 (5.0)	2 (2.9)	
Pregnancy complications, n (%)			
Gestational diabetes	5 (12.5)	5 (7.4)	0.373
Gestational hypertension	4 (10.0)	13 (19.1)	0.209
Acute fatty liver of pregnancy	2 (5.0)	5 (7.4)	0.483
Placenta previa	12 (30.0)	29 (42.6)	0.191
Placental abruption	1 (2.5)	4 (5.9)	0.386
Gravidity, n (%)			0.101
0	18 (45.0)	20 (29.4)	
≥1	22 (55.0)	48 (70.6)	
Parity, n (%)			1.000
0	20 (50.0)	34 (50.0)	
≥1	20 (50.0)	34 (50.0)	
Prior history of CS, n (%)	16 (40.0)	36 (52.9)	0.194
Marital status, n (%)			1.000
Married	39 (97.5)	66 (97.1)	
Unmarried	1 (2.5)	2 (2.9)	
Divorced	0 (0)	0 (0)	
Educational level, n (%)			0.373
Master or above	35 (87.5)	63 (92.6)	
Bachelor or below	5 (12.5)	5 (7.4)	
Employment, n (%)			0.913
Employed	35 (87.5)	59 (86.8)	
Unemployed	5 (12.5)	9 (13.2)	
Pressure during pregnancy, n (%)			0.405
High	6 (15.0)	6 (8.8)	
Moderate	13 (32.5)	18 (26.5)	
Low	21 (52.5)	44 (64.7)	

Table 5 (*continued*)

Table 5 (*continued*)

Variables	Low-dose group	High-dose group	P value
Type of CS, n (%)			0.364
Elective	37 (92.5)	58 (85.3)	
Emergency	3 (7.5)	10 (14.7)	
Operation time (minute), mean ± SD	44.5±15.0	42.7±17.4	0.581
Anesthesia time (minute), mean ± SD	78.5±33.9	78.0±30.9	0.936
Volume of blood loss (mL), mean ± SD	541.0±300.3	507.9±255.5	0.544
Blood transfusion, n (%)	2 (5.0)	2 (2.9)	0.626
Fetus, n (%)			0.708
1	37 (92.5)	64 (94.1)	
≥2	3 (7.5)	4 (5.9)	
Dose of esketamine (mg/kg), mean ± SD	0.25±0.05	0.42±0.08	<0.001

BMI, body mass index, CS, cesarean section; SD, standard deviation.

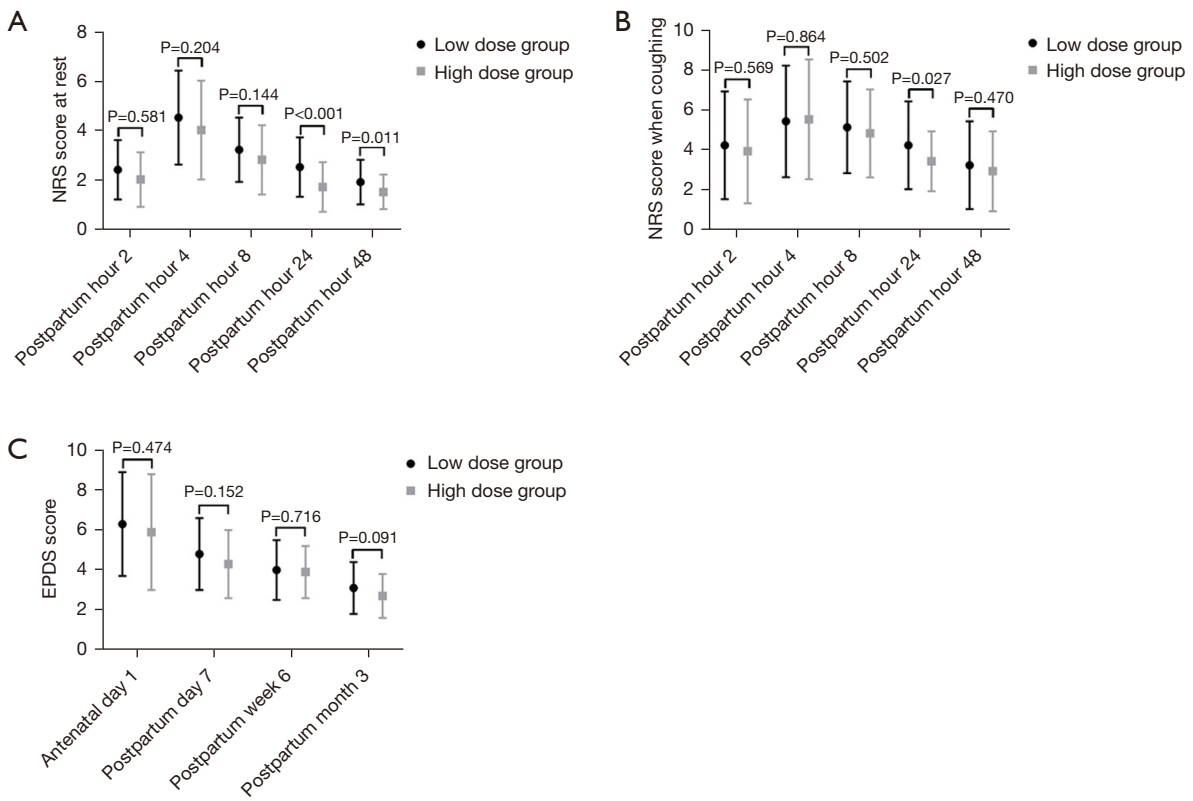

Figure 3 Numeric rating scale (NRS) scores at rest (A) and when coughing (B) at 2, 4, 8, 24, and 48 hours postpartum, and Edinburgh postnatal depression scale (EPDS) scores (C) at antenatal day 1, 7 days postpartum, 6 weeks postpartum, and 3 months postpartum were compared between the low-dose esketamine group and high-dose esketamine group.

Table 6 Subgroup analysis of secondary outcomes of included parturients receiving different doses of esketamine

Variables	Low-dose group	High-dose group	P value
Analgesia-related adverse events, n (%)			
Nausea and vomiting	7 (17.5)	20 (29.4)	0.167
Dizziness	14 (35.0)	28 (41.1)	0.525
Pruritus	3 (7.5)	8 (11.8)	0.743
Sleep quality within 1 week postpartum, n (%)			0.968
Good	11 (27.5)	20 (29.4)	
Moderate	11 (27.5)	19 (27.9)	
Poor	18 (45.0)	29 (42.6)	
Morphine consumption within 24 hours postpartum (mg), mean ± SD	23.7±10.9	24.3±11.6	0.787
Postpartum anxiety within 1 week postpartum, mean ± SD	6.1±2.1	6.3±2.3	0.754
Quality of recovery within 3 months postpartum, mean ± SD	122.2±26.2	126.5±25.8	0.254

SD, standard deviation.

at rest at 24 and 48 hours postpartum in the high-dose group were much lower than those in the low-dose group (P<0.001 and P=0.011, respectively). Also, the NRS score when coughing at 24 hours postpartum was lower in the high-dose group compared with the low-dose group. No significant difference was found between the 2 subgroups in postpartum EPDS scores. However, the incidence of analgesia-related adverse events was slightly higher in the high-dose group. Therefore, low-dose esketamine may be more suitable for pregnant women undergoing CS, considering the potential adverse events and similar effects to high-dose esketamine.

There were some limitations in this study. Firstly, our center has used esketamine for analgesia after CS since 2019. There was a certain time difference between the control group and the esketamine group. This may have led to certain differences in the medical level and parturient prognosis. Secondly, the dose of esketamine used in this study was 20 mg, thus, the different doses in the subgroup analysis were mainly dependent on the different body weights of pregnant women. This may have led to selection bias in this study. A randomized controlled study will be more helpful to verify the effect of different doses of esketamine on the prognosis of parturients. Thirdly, this study was a retrospective study, which may have contributed to some errors in the collected data. Also, some data, such as spousal relationship, family income, and domestic violence, could not be obtained in this study.

Conclusions

This retrospective study confirmed the effects of esketamine on pain control and the incidence of PPD in pregnant women who underwent CS. Furthermore, the use of esketamine could reduce the consumption of morphine and improve the quality of recovery. The subgroup analysis revealed that low-dose and high-dose esketamine provided similar improvement of postoperative pain and PPD. Considering the potential adverse events induced by esketamine, low-dose esketamine may be more suitable for pregnant women who have undergone CS.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3343/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3343/coif).

The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by institutional ethics board of Wuxi No. 9 People's Hospital Affiliated to Soochow University (No. 0021022). Individual consent for this retrospective analysis was waived.

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