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Esketamine combined with low-dose propofol induction strategy for category-1 cesarean section: a case series

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Abstract

Background General anesthesia (GA) is the most accepted option for category-1 emergency cesarean sections (CSs). A low dose of esketamine has been used as an excellent adjunct to neuraxial anesthesia (NA) with little effect on newborns. However, literature on the use of esketamine for GA induction in emergency CS is limited. This case series describes our experience with an esketamine-based combined low-dose propofol induction strategy for category-1 CS.

Methods We retrospectively analyzed esketamine-based anesthesia induction for category-1 emergency CS at our hospital between November 2022 and November 2024. Modified rapid sequence induction included 0.5 mg/kg esketamine, 1 mg/kg propofol, and 1 mg/kg rocuronium, respectively. Anesthesia was maintained by propofol infusion at 4 mg/kg/h and inhalation of 1.5% sevoflurane. The dose of propofol and sevoflurane was adjusted to maintain the BIS value at 40–60.

Results The final cohort comprised 11 patients. The median 1-minute Apgar score was 9 points [range, 6–10], and the 5-minute Apgar score was 10 points for all newborns. The mean decision-to-delivery interval (DDI) was 10.9 ± 2.4 min. Only one newborn required temporary mask ventilation due to acute fetal distress, mainly caused by major placental abruption. No newborns were admitted to the intensive care unit (ICU). No episodes of hypotension (MAP < 70 mmHg) were observed from anesthesia induction to delivery of the newborns. In all cases, there was no intraoperative awareness, reflux aspiration, or adverse psychiatric effects.

Conclusions The esketamine-based combination low-dose propofol induction strategy can effectively maintain maternal hemodynamic stability without causing neonatal depression, making it suitable for category-1 emergency CSs. However, further randomized controlled trials are needed to confirm these findings.

Keywords Esketamine, Propofol, Cesarean section, Emergency, General anesthesia

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Background

Category-1 cesarean section (CS) is defined as an emergency operation due to an immediate threat to the life of the mother or fetus, with a decision-to-delivery interval (DDI) that should be within 30 min [1]. Anesthesia for Category-1 CS is challenging because it must be performed in a limited time while considering the safety of the compromised fetus or mother. General anesthesia (GA) is a generally accepted option for Category-1 CS due to its rapid and predictable onset time [2]. However, GA has been shown to lower neonatal Apgar scores compared to neuraxial anesthesia (NA) [3–7], and there is currently no optimal GA induction protocol for Category-1 CS.

Ketamine, a noncompetitive NMDA receptor antagonist characterized by rapid onset and short duration, possesses analgesic, hypnotic, and anti-postpartum depression properties and has been used for CS anesthesia for decades [8, 9]. Ketamine can be transferred across the placenta to the neonate [10, 11], and its adverse effects are dose-dependent. A low dose of ketamine (≤ 1.5 mg/kg) has been shown to maintain maternal hemodynamic stability and improve uterine perfusion with little newborn suppression [8, 12]. This makes ketamine an appealing option, even in cases of severe fetal distress [8, 13]. In recent years, the use of ketamine in obstetric anesthesia has fallen out of favor because of its adverse effects, including unpleasant hallucinations, nightmares, and nausea [8].

Ketamine is a racemic mixture of 50% S(+)-ketamine and 50% R(-)-ketamine. Esketamine (S(+)-ketamine) has similar pharmacological properties to ketamine, with a lower incidence of adverse effects, faster clearance, and shorter recovery time [14–16]. Low-dose esketamine has been used as an adjunct to NA prior to incision without adverse effects on neonatal outcomes [14, 17, 18]. Esketamine is particularly suitable for GA induction in CS [19]; however, the relevant literature is very limited. This case series reports our experience with low-dose esketamine for the induction of GA in category-1 emergency CSs.

Methods

After obtaining approval with written consent waived by the Ethics Committee of Taizhou Hospital of Zhejiang Province (Approval no: KL20241024), we retrospectively analyzed esketamine-based anesthesia induction for category-1 emergency CSs in our hospital from November 2022 to November 2024. All the experiments were performed in accordance with the Declaration of Helsinki. Eligible cohorts were identified using data from the electronic medical records database of Taizhou Hospital of Zhejiang Province. Clinical trial number: not applicable.

A series of 11 women undergoing category-1 emergency CS were included, with a mean age of 30.7 ± 5.8 years, a mean body mass index (BMI) of 25.3 ± 2.3 kg/m^2, and a mean gestational age of 37.5 ± 2.2 weeks. There were four cases of premature CS and seven cases of full-term CS. The reasons for emergency CS included one case of placenta previa with antenatal bleeding, one case of placental abruption, six cases of acute fetal distress, and three cases of umbilical cord prolapse.

All the procedures were performed in an obstetric operating room adjacent to the delivery room. Electrocardiography, pulse oxygen saturation, non-invasive blood pressure, and partial pressure of end-tidal CO_2 were regularly monitored. The patients were positioned in a 30° head-up position [20, 21] with a 15° left tilt [22, 23] and preoxygenated with a tight-fitting mask using oxygen flows of 10 to 15 L/min. Gentle bag-mask ventilation (< 20 cmH_2O) in combination with cricoid pressure was performed during modified rapid sequence induction [20, 24]. GA was induced simultaneously with surgical disinfection. Modified rapid sequence induction was performed using 0.5 mg/kg of esketamine, 1 mg/kg propofol, and 1 mg/kg rocuronium, followed by tracheal intubation using a videolaryngoscope 60 s later. Anesthesia was maintained by the intravenous infusion of propofol at 4 mg/kg/h and inhalation of 1.5% sevoflurane. The dose of propofol and sevoflurane was adjusted to maintain the BIS value at 40–60. After umbilical cord clamping, 0.5 μg/kg sufentanil was injected intravenously, and remifentanil was infused at 0.2 μg/kg/min intravenously. The incision was locally infiltrated with 0.75% ropivacaine (20 mL), and the neuromuscular blockade was reversed with sugammadex at the end of the procedure.

The DDI was calculated based on electronic medical records. Apgar scores of newborns at 1 and 5 min, as well as data on neonatal resuscitation and outcomes, were collected. The occurrence of hypotension (MAP < 70 mmHg [25]) during the period from GA induction to umbilical cord clamping was recorded. Esketamine-related adverse effects such as hallucinations, nightmares, and nausea were specifically recorded. Intraoperative awareness was assessed postoperatively using a standardized questionnaire (modified Brice questionnaire) [26, 27]. Reflux aspiration was evaluated by videolaryngoscopy during intubation and by chest auscultation postoperatively.

Normally distributed data are presented as mean ± standard deviation (SD), while non-normally distributed data are presented as median [range].

Results

The mean DDI was 10.9 ± 2.4 min. The median 1-minute Apgar score was 9 points [range, 6–10], and the 5-minute Apgar score was 10 points for all newborns. Only one newborn required temporary mask ventilation due to neonatal asphyxia, which was primarily caused by major

Table 1 Maternal and neonatal outcomes

Variable	Value
Maternal Characteristics	
Number of patients	11
Age (years)	30.7 ± 5.8 (mean ± SD)
BMI (kg/m^2)	25.3 ± 2.3 (mean ± SD)
Gestational age (weeks)	37.5 ± 2.2 (mean ± SD)
Preterm CS / Term CS	4 (36.4%) / 7 (63.6%)
Indications for CS	
Placenta previa	1 (9.1%)
Placental abruption	1 (9.1%)
Acute fetal distress	6 (54.5%)
Umbilical cord prolapse	3 (27.3%)
Neonatal Outcomes	
1-minute Apgar score	9 [6–10] (median [range])
5-minute Apgar score	10 (all cases)
Temporary mask ventilation	1 (9.1%)
ICU admission	0
Maternal Complications	
Hypotension[†]	0
Esketamine-related adverse effects	None observed

[†] Defined as MAP < 70 mmHg during the period from anesthesia induction to umbilical cord clamping. BMI, body mass index; CS, cesarean section; ICU, intensive care unit; MAP, mean arterial pressure

placental abruption. No newborns were admitted to the ICU (Table 1).

No episodes of hypotension (MAP < 70 mmHg) were recorded during the interval from anesthesia induction to umbilical cord clamping in any of the 11 patients (Table 1). No adverse effects related to esketamine, such as hallucinations, nightmares, or nausea, were observed. No intraoperative awareness was observed.

Discussion

In recent years, the anesthesia induction protocol for CS has evolved from the traditional use of sodium thiopental plus succinylcholine to a combination of propofol and rocuronium. Propofol has a rapid onset, short duration of action, and rapidly crosses the placenta; however, it is rapidly eliminated from the fetus [28–30]. The recommended induction dose of propofol is approximately 2.0–2.8 mg/kg, which tends to lower maternal blood pressure and increases the incidence of Apgar scores of 7 or less [31, 32]. The depressant effect of propofol in neonates is dose-dependent. Therefore, we used a low dose of propofol (1 mg/kg) in combination with esketamine to reduce the suppressive effects of propofol in newborns. During gastroscopy in adults, the administration of esketamine at a dose of 0.5 mg/kg was found to reduce the median effective concentration of propofol by 50% and result in more stable hemodynamics [33]. In addition, propofol has anti-anxiety and intrinsic antiemetic properties that inhibit the adverse effects caused by esketamine [34], while the increased sympathetic tone and analgesic effects of esketamine can reduce propofol-related cardiovascular depression and injection pain [35]. A combination of esketamine and propofol can decrease adverse reactions to both drugs. Category-1 emergency CSs typically involve life-threatening maternal or acute fetal distress, and anesthesia must be carefully managed to avoid further pharmacological suppression of an already compromised mother or fetus. Esketamine has a potent analgesic effect that can reduce the stress response caused by endotracheal intubation and skin incision and has little effect on newborns, making it suitable for anesthetic induction in emergency CS [15]. Although ketamine readily crosses the placental barrier, its rapid metabolism and redistribution in the fetus ensure neonatal safety within a certain dose range.An induction dose of 2.0 mg/kg ketamine for CS was associated with a high incidence of maternal complications and neonatal suppression [36]. It is generally accepted that intravenous ketamine 1–1.5 mg/kg produces normal Apgar scores in CS [8, 37].

Given the well-established 2:1 anesthetic potency ratio of ketamine to esketamine [14, 16, 17], a dose of 0.5–0.75 mg/kg of esketamine is safe for induction of anesthesia for CS. Therefore, we used a relatively low dose of esketamine (0.5 mg/kg) in combination with a low dose of propofol for GA induction to minimize neonatal suppression. Esketamine (0.5 mg/kg) in combination with low-dose propofol has been demonstrated to significantly shorten the induction time for elective CS and maintain hemodynamic stability better, resulting in improved neonatal Apgar scores [19]. We used an esketamine-based induction strategy for emergency CS and obtained consistent results.

Esketamine is advantageous for parturients with a high risk of hypotension [38], as it helps maintain adequate placental blood flow and prevents fetal hypoxia. In our cases, maternal hemodynamics remained stable after induction with esketamine without the need for vasoactive drug intervention. However, esketamine may not be appropriate for patients with pregnancy-induced hypertension syndrome because of its blood pressure-increasing properties. None of these patients were included in the case series.

Rocuronium is a highly water-soluble, non-depolarizing blocker with a large molecular weight that has difficulty passing through the placental barrier and has no significant adverse effects on the fetus during CS [39]. A higher dose of rocuronium (1 mg/kg) provided faster and better intubation conditions for CS without increasing the sedative dose [40].

In addition, it is very important to set up an operating room in or adjacent to the delivery room and to provide regular simulation training for emergency CS to shorten the DDI [41].

This study has some limitations. One limitation of this study was that it was a single-center retrospective case series with a small sample size. Further investigations are required to determine the effect of esketamine on maternal and neonatal outcomes during emergency CS. Additionally, the safety concerns of sugammadex in pregnant women and the potential long-term effects of esketamine on the central nervous system and physical growth of the newborn need further investigation.

Conclusions

Esketamine combined with a low-dose propofol induction strategy can effectively maintain maternal hemodynamic stability without causing neonatal depression, making it suitable for category-1 emergency CSs. However, further randomized controlled trials are needed to confirm these findings.

Abbreviations

CS Cesarean section
DDI Decision-to-delivery interval
GA General anesthesia
NA Neuraxial anesthesia

Author contributions

GQ Z, XX W, Y W, HT C and WL M co-designed the study. GQ Z, Y W, and XX W collected the data. GQ Z and XX W wrote the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and analyzed in the current study are available from the corresponding author in response to reasonable requests.

Declarations

Ethics approval and consent to participate

This case series study was approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province with consent waived (Approval no: KL20241024). All methods followed the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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