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Original Article

The effect and safety of desflurane combined with remifentanil in general anesthesia for cesarean section

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Abstract: Objective: As anesthesia is essential in cesarean section, the clinical application of remifentanil and desflurane needs further exploration. We hypothesize that using desflurane combined with remifentanil in anesthesia helps maintain the hemodynamics stability of pregnant women undergoing cesarean section without affecting the newborn. Methods: Patients scheduled for cesarean section under general anesthesia were randomly divided into the control group (sevoflurane and remifentanil, n=135) and the observation group (desflurane and remifentanil, n=143). The patients' heart rates and mean arterial pressures were measured before the intubation (T0), during the intubation (T1), during the skin incision (T2), and during fetal the delivery (T3). The clinical indexes, the pH values of the umbilical arterial blood, the Apgar scores, and the occurrences of adverse reactions were evaluated. Results: The mean arterial pressures and heart rates in the observation group were significantly improved compared to the control group at the T1 and T3 time points (both P<0.001) but not at the T0 and T2 time points. The operation times, the fetal delivery times, the intraoperative bleeding volumes, the oxytocin volumes and the carboprost tromethamine proportions were not significantly different between the two groups, nor were the blood pH values of the umbilical arteries or the Apgar scores at 1, 5, and 10 minutes after birth (all P>0.05). The observation group showed significantly shorter recovery and extubation times than the control group did (both P<0.001). The incidence of adverse reactions was not significantly different between the two groups (P>0.05). Conclusion: The application value of desflurane combined with remifentanil in general anesthesia in cesarean section.

Keywords: Cesarean section, desflurane, general anesthesia, remifentanil, combination therapy

Introduction

According to statistics, the cesarean section rate in some cities in China can be as high as 60%, and the proportion is still increasing, with elderly primiparas being the principal candidates [1-3]. Because of the unique physiology of pregnant women, the anesthesia method is critical during cesarean section. The main principle of anesthesia in cesarean section is to ensure the wellbeing of the parturient and the newborn, without affecting the contractions. With the continuous development of anesthesia technology, combined spinal epidural anesthesia (CSEA) is increasingly favored by obstetrics clinics [4]. Although the CSEA technique is highly effective, this method only applies to parturient women who have no contraindication for intraspinal anesthesia. For patients with a history of spinal surgery, puncture site infections, spinal deformities, etc., general anesthesia is still the preferred choice clinically [5]. The selection and dose control of narcotic drugs are the key factors in the implementation of general anesthesia.

Remifentanil, a commonly used analgesic drug, can maintain the hemodynamic stability of the body, but may expose the patients to risks such as intraoperative awareness [6]. Desflurane is an inhaled anesthetic, with the advantages of low tissue solubility and good postoperative resuscitation effects [7]. In some studies, compared with sevoflurane plus remifentanil anesthesia, desflurane plus remifentanil anesthesia in total hysterectomies showed better effects in controlling the hemodynamics throughout the perioperative period, shorting the postoperative recovery times and reducing the incidence of adverse reactions [8]. However, at

present, there is no clinical report on the application of desflurane combined with remifentanil in cesarean section in China. Therefore, in this study, we hypothesize that desflurane combined with remifentanil have a good effect and are safe as anesthetics in cesarean section.

Materials and methods

General information

From January 2015 to February 2019, 278 parturients who had caesarean section delivery were recruited as the study cohort. None of the participating parturients had any special anesthesia requirement. The parturients were randomly divided into the observation group (n=143) and the control group (n=135). This study was approved by the medical Ethics Committee of Liaocheng Dongchangfu District Maternity and Child Health Care Hospital, and the participants and their families signed the informed consents.

Inclusion criteria: Patients (1) without gestational hypertension or gestational diabetes, (2) with singleton and full-term pregnancies; (3) with stable hemodynamics, (4) with complete clinical data, (5) without cognitive impairments, (6) with good compliance and effective communication, and (7) who were primiparas.

Exclusion criteria: Patients (1) with multiple pregnancies, (2) with poor compliance, (3) with neurological diseases, (4) who withdrew from the study halfway, and (5) with abnormal coagulation.

Methods

The patients in the control group were anesthetized with sevoflurane and remifentanil. To be specific, after the parturient entered the operating room, the upper limb vein was opened, and the induction of general anesthesia was performed with 8% sevoflurane, 2 mg/kg propofol and 1-2 mg/kg Scoline, and then tracheal intubation was given. During the operation, breathing was controlled by ventilator, and propofol was pumped at a rate of 2.5 mg/kg until the delivery of the fetus. During this period, sevoflurane was continuously inhaled to keep the end-expiratory concentration of sevoflurane at 1.3%. After delivery, 0.01 mg sufentanil and 0.05 mg/kg vecuronium were given for anesthesia maintenance.

The patients in the observation group were anesthetized with desflurane combined with remifentanil. The specific methods were as follows. The general anesthesia mode of rapid induction by tracheal intubation was the same as it was in the control group, and the vital signs of the patients were monitored in real time. After the blood pressure and heart rate stabilized, the patients were intubated in the trachea and were kept at stable respiration by changing the respiratory parameters. During the operation, propofol was pumped at a rate of 2.5 mg/kg until the fetus was delivered. Desflurane was inhaled continuously until the end expiratory concentration of desflurane reached 7%, namely, the minimum effective alveolar concentration of 1.0. After delivery, sufentanil and vecuronium were given for anesthesia maintenance. The dosage and usage were the same as in the control group [9]. The uterine contractions of the two groups were evaluated by the obstetrician on the operating table. If the uterine contractions were not satisfactory, 5 units of carboprost tromethamine were added within 3 min.

Outcome measures and clinical efficacy evaluation

Before intubation (T0), during intubation (T1), during skin incision (T2), and during fetal delivery (T3), the average arterial pressure and blood pressure of the two groups were measured. The two groups' operation times, fetal delivery times, intraoperative hemorrhage volumes, oxytocin dosages, carboprost tromethamine dosages, resuscitation times, and extubation times were recorded and compared. The evaluation criteria for resuscitation were stable vital signs, consciousness, responsiveness, physical activity, and limited lift of the head. The evaluation criteria for extubation were spontaneous breathing, good swallowing and coughing reflexes, normal breathing sounds in both lungs, a significant reduction of tracheal secretions, normal ventilation volumes, and no significant hypoxia symptoms after being weaned from oxygen inhalation. Then 2 mL of neonatal umbilical artery blood was extracted and measured using a blood gas analyzer, and the pH values of the two groups' neonatal umbilical artery blood were compared. The Apgar scores were recorded and compared between the two groups 1, 5, and 10 min after birth. The incidence of adverse reactions,

Table 1. Comparison of the clinical data ($\bar{x} \pm sd$, n)

Group	Observation group (n=143)	Control group (n=135)	t/χ^2	P
Average age (years)	29.4±2.3	29.7±2.5	1.042	0.298
Average gestational age (weeks)	38.54±1.22	38.61±1.24	0.474	0.636
Hemoglobin (g/L)	120.43±2.11	120.17±2.09	1.032	0.303
Average BMI (kg/m^2)	23.33±2.45	23.19±2.68	0.455	0.649
ASA grading			0.022	0.882
Grade I	92	88		
Grade II	51	47		

Note: ASA: American Society of Anesthesiologists; BMI: body mass index.

Table 2. Comparison of the mean arterial pressures and heart rates ($\bar{x} \pm sd$)

Group	Observation group (n=143)	Control group (n=135)	P
Mean arterial pressure (mmHg)			
T0	90.17±8.32	90.20±8.25	0.976
T1	91.42±8.06	110.09±8.17	<0.001
T2	118.56±8.82	118.33±8.74	0.827
T3	94.84±8.05	121.31±7.48	<0.001
F	2.210	2.164	
P	0.173	0.145	
Heart rate (times/min)			
T0	77.94±16.98	77.89±17.01	0.980
T1	85.97±19.44	115.02±14.87	<0.001
T2	101.88±18.47	102.20±16.99	0.881
T3	83.93±21.44	101.44±20.94	<0.001
F	2.967	3.270	
P	0.309	0.238	

Note: T0: before intubation; T1: during intubation; T2: during skin incision; T3: during fetal delivery.

including shivering, bradycardia, and nausea and vomiting, were statistically analyzed in the two groups.

Statistical methods

SPSS 20.0 was used for the statistical analysis of the research data. The measurement data were expressed as the mean ± standard deviation ($\bar{x} \pm sd$). The measurement data consistent with a normal distribution were compared using paired t-tests for the intra-group comparison and independent t-tests for the inter-group comparison, and represented as t. The count data were expressed as the number of cases/percentage (n/%), tested using chi-square tests and represented as χ^2. The repeated measured data at multiple time points were compared using repeated measurement analysis of variance combined with post-Bonferroni tests. $P<0.05$ was considered statistically significant.

Results

Comparison of the clinical data

The main clinical baseline data of the patients in the two groups, including their average age, average gestational age, hemoglobin, average body mass index, and ASA grading, did not show any significant differences in the statistical analysis (all $P>0.05$), so the comparative analysis between the two groups could therefore be continued (**Table 1**).

Comparison of the mean arterial pressures and heart rates

There was no significant difference in the mean arterial pressures and heart rates between the two groups at the T0 and T2 time points (all $P>0.05$). The mean arterial pressures and heart rates of the observation group at the T1 and T3 time points were more significantly improved compared to the control group (all $P<0.001$, **Table 2**).

Comparison of the clinical indices

There were no significant differences in the operation times, fetal delivery times, intraoperative bleeding volumes, oxytocin volumes, or the proportions of carboprost tromethamine

Table 3. Comparison of the clinical indices ($\bar{x} \pm sd$)

Group	Observation group (n=143)	Control group (n=135)	t/χ^2	P
Operation time (min)	48.55±3.17	48.17±3.20	0.994	0.321
Fetal delivery time (min)	5.06±1.48	5.12±1.30	0.358	0.720
Intraoperative bleeding volume (mL)	338.07±10.48	339.15±9.37	0.904	0.367
Oxytocin dosage (million units)	31.20±4.90	30.90±5.20	0.495	0.621
The proportion of carboprost tromethamine (n, %)	28 (19.58)	33 (24.44)	0.959	0.327
Resuscitation time (min)	8.11±1.52	11.48±1.29	19.874	<0.001
Extubation time (min)	13.34±3.15	17.87±2.88	12.492	<0.001

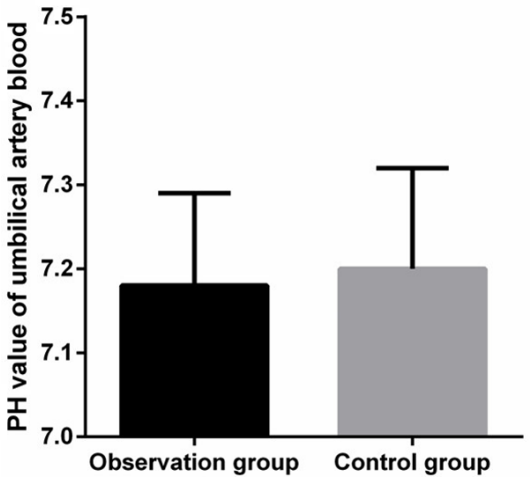

Figure 1. Comparison of the umbilical artery blood pH values.

used in the two groups (all P>0.05). The resuscitation and extubation times in the observation group were significantly shorter than they were in the control group (both P<0.001, **Table 3**).

Comparison of the umbilical artery blood pH values

The umbilical artery blood pH value in the observation group was 7.18±0.11, and the corresponding value in the control group was 7.20±0.12. There was no significant difference between the two groups (P>0.05, **Figure 1**).

Comparison of the Apgar scores

There was no significant difference in the Apgar scores between the two groups at 1, 5, and 10 minutes after birth (all P>0.05, **Table 4**).

Comparison of the postoperative adverse reactions

There was no significant difference in the incidence of adverse reactions between the two groups (P>0.05, **Table 5**).

Discussion

Anesthesia, one of the most critical steps in cesarean section, is a key factor in determining the success of the operation. Clinical results show that intraspinal anesthesia is the first choice for cesarean section [10]. The value of CSEA in lower abdominal and lower extremity operations has been widely demonstrated [11, 12]. Apart from the effectiveness of the anesthesia, the advantages include an inhibition of the intraoperative bleeding and a reduction of the incidence of thrombosis. However, the safe dose of the drugs used in CSEA is very close to the toxic dose, so a combination with ephedrine or clonidine is needed to prolong the anesthesia time. Intraspinal anesthesia can induce systemic or spinal nerve side effects; at the same time, this anesthesia mode is contraindicated for the parturient with complications such as abnormal coagulation function and low blood volume [13]. It has been reported that, compared with intraspinal anesthesia, general anesthesia helps manage the patients' airways and circulation and helps reduce the patients' anxiety and tension [14]. But the selection of the anesthetic drugs and the impacts on the mothers and newborns after the operation are still the main issues to be considered.

Remifentanil is a new type of opioid receptor agonist with potent short-term lipophilic effects, with the advantages of rapid action, a good analgesic effect, and fast metabolism. Although it can penetrate the maternal placental bar-

Table 4. Comparison of the Apgar scores ($\bar{x}$ ± sd, score)

Group	Observation group (n=143)	Control group (n=135)	P
1 min after birth	9.03±0.77	9.10±0.79	0.455
5 min after birth	9.18±0.80	9.15±0.81	0.756
10 min after birth	9.20±0.74	9.19±0.76	0.912
F	0.884	0.847	
P	0.139	0.127	

Table 5. Comparison of the postoperative adverse reactions (n)

Group	Observation group (n=143)	Control group (n=135)	χ^2	P
Shivering	22	28	1.351	0.245
Bradycardia	15	17	0.302	0.583
Nausea and vomiting	32	30	0.001	0.975
Rate of adverse reactions (n, %)	69 (48.25)	75 (55.56)	0.405	0.525

rier, it can be rapidly metabolized in the fetus and be discharged through the kidneys. So, remifentanil does not affect the respiratory or nervous system of the newborn. In addition, this drug has a significant effect on inhibiting the secretion of the adrenal medulla and improving the vagal tension. Therefore, when choosing remifentanil in general anesthesia, the intake dose should be strictly controlled to prevent adverse effects on mothers and newborns [15, 16]. Desflurane is a kind of third-generation halogenated alkyl drug commonly used in the clinic. Compared with traditional inhaled anesthetics, desflurane has a better pharmacological effect and a higher safety [17]. Clinically, desflurane is rapidly metabolized in the body with no metabolite, so it does not have a significant impact on liver or kidney function. Meanwhile, it contributes to patients' induction and recovery, significantly making the depth of anesthesia more controllable [18]. Desflurane in laparoscopic surgery has been found to significantly accelerate the postoperative recovery of consciousness and reduce the incidence of adverse reactions [19]. It has also been pointed out that, compared with sevoflurane combined with remifentanil, desflurane combined with remifentanil can significantly shorten patients' resuscitation and extubation times after laparoscopic cholecystectomy, and their cognitive function can recover quickly after the anesthesia [20]. It is reported that sevoflurane can inhibit the microcirculation to a certain extent, but desflurane can better maintain the microcirculation [21]. Although microcirculation can be affected by inhaled anesthetics, it can return to baseline levels within 24 hours after surgery following desflurane anesthesia. However, there is no clinical report on the application of desflurane combined with remifentanil in cesarean section.

The results of this study showed that there was no significant difference in the mean arterial pressure or heart rate between the two groups before intubation and during skin cutting, but the mean arterial pressure and heart rate during the intubation and fetal delivery in the observation group were significantly improved compared to the control group; meanwhile, the resuscitation and extubation times in the observation group were significantly shorter than they were in the control group. But there was no statistical significance in the clinical indicators such as operation time, delivery time of the fetus, intraoperative blood loss, oxytocin dosage, or the proportion of carboprost tromethamine used, nor in the incidence of adverse reactions after the operation between the two groups. The results showed that desflurane combined with remifentanil anesthesia is more conducive to maintaining the stability of maternal hemodynamics, without producing a greater stress response that increases the incidence of adverse reactions. This may be due to the lower tissue solubility of desflurane, the faster elution speed, and the better anesthesia recovery effect. The results of this study also showed that there was no significant difference between the two groups in their umbilical artery blood pH values or their Apgar scores at 1, 5, and 10 min after birth. This shows that desflurane combined with remifentanil anesthesia will not have a great impact on the newborn or inhibit the newborn's breathing or cause other symptoms. However, the number of patients in this study was limited, so the exact mechanism and pharmacological effect of desflurane combined with remifentanil in cesarean section still needs to be studied with a larger cohort and using a multi-center approach.

To sum up, desflurane combined with remifentanil anesthesia is an effective anesthetic combination in cesarean section delivery. It is also conducive to maintaining the stability of maternal hemodynamics and has no significant postoperative adverse reactions. The desflurane/remifentanil anesthetic combination is worthy of clinical application.

Disclosure of conflict of interest

None.

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