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Original Article

Application effect of sevoflurane in the cesarean section of pregnant women with pernicious placenta previa and its influence on maternal hemodynamics

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Abstract: Objective: To evaluate the application effect of sevoflurane in pregnant women with pernicious placenta previa who conduct the cesarean section and its influence on maternal hemodynamics. Methods: A total of 94 women with pernicious placenta previa (PPP) admitted to our hospital were recruited in this study. They were randomly divided into two groups, with 47 each group. The control group was given ketamine, propofol and rocuronium while the observation group was given sevoflurane base on conventional general anesthesia. The available data, intraoperative indexes, coagulation function before and after operation, hemodynamics, umbilical arterial partial pressure of oxygen and carbon dioxide before the procedure (T0), 5 min after anesthesia (T1), 15 min after anesthesia (T2) and during fetal delivery (T4) were observed. The Apgar scores of 1 min, 5 min and 10 min after birth were recorded. Results: No significant difference was seen in related indicators during operation and blood coagulation function before and after the operation between the two groups (P>0.05). The diastolic blood pressure and systolic blood pressure decreased at T1, T2 and T3 compared with T0 time (P<0.05). The decrease was more evident in the control group than in the observation group (P<0.001). The mean arterial pressure in the two groups at T1, T2 and T3 was higher than that at T0 (P<0.05). At T2, the increase in the control group was more obvious than that in the observation group (P<0.001). The heart rate at T1 and T2 was higher than that at T0 (P<0.05). Compared with the control group, the oxygen pressure increased and the carbon dioxide pressure decreased in the observation group (P<0.001). The Apgar score of the observation group was higher than that of the control group at 1 min and 5 min (P<0.001). Conclusion: Sevoflurane can stabilize hemodynamics, improve neonatal oxygen uptake rate and increase the safety of operation without affecting coagulation function, which is worthy of clinical application.

Keywords: Sevoflurane, pernicious placenta previa, cesarean section, hemodynamics

Introduction

Placenta previa is the placenta attached to the lower uterine segment or beyond the internal cervical orifice after 28 weeks of gestation, which is lower than the first exposed part of the fetus. If a pregnant woman with a history of cesarean section was complicated with placenta previa, she may have severe postpartum hemorrhage or adverse maternal and infant outcomes, which is clinically known as pernicious placenta previa (PPP) [1, 2]. With the age increase of pregnant women, the cesarean section rate has increased year by year, and the number of PPP cases has also increased [3]. For PPP, the cesarean section should be performed under general anesthesia. Previous studies showed that the use of narcotic drugs could lead to uterine contraction, which is easy to cause neonatal respiratory repression [4]. Therefore, attention should be paid to the selection of anesthetics. The way and effect of anesthesia are significant in cesarean section. The ideal state of anesthesia is not only to maintain the stability of heart rate, but also to maintain the stability of hemodynamics, ensure the regular blood supply of various organs, and maintain the stable state of the body during and after operation [5]. Sevoflurane is a kind of inhalation anesthetic, which has the advantages of rapid onset, rapid elimination, more comfortable control of anesthesia depth, and less

impact on maternal hemodynamics [6, 7]. However, studies have shown that sevoflurane can inhibit platelet aggregation and prolong the bleeding time of breast cancer patients [8]. The most severe complication of PPP is postpartum hemorrhage. Therefore, the use of sevoflurane in PPP maternal is still controversial. Here, we investigate the effect of sevoflurane on hemodynamics and safety of PPP maternal.

Materials and methods

Clinical data

This study was approved by the ethics committee of The People's Hospital of Guangrao. About 94 cases of pregnant women with pernicious placenta previa (PPP) admitted to The People's Hospital of Guangrao from December 2018 to July 2020 were selected and randomly grouped with 47 cases in each group. Routine general anesthesia was used as the control group, and sevoflurane was added as the observation group. The average age was 28.3±2.6 years (range, 24-46 years). All the parturient in this study has signed the consent form.

Inclusion criteria

(1) According to the diagnosis of placenta previa, the cesarean section under general anesthesia is required [1]; (2) Previous cesarean section history; (3) American Society of anesthesiologist (ASA) grade I-III [9]; (4) Patients with normal coagulation and bone marrow function; (5) Complete clinical data.

Exclusion criteria

(1) Patients with severe cardiopulmonary disease; (2) Patients with abnormal coagulation or bone marrow function; (3) Patients with liver and kidney dysfunction; (4) Pregnant women with difficult follow-up.

Methods

ECG monitoring (Nanjing Shidi Medical Technology Co., Ltd., China) and radial artery catheterization were performed for the pregnant women included in the study. Anesthesia induction: After 4-6 L/min oxygen flow was directly inhaled in both groups, Ketamine (China, Fujian Gutian Pharmaceutical Co., Ltd.) 0.5 mg/kg, propofol (Xi'an Libang Pharmaceutical Co., Ltd., China) 1 mg/kg and rocuronium (North China Pharmaceutical Co., Ltd., China) 0.6 mg/kg were given intravenously. The observation group was assigned 1.3% sevoflurane (China, Shanghai Baite medical supplies Co., Ltd.) while the control group was only given oxygen. Mechanical ventilation was performed after laryngeal mask implantation in the two groups. Anesthesia maintenance: the control group was given propofol injection 4-8 mg/(kg·h), while the observation group was given 1.3% sevoflurane inhalation combined with propofol infusion. Midazolam (Yichang humanwell Pharmaceutical Co., Ltd., China) 0.05-0.1 mg/kg and sufentanil (Yichang humanwell Pharmaceutical Co., Ltd., China) 0.5-1 μg/kg were injected intravenously after the delivery. The fresh airflow was adjusted to 2 L/min (air 1 L: oxygen 1 L) until the end of the operation. Muscle relaxants were only given during induction in both groups. The withdrawal time of the two groups was selected at the end of the suture.

Outcome measures

Main outcome measures: Intraoperative and postoperative indicators of the two groups included: operation time, intraoperative blood loss, time from anesthesia to fetal delivery, laryngeal mask extraction time and incidence of postoperative nausea and vomiting.

About 5 mL venous blood was drawn 30 min before the operation and one day after the operation to determine coagulation function indexes.

Hemodynamics such as systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (map) and heart rate (HR) were measured before the operation (T0), 5 min after anesthesia (T1), 15 min after anesthesia (T2) and at the time of fetal delivery (T4).

Secondary outcome measures: Umbilical artery partial pressure of oxygen and carbon dioxide were detected.

The Apgar scores of 1 min, 5 min and 10 min were recorded.

Statistical methods

SPSS 17.0 was used to analyze the data. Continuous variables were expressed by mean ± standard deviation ($\bar{x}$±sd), and non-normal distribution was represented by M (P25, P75). Independent sample t-test was used for normal

Table 1. Comparison of general data of two groups (($\bar{x}$±sd), n)

Groups	Observation group (n=47)	Control group (n=47)	χ^2/t	P
Age (year)	28.4±2.7	28.1±2.3	0.563	0.580
Gestational weeks (week)	38.2±1.5	38.4±1.6	0.533	0.625
Gravidity			1.106	0.293
2	41	44		
≥3	6	3		
Number of cesarean sections			0.547	0.460
1	42	44		
≥2	5	3		
Preoperative hemoglobin level (g/L)	134.12±6.39	133.24±6.47	0.663	0.509
BMI (kg/m^2)	24.23±2.61	23.92±2.83	0.552	0.582
Complications				
Gestational hypertension	6	8	0.336	0.562
Gestational diabetes	7	6	0.089	0.765
ASA grade			0.177	0.674
I	27	29		
II	20	18		

Table 2. Comparison of intraoperative indicators ($\bar{x}$±sd)

Groups	Observation group (n=47)	Control group (n=47)	χ^2/t	P
Anesthesia induction time (min)	3.15±0.76	3.22±0.81	0.432	0.667
Operation time (min)	45.32±7.97	46.23±7.86	0.557	0.579
Intraoperative blood loss (mL)	892.23±270.33	902.33±269.45	0.181	0.856
Time from anesthesia to fetal delivery (min)	21.23±2.92	20.67±2.86	0.939	0.350
Removal time of LMA (min)	7.43±2.11	7.36±2.21	0.157	0.876
Number of blood transfusion cases	4	5	0.123	0.726
Intraoperative urine volume (mL)	208.23±40.23	200.72±45.23	0.851	0.397
Postoperative recovery time (min)	13.24±4.87	12.57±4.95	0.661	0.510
Incidence of nausea and vomiting (n, %)	7 (14.89)	9 (19.15)	0.301	0.583

distribution and homogeneity of variance. Independent sample t-test was used for inter-group comparison. Paired sample t-test was used for intra-group comparison. The data of multiple time points were analyzed by repeated measurement analysis of variance combined with post Bonferroni test. The count data were analyzed by the Pearson Chi- square test. The difference was statistically significant when P<0.05.

Results

Comparison of general data of two groups of puerpera

There was no difference in general information (all P>0.05). See **Table 1**.

Comparison of intraoperative and postoperative indicators

The comparison of intraoperative and postoperative indicators between the two groups showed no difference (P>0.05), as shown in **Table 2**.

Comparison of coagulation function before and after operation

There was no difference in thrombin time, prothrombin time and partial thromboplastin time between the two groups before and after the operation (P>0.05). FIB was lower than that before treatment, while D-dimer and platelet were higher than those before treatment (all P<0.05). See **Table 3**.

Table 3. Comparison of coagulation function before and after operation ($\bar{x}\pm sd$)

Projects	Before the treatment		After the treatment	
	Observation group	Control group	Observation group	Control group
Thrombin time (s)	15.34±2.43	15.53±2.32	15.78±2.41	16.21±2.63
Prothrombin time (s)	10.21±0.56	10.45±0.61	10.98±0.81	11.02±0.73
Partial thromboplastin time (s)	24.32±3.21	24.58±3.45	25.46±3.56	25.62±3.72
Fibrinogen (g/L)	3.07±0.74	3.09±0.76	1.94±0.71*	1.92±0.75*
D-Dimer (mg/L)	0.68±0.27	0.73±0.23	0.91±0.25*	0.93±0.26*
Platelet count (× 10^9/L)	284.58±32.47	286.47±34.78	303.58±34.17*	304.14±35.26*

Note: Compared with before the treatment, *P<0.05.

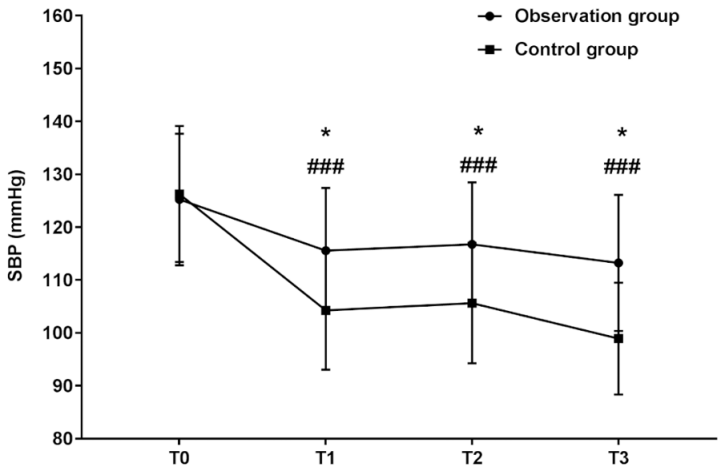

Figure 1. Comparison of systolic blood pressure of two groups at different time points. Compared with T0 time, *P<0.05; compared with the control group, ###P<0.001. SBP: systolic blood pressure.

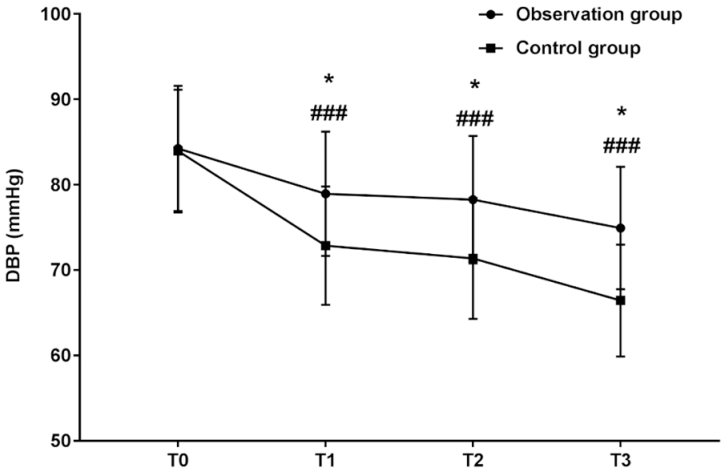

Figure 2. Comparison of diastolic blood pressure at different time points. Compared with T0, *P<0.05; Compared with the control group, ###P<0.001. DBP: diastolic blood pressure.

Comparison of intraoperative hemodynamics

There were significant differences in systolic blood pressure, diastolic blood pressure and mean arterial pressure between the observation group and the control group (P<0.05) by repeated measurement ANOVA. The systolic blood pressure and diastolic blood pressure of the two groups at T1, T2 and T3 were lower than those at T0 (P<0.05). Compared with the observation group, the decrease was more obvious (P<0.001) in the control group. The mean arterial pressure of the two groups at T1, T2, T3 were increased significantly (P<0.05). At T2, the control group was significantly higher than the observation group (P< 0.001), and the heart rate of the two groups at T1 and T2 were higher than that at T0 (P<0.05). See **Figures 1**-**4**.

Comparison of the partial pressure of oxygen and carbon dioxide

The partial pressure of oxygen increased while the partial pressure of carbon dioxide decreased in the observation group compared with the control group (P<0.001). See **Table 4**.

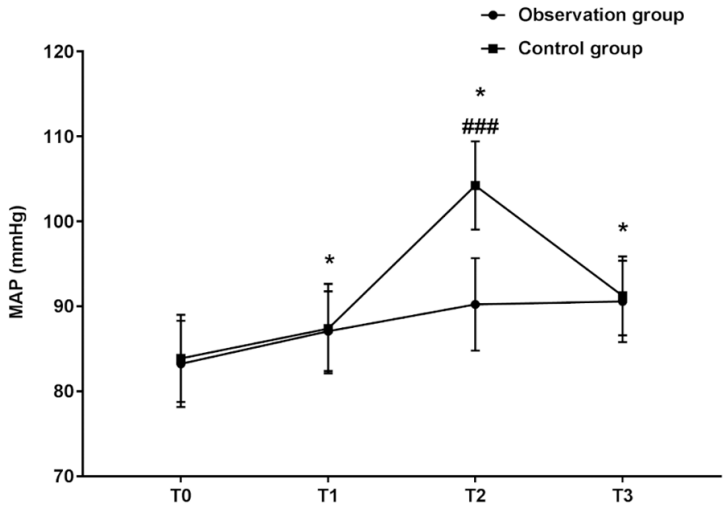

Figure 3. Comparison of MAP at different time points. Compared with T0, *P<0.05; Compared with the control group, ###P<0.001. MAP: mean arterial pressure.

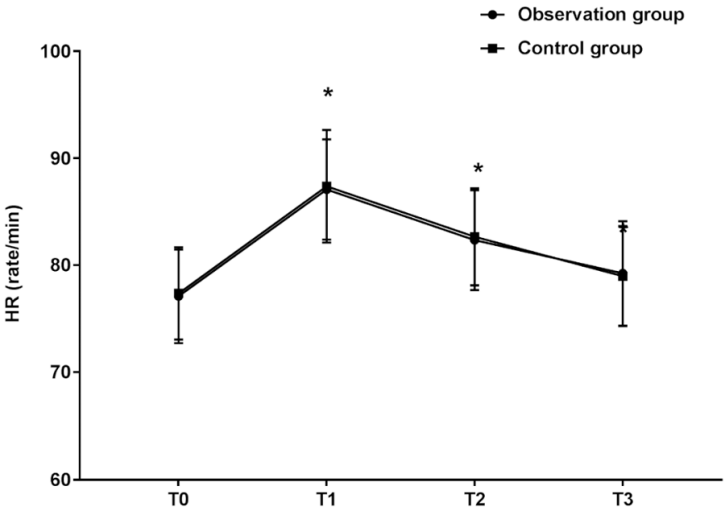

Figure 4. Comparison of heart rate in two groups at different time points. Compared with T0, *P<0.05. HR: heart rate.

Comparison of neonatal Apgar score

The neonatal Apgar score of the observation group was higher than that of the control group at 1 min and 5 min (P<0.001), but there was no difference between the two groups at 10 min (P>0.05). See **Table 5**.

Discussion

The placenta is mainly for the supply of fetal nutrition. The placenta extends to the lower part of the uterus, leading to placenta previa, which increases the risk of postpartum hemorrhage [10]. For pernicious placenta previa (PPP), general anesthesia should be carried out. Sevoflurane is an induction anesthetic, which takes effect quickly and the deepness of anesthesia can be effectively controlled, which has been utilized in the clinic [11].

Because of its high safety, it is used in pediatrics and cardiothoracic surgery [12]. Hemodynamics plays a vital role in surgery. Previous studies have shown that sevoflurane anesthesia has little impact on hemodynamics of patients. In another study, sevoflurane used in Caesarean section can inhibit oxytocin, and the degree of inhibition is positively correlated with the dosage of sevoflurane, but the low concentration of sevoflurane does not increase the bleeding caused by uterine relaxation and can improve the hypercoagulable state of pregnant women with hypercoagulation [6, 13]. Some studies have shown that sevoflurane combined with opioid anesthesia can make hemodynamics more stable [14]. Studies have also shown that sevoflurane has a less inhibitory effect on the cardiovascular system and protects myocardial cells to a certain extent [15-18]. Sevoflurane in cardiac surgery can reduce the oxidative stress reaction of patients and prevent myocardial injury caused by ischemia and hypoxia [19, 20]. In this study, sevoflurane can make maternal hemodynamics stable, blood pressure, heart rate mean and arterial pressure fluctuate less, which may be related to the above mechanisms.

Sevoflurane has been shown to inhibit platelet aggregation and prolong the bleeding time of breast cancer patients [8]. Sevoflurane may significantly increase the inhibition of platelet aggregation and increase the risk of bleeding compared with isoflurane [20]. This study showed that there was no difference in the

Table 4. Comparison of partial pressure of oxygen and carbon dioxide in umbilical artery ($\bar{x}$±sd)

Groups	Observation group (n=47)	Control group (n=47)	χ^2/t	P
Partial pressure of oxygen (mmHg)	64.25±2.18	60.05±2.08	9.556	<0.001
Partial pressure of carbon dioxide (mmHg)	41.04±2.01	44.83±2.19	0.181	<0.001

Table 5. Comparison of Apgar score of newborns between the two groups ($\bar{x}$±sd)

Groups	Apgar score of newborns		
	1 min	5 min	10 min
Observation group (n=47)	8.92±0.83	9.52±0.21	9.67±0.29
Control group (n=47)	8.03±0.76	8.92±0.24	9.57±0.31
t	5.422	12.923	1.615
P	<0.001	<0.001	0.110

effect of sevoflurane anesthesia on the coagulation function of pregnant women between two groups. Patients with PPP often have a hypercoagulable state. The reason may be that although sevoflurane has an impact on its coagulation function, it does not increase bleeding. It may also be related to the small number of samples included in this study. We further investigated the partial pressure of oxygen and carbon dioxide in umbilical cord blood. The partial pressure of oxygen in umbilical cord blood of puerpera using sevoflurane is higher. In comparison, the partial pressure of carbon dioxide is lower, which may be related to sevoflurane making maternal hemodynamics more stable [21]. Apgar score is of great value for the evaluation of newborns, and some studies have shown that it is the most accurate and reliable to judge the neonatal respiratory function at 1 minute and 5 minutes after birth [22]. Some studies have shown that umbilical cord blood gas analysis is helpful to evaluate the neonatal respiratory function [23]. In this study, the Apgar scores for 1 minute and 5 minutes of newborns using sevoflurane were higher than those of the control group.

Deficiencies and prospects: This study is a single-center study and the sample size is small. We can further conduct multi-center randomized controlled trials with larger sample size.

To sum up, Sevoflurane in the application of general anesthesia in dangerous placenta previa can stabilize hemodynamics, improve neonatal oxygen uptake rate, increase the safety of surgery and do not affect coagulation function, which is worthy of clinical application.

Disclosure of conflict of interest

None.

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