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Effect of Hemabate combined with packing therapy on the systemic stress response in patients with postpartum hemorrhage after placenta previa cesarean section

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ABSTRACT

Objective: To discuss the effect of Hemabate combined with packing therapy on the systemic stress response in patients with postpartum hemorrhage after placenta previa cesarean section. **Methods:** 70 patients with postpartum hemorrhage after placenta previa cesarean section who were treated in Chengdu Women & Children′s Central Hospital between January 2014 and February 2017 were collected and then divided into the control group (n=35) who received uterine packing therapy and the observation group (n=35) who received Hemabate combined with packing therapy according to random number table. Serum levels of oxidative stress indexes and stress hormones immediately after operation and 24 h after operation were compared between two groups of patients. **Results:** Immediately after operation and 24 h after operation, serum oxidative stress indexes ROS and MDA levels of observation group were significantly lower than those of control group while SOD, GSH-px and CAT levels were significantly higher than those of control group, and serum stress hormones NE, E and Cor levels were significantly lower than those of control group. **Conclusion:** Hemabate combined with packing therapy can effectively reduce systemic stress response in patients with postpartum hemorrhage after placenta previa cesarean section, is a more ideal way of the bleeding.

1. Introduction

Placenta previa is the situation that the placental location is lower than fetal presentation after 28 weeks of gestation, and it is one of the main causes of late pregnancy bleeding and maternal death[1,2]. Multiple gestation, induced abortion history, smoking, drug use, etc., are all important causes of placenta previa, pregnant women with repeated massive bleeding need early termination of pregnancy. Cesarean section is the main mode of delivery for pregnant women with placenta previa, but the bleeding volume during birth process is greater than that in normal puerperae, and postpartum hemostasis is difficult, so choosing efficient and reasonable way of hemostasis is the focus of current obstetrics research. Uterine packing is a physical hemostatic method that has significant hemostatic effect on the bleeding caused by poor overall/local contraction, but hemostasis is still difficult for some patients. Hemabate was mostly used for abortion between 13-20 weeks of gestation in the past, many scholars believe that it helps the hemostasis of fatal haemorrhage, and therefore, it is recommended for patients with postpartum hemorrhage of placenta previa cesarean delivery[3,4]. In the research, Hemabate combined with packing therapy was used for patients with postpartum hemorrhage after placenta previa cesarean section, and its application value was explored from the aspect of stress response in the body, now reported as follows.

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2. Information and methods

2.1 Case information

70 patients with postpartum hemorrhage after placenta previa cesarean section who were treated in Chengdu Women & Children's Central Hospital in Sichuan Province between January 2014 and February 2017 were collected as the research subjects, and family members of patients signed the informed consent. Random number table was used to divide the enrolled patients into two groups, 35 cases in each group. Control group were 25-39 years old, the gravidity was 1-4 and (2.11±0.67) in average, and the parity was 1-3 and (1.34±0.19) in average; observation group were 24-38 years old, the gravidity was 1-3 and (2.07±0.64) in average, and the parity was 1-3 and (1.29±0.24) in average. The differences in general information were not statistically significant between the two groups (P>0.05), and the hospital ethics committee approved the study.

2.2 Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with placenta previa before childbirth; (2) without placenta previa history; (3) receiving cesarean delivery for the first time; (4) surviving after treatment. Exclusion criteria: (1) associated with gestational diabetes, pre-eclampsia and other pregnancy complications; (2) with systemic infectious disease before delivery; (3) associated with severe coagulation dysfunction.

2.3 Therapy

Control group of patients received uterine packing treatment, specifically as follows: after childbirth, oxytocin (Tianjin Biochem Pharmaceutical Co., Ltd., approved by H12020482) 20 U was injected via uterine wall, and oxytocin 20 U was added in 5% glucose liquid, which was by intravenous drip. Gauze was packed from the cornua uteri, the part above the superior border of incision of lower uterine segment was filled at first, then sponge forceps were used to insert the gauze into the vagina via cervix, and the area around the uterine incision, lower uterine segment and uterine orifice were filled at last. The uterus was sewn up after confirming that there was no further bleeding. Observation group of patients received Hemabate combined with packing therapy, specifically as follows: oxytocin and gauze packing methods were the same as those of control group, and Hemabate (Changzhou Siyao Pharmaceutical Co., Ltd., approved by H20094183) 250 μg was injected via uterine wall after childbirth.

2.4 Serological indicators

Immediately after surgery and 24 h after surgery, 2-3 mL fasting cubital venous blood was extracted from two groups of puerperae respectively, joined by heparin sodium (Jilin Yinglian Biopharmaceutical Co., Ltd., approved by H22021912) for anti-coagulation and centrifuged at 3 500 r/min in 4 ℃ environment for 10-15 min to get upper serum, and the levels of oxidative stress indexes and stress hormones were determined, including oxidative stress indicators: reactive oxygen species (ROS), malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GSH-px) and catalase (CAT) as well as stress hormones: norepinephrine (NE), epinephrine (E) and cortisol (Cor).

2.5 Statistical processing

Data in the study were recorded and analyzed by specially-assigned person, and statistical software was SPSS 20.0. Oxidative stress indexes, stress hormones and other measurement data were in terms of mean ± standard deviation, and comparison between groups was by t test. P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Oxidative stress indexes

Comparison of serum oxidative stress indexes ROS (μmol/L), MDA (μmol/L), SOD (U/L), GSH-px (nmol/L) and CAT (U/L) levels between two groups of puerperae at different points in time was as follows: immediately after operation and 24 h after operation, serum oxidative stress indexes ROS and MDA levels of observation group were significantly lower than those of control group while SOD, GSH-px and CAT levels were significantly higher than those of control group. Differences in serum oxidative stress indexes ROS, MDA, SOD, GSH-px and CAT levels were statistically significant between two groups of puerperae immediately after operation and 24 h after operation (P<0.05), shown in Table 1.

Table 1.

Comparison of oxidative stress index levels between two groups of puerperae at different points in time.

Groups	n	Time	ROS	MDA	SOD	GSH-px	CAT
Control group	35	Immediately after operation	8.93±0.97	15.48±2.11	231.39±27.85	273.46±30.71	227.84±31.65
		24 h after operation	7.03±0.84	12.05±1.74	320.61±3.53	326.83±40.19	295.71±34.26
Observation group	35	Immediately after operation	6.11±0.75[a]	11.93±1.75[a]	318.46±40.55[a]	341.55±38.94[a]	224.97±30.45[a]
		24 h after operation	4.27±0.56[b]	6.18±0.74[b]	427.53±52.79[b]	452.35±50.18[b]	384.26±41.57[b]

Note: compared with control group immediately after operation, [a]P<0.05; compared with control group 24h after operation, [b]P<0.05.

Table 2.

Comparison of stress hormone levels between two groups of puerperae at different points in time.

Groups	*n*	Time	NE	E	Cor
Control group	35	Immediately after operation	489.26±51.77	84.92±9.16	29.37±3.88
		24 h after operation	371.05±42.63	57.39±7.11	20.52±2.75
Observation group	35	Immediately after operation	411.95±46.63[a]	70.53±8.14[a]	21.52±2.84[a]
		24 h after operation	218.57±26.92[b]	30.25±4.18[b]	11.63±1.79[b]

Note: compared with control group immediately after operation, [a]$P<0.05$; compared with control group 24 h after operation, [b]$P<0.05$.

3.2 Stress hormones

Comparison of serum stress hormones NE (pg/mL), E (pg/mL) and Cor (ng/mL) levels between two groups of puerperae at different points in time was as follows: immediately after operation and 24 h after operation, serum stress hormones NE, E and Cor levels of observation group were significantly lower than those of control group. Differences in serum stress hormones NE, E and Cor levels were statistically significant between two groups of puerperae immediately after operation and 24 h after operation ($P<0.05$), shown in Table 2.

4. Discussion

Postpartum bleeding volume is huge after placenta previa cesarean section, and the hemostasis is difficult, some patients may die for uncontrolled hemorrhagic shock, and choosing effective treatment is the key to optimize the outcome of patients with postpartum hemorrhage after placenta previa cesarean delivery[5–7]. Uterine packing is the most common clinical hemostatic way for cesarean delivery, gauze can directly compress the uterine wall and achieve hemostatic effect, and it can also stimulate related receptors and cause uterine contractions, which is conducive to the hemostasis[8,9]. Previous study shows that uterine packing alone may effectively terminate the intraoperative bleeding in general cesarean delivery, but its separate application value is controversial for patients with postpartum hemorrhage of placenta previa cesarean delivery. Hemabate is methyl prostaglandin with long biological half-life and strong biological activity, it was mostly used for hemostasis of abortion women, and some scholars have recommended it for the adjuvant treatment of patients with intractable postpartum hemorrhage[10]. In this study, the values of uterine packing alone and Hemabate combined with uterine packing for postpartum hemorrhage after placenta previa cesarean section were analyzed in detail in order to lay practical foundation for the selection of hemostatic schemes for subsequent similar puerperae.

Continuous massive hemorrhage can cause secondary maternal systemic oxidative stress response, and the generation of a large number of oxide metabolites can cause oxidative damage to body, further affect blood coagulation function and increase postpartum haemorrhage amount[11,12]. ROS and MDA are the typical oxidative metabolites, and their levels are highly correlated with postpartum bleeding volume; SOD, GSH-px and CAT are antioxidant molecules, oxidant/antioxidant factor levels are in dynamic equilibrium under physiological state, oxidation metabolites are produced excessively after massive hemorrhage and they consume a large amount of antioxidant factors, so the antioxidants are relatively insufficient in circulating blood[13,14]. In the study, serum contents of the oxidative stress indexes were compared between two groups of puerperae at different time points, and it was found that compared with control group, the observation group were with lower serum ROS and MDA levels and higher SOD, GSH-px and CAT levels immediately after operation and 24h after operation, it indicates that Hemabate on the basis of the uterine packing can effectively reduce the massive hemorrhage stimulation to the oxidative stress system, and in other words, Hemabate combined with packing therapy can effectively reduce the perioperative blood loss in patients with placenta previa cesarean delivery. Hemabate can inhibit the role of adenylate cyclase, has bi-directional regulating effect on the expression of clotting factors, and can also promote uterine cavity surface vasoconstriction and close uterine blood sinus, and this is also the fundamental mechanism for it to exert hemostatic effect.

Continued massive bleeding can also lead to systemic stress response, and it works together with oxidative stress to damage the body's blood coagulation system and aggravate the systemic consumption state, which does not favor the maternal body function recovery after surgery. NE, E and Cor are the most commonly studied stress hormones at present, they are excessively expressed in the central nervous system and released into the blood under the stimulation of surgery, trauma and other stimuli, the body′s catabolism is enhanced after that, massive hemorrhage is an important cause of stress system activation, and the bleeding amount is closely related to the intensity of stress reaction[15,16]. In the study, serum levels of stress hormones were compared between two groups of puerperae at different points in time, and it was found that compared with control group, the observation group were with lower serum NE, E and Cor contents immediately after operation and 24 h after operation, indicating that Hemabate combined with packing therapy can effectively reduce the maternal systemic stress reaction, and indirectly showing the efficiency of the hemostatic solution.

Above all, it can be concluded as follows: Hemabate combined with packing therapy for patients with postpartum hemorrhage after placenta previa cesarean section can effectively reduce the maternal perioperative stress response, which indirectly shows that it is efficient in hemostasis and is worthy of popularization and application in clinical practice in the future.

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