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Clinical study on preventive treatment of postpartum hemorrhage with carboprost tromethamine combined with oxytocin and misoprostol

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Abstract: To study the clinical effect of carboprost tromethamine combined with oxytocin and misoprostol in the preventive treatment of postpartum hemorrhage. 94 cases of postpartum hemorrhage patients from October, 2022 to October, 2023 were divided into the reference group (treated with oxytocin and misoprostol) and the observation group (treated with carboprost tromethamine, oxytocin and misoprostol) and the treatment situation was analyzed. Compared with the reference group, the stress and serum indexes in the observation group were significantly decreased. Except oxygen saturation, the postpartum hemorrhage and hemostasis time in the observation group were significantly lower than those in the reference group and the hemoglobin content was relatively high. After treatment, the improvement of coagulation function in the observation group was better than that in the reference group. The incidence of complications was 21.28% in the reference group and 4.26% in the observation group, the difference was statistically significant ($P < 0.05$). In the preventive treatment of postpartum hemorrhage, triple medication is more effective, which can improve patients' stress response and serum indexes, reduce the amount of bleeding and improve patients' coagulation function. At the same time, it is also very beneficial to control complications and has high safety.

Keywords: Carboprost tromethamine; oxytocin and; misoprostol; postpartum hemorrhage

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INTRODUCTION

In obstetrics, there is a high incidence of postpartum hemorrhage, which is related to excessive stretching of uterine muscle fibers caused by multiple pregnancies, polyhydramnios and macrosomia, resulting in uterine contraction weakness, which can easily lead to disseminated intravascular coagulation, organ failure, hemorrhagic shock and even death in severe cases, so preventive treatment should be carried out in time (Jaffer, D *et al*., 2022). Weakness of uterine contraction is the key factor to induce postpartum hemorrhage, which usually occurs 2 hours after delivery, so strengthening postpartum uterine contraction can reduce the risk of postpartum hemorrhage. It is necessary to pay attention to the signs, vaginal bleeding and uterine contraction of pregnant women after delivery. Oxytocin plays an important role in the treatment of postpartum hemorrhage, which can promote extracellular calcium ions to enter uterine smooth muscle cells and then increase intracellular calcium ion concentration (Gong, X and Wu, X *et al*., 2022). It can induce muscle cells to contract as soon as possible under the action of calmodulin and protein kinase and achieve the goal of stopping bleeding while relieving the symptoms of uterine inertia of patients. Oxytocin has a relatively short half-life and therefore needs to be reused. If the receiving position is saturated, the dosage of drugs should be increased, but because some patients are relatively less sensitive to drugs, their application will be limited and side effects will be induced. Oxytocin is mainly composed of polypeptide hormones, which can bind to oxytocin receptor in pregnant women and stimulate uterine smooth muscle contraction, thus preventing uterine atony (Erickson, E N *et al*., 2023). However, due to the obvious differences in the physical conditions of different parturients, it is necessary to use drugs scientifically from the actual situation. In clinic, oxytocin is a preventive drug for postpartum hemorrhage with high frequency of application, which can effectively improve the bleeding of patients. Misoprostol is a prostaglandin preparation. The combination of misoprostol and oxytocin can further improve the sensitivity of lying-in women to oxytocin, avoid the adverse reactions caused by large doses of oxytocin as much as possible and effectively reduce postpartum hemorrhage. Carboprost tromethamine is an abortion drug, which is suitable for postpartum hemorrhage induced by ineffective uterine contraction and the treatment efficiency is high. The combined application of the three drugs can further reduce the rate of postpartum hemorrhage, reduce the negative impact on patients and avoid the aggravation of the disease while controlling the disease (Zong, F and Cao, Y *et al*., 2021). This study aimed to comprehensively evaluate the clinical efficacy of carboprost tromethamine combined with oxytocin and misoprostol in the preventive treatment of postpartum hemorrhage. This research is expected to provide valuable evidence-based support for clinical practice in preventing postpartum hemorrhage.

MATERIALS AND METHODS

General information

94 cases of postpartum hemorrhage in our hospital from October, 2022 to October, 2023 were selected and divided

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into two groups, with 47 cases in each group. Inclusion indicators: (1) No history of cardiovascular and cerebrovascular diseases; (2) No history of drug allergy; (3) Patients can tolerate treatment and have good compliance; (4) All patients are aware of this study. Exclusion indexes: (1) those with cyst and hysteromyoma; 2 mental disorders and confusion; (3) Patients with severe liver and kidney dysfunction; (4) Those who have a history of drug allergy and quit halfway (Erickson, E N *et al*., 2023). There was no significant difference in general data of patients ($P > 0.05$). See table 1 for details.

METHODS

Reference group

After the fetus is delivered, 2.5-5 IU of oxytocin should be added to 500 mL of 0.9% sodium chloride solution for intravenous drip. The initial drip rate is set at 4-6 drops per minute and then adjusted according to the uterine contractions of the parturient and vaginal bleeding. The maximum drip rate should not exceed 40 drops per minute. The intravenous drip of oxytocin should continue until 2 hours after delivery. At the same time, after 30 minutes of initiating intravenous infusion of oxytocin, 400μg misoprostol was administered rectally to the parturient. The study was approved for the affiliated hospital of Jiangnan University No. 202312008

Observation group

Immediately after fetal delivery, 250μg of carboprost tromethamine is injected into the deep gluteal muscles. If vaginal bleeding doesn't improve within 15-30 minutes and exceeds the set standard, reinjection can be done every 15-90 minutes, up to 8 times. In both the observational and Reference groups, after delivery, 2.5-5 IU of oxytocin in 500 mL of 0.9% saline is intravenously dripped at 4-6 drops/min (Yan, D *et al*., 2022).

Observation indicators

The stress and serum indexes of the two groups before and after treatment were compared and analyzed; Observe the changes of bleeding related indexes and coagulation function in the two groups; Analyze the complications, including infection, hemorrhagic shock and visceral failure and record their incidence.

STATISTICAL ANALYSIS

The data were analyzed by SPSS21.0 statistical software and the measurement data were expressed by (S); The counting data were expressed in percentage (%) and the difference was statistically significant by using $\chi 2$ test, with $P < 0.05$.

RESULTS

Analysis of maternal stress and serum indexes in two groups

Compared with the reference group, the stress and serum indexes in the observation group were significantly decreased ($P < 0.05$). See table 2 for details.

Compare the bleeding related indexes between the two groups

Except the oxygen saturation, the amount of postpartum hemorrhage and hemostasis time in the observation group were significantly lower than those in the reference group and the hemoglobin content was relatively high ($P < 0.05$). See table 3 for details.

Comparison of changes of coagulation function between two groups of parturients

After treatment, the improvement of coagulation function in the observation group was better than that in the reference group ($P < 0.05$). See table 4 for details.

Comparison of complications between the two groups

The incidence of complications was 21.28% in the reference group and 4.26% in the observation group ($P < 0.05$). See table 5 for details.

DISCUSSION

Clinically, postpartum hemorrhage, a childbirth complication, is related to soft birth canal injury, uterine inertia, etc. Excessive amniotic fluid and uterine hypofunction are all high-risk factors that induce postpartum hemorrhage (Vizheh, M *et al*., 2023). If postpartum hemorrhage occurs, blood coagulation function and hemoglobin examination should be carried out in time to judge its severity and symptomatic treatment should be carried out to avoid other complications such as water-electrolyte disorder and reproductive tract infection (Fan, L *et al*., 2021). Postpartum hemorrhage has always been a serious complication in the field of obstetrics and its incidence rate is high, which has gradually attracted the general attention of obstetricians (Wen, Y *et al*., 2022). Postpartum hemorrhage will not only induce coagulation dysfunction and hemorrhagic shock, but also pose a threat to maternal life safety. It is necessary to actively explore safe and effective preventive and therapeutic measures to ensure maternal health while controlling postpartum hemorrhage.

Uterine atony is one of the key causes of postpartum hemorrhage. It usually occurs within 2 hours after delivery. Therefore, strengthening uterine contractions after delivery is the key to prevention and treatment. Clinically, oxytocin is often used to control the amount of bleeding (Zhang, Y and Xie, S *et al*., 2022). Oxytocin can enhance the excitability and contractility of uterine smooth muscle, accelerate the closure of blood sinuses, but its half-life is short (about half an hour). Different pregnant women have significant differences in their sensitivity to it. Its single use effect is limited and it may increase the myocardial load of pregnant women with heart disease. Therefore, it should be used with caution. During delivery, the maternal vital signs,

uterine contraction and vaginal bleeding should be closely observed 2 hours after delivery of placenta and drugs should be used for treatment in time. Oxytocin has a relatively short half-life and lasts for about half an hour, which can improve the excitement of uterine smooth muscle, enhance uterine contractility and then accelerate sinus closure. But at the same time, the drug will increase the myocardial load of patients to a certain extent and it should be used cautiously for pregnant women with heart disease (Pascali, M *et al*., 2021). During the period of medication, the therapeutic effectiveness will be high with the increase of drug dosage, but the effect of single medication is not obvious because of the obvious differences in the sensitivity of different parturients to drugs, so joint medication can be carried out to consolidate the therapeutic effect and play its coordinating role (Sarimov, R M *et al*., 2023).

Misoprostol can soften the cervix, promote the maturation of the cervix, accelerate the release of oxytocin and enhance uterine contractions. However, its effect on promoting the maturation of the cervix varies from person to person. Some parturients may experience adverse reactions such as uterine spastic contractions after taking it (Schalkwyk, *et al*., 2022). Therefore, it is often used in combination with oxytocin to make up for the deficiency of single medication. Therefore, it is necessary to strengthen monitoring and reduce adverse events during medication. In the process of applying misoprostol, it is generally used together with oxytocin, which can make up for the problem of adverse reactions of women with low drug sensitivity, ensure safe hemostasis and ensure maternal health and safety. Studies have found that in the prevention and treatment of postpartum hemorrhage, the combination of oxytocin and misoprostol has special advantages, but there are still some parturients whose effect is not obvious. Therefore, it is generally recommended to use carboprost tromethamine in combination to prevent and treat postpartum hemorrhage while ensuring safety. This medicine has obvious contractile function and it is an important medicine to dilate the cervix in clinic. It can control the bleeding of uterine sinus in time, increase the number of oxytocin receptors in uterine myometrium and fully display its hemostatic effect (Bloska J, *et al*., 2024). Studies have shown that the combination of this drug and oxytocin can further improve the therapeutic effect of the drug. At present, its synergistic effect has been gradually paid attention to in clinic and the contraction function formed is in direct proportion to the content, thus promoting uterine contraction. In blood, the drug can effectively stimulate the release of calcium ion and the concentration of calcium ion is relatively high after taking the drug, which can effectively relieve the vascular compression of blood sinus while accelerating the contraction of uterine smooth muscle, with a half-life of about 2-3 hours and obvious hemostatic effect (Yu, J and Chen, L *et al*., 2022).

Carboprost tromethamine can promote regular uterine contraction, reduce postpartum hemorrhage and discharge pregnancy products in time. After medication, uterine muscle contraction can fully display its hemostatic effect in placenta. Carboprost tromethamine is a uterine contractile agent, which currently plays an important role in the prevention and treatment of postpartum hemorrhage. It mainly stimulates uterine smooth muscle contraction to enhance uterine contractility, thus achieving the goal of hemostasis. Clinically, it is generally used in combination with other drugs to minimize the incidence of postpartum hemorrhage while exerting its hemostatic effect (Wang, W *et al*., 2022). The drug is common in the second trimester of pregnancy and abortion and the dosage should be determined according to the physical condition during the medication. However, the drug can also induce side effects such as nausea and vomiting, diarrhea, chest pain, etc. Generally, it can recover itself after treatment (Sun, L *et al*., 2024).

During the application of misoprostol, it is generally administered by anal plugging, which can reduce the negative impact of oral administration on gastrointestinal system and reduce gastrointestinal discomfort. Combined with oxytocin, it can also play a synergistic role and then better prevent and treat postpartum hemorrhage. The combined application of carboprost tromethamine, oxytocin and misoprostol compared with the use of oxytocin and misoprostol alone can enhance uterine contractility through multiple pathways, more effectively control postpartum hemorrhage and show better preventive effects. The combined strategy of the three drugs may exert a synergistic effect through complementary mechanisms, increase the sensitivity of the uterus to the drugs and is particularly suitable for patients who do not respond well to oxytocin. (Wang, W *et al*., 2022). Postpartum hemorrhage has always been the top priority in obstetric prevention and treatment, so promoting uterine contraction is extremely critical and promoting cervical maturity is very important in the prevention of postpartum hemorrhage. In the process of selecting drugs, we should pay attention to promoting cervical maturity and uterine contraction and give play to the synergistic effect between drugs, so as to improve the overall effect of treatment while improving the uterine contraction of patients, ensure the health of parturient and then fully display its application value and role (Pahan, S *et al*., 2023). The results showed that compared with the control group, the stress and serum indicators in the observation group were significantly reduced. Except for oxygen saturation, the postpartum hemorrhage volume and hemostasis time in the observation group were significantly lower than those in the control group and the hemoglobin content was relatively higher. After treatment, the improvement of coagulation function in the observation group was better than that in the control group. The complication rate of the control group was 21.28%, while that of the observation group was 4.26% and

Table 1: Comparison of general data between two groups of patients ($\bar{x}$±s)

group	Number of cases	age	Average age	Average gestational age
Reference group	47	23~40	(29.45±2.19)year	(38.41±0.18)week
Observation group	47	24~39	(29.33±2.60)year	(38.12±0.20)week

Table 2: Analysis of maternal stress and serum indexes in two groups [n ($\bar{x}$±s)]

Group	n	Malondialdehyde (μmol/L)		Norepinephrine (pg/mL)		Brain natriuretic peptide (pg/mL)		Nitric oxide (μmol/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Reference group	47	13.31 ±1.25	7.14 ±0.25	214.23 ±23.68	344.53 ±26.71	202.42 ±21.15	71.26 ±7.35	113.41 ±12.52	92.36 ±9.17
Observation group	47	13.50 ±1.14	5.61 ±0.22	214.46 ±23.74	291.58 ±31.20	202.61 ±21.33	42.87 ±8.24	112.33 ±12.36	85.50 ±13.20
P		0.443	0.000	0.962	0.000	0.965	0.000	0.674	0.004

Table 3: Comparison of bleeding related indexes between the two groups [n ($\bar{x}$±s)]

Group	N	Oxygen saturation (%)	Total postpartum hemorrhage (mL)	Hemostasis time (min)	Hemoglobin content (g/L)
Reference group	47	92.31±8.52	348.51±52.22	39.51±5.54	95.12±12.41
Observation group	47	93.20±8.01	256.23±41.07	13.24±6.33	123.50±15.20
P		0.603	0.000	0.000	0.000

Table 4: Comparison of coagulation function between two groups [n ($\bar{x}$±s)]

Group	N	Prothrombin Time (s)		Fibrin Degradation Products (mg / L)		Erythrocyte sedimentation rate (mm/h)		Plasma viscosity (mPa·s)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Reference group	47	20.62 ±3.45	12.31 ±3.24	8.24 ±2.54	4.40 ±2.34	22.65 ±3.51	11.33 ±1.67	1.68 ±0.27	1.36 ±0.13
Observation group	47	20.60 ±3.35	10.34 ±2.25	8.30 ±2.56	3.37 ±2.51	22.46 ±3.60	13.58 ±1.26	1.63 ±0.32	1.07 ±0.04
P		0.977	0.000	0.909	0.042	0.796	0.000	0.415	0.000

Table 5: Comparison of complications between the two groups [n(%)]

Group	N	infect	Hemorrhagic shock	Organ failure	incidence rate
Reference group	47	3	4	3	21.28
Observation group	47	1	1	0	4.26
x^2					6.113
P					0.013

the difference was statistically significant ($P < 0.05$). This indicates that in the preventive treatment of postpartum hemorrhage, the effect of triple drug administration is more significant than that of dual drug administration. It can improve the stress response and serum indicators of patients, reduce the amount of hemorrhage and improve the coagulation function of patients. At the same time, it is also very beneficial for controlling complications and has certain safety (Zheng, J *et al*., 2023). It can be seen that triple drug administration can regulate the coagulation function of patients, accelerate platelet aggregation, promote blood circulation to improve as soon as possible, effectively inhibit the effect of angiotensin-converting enzyme and reduce the oxidative stress response of patients. Moreover, through combined medication, patients will not have serious adverse reactions and have a higher safety.

CONCLUSION

In conclusion, the combined application of carbetocin ammonium triacetate, oxytocin and misoprostol can exert a more significant synergistic effect compared with the use of oxytocin and misoprostol alone. In particular, it can accelerate postpartum hemostasis, improve the coagulation indicators of the parturient, effectively alleviate the stress response and has certain promotion and application value.

Conflicts of interest

The authors declare no conflicts of interest.

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