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*Review Article*

# Clinical study of oxytocin combined with prostaglandins in preventing postpartum hemorrhage and improving delivery outcomes in high-risk pregnancy after cesarean section

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**Abstract:** Objective: To investigate the effect of oxytocin combined with prostaglandins (PGs) on preventing hemorrhage and improving delivery outcomes after cesarean section (C-section) in high-risk pregnancy. Methods: One hundred and six parturients with high risk pregnancy who underwent C-section in our hospital from September 2016 to November 2018 were selected as the research participants, among which 54 cases were treated with oxytocin alone and were selected as the control group (CG), and 52 cases that were treated with PGs in addition to the CG were selected as the observation group (OG). The therapeutic effect, blood loss, blood pressure, heart rate, treatment and recovery, occurrence of adverse reactions and recent menstruation were compared between the two groups. Results: The therapeutic effect in the OG was remarkably better than that in the CG after treatment ($P<0.05$). The maternal blood loss in the OG was evidently less than that in the CG during operation and postpartum (3 h, 24 h) ($P<0.05$). The OG showed a more significant increase in indicators such as diastolic blood pressure (DBP), systolic blood pressure (SBP), and heart rate ($P<0.05$) at 1 h after medication, but all of them returned to the normal stable value 3 h after medication. The OG was superior to the CG in terms of hemostasis time, hospital stay and anal exhaust time ($P<0.05$). The incidence of adverse reactions did not differ statistically between the two groups ($P>0.05$). The menstrual recovery of the OG at 2 and 6 months postpartum was better than that of the CG ($P<0.05$). Conclusion: Compared with oxytocin alone, the combination therapy of oxytocin and PGs is more effective in preventing hemorrhage after C-section in pregnant women with high-risk pregnancy, which can effectively reduce the intraoperative and postoperative blood loss and improve delivery outcome.

**Keywords:** Oxytocin, prostaglandins, high-risk pregnancy, cesarean section, postpartum hemorrhage

## Introduction

High-risk pregnancy refers to a type of pregnancy that can be risky and may cause damage to the fetus or mother [1]. High risk factors such as advanced age, gestational hypertension, gestational diabetes mellitus, placenta previa, multiple births, polyhydramnios or oligohydramnios will increase the risk of issues durring pregnancy and birth [2, 3]. C-section is an operation that extracts the fetus and remaining supportive tissues after opening the abdominal wall and uterus; it is often used in dystocia and some high-risk pregnancy patients [4]. With the continuous relaxation of hospital indications for C-sections in recent years, more pregnant women decide on a C-section, increasing the rate of C-sections, and therefore an increasing number of cases of C-section-induced postpartum hemorrhage are occuring [5]. Compared with natural delivery, the probability of postpartum hemorrhage after C-section is higher. Postpartum hemorrhage, which is one of the major manifestations of severe complications during C-section and a common cause of maternal death, refers to blood loss of more than 500 mL within 24 h after the delivery of the fetus, which in most cases, occurs within 2 h after delivery [6]. The incidence of postpartum hemorrhage also increases with the occurrence of

pregnancy risk factors such as placenta previa, scarred uterus, placental abruption, macrosomia, polyhydramnios and abnormal labor process [7]. Therefore, the control of hemorrhage after C-section has become the focus and hotspot of obstetrics and gynecology research. Uterine inertia, which accounts for the most of the postpartum hemorrhage after C-section, can even lead to shock, disseminated intravascular coagulation (DIC), multi-organ damage, and refractory postpartum hemorrhage if it is left without timely treatment, all of which increase maternal mortality [8, 9]. On the contrary, timely and effective treatment of maternal uterine inertia can effectively prevent the occurrence of postpartum hemorrhage and play a positive role in ensuring maternal life safety and retaining fertility [10]. Clinically, postpartum hemorrhage can be treated by conservative methods such as uterotonic agents, uterine massage and intrauterine tamponade, and if necessary, surgery, or even hysterectomy [11].

Oxytocin, as a commonly used hemostatic drug in clinical C-section, is a potent uterotonic agent, which can effectively treat uterine inertia, but its hemostatic effect is not ideal when used alone, and it has shown medication contraindications or little efficacy in some patients [12]. Clinical literature has revealed that the main action of carboprost tromethamine is to make the uterus contract regularly, which is an effective method to treat and prevent postpartum hemorrhage caused by uterine inertia [13]. However, the therapeutic effect of carboprost tromethamine combined with oxytocin, a clinically effective drug for the suppression of postpartum hemorrhage, in high-risk pregnant women has not been clearly defined. Therefore, the purpose of this study is to explore the effect of carboprost tromethamine combined with oxytocin to control the total blood loss during C-section in high-risk pregnancy and optimize the delivery outcome. The report is as follows.

## Materials and methods

### *General information*

From September 2016 to November 2018, 106 parturients with high risk pregnancy who underwent C-section in Chongqing Health Center for Women and Children were selected as the research participants, among which 54 cases treated with oxytocin alone were selected as the CG, and 52 cases treated with PGs in addition to treatment in the CG, were grouped into the OG. Inclusion criteria: (1) All parturients met the clinical diagnostic criteria for high-risk pregnancy [14]; (2) Parturients without prostaglandin contraindications; (3) Parturients who met the indications for C-section surgery. Exclusion criteria: (1) Patients with coagulation dysfunction or disorder; (2) Patients with severe impairment of liver and kidney function; (3) Pregnant patients with severe organ disease. The study has been approved by the ethics committee of Chongqing Health Center for Women and Children, and is in line with the Declaration of Helsinki. The parturients and their families had a clear understanding of the content of this study and voluntarily signed the informed consent. The participants enrolled in this study were aged (32.86±5.55) years, and the gestational age was (38.54±1.55) weeks.

### *Methods*

Both groups of high-risk parturients underwent continuous epidural anesthesia (CEA) and were maintained with good anesthesia for C-section. The CG was given oxytocin injection (Chengdu Hepatunn Pharmaceutical Co., Ltd., State Drug Approval Document Number: H51021982, 1 mL:5 U) and 0.9% sodium chloride injection to dilute a solution of 0.01 U/mL after the fetus was delivered, and the maintenance rate was 0.02-0.04 U/min. In the OG, 250 μg of carboprost tromethamine injection (Changzhou Siyao Pharmaceutical Co., Ltd., registration number: H20094183, 1 mL:250 μg) was injected intramuscularly in addition to the treatment in the CG. If the maternal contractions were not improved after administration, other effective hemostasis measures were taken according to parturients' situation, such as uterine (artery ligation, compression suture, resection) surgery or second-line treatment like intrauterine tamponade.

### *Outcome measures*

(1) Therapeutic effect [15]: Markedly effective (significant enhanced uterine contraction ability, disappearance of vaginal bleeding), effective (enhanced uterine contraction ability, improvement in vaginal bleeding volume), ineffective (insufficient uterine contraction capacity, decreased or even exacerbated vaginal bleed-

**Table 1.** Comparison of basic data between the two groups

| Groups | CG (n=54) | OG (n=52) | $\chi^2$/t | P |
|---|---|---|---|---|
| Age (years old) | 32.42±5.65 | 33.13±5.36 | 0.663 | 0.509 |
| Number of births (times) | 2.01±0.73 | 1.97±0.78 | 0.273 | 0.786 |
| Gestational age (week) | 38.57±1.53 | 38.40±1.57 | 0.565 | 0.574 |
| placenta previa (cases) | | | 0.385 | 0.535 |
| Yes | 8 (14.81) | 6 (11.54) | | |
| No | 46 (85.19) | 46 (88.46) | | |
| Placental abruption (cases) | | | 0.046 | 0.831 |
| Yes | 7 (12.96) | 6 (11.54) | | |
| No | 47 (87.04) | 46 (88.46) | | |
| Diabetes mellitus (cases) | | | 0.243 | 0.622 |
| Yes | 14 (25.93) | 12 (23.08) | | |
| No | 40 (74.07) | 40 (76.92) | | |
| Thyroid disease (cases) | | | 1.607 | 0.205 |
| Yes | 6 (11.11) | 3 (5.77) | | |
| No | 48 (88.89) | 49 (94.23) | | |
| Anemia (cases) | | | 0.362 | 0.548 |
| Yes | 19 (35.19) | 16 (30.77) | | |
| No | 35 (64.81) | 36 (69.23) | | |

**Table 2.** Comparison of therapeutic effects between the two groups [n (%)]

| Groups | CG (n=54) | OG (n=52) | $\chi^2$ | P |
|---|---|---|---|---|
| Markedly effective | 20 (37.04) | 29 (55.77) | - | - |
| Effective | 27 (50.00) | 21 (40.38) | - | - |
| Ineffective | 7 (12.96) | 2 (3.85) | - | - |
| Total effective rate | 47 (87.04) | 50 (96.15) | 5.207 | 0.023 |

ing volume). Total effective rate of treatment = (markedly effective cases + effective cases)/ total cases × 100%. (2) Blood loss: The blood loss was recorded during the operation, at 3 h and 24 h postpartum, and compared by the combined weighing method, volume method and area method. (3) The blood pressure indexes and heart rate of parturients in the two groups before, 1 h and 3 h after medication were recorded and compared. (4) Treatment and recovery: the maternal blood transfusion rate, intervention rate of additional hemostasis measures, and time of operation, hemostasis, hospitalization and anal exhaust were calculated and compared between the two groups. (5) The adverse reactions such as nausea and vomiting, fever, postpartum infection and urinary retention were compared between the two groups. (6) Recent menstruation: the patients were followed up by telephone for more than 6 months, and the menstruation of patients 2 months and 6 months postpartum was statistically analyzed.

*Statistical methods*

The collected data were processed using SPSS 20.0 statistical software. The measurement data were expressed as mean ± standard deviation and verified by t test, and the multiple time -point data were compared by repeated measures analysis of variance, and analyzed by LSD method. The counting data were analyzed by $\chi^2$ test. P<0.05 indicated a statistically significant difference.

## Results

*Comparison of basic data between the two groups*

There were no significant statistical differences between the OG and the CG regarding age, number of births, gestational weeks and disease-related etiology (P>0.05). The included cases can be compared and referenced experimentally (**Table 1**).

*Comparison of therapeutic effects between the two groups*

Statistical results showed that the therapeutic effect in the OG was significantly better than that in the CG after treatment (P<0.05) (**Table 2**).

*Comparison of intraoperative and postpartum blood loss in the two groups*

The amount of maternal blood loss during operation and postpartum (3 h and 24 h) in the OG was notably less than that in the CG (P<0.05) (**Table 3**).

*Comparison of maternal blood pressure changes before, 1 h and 3 h after medication in the two groups*

Before medication, the blood pressure was mostly low in parturients, and the blood pressure indexes of parturients in the two groups were not statistically significant (P>0.05). After 1 h of medication, the DBP and SBP increased in both groups, and the DBP and SBP in the OG was higher than those in the CG. The blood pressure indexes of the two groups showed a

**Table 3.** Comparison of intraoperative and postpartum blood loss between the two groups (mL)

| Groups | CG (n=54) | OG (n=52) | T | P |
|---|---|---|---|---|
| Intraoperative | 394.64±127.35 | 342.53±114.42 | 2.213 | 0.029 |
| 3 h postpartum | 154.74±59.45 | 104.37±43.63 | 4.958 | <0.001 |
| 24 h postpartum | 89.38±30.62 | 61.55±27.36 | 4.928 | <0.001 |

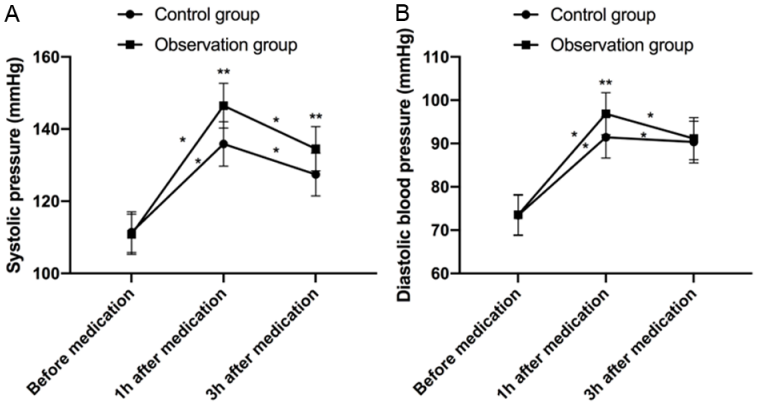


**Figure 1.** Comparison of maternal blood pressure changes before, 1 h and 3 h after medication in the two groups. A: The maternal SBP in both groups increased at 1 h after medication, and decreased at 3 h after medication, and the SBP in the OG was significantly higher than that in the CG at 1 h and 3 h after medication. B: The maternal DBP in both groups increased at 1 h after medication, and decreased at 3 h after medication, and the DBP in the OG was markedly higher than that in the CG at 1 h after medication. Note: * indicated P<0.05 compared with the same group at different time points, and ** indicated P<0.05 compared between the two groups at the same time point.

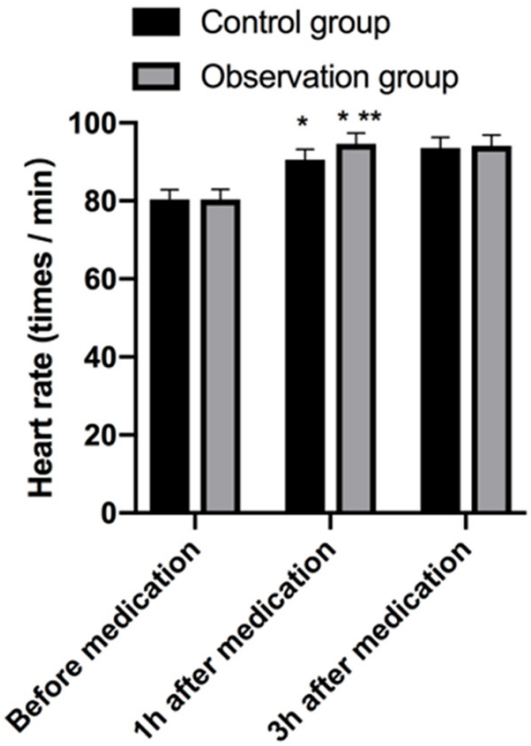


**Figure 2.** Comparison of maternal heart rates before, 1 h and 3 h after medication between the two groups. After 1 h of medication, the maternal heart rate of both groups increased compared with that before treatment, and the maternal heart rate in the OG was remarkably higher than that in the CG (P<0.05). Note: * indicated P<0.05 compared with the same group before and 1 h after medication, and ** indicated P<0.05 compared between the two groups at the same time point.

downward trend 3 h after medication, and the OG was significantly higher than the CG in SBP (P<0.05) (**Figure 1**).

*Comparison of maternal heart rates before, 1 h and 3 h after medication between the two groups*

Before medication, the heart rate was mostly low in parturients, and the heart rate did not differ significantly between the two groups (P>0.05). After 1 h of medication, the maternal heart rate of both groups increased compared with that before medication, and the maternal heart rate in the OG was noticeably higher than that in the CG (P<0.05). There was no significant difference in maternal heart rate between the two groups after 3 h of medication, and both remained stable in the normal range with small amplitude changes (**Figure 2**).

*Maternal treatment and recovery in the two groups*

There were no statistically significant differences between the two groups in maternal blood transfusion rate, intervention rate of additional hemostasis measures and operation time (P> 0.05). The OG was superior to the CG in terms of hemostasis time, hospital stay and anal exhaust time (P<0.05) (**Table 4**).

*Comparison of postpartum adverse reactions between the two groups*

The incidence of adverse reactions in the OG (19.23%) was not statistically different from

**Table 4.** Comparison of maternal treatment and recovery between the two groups

| Groups | CG (n=54) | OG (n=52) | $\chi^2$/t | P |
|---|---|---|---|---|
| Blood transfusion rate (%) | 9 (16.67) | 6 (11.54) | 1.008 | 0.315 |
| Intervention rate of additional hemostasis measures (%) | 11 (20.37) | 8 (15.38) | 0.866 | 0.352 |
| Operation time (h) | 2.61±0.70 | 2.53±0.67 | 0.601 | 0.549 |
| Hemostasis time (min) | 33.35±5.23 | 18.53±4.34 | 15.840 | <0.001 |
| Hospital stay (d) | 6.97±2.53 | 5.53±2.22 | 3.110 | 0.002 |
| Anal exhaust time (h) | 15.45±3.48 | 9.45±2.64 | 9.972 | <0.001 |

**Table 5.** Comparison of postpartum adverse reactions between the two groups

| Groups | CG (n=54) | OG (n=52) | $\chi^2$ | P |
|---|---|---|---|---|
| Nausea and vomiting | 4 (7.41) | 3 (5.77) | - | - |
| Fever | 2 (3.70) | 2 (3.85) | - | - |
| Postpartum infection | 1 (1.85) | 2 (3.85) | - | - |
| Uroschesis | 2 (3.70) | 3 (5.77) | - | - |
| Incidence of adverse reactions (%) | 9 (16.67) | 10 (19.23) | 0.136 | 0.713 |

that in the CG (16.67%) (P>0.05). In the OG, 1 parturient showed severe postpartum infection, which was improved after symptomatic treatment, and the remaining cases showed improvement in short time without special treatment (**Table 5**).

*Comparison of menstrual efficacy between the two groups*

The effect of C-section on normal physiological functions of uterus and appendages was judged by comparing the menstrual regularity of puerperae. It was found that the menstrual recovery in the OG at 2 and 6 months postpartum was better than that in the CG (P<0.05) (**Table 6**).

## Discussion

Following the continuous improvement of modern living standards and the influence of external factors such as society and the environment, more women choose C-section instead of natural delivery as the first choice for delivery, and the ensuing negative clinical effects have become a hot issue in society as they draw more attention [16]. After 28 weeks of gestation, placenta previa is a common condition in which the placenta is attached to the lower segment of the uterus, the cervix, or is covered below the exposed part of the fetus, and in which cases, C-section is mainly used in clinical practice to help the puerpera complete delivery, so as to avoid damage to the fetus caused by tearing of the mother's cervix [17]. However, during C-section, postpartum hemorrhage often occurs due to the difficulty in closing and opening the blood sinuses caused by thin tissue and poor contraction of the lower uterine segment [18]. Most clinicians believe that postpartum hemorrhage occures if the amount of postpartum hemorrhage exceeds 500 ml within 24 h, while as the qualifying amount of postpartum hemorrhage is often limited due to the statistical criteria, methods and other factors, the standardization of the amount of postpartum hemorrhage lacks accuracy and effectiveness [19]. According to research [20], the high incidence of postpartum hemorrhage keeps updating and increasing. The process of C-section poses certain risks to women's health. If bleeding is not controlled in a timely manner, it will easily cause massive postpartum hemorrhage and affect the physical and mental health of pregnant women, and in severe cases, can be life-threatening. Hence, the process of childbirth and the occurrence of postpartum hemorrhage should be paid close attention to, and meanwhile timely and effective hemostasis measures are essential. Therefore, in this study, two conventional clinical drugs, oxytocin and carboprost tromethamine, were used to regulate uterine contractile function to compare the effects of single and combined use on uterine function in patients with high-risk pregnancy undergoing C-section, in order to better understand how to use appropriate and effective drugs to control hemorrhage and other adverse reactions in patients after C-section.

**Table 6.** Comparison of postpartum menstrual efficacy between two groups [n (%)]

| Groups | CG (n=54) | OG (n=52) | $\chi^2$ | P |
|---|---|---|---|---|
| Recovery rate of menstruation within 2 months | 34 (62.96) | 45 (86.54) | 15.361 | <0.001 |
| Recovery rate of menstruation within 6 months | 46 (85.19) | 50 (96.15) | 7.037 | 0.008 |

Statistical analysis on the efficacy of the two groups revealed that the therapeutic effect of the combination therapy was better. As the accurate measurement of the blood loss can more objectively reflect the efficacy of the two drugs on pregnant women with high-risk pregnancy C-section, we recorded and analyzed the maternal blood loss during operation and at different postpartum periods, and found that the maternal blood loss in the OG at each period was remarkably less than that in the CG. Oxytocin, as a universal clinical treatment drug for postpartum hemorrhage, has the effect of strengthening the contraction of uterine smooth muscle and effective hemostasis. Currently, it is commonly used in clinical practice to prevent postpartum hemorrhage by intravenous infusion of 20 U oxytocin after delivery, and the best effect is achieved within 2 h after delivery [21]. It has also been confirmed in the literature that among the PGs, carboprost tromethamine has shown efficacy on uterine contraction in various stages of pregnancy, and can effectively inhibit the increase of uterine blood flow [22]. The use of oxytocin combined with carboprost tromethamine injection has the advantages of long half-life, rapid absorption and strong biological activity, which can maintain the contraction of pregnant uterine smooth muscle and reduce the amount of bleeding. Further monitoring of the normal vital signs and adverse reactions of the two groups showed that the OG increased significantly in DBP, SBP, heart rate and other indicators 1 h after medication, but all of them returned to the normal stable value 3 h after medication. In addition, the OG was superior to the CG in terms of hemostasis time, hospital stay and anus exhaust time. What's more, the combination of the two drugs did not cause changes in adverse reactions compared to the monotherapy. By inhibiting adenylate cyclase, carboprost tromethamine injection stimulates uterine contraction and affects the contraction frequency, so as to promote vasoconstriction and intrauterine closure (sinus, blood vessels), thereby achieving the goal of hemostasis. In the case of low dosage, it can achieve effective hemostatic effect, which is beneficial to the stability of patients' normal life characteristics, and greatly reduces the burden of adverse reactions [23, 24]. All these indicate that the combination of the two in this study can promote the homeostasis balance of vital signs, lower the difficulty of operation, and help the recovery of maternal body and uterine function, so as to avoid malignant delivery outcomes and invasive intervention. Combined with the description and analysis of the adverse reactions in the results of this paper, the reason behind the small difference in adverse reactions between the two groups may be that carboprost tromethamine itself has a good uterine smooth muscle contraction control function to help hemostasis, which reduces the occurrence of related complications and enables the combined treatment with oxytocin to possess a synergistic hemostasis effect without increasing the adverse reactions. Therefore, the application of oxytocin combined with PGs in the treatment of parturients undergoing C-section is a safe and feasible combination therapy. At last, we followed up and observed the menstrual condition of the patients within 6 months after delivery. The menstrual recovery of the OG at 2 and 6 months after delivery was better than that of the CG. As C-section scar defects and decreased ovarian function will lead to abnormal menstrual time disorders [25], the preceding results indicate that the combination therapy brings faster and more effective postoperative recovery.

PGs are effective in the treatment of parturients at high risk of postpartum hemorrhage, especially under the treatment of oxytocin combined with carboprost tromethamine, which can control the amount of perinatal hemorrhage and reduce the related complications caused by massive hemorrhage, with the advantages of high safety, rapidity and good recovery. Carboprost tromethamine can be considered as the first choice for preventing postpartum hemorrhage in C-section. In this study, we analyzed the postpartum menstrual recovery of women undergoing cesarean sec-

tion after carboprost tromethamine treatment to understand the therapeutic effect and strengthen the effectiveness of the drug effect. However, there are still some shortcomings in this study. For example, this paper did not monitor the treatment and recovery of patients with multiple indicators. In future research, we will conduct an in-depth analysis of the impact of related indicators on the cesarean delivery women combined with the results of this paper, so as to improve the accuracy of the results to achieve the exact research value, thereby providing effective hemostasis measures for the judgment of postpartum hemorrhage applicable to C-section.

**Disclosure of conflict of interest:**

None.

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