Tropical Journal of Pharmaceutical Research April 2020; 19 (4): 899-904
ISSN: 1596-5996 (print); 1596-9827 (electronic)

Available online at http://www.tjpr.org
http://dx.doi.org/10.4314/tjpr.v19i4.32

Original Research Article

Carboprost tromethamine prevents caesarean section-associated postpartum hemorrhage

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Sent for review: 23 October 2019 *Revised accepted: 29 January 2020*

Abstract

Purpose: *To investigate the effect of carboprost tromethamine on post-partum hemorrhage associated with caesarean section.*
Methods: *One hundred patients with postpartum hemorrhage induced by cesarean section who were admitted to Binzhou People's Hospital from October 2016 to August 2018 were selected. They were randomly assigned to two groups: control group and treatment group. Patients in the control group were administered oxytocin, while those in the treatment group received oxytocin in combination with carboprost tromethamine. The incidence of hemorrhage and adverse reactions were compared for the two groups.*
Results: *The two groups showed gradually increasing degrees of postpartum hemorrhage within 24 h, but the treatment group had significantly lower volume of postpartum hemorrhage than the control group at different time points ($p < 0.05$). At the 1st, 3rd and 5th days after delivery, the height of the uterine fundus decreased gradually in the two groups, but was smaller in the treatment group than in the oxytocin group at all time points ($p < 0.05$). Total response in the treatment group was 98 %, which was significantly higher than 78 % in the control group ($p < 0.05$). The incidence of adverse reactions in the treatment group (12 %) was significantly lower than that in the control group (24 %, $p < 0.05$).*
Conclusion: *Carboprost tromethamine prevents postpartum hemorrhage after cesarean section. It effectively reduces bleeding and promotes uterine involution, without obvious adverse reactions.*

Keywords: *Carboprost tromethamine, Oxytocin, Cesarean section, Postpartum hemorrhage*

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, International Pharmaceutical Abstract, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

INTRODUCTION

Due to continuous improvements in the qualities of obstetric treatments and anesthesia technology, the frequency of application of cesarean section in obstetric clinical practice has increased in recent years, and it has become the main treatment method for dystocia and obstetric complications [1].

Postpartum hemorrhage, a common complication after cesarean section, poses a serious threat to maternal life [2]. It refers to a condition where the volume of hemorrhage of puerpera exceeds 500 mL within 24 h after delivery of the fetus. Sometimes, the amount of hemorrhage of puerpera after cesarean delivery may be more than 1000 mL within 24 h, and the increased

amount of hemorrhage may be accompanied by hypovolemia [3,4]. In addition, postpartum erythrocyte loss of up to, or more than 10 % is considered as postpartum hemorrhage. Postpartum hemorrhage is also considered as one of the most common causes of maternal mortality.

Currently, 66 to 93 % of global deaths due to hemorrhage are preventable. Therefore, the prevention and effective treatment of postpartum hemorrhage are of clinical importance. Some clinical studies have shown that uterine inertia is a key factor involved in the induction of most postpartum hemorrhage events, and that postpartum hemorrhage can be treated by improving the intensity of uterine contraction, as well as timely hemostasis [5,6].

Oxytocin is currently the most widely used uterine contraction drug, but it has a short-lasting effect in postpartum hemorrhage, leading to a poor effect in a single use [7]. Carboprost tromethamine promotes the contraction of uterine smooth muscle in pregnancy. Moreover, the effect of carboprost tromethamine on uterine smooth muscle contraction is prolonged due to its long half-life period, thereby effectively preventing postpartum hemorrhage. This study was aimed at investigating the clinical effect of carboprost tromethamine on postpartum hemorrhage.

METHODS

General patient profile

One hundred patients who had postpartum hemorrhage after cesarean section in Binzhou People's Hospital between October 2016 and August 2018 were recruited for the study. All selected subjects had indications for cesarean section [8]. Patients who had impaired coagulation, blood disease, liver disease, scarred uterus, myoma of uterus, or abruption, adhesion, implantation and previa of placenta, were excluded. The patients were grouped into a treatment group and a control group (50 patients per group), using the random number table. The ages of patients in the treatment group ranged from 20 to 36 years (mean age = 27.6 ± 3.8 years), and their gestational ages were 35 - 40 weeks (mean age = 38.2 ± 1.4 weeks). In the observation group, there were 26 cases of primipara and 24 cases of multipara.

With respect to causes of hemorrhage, 4 cases were due to twin pregnancy, 6 cases were caused by placental abruption, 4 cases were from placenta previa, 24 cases were due to giant placenta, while 12 cases were as a result of polyhydramnios. The ages of patients in the control group ranged from 20 to 36 years (mean age = 27.2 ± 3.5 years), and the gestational ages ranged from 35 to 40 weeks (mean = 37.6 ± 2.3 weeks). There were 25 cases of primipara and 25 cases of multipara. With respect to causes of hemorrhage, 3 cases were caused by twin pregnancy, 7 cases by placental abruption, 4 cases by placenta previa, 22 cases by giant placenta, and 14 cases by polyhydramnios. There were no significant differences between the two groups in terms of general data such as age, gestational age, parity and causes of hemorrhage ($p > 0.05$). The study was approved by the Medical Ethics Committee of Binzhou People's Hospital (approval no. WL20170120), and the experiments were performed in line with the guidelines of the Declaration of Helsinki [9].

Treatments

The two groups of puerperae were delivered by cesarean section. A transverse incision was made in the lower part of the uterus. After the lower part of the uterus was opened, the amniotic fluid was removed. Each puerpera in the control group was given 40 U of oxytocin (Jiuquan Dadeli Pharmaceutical Co. Ltd, China; approval no. H62020713) after the delivery of the fetus by means of intrauterine injection and intravenous drip at a dose of 20 U/time. If the patient's contraction condition was not good, continuous uterine contraction treatment with 20 - 50 U of oxytocin was applied. Patients in the treatment group were given 250 μg of carboprost tromethamine injection (Xinmupei; Pharmacia & Upjohn Company; registration no. H20120388) in addition to oxytocin treatment after the delivery of the fetus. If the drugs did not take effect, injection was repeated as long as the interval between injections was more than 15 min, and the total dosage was < 2 mg.

Treatment indicators

Postpartum hemorrhage in the two groups were monitored and recorded at the 2^{nd}, 6^{th}, 12^{th} and 24^{th} hour after delivery. The degree of hemorrhage was measured in terms of volume of blood. The amniotic fluid was first received in the negative pressure bottle during cesarean section. Then, the intraoperative hemorrhage was obtained using a suction device, and the volume of hemorrhage was obtained by subtracting the volume of amniotic fluid from the blood volume in the negative pressure bottle at the end of operation. Ten mL of blood loss was recorded if there was no blood dropping from a permeant 10 cm × 10 cm gauze.

On the morning of 1st, 3rd, and 5th days after delivery, the uterus was massaged after the puerperae urinated and when the bladder was empty. The vertical distance from the midpoint of the upper edge of pubic symphysis to the bottom of the uterus was taken as the height of the uterus floor.

Hemostasis was monitored in the two groups. The criteria for curative effect were classified as significant, effective or ineffective as follows[10]: curative effect was deemed significant if uterine contraction was obvious within 15 min after medication, and if volume of vaginal bleeding was significantly controlled; hemostasis effect was classified as effective if uterine contraction was good within 30 min after repeated medication, and vaginal bleeding was controlled. On the other hand, the hemostasis effect was considered ineffective if uterine contraction was weak after repeated medication, and vaginal bleeding was not arrested. Total response (W) was computed as in Eq 1.

$$W = \{(A+B)/N\}100 \ldots\ldots\ldots (1)$$

where *W* stands for the total response, *A* stands for the number of significantly effective cases, and *B* stands for the number of effective cases.
The incidence postpartum adverse reactions (nausea, vomiting, chest tightness and facial flushing) in the two groups was monitored and recorded.

Statistical analysis

Measurement data are expressed as mean ± SD. Pairwise comparison was performed using t-test. Qualitative data are expressed as percentage, and statistical analysis was done with Chi-square test. All data were statistically analyzed and processed using SPSS version 21.0. Differences were considered significant at $p < 0.05$.

RESULTS

Postpartum hemorrhage

The amount of postpartum hemorrhage in the two groups showed an increasing trend from the 2nd, 6th, 12th and 24th hour after delivery, and the volume of postpartum hemorrhage in the treatment group was significantly lower than that in the oxytocin group ($p < 0.05$, Table 1).

Height of fundus of uterus

On the 1st, 3rd and 5th days post-delivery, the height of uterine fundus was decreased in the two groups, but was significantly smaller in the treatment group than that in the control group ($p < 0.05$, Table 2).

Hemostatic effect

After treatment, the total response of the treatment group was 97.50 %, while that of the control group was 77.50 %. Thus, the total effectiveness of the treatment group was significantly higher than that of the control group ($p < 0.05$, Table 3).

Adverse reactions

In the control group, there were 2 cases of nausea and vomiting, 3 cases of chest tightness, and 5 cases of facial flusing, accounting for 24 % incidence of adverse reactions (12/41). In the treatment group, nausea and vomiting occurred in one puerpera; chest tightness occurred in 2 cases, while facial flushing was seen in 2 cases. The incidence of adverse reactions in this group was 12 % (6/41). The treatment group had significantly lower total incidence of adverse reactions than the control group ($X^2 = 4.672$, $p < 0.05$).

Table 1: Postpartum hemorrhage in the two groups

Group	Treatment group	Control group	t	*P-value*
2 h after delivery	265.36±16.48	289.45±18.24	10.731	<0.05
6 h after delivery	321.96±29.85	373.81±20.16	15.765	<0.05
12 h after delivery	376.85±37.36	427.44±29.50	11.617	<0.05
24 h after delivery	468.94±39.75	409.49±24.61	13.895	<0.05

Data are mean ± SD, cm^3

Table 2: Height of fundus of uterus after delivery

Group	Treatment group	Control group	t	*P*-value
1st day after delivery	15.35±0.94	16.77±1.36	9.487	<0.05
3rd day after delivery	13.78±0.95	14.62±1.06	6.459	<0.05
5th day after delivery	11.56±0.77	13.17± 0.86	15.196	<0.05

Data are mean ± SD, cm

Table 3: Hemostatic effect ps (%)

Group	Treatment group	Control group	t	*P*-value
Significantly effective	36(72)	25(50)		
Effective	13(26)	14(28)		
Ineffective	1(2)	11(22)		
Total response (effectiveness)	49(98)	39(78)	8.785	<0.05

DISCUSSION

Postpartum hemorrhage often occurs within 24 h after delivery, and the condition develops rapidly. If hemostasis is not treated timely, it will easily lead to dysfunctional coagulation and hysterectomy or pituitary infarction, which endanger the lives of puerperae. Most scholars [11] believe that postpartum hemorrhage is affected by injury to the soft birth canal, uterine atony, dysfunctional coagulation and placental factors, among which uterine atony is the most common factor. Therefore, the key issue in preventing postpartum hemorrhage is how to strengthen the contractibility of the uterus.

Oxytocin is a synthetic polypeptide hormone. It is a classical drug used for preventing and treating postpartum hemorrhage. However, after injection of oxytocin, it is rapidly metabolized, inactivated and eliminated. Thus, the half-life period of oxytocin is short, and the effective concentration can only be maintained by constantly increasing the dose. Moreover, increasing the dose of oxytocin will not only be ineffective at saturating concentrations, but may also increase the incidence of adverse reactions [12].

Carboprost tromethamine, a synthetic derivative of prostaglandin F2, increases the concentration of intracellular calcium, stimulates contraction of fibrous tissue and increases intra-uterine pressure by binding to a calcium receptor. Moreover, it effectively inhibits adenylate cyclase, reduces the generation of adenosine cyclic monophosphate, inhibits the phosphorylation of sarcoplasmic reticulum protein, and indirectly promotes increases in intracellular calcium concentration. In addition, the 15-methyl group in the molecular structure of carboprost tromethamine canfers on it resistance to inactivation by 15-hydroxydehydrogenase, thereby prolonging its half-life period and promoting sustained contraction of uterus [13].
Moreover, it activates blood platelets, shortens platelet aggregation time, increases coagulation, thrombosis and the release of blood coagulation factor; strengthens coagulation reaction, and stops hemorrhage by blocking the blood vessels and exfoliated placental wound. Blood supply to the endometrial basal layer is improved under the effect of carboprost tromethamine, resulting in regulation and repair of the uterus. Compared to oxytocin, carboprost tromethamine has longer action time, and more significant effect in preventing post-caesarean section hemorrhage.

This study demonstrated that the total response of the observation group (98 %) was significantly higher than that of the control group (78 %). This finding suggests that the application of carboprost tromethamine in the treatment of postpartum hemorrhage could enhance hemostatic effect, which is similar to findings of Hu [14].

In addition, the results of this study suggest that the volumes of postpartum hemorrhage at the post-delivery 2^{nd}, 6^{th}, 12^{th} and 24^{th} h in the treatment group were significantly lower than the corresponding volumes in the control group, and the height of uterine fundus gradually decreased on the 1^{st}, 3^{rd} and 5^{th} day after delivery. Therefore, the combination of oxytocin with carboprost tromethamine injection can reduce the amount of postpartum hemorrhage, promote uterine involution, and lower the risk of coagulation dysfunction. It is likely that the combination of carboprost tromethamine and oxytocin improves the excitability of uterine smooth muscle and maintains the contraction of the uterus, thereby achieving hemostatic effect. The enhancement of uterine involution by increasing uterine contraction amplitude, frequency and tension has rarely been reported in previous studies [15,16].

Repeated use of oxytocin easily leads to side effects such as hypotension and water intoxication, resulting in poor tolerance which affects prognosis. The present study has shown that the treatment group had significantly lower incidence of adverse reactions such as nausea, vomiting and chest tightness (24 %) than the control group (12 %). This is basically consistent with a previous report [17]. It might be that the high water-solubility of carboprost tromethamine effectively resists the elimination of drugs by enzymes, thereby enhancing the action time of drugs, and reducing the clinical doses and risk of adverse reactions.

Limitations of the study

The size of samples was small. Moreover, the follow-up time was short, and the long-term prognosis was not further observed. Therefore, the number of cases should be increased in the future study, and a multi-center, long-term observation study is expected for further classification.

CONCLUSION

The results obtained in this study demonstrate that the application of carboprost tromethamine has a significant effect in the treatment and prevention of postpartum hemorrhage after cesarean section. It effectively prevents the occurrence of postpartum hemorrhage in puerperae who underwent cesarean section, reduces the volume of hemorrhage, and enhances uterine involution. Thus, carboprost tromethamine has potential for application in the clinical prevention and treatment of postpartum hemorrhage.

DECLARATIONS

Conflict of interest

No conflict of interest is associated with this work.

Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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