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Original Article

Clinical effect of tranexamic acid combined with carbetocin on reducing postpartum hemorrhage in high-risk pregnant women

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Abstract: Objective: To evaluate the efficacy and safety of tranexamic acid combined with carbetocin for postpartum hemorrhage (PPH) in high-risk parturients. Methods: A total of 200 high-risk parturients were divided into an observation group (tranexamic acid combined with carbetocin, n=118) and a control group (carbetocin alone, n=82). Postpartum blood loss, PPH incidence, blood transfusion rate, hysterectomy rate, hemoglobin level, hemoglobin decrease, length of hospital stay, lochia duration, adverse drug reactions, and postpartum recovery were compared. Results: The observation group had significantly lower 2-h blood loss, 24-h blood loss, PPH incidence, blood transfusion rate, and hysterectomy rate (all P<0.05). Hemoglobin at 24 h was higher and hemoglobin decrease was smaller in the observation group (both P<0.05). No significant differences were observed in length of hospital stay, lochia duration, adverse drug reactions, or postpartum recovery indicators between the two groups (all P>0.05). Conclusion: Tranexamic acid combined with carbetocin effectively reduces postpartum blood loss and the incidence of PPH, lowers the blood transfusion and hysterectomy rates, improves hemoglobin levels, and does not increase adverse drug reactions or affect postpartum recovery, demonstrating good efficacy and safety in high-risk parturients.

Keywords: High-risk pregnant women, postpartum hemorrhage, tranexamic acid, carbetocin, clinical effect

Introduction

Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide, accounting for approximately 25%-30% of all maternal deaths [1, 2]. Refractory bleeding caused by uterine atony and traumatic factors often progresses rapidly and can endanger the lives of parturients within a short time. Therefore, reducing blood loss and the hysterectomy rate and improving the short-term and long-term prognosis of parturients have become the focus of obstetric research [3, 4].

Carbetocin, a long-acting oxytocin analogue, is widely recommended for the prevention and treatment of postpartum uterine atony because of its rapid onset and long-lasting effect. Tranexamic acid, an antifibrinolytic agent, stabilizes blood clots by competitively inhibiting plasminogen activation and has shown favorable outcomes in the treatment of traumatic and obstetric hemorrhage [5, 6]. However, high-quality clinical studies on the synergistic effect and safety of tranexamic acid combined with carbetocin in high-risk parturients are still limited in China. Whether the combined regimen can further enhance hemostatic efficacy without increasing the risk of adverse events such as thromboembolism remains to be determined [7, 8]. In addition, single-center studies have shown that early administration of tranexamic acid for PPH can significantly reduce bleeding-related deaths. However, previous studies have mainly focused on the effect of administration timing on prognosis after hemorrhage. The combination of tranexamic acid with carbetocin as preventive medication in high-risk groups has not been systematically evaluated, especially regarding postpartum recovery indicators and the adverse reaction profile [9].

Based on this, this study retrospectively analyzed the clinical data of parturients with high-risk factors for PPH, and compared tranexamic acid combined with carbetocin with carbetocin

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alone in terms of postpartum blood loss, PPH incidence, blood transfusion rate, hysterectomy rate, hemoglobin level, and adverse drug reactions, aiming to provide a stronger evidence base for the combined preventive strategy for PPH in high-risk parturients.

Materials and methods

Study participants

The clinical data of parturients with high-risk factors for PPH who delivered at Qinghai Red Cross Hospital from January 2023 to December 2025 were retrospectively collected. According to the medication regimen received after delivery, the parturients were divided into an observation group (tranexamic acid combined with carbetocin, n=118) and a control group (carbetocin alone, n=82). This study was approved by the ethics committee of Qinghai Red Cross Hospital.

Sample size determination

This retrospective study included 200 consecutively enrolled high-risk parturients. Post-hoc power analysis was performed to validate the adequacy of the sample size. For the primary outcome (24-h postpartum blood loss), the power of the two independent samples t-test was calculated using the following formula:

$1-\beta=\Phi(|\mu 1-\mu 2|\sigma 1/n1+1/n2-z1-\alpha/2)1-\beta=\Phi(\sigma 1/n1+1/n2|\mu 1-\mu 2|-z1-\alpha/2)$

With the observed data ($\mu 1=312.5$, $\mu 2=425.3$, $\sigma=76.8$, $n1=118$, $n2=82$; two-tailed $\alpha=0.05$), the achieved power was $1-\beta\approx0.999$. For the secondary binary outcome (incidence of PPH), the post-hoc power of the chi-square test was calculated with a non-centrality parameter $\lambda=4.54$, yielding a power of ≈0.85. All primary and secondary outcomes achieved powers ≥0.85, confirming an adequate sample size and reliable statistical conclusions.

Inclusion criteria: ① Age ≥18 years; ② Singleton, full-term (gestational age ≥37 weeks) delivery (vaginal or cesarean section); ③ At least one of the following high-risk factors for PPH: placenta previa, placental abruption, polyhydramnios (AFI ≥25 cm), macrosomia (estimated fetal weight ≥4000 g), history of uterine atony, previous cesarean section, preeclampsia, prenatal hemoglobin <90 g/L, or coagulation dysfunction (platelet count $<100\times10^9$/L or INR >1.5); ④ Voluntary acceptance of the corresponding prophylactic medication regimen after fetal delivery; ⑤ Complete clinical data.

Exclusion criteria: (1) Known severe prenatal coagulation dysfunction or platelet count <50×10/L; (2) Severe hepatic or renal dysfunction (alanine aminotransferase >3× the upper limit of normal, or serum creatinine >177 μmol/L); (3) History of allergy to tranexamic acid or carbetocin; (4) Active thrombotic disease (e.g., deep vein thrombosis, pulmonary embolism) or a history of thrombotic tendency; (5) Severe infection, malignant tumor, or mental disorder that precluded cooperation with data collection; (6) The neonate was admitted to the intensive care unit immediately after delivery.

Treatment methods

After admission, all parturients received standardized perinatal management according to the guidelines for the prevention and treatment of PPH, including labor monitoring, vital signs assessment, and basic supportive care. After delivery of the fetus, the control group received an immediate intravenous injection of 100 μg carbetocin, and the observation group additionally received an intravenous infusion of 1 g tranexamic acid dissolved in 100 mL of 0.9% sodium chloride injection over no less than 10 min. Both groups were routinely monitored for vital signs, uterine contractions, and vaginal bleeding after delivery. When necessary, additional uterotonics were administered, and blood transfusion or escalation of hemostatic interventions was initiated.

Observation indicators

Primary outcomes: (1) Postpartum blood loss: the cumulative blood loss at 2 h and 24 h after delivery, measured by the weighing method and the volumetric method, was compared between the two groups. (2) Incidence of PPH: PPH was defined as cumulative blood loss within 24 h after delivery of ≥500 mL for vaginal delivery or ≥1000 mL for cesarean section. (3) Blood transfusion rate and hysterectomy rate: red blood cell transfusion within 24 h after delivery and performance of hysterectomy were recorded.

Table 1. Comparison of general data between the two groups of parturients

Item	Observation group (n=118)	Control group (n=82)	Statistical value (t/χ^2)	*P* value
Age (years, $\bar{x} \pm s$)	31.2±4.5	30.8±4.7	0.613	0.541
Gestational weeks (weeks, $\bar{x} \pm s$)	38.5±1.6	38.7±1.5	-0.902	0.368
Gravidity (times, $\bar{x} \pm s$)	2.4±1.1	2.3±1.0	0.655	0.514
Parity (times, $\bar{x} \pm s$)	1.2±0.5	1.3±0.6	-1.278	0.203
Mode of delivery [n (%)]			0.108	0.742
Vaginal delivery	72 (61.0)	48 (58.5)		
Cesarean section	46 (39.0)	34 (41.5)		
Neonatal weight (g, $\bar{x} \pm s$)	3356.4±452.7	3402.1±468.3	-0.701	0.484
Types of high risk factors for postpartum hemorrhage [case (%)]			0.256	0.993
Uterine atony	56 (47.5)	39 (47.6)		
Placental factors	31 (26.3)	21 (25.6)		
Birth canal injury	18 (15.3)	13 (15.9)		
Coagulation dysfunction	13 (11.0)	9 (11.0)		
Gestational hypertension [n (%)]	22 (18.6)	15 (18.3)	0.004	0.951
Gestational diabetes mellitus [n (%)]	28 (23.7)	20 (24.4)	0.012	0.913

Note: $\bar{x} \pm s$ means mean ± standard deviation; placental factors include placenta previa, placental abruption, placental adhesion/implantation, etc.

Secondary outcomes: (1) Hemoglobin level and decrease: fasting venous blood was collected before delivery and at 24 h after delivery; the hemoglobin level at 24 h and its decrease from the prenatal baseline were compared between the two groups. (2) Length of hospital stay and lochia duration. (3) Adverse drug reactions: reactions such as nausea, vomiting, dizziness, facial flushing, hypotension, and diarrhea occurring within 24 h after administration were recorded. (4) Postpartum recovery: including the incidence of poor uterine involution at 42 days postpartum (evaluated by B-ultrasound, defined as inadequate descent of the uterine fundus or uterine effusion) and the time to lactation initiation (the first day of postpartum breast fullness with colostrum overflow).

Statistical methods

All statistical analyses were performed using SPSS 26.0. Continuous variables were first tested for normality using the Shapiro-Wilk test. Normally distributed data were expressed as mean ± standard deviation ($\bar{x} \pm s$) and compared between groups using the independent samples t-test; paired comparisons of prenatal and postnatal values within groups were performed using the paired samples t-test. Non-normally distributed data were expressed as median (interquartile range) [M (P25, P75)] and compared using the Mann-Whitney U test. Categorical variables were expressed as case numbers (percentages) [n (%)] and compared using the χ^2 test; Fisher's exact test was applied when the expected frequency in any cell of the 2×2 table was <5. All tests were two-tailed, and P<0.05 was considered statistically significant.

Results

Comparison of baseline data

There were no significant differences between the two groups in age, gestational age, gravidity, parity, mode of delivery, neonatal weight, types of high-risk factors for PPH, gestational hypertension, or gestational diabetes mellitus (all P>0.05; **Table 1**).

Comparison of postpartum blood loss and PPH incidence

Postpartum blood loss at 2 h and 24 h after delivery and the incidence of PPH were significantly lower in the observation group than in the control group (all P<0.05). Specifically, 24-h blood loss was approximately 112.8 mL lower and the PPH incidence was approximately 11.0 percentage points lower in the observation group than in the control group (all P<0.05, **Table 2**).

Table 2. Comparison of postpartum blood loss and PPH incidence between the two groups

Item	Observation group (n=118)	Control group (n=82)	Statistical value (t/χ^2)	*P* value
2-h blood loss (mL)	185.6±42.3	268.4±58.7	-11.372	<0.001
24-h blood loss (mL)	312.5±68.4	425.3±85.6	-10.340	<0.001
Incidence of postpartum hemorrhage [(%)]	10 (8.5)	16 (19.5)	5.117	0.024

Table 3. Comparison of maternal blood transfusion rate and hysterectomy rate between the two groups

Item	Observation group (n=118)	Control group (n=82)	χ^2 value	*P* value
Blood transfusion rate [n (%)]	5 (4.2)	10 (12.2)	4.420	0.036
Hysterectomy rate [n (%)]	1 (0.8)	4 (4.9)	-	0.048

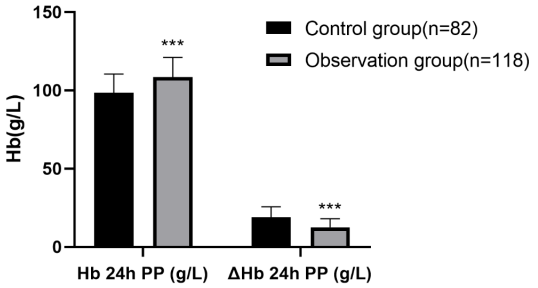

Figure 1. Data are presented as mean ± standard deviation. ***P<0.001 vs. control group (independent samples t-test). The observation group received tranexamic acid combined with carbetocin, while the control group received carbetocin alone. Hb 24h PP, 24-hour postpartum hemoglobin; ΔHb 24h PP, 24-hour postpartum hemoglobin drop value.

Comparison of blood transfusion and hysterectomy rates

Both the blood transfusion and hysterectomy rates were lower in the observation group than in the control group (both P<0.05). The blood transfusion rate was 4.2% (5/118) in the observation group and 12.2% (10/82) in the control group, with a statistically significant difference (χ^2=4.420, P=0.036). The hysterectomy rate was 0.8% (1/118) and 4.9% (4/82), respectively, and the difference was statistically significant (Fisher's exact test, P=0.048; **Table 3**).

Comparison of hemoglobin levels

At 24 h after delivery, the hemoglobin level was significantly higher in the observation group (108.5±12.6 g/L) than in the control group (98.6±11.8 g/L) (t=5.683, P<0.001), and the hemoglobin decrease was significantly smaller in the observation group (12.5±5.6 g/L) than in the control group (18.9±6.8 g/L) (t=-7.236, P<0.001, **Figure 1**).

Comparison of length of hospital stay and lochia duration

The length of hospital stay was (5.2±1.3) d in the observation group and (5.5±1.4) d in the control group, with no significant difference (t=-1.560, P=0.121). Lochia duration was (21.5±4.2) d and (22.3±4.5) d, respectively, also without a significant difference (t=-1.291, P=0.198). These results suggest that the combination therapy does not prolong hospital stay or lochia duration (**Table 4**).

Comparison of adverse drug reactions

Adverse drug reactions occurred in 7 cases (5.9%, 7/118) in the observation group and in 4 cases (4.9%, 4/82) in the control group, with no significant difference in the total incidence (χ^2=0.102, P=0.750). The main adverse reactions were nausea, vomiting, diarrhea, and dizziness. All symptoms were mild and resolved spontaneously or with symptomatic supportive treatment, and no serious adverse drug reactions occurred. These findings indicate that tranexamic acid combined with carbetocin does not increase the risk of additional adverse drug reactions (**Table 5**).

Comparison of postpartum recovery

The incidence of poor uterine involution was 3.4% (4/118) in the observation group and 3.7% (3/82) in the control group, with no signifi-

Table 4. Comparison of length of hospital stay and lochia duration between the two groups

Item	Observation group (n=118)	Control group (n=82)	t value	*P* value
Length of hospital stay (d)	5.2±1.3	5.5±1.4	-1.560	0.121
Lochia duration (d)	21.5±4.2	22.3±4.5	-1.291	0.198

Table 5. Comparison of adverse drug reactions between the two groups

Types of adverse reactions	Observation group (n=118)	Control group (n=82)	χ^2 value	*P* value
Nausea [n (%)]	3 (2.5)	2 (2.4)		
Vomiting [n (%)]	2 (1.7)	1 (1.2)		
Diarrhea [n (%)]	1 (0.8)	1 (1.2)		
Dizziness [n (%)]	1 (0.8)	0 (0)		
Total [n (%)]	7 (5.9)	4 (4.9)	0.102	0.750

cant difference (continuity-corrected χ^2=0.010, P=0.922). Uterine fundus descent at 24 h after delivery was (2.1±0.6) cm and (2.0±0.7) cm, respectively (t=1.081, P=0.281). Time to lactation initiation was (23.5±6.8) h in the observation group and (24.2±7.2) h in the control group (t=-0.711, P=0.478). At the 42-day follow-up, the rate of good uterine involution was 97.5% (115/118) in the observation group and 97.6% (80/82) in the control group, with no significant difference (Fisher's exact test, P=1.000). These results indicate that adding tranexamic acid to carbetocin does not affect postpartum physiological recovery, including uterine involution and lactation initiation (**Table 6**).

Subgroup analysis of different delivery modes

To further assess the consistency of the hemostatic effect across delivery modes, parturients were divided into vaginal delivery and cesarean section subgroups, and 24-h postpartum blood loss was compared between the two treatment groups within each subgroup. In the vaginal delivery subgroup, 24-h blood loss was significantly lower in the observation group (285.6± 58.3 mL) than in the control group (396.4±72.5 mL) (t=-9.142, P<0.001). In the cesarean section subgroup, the observation group also had significantly lower blood loss (354.7±65.2 mL) than the control group (466.1±78.4 mL) (t=-6.895, P<0.001). These findings indicate that the hemostatic effect of the combination therapy is consistent across delivery modes (**Table 7**).

Logistic regression analysis of influencing factors of postpartum hemorrhage

Multivariate logistic regression (Enter method) was performed with PPH as the dependent variable. Variables with P<0.10 in univariate analysis (combined medication, mode of delivery, placental factors) and clinically recognized confounding factors (age, gravidity, gestational hypertension, gestational diabetes mellitus) were entered as independent variables. Combined medication was an independent protective factor for PPH (OR= 0.276, 95% CI: 0.114-0.669, P=0.004), whereas cesarean section (OR= 1.844, 95% CI: 1.051-3.235, P=0.033) and placental factors (OR=2.677, 95% CI: 1.358-5.276, P=0.004) were independent risk factors for PPH (**Table 8**).

Discussion

PPH remains the leading cause of maternal death worldwide [10-12], and uterine atony accounts for the highest proportion of PPH causes (approximately 70%-80%) [13, 14]. Parturients with high-risk factors face a significantly higher risk of hemorrhage than ordinary women. Strengthening hemostasis while effectively promoting uterine contraction is therefore a key challenge in obstetric practice. In the present study, tranexamic acid combined with carbetocin significantly reduced postpartum blood loss and the incidence of PPH compared with carbetocin alone in high-risk parturients [15].

The potential mechanisms are as follows. Carbetocin binds to oxytocin receptors on uterine smooth muscle cells, activates the phosphatidylinositol signaling pathway, and promotes intracellular calcium release, thereby inducing strong rhythmic uterine contractions and mechanically compressing the uterine spiral arteries to achieve hemostasis [16]. Tranexamic acid competitively occupies the lysine-binding site of plasminogen, preventing its binding to fibrin and inhibiting plasmin formation, which reduces fibrin degradation and sta-

Table 6. Comparison of postpartum recovery between the two groups

Item	Observation group (n=118)	Control group (n=82)	Statistic	*P* value
Uterine fundus descent at 24 h postpartum (cm)	2.1±0.6	2.0±0.7	1.081	0.281
Lactation start time (h)	23.5±6.8	24.2±7.2	-0.711	0.478
Poor uterine involution [n (%)]	4 (3.4)	3 (3.7)	0.010	0.922
Good uterine involution at 42 d postpartum [n (%)]	115 (97.5)	80 (97.6)	-	1.000*

Note: *Fisher's exact test was applied for "good uterine involution at 42 d postpartum" due to the presence of cells with extremely low expected frequencies in the 2×2 table; accordingly, only *P* value is reported.

Table 7. Comparison of 24-h postpartum blood loss between the two groups by delivery mode (mL)

Mode of delivery	Observation group (n=118)	Control group (n=82)	t value	*P* value
Vaginal delivery	285.6±58.3	396.4±72.5	-9.142	<0.001
Cesarean section	354.7±65.2	466.1±78.4	-6.895	<0.001

bilizes formed blood clots [17, 18]. In addition, the significantly lower blood transfusion and hysterectomy rates in the observation group suggest that the combination therapy not only reduced blood loss but also improved clinical outcomes, consistent with previous studies [19].

Postpartum hemoglobin level has been confirmed as an objective biochemical indicator of postpartum blood loss [20]. In this study, the observation group had a significantly higher hemoglobin level and a significantly smaller hemoglobin decrease at 24 h after delivery than the control group. However, the length of hospital stay and lochia duration did not differ significantly between the two groups, indicating that the combination therapy reduced postpartum blood loss but did not shorten hospital stay or lochia duration. Hospital stay is mainly determined by clinical pathways and routine management processes rather than by blood loss alone, whereas lochia duration is influenced by individual differences, the rate of uterine involution, postpartum activity, and lactation; a modest reduction in blood loss may therefore not affect lochia duration, consistent with previous findings [21].

Drug safety is a prerequisite for clinical application, particularly for tranexamic acid, which carries a theoretical risk of thrombosis as an antifibrinolytic agent [22]. In this study, the total incidence of adverse drug reactions did not differ significantly between the two groups. At the standard dose (1 g intravenous infusion), the combination regimen did not increase the risk of additional adverse reactions and showed good short-term safety, consistent with previous safety reports of tranexamic acid in the prevention and treatment of PPH [23]. Postpartum recovery is another important indicator of whether the combination therapy interferes with maternal physiological recovery. The incidence of poor uterine involution, uterine fundus descent at 24 h after delivery, time to lactation initiation, and the rate of good uterine involution at 42 days postpartum did not differ significantly between the two groups. These results indicate that the antifibrinolytic effect of tranexamic acid is highly targeted and does not interfere with the normal contraction rhythm of uterine smooth muscle, endometrial repair, or the regulation of the pituitary-lactation axis, consistent with previous reports [24, 25].

We further analyzed the consistency of the treatment effect across clinical subgroups. In both the vaginal delivery and cesarean section subgroups, 24-h blood loss was significantly lower in the observation group than in the control group, indicating that the hemostatic effect of the combination therapy was consistent across delivery modes. Blood loss was higher in the cesarean section subgroup than in the vaginal delivery subgroup, consistent with the larger surgical wound and the need for additional hemostasis at the uterine incision [26]. After adjusting for potential confounders (age, gravidity, mode of delivery, placental factors, gestational hypertension, and gestational diabetes mellitus), multivariate logistic regression showed that the combination therapy was an independent protective factor for PPH, consistent with previous reports [27]. Placental fac-

Table 8. Logistic regression analysis of influencing factors of postpartum hemorrhage

Variable	β	SE	Wald χ^2	OR	95% CI	P
Combination therapy (observation vs. control)	-1.286	0.452	8.104	0.276	0.114-0.669	0.004
Age (≥35 vs. <35 years)	0.418	0.315	1.762	1.519	0.819-2.816	0.184
Gravidity (≥3 vs. <3)	0.325	0.298	1.189	1.384	0.772-2.482	0.276
Cesarean section (vs. vaginal delivery)	0.612	0.287	4.548	1.844	1.051-3.235	0.033
Placental factors (yes vs. no)	0.985	0.346	8.104	2.677	1.358-5.276	0.004
Gestational hypertension (yes vs. no)	0.453	0.372	1.482	1.573	0.758-3.261	0.224
Gestational diabetes mellitus (yes vs. no)	0.287	0.341	0.708	1.332	0.682-2.601	0.400

tors had the largest OR, suggesting the strongest association with bleeding risk and supporting previous conclusions [28].

This study has several limitations. First, as a retrospective single-center study, it is subject to selection and information bias, and the generalizability of the findings requires further validation. Second, the sample size was relatively limited (200 cases), which precluded detailed stratified analyses (e.g., by type of high-risk factors, age, or complications) and may have reduced the precision of the results; larger multicenter prospective randomized controlled trials are needed. Third, dynamic changes in coagulation indicators (e.g., fibrinogen, D-dimer, platelet count) were not measured, so the specific antifibrinolytic mechanism of tranexamic acid could not be explored in depth; future studies should include these laboratory indicators to further clarify the hemostatic pathway. Fourth, only short-term efficacy and safety during hospitalization and up to 42 days postpartum were assessed, without long-term follow-up (e.g., 6 months or 1 year after delivery); therefore, the effects of the combination therapy on long-term anemia, uterine recovery, and subsequent pregnancy outcomes remain unclear. In addition, future prospective studies should adopt a standardized perinatal risk assessment tool (e.g., the ACOG hemorrhage risk calculator) to standardize the indications for combination therapy and further strengthen the evidence base.

In summary, adding tranexamic acid to carbetocin significantly reduced postpartum blood loss, the incidence of PPH, the blood transfusion rate, and the hysterectomy rate, and improved postpartum hemoglobin levels in parturients with high-risk factors for PPH, without increasing adverse drug reactions or affecting postpartum physiological recovery such as uterine involution and lactation initiation. The hemostatic effect was consistent across delivery modes. This combination regimen is therefore worthy of clinical recommendation.

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Disclosure of conflict of interest

None.

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