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POSTPARTUM HEMORRHAGE AND TRANEXAMIC ACID: CURRENT EVIDENCE

Abstract

Postpartum hemorrhage (PPH) remains one of the leading causes of maternal mortality and disability worldwide. According to national clinical guidelines, PPH is defined as blood loss of 500 mL or more following childbirth or any amount of blood loss resulting in hemodynamic instability. The primary etiological factor is uterine atony, accounting for approximately 70% of cases, along with other components of the "4Ts" concept (Tissue, Trauma, Thrombin). Tranexamic acid is a potent synthetic antifibrinolytic agent and a lysine analogue that stabilizes the fibrin clot by competitively inhibiting plasminogen activation and directly suppressing plasmin activity. The drug rapidly reaches therapeutic plasma concentrations, has a relatively short elimination half-life, and demonstrates a favorable safety profile.

The aim of the study was to substantiate the clinical rationale and pathogenetic effectiveness of tranexamic acid in the comprehensive treatment and prevention of postpartum hemorrhage in order to reduce blood loss, prevent coagulopathy, and decrease the need for blood transfusions.

The article analyzes data from large randomized controlled trials, systematic reviews, and meta-analyses. Timely administration of tranexamic acid within the

first three hours after the onset of bleeding significantly reduces hemorrhage-related mortality, the risk of life-threatening complications, the volume of blood loss (by 32–92 mL depending on the mode of delivery), and the need for blood transfusions (by 38–39%). Prophylactic use in high-risk women reduces the incidence of hemorrhagic complications. The greatest therapeutic benefit is achieved when the drug is administered within the so-called "golden hour."

The safety profile of tranexamic acid is favorable, with the incidence of thromboembolic events not exceeding that observed in placebo groups. The most commonly reported adverse effects are nausea and vomiting.

Current evidence confirms the high efficacy and safety of tranexamic acid, supporting its widespread incorporation into modern protocols for the management of obstetric hemorrhage and the improvement of maternal outcomes.

Keywords: postpartum hemorrhage, tranexamic acid, antifibrinolytics, maternal mortality, hemorrhage prevention, hemostasis, obstetric hemorrhage.

Problem statement. Postpartum hemorrhage (PPH) remains one of the most pressing challenges in modern obstetrics, representing a leading cause of maternal mortality and long-term morbidity worldwide. According to Order No. 205 of the Ministry of Health of Ukraine dated March 24, 2014, postpartum hemorrhage is defined as blood loss of 500 mL or more following the completion of the second stage of labor or any amount of blood loss resulting in hemodynamic instability. Clinical classification distinguishes between primary (early) PPH, occurring within the first 24 hours after delivery, and secondary (late) PPH, which develops within six weeks postpartum [5].

The strategy for emergency management is based on the rapid identification of the underlying cause according to the internationally recognized “4Ts” concept. The most common etiological factor is Tone (uterine atony), which accounts for approximately 70% of cases of early PPH and is characterized by the inability of

the myometrium to contract effectively. Other causes include retained placental tissue (Tissue) in about 10% of cases, trauma to the birth canal (Trauma) in approximately 20%, and coagulation disorders (Thrombin) in about 1% [5]. Although coagulation abnormalities represent the smallest proportion of primary causes, they frequently play a crucial role in the development of massive hemorrhage through the onset of disseminated intravascular coagulation (DIC) and consumptive coagulopathy [5].

The search for effective hemostatic strategies remains highly relevant because successful control of postpartum hemorrhage largely depends on the timely initiation of pathogenetically targeted therapy. In this context, the use of tranexamic acid has attracted considerable attention. As a potent antifibrinolytic agent, tranexamic acid promotes stabilization of the fibrin clot, which is critically important regardless of the underlying “4T” mechanism, since severe blood loss inevitably triggers excessive fibrinolytic activity. The incorporation of tranexamic acid into treatment algorithms within the “golden hour” not only minimizes blood loss but also substantially reduces the need for blood transfusions, fully aligning with the principles of safety and effectiveness established in national clinical guidelines [5].

Analysis of recent research and publications. The current evidence supporting the use of tranexamic acid in postpartum hemorrhage is based on large randomized controlled trials (RCTs) and meta-analyses.

The landmark WOMAN trial (2017), which included more than 20,000 women with clinically diagnosed postpartum hemorrhage, demonstrated that early administration of 1 g of intravenous tranexamic acid, with the option of a second dose after 30 minutes if bleeding persisted, reduced death due to hemorrhage by 31% (RR 0.69; 95% CI 0.52–0.91) when administered within the first three hours after the onset of bleeding. The beneficial effect was particularly pronounced in

women with severe blood loss. In addition, the rates of hysterectomy and laparotomy were reduced by approximately one-third [7].

The TRAAP trial (2018) evaluated the prophylactic administration of 1 g of tranexamic acid following vaginal delivery in 3,891 women. Although no significant reduction in blood loss exceeding 500 mL was observed, the incidence of hemorrhagic complications decreased by 32%, and the need for additional uterotonic agents was lower compared with the control group [6].

The large international WOMAN-2 trial (2024), conducted among women with anemia, did not demonstrate a significant preventive effect of tranexamic acid when administered after childbirth. These findings highlight the importance of earlier administration and more appropriate patient selection for prophylactic treatment [13].

Recent meta-analyses published between 2023 and 2025 (Al-Dardery, Daghmouri, Rohwer, and colleagues) have consistently confirmed a reduction in perioperative blood loss during both cesarean delivery and vaginal birth, particularly among women at high risk of hemorrhage [14–16].

A systematic review by Ali et al. (2025) further demonstrated that tranexamic acid effectively reduces postpartum blood loss and the need for blood transfusions following both vaginal and operative deliveries [3].

Similarly, a Cochrane-style systematic review on postpartum hemorrhage prevention conducted by Rohwer et al. (2025) confirmed the effectiveness of tranexamic acid, particularly among women with an increased risk of hemorrhagic complications [16].

Collectively, these findings support the recommendations of the World Health Organization and national clinical guidelines advocating the routine use of tranexamic acid in the management of postpartum hemorrhage within the "golden hour" and consideration of its prophylactic administration in selected high-risk populations.

Purpose of the article. To substantiate the clinical rationale and pathogenetic effectiveness of tranexamic acid in the comprehensive management of postpartum hemorrhage in order to reduce blood loss, prevent the development of coagulopathy, and decrease the need for blood transfusions in accordance with current standards of obstetric care.

Presentation of the main material of the study. Analysis of the pharmacological properties of tranexamic acid (TXA) confirms its status as one of the most potent antifibrinolytic agents currently available. As a synthetic analogue of the amino acid lysine, TXA exhibits a binding affinity for plasminogen that is 6–10 times greater than that of its predecessor, ε-aminocaproic acid, while its individual antiplasmin activity is approximately 27 times higher. Following intravenous administration, TXA rapidly achieves therapeutic plasma concentrations and has a relatively short elimination half-life of approximately 3 hours, allowing precise control of hemostasis in acute clinical settings. The drug is primarily excreted unchanged by the kidneys within 6–8 hours [1, 4].

The mechanism of action of TXA is based on the competitive inhibition of plasminogen activation. By blocking lysine-binding sites on fibrin molecules, TXA prevents the binding of plasminogen to fibrin and its subsequent conversion into the active enzyme plasmin. At higher doses, the drug is also capable of directly inhibiting plasmin activity. This dual mechanism ensures effective stabilization of the fibrin clot and protects it from degradation mediated by tissue plasminogen activator (tPA). In obstetric practice, this property is particularly important because it counteracts hyperfibrinolysis, a key pathogenetic mechanism underlying massive hemorrhage. This effect is supported by evidence demonstrating reduced D-dimer levels in women receiving TXA therapy [1, 4].

Additional systemic effects of tranexamic acid include preservation of platelet function through inhibition of plasmin-induced platelet aggregation. Furthermore, TXA has been shown to modulate the immune response by reducing

the production of pro-inflammatory cytokines, particularly interleukin-6 (IL-6). This effect may be of considerable clinical importance in critical obstetric conditions, where massive blood loss is frequently accompanied by a systemic inflammatory response and the development of organ dysfunction [1, 2].

The clinical efficacy of TXA in reducing maternal mortality has been convincingly demonstrated in the landmark WOMAN trial. Administration of the drug within the first three hours after the diagnosis of postpartum hemorrhage was associated with a 33% reduction in death due to bleeding. Notably, TXA demonstrates a unique degree of versatility, as its hemostatic effect is independent of the underlying cause of hemorrhage, whether uterine atony, birth canal trauma, or coagulation disorders. This distinguishes TXA from uterotonic agents, whose effects are limited to specific mechanisms of bleeding. These findings were further supported by a 2024 meta-analysis involving 54,404 women, which demonstrated a 23% reduction in the risk of life-threatening hemorrhage [2, 3, 7].

Time to treatment, often referred to as the “golden hour” principle, is a critical determinant of patient survival. Mathematical modeling has shown that every 15-minute delay in TXA administration reduces its survival benefit by approximately 10%. Administration later than three hours after the onset of bleeding not only diminishes its effectiveness but may also be associated with an increased risk of disseminated intravascular coagulation (DIC). Consequently, contemporary research is increasingly focused on preventive strategies. Recent studies published in 2024 indicate that prophylactic administration of TXA to women at high risk of postpartum hemorrhage, even before the diagnosis is formally established, is both safe and clinically justified [3, 4].

Particular emphasis in recent studies has been placed on the safety profile of tranexamic acid. The most up-to-date meta-analyses published in 2024 have largely refuted concerns regarding an increased risk of thromboembolic complications associated with its use. The incidence of thrombotic events in the

TXA group was 0.2% (50 cases among 26,571 women), which was comparable to that observed in placebo groups. Such findings support the favorable safety profile of TXA and allow its use even in patients with complicated medical histories, where the risk of death from hemorrhage substantially outweighs the potential risk of coagulation-related adverse events. Furthermore, TXA has been shown to reduce the need for blood transfusions by approximately 38–39%, thereby minimizing the risks associated with transfusion-transmitted infections and other transfusion-related complications [1, 3].

In obstetric practice, TXA has demonstrated a statistically significant ability to reduce blood loss during both vaginal delivery and cesarean section. Average reductions in blood loss of approximately 92 mL during vaginal birth and 32.5 mL during cesarean delivery have been reported. In addition, the efficacy of TXA has been well established in the management of menorrhagia, where reductions in menstrual blood loss ranging from 34% to 59% have been observed. By preserving maternal blood volume, TXA contributes to the prevention of severe iron-deficiency anemia, facilitates postpartum recovery, and improves overall maternal well-being [1, 2].

The TRAAP trial, a multicenter double-blind randomized controlled study, was designed to evaluate the prophylactic efficacy of tranexamic acid in preventing postpartum hemorrhage following vaginal delivery. Analysis of data from 3,891 participants demonstrated that administration of 1 g of TXA was associated with a 32% reduction in postpartum hemorrhagic complications and a lower need for additional uterotonic therapy. However, no statistically significant difference was observed in the incidence of blood loss exceeding 500 mL. It is important to note that the study included a substantial proportion of women at increased risk of postpartum hemorrhage. One limitation of the study was the variability in the timing of hemoglobin and hematocrit measurements, as sample collection procedures were not standardized [6].

The multicenter open-label randomized controlled EXADELI trial demonstrated that early administration of high-dose tranexamic acid (4 g) in patients with postoperative bleeding produced a clinically significant hemostatic effect [8]. In patients with traumatic injuries accompanied by hemodynamic instability, an additional 3 g dose administered within the first hour after injury was associated with reduced 30-day mortality compared with placebo. Nevertheless, the use of high-dose TXA was linked to an increased risk of adverse events, including seizures, venous thromboembolic complications, and potential renal impairment. In contrast, prehospital administration of TXA at doses of 1 g or 2 g did not demonstrate clear clinical benefits [9].

Pregnancy is characterized by physiological activation of the hemostatic system and the development of a prothrombotic state, which increases the risk of venous thromboembolism. Consequently, concerns have been raised regarding the possibility that TXA administration for the prevention and treatment of postpartum hemorrhage might further increase thrombotic risk. However, the majority of contemporary studies have failed to demonstrate a significant association between TXA use and an increased incidence of venous thromboembolic events [6, 7, 10].

At the same time, findings from a recent randomized controlled trial indicated a slightly higher incidence of thromboembolic events during the first three months postpartum among women receiving tranexamic acid compared with those receiving placebo (0.4% vs. 0.1%; adjusted hazard ratio = 4.01; p = 0.08). The investigators suggested that this observation may be related to the use of higher doses and prolonged treatment duration. Therefore, when prescribing TXA, clinicians should carefully consider each patient's individual thrombotic risk profile and exercise caution, particularly in women with pre-existing risk factors for thromboembolic complications [11].

Among the adverse events associated with tranexamic acid administration, nausea and vomiting were reported most frequently. An increase in drug dosage was associated with a higher incidence of gastrointestinal side effects, and isolated cases of seizures have also been documented. According to a meta-analysis, symptoms of nausea and vomiting occurred more often in patients receiving tranexamic acid than in those assigned to the control group. However, no significant differences were observed between groups regarding the incidence of dizziness or photopsia [12].

The thermostability of tranexamic acid and its long shelf life make it particularly valuable in low-resource settings and in emergency prehospital care. The World Health Organization recognizes TXA as a life-saving medication, as its timely administration can prevent the need for radical surgical interventions, including hysterectomy and repeat laparotomy [4].

Conclusions. Tranexamic acid occupies an important place in contemporary strategies for the prevention and treatment of postpartum hemorrhage due to its potent antifibrinolytic activity, well-established clinical efficacy, and favorable safety profile. Timely administration of the drug contributes to a reduction in blood loss, decreases the need for blood transfusion therapy, and improves maternal outcomes. Current evidence supports the incorporation of tranexamic acid into comprehensive algorithms for the management of obstetric hemorrhage, particularly in women at high risk of hemorrhagic complications. Future research should focus on optimizing dosing regimens, refining indications for prophylactic administration, and evaluating long-term clinical outcomes associated with its use.

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