The role of tranexamic acid in reducing postpartum hemorrhage in high-risk pregnancies

Postpartum hemorrhage (PPH) continues to be a major cause of maternal death and illness worldwide, approximately 14 million women experience PPH each year, leading to an estimated 70,000 maternal deaths.[1] This condition, refers to a total blood loss of 1000 mL or more, along with symptoms or signs of hypovolemia, irrespective of the delivery method. Primary PPH takes place within 24 hours after childbirth, whereas secondary PPH can arise up to 12 weeks postpartum.[2] It can result in severe complications and even death if not promptly managed. Tranexamic acid (TXA), an antifibrinolytic drug, has shown effectiveness in reducing blood loss in trauma cases, and recent research indicates its potential in managing PPH, particularly in high-risk populations. Through this letter, we aim to emphasize the efficacy and safety of TXA in preventing and managing PPH, a leading cause of maternal mortality worldwide.

Studies have shown that TXA can play a significant role in both the prevention and treatment of PPH. Administered either prophylactically before delivery or within 3 hours postpartum, TXA works by inhibiting fibrinolysis, thereby stabilizing blood clots and reducing further bleeding.[3,4] The World Health Organization has included TXA in its PPH treatment guidelines, recognizing its life-saving potential.[5]

In a multi-center randomized controlled trial conducted at the Institute of Maternal and Child Health in Lagos, Nigeria, TXA administration in high-risk cesarean sections significantly lowered the prevalence of PPH.[3] The placebo group experienced four times the incidence of PPH compared to the TXA group, emphasizing the drug's efficacy in reducing severe blood loss during cesarean deliveries.

Numerous trials have underscored TXA's impact on blood loss. One such study focused on cesarean deliveries at the Karnatak Lingayat Education Society Medical Research Centre in India and included 212 women randomized to receive either TXA or a placebo.[6] The results were striking: The TXA group had a mean blood loss of about 400.9 mL, significantly lower than the 597.9 mL observed in the placebo group ($P<.001$). The study also reported gravimetric measurement, showing TXA reduced blood loss to 379.2 mL compared to 431.1 mL for the placebo group.

In a broader meta-analysis encompassing 59 randomized controlled trials with 18,649 participants, TXA's role in PPH prevention was confirmed.[7] The analysis found that TXA significantly reduced blood loss in cesarean (MD=−2.11 mL, $P<.001$) and vaginal births (MD=−0.89 mL, $P<.02$). However, TXA increased nausea or vomiting in cesarean (OR=1.36, $P=.01$) and vaginal deliveries (OR=2.36, $P=.02$), with no significant hemoglobin changes in vaginal births. Study bias risk ranged from low to high. This statistical reduction reflects TXA's potential as a preventive measure for women at high risk of PPH.

In addition to blood loss, secondary outcomes such as changes in hemoglobin and hematocrit levels were measured in these studies. At the Karnataka trial, women receiving TXA showed a decrease in hemoglobin levels of just 1.04 g/dL compared to 1.61 in the placebo group.[6] Similarly, hematocrit levels dropped by only 3.2% in the TXA group, as opposed to a 4.95% decrease in the placebo group. These differences were statistically significant, underscoring the effectiveness of TXA in stabilizing blood values following childbirth.

While TXA is generally well-tolerated, some mild adverse effects have been reported. The meta-analysis found a slight increase in the risk of mild adverse reactions, with an RR of 1.55 ($P=.007$) for events like nausea or vomiting.[7] TXA, when used alongside prophylactic uterotonic agents during cesarean delivery, effectively reduced the risk of significant blood loss (>1000 mL) or red-cell transfusion within 2 days. However, this benefit did not extend to reducing secondary clinical outcomes associated with hemorrhage, highlighting the need for a balanced assessment of its overall efficacy. The statistical significance of TXA's reduction in postpartum blood loss does not equate to clinical significance, as key outcomes like mortality, transfusion, and severe maternal morbidity remain unaffected. Moreover, the TRAPP study reports a fourfold increase in thromboembolic events with TXA use, emphasizing the importance of evaluating both benefits and risks in clinical contexts.[8]

The economic aspect of TXA in obstetrics is equally promising. A cost-effectiveness analysis from the TRAAP2 trial, conducted in France, found that using TXA during cesarean sections resulted in a modest increase in hospital costs (€3321 vs. €3260) but yielded a high probability of cost-effectiveness, particularly in preventing PPH complications.[9] With an incremental cost-effectiveness ratio of €762 per additional cesarean delivery without complication, TXA is positioned as an economically viable intervention for reducing PPH risks.

Despite promising results, some limitations warrant consideration. First, studies in low-resource settings highlighted challenges in adopting TXA as a standard prophylactic measure due to limited healthcare infrastructure and lack of widespread accessibility.[10] Additionally, while TXA's efficacy is well-documented for both trauma-related and surgical hemorrhage, optimal dosing protocols for PPH prevention require further refinement.

Ongoing trials like the World Maternal Antifibrinolytic-2 study continue to explore the utility of TXA in high-risk populations, such as women with anemia, who are more susceptible to severe PPH.[11] Preliminary data suggest that lower red

blood cell counts enhance TXA's antifibrinolytic effects due to its impact on fibrin structure and clot stability, further supporting its role in mitigating PPH risks in vulnerable groups.

The body of evidence supporting TXA's role in PPH prevention and treatment is both extensive and compelling. Its effectiveness in reducing maternal blood loss, stabilizing hemoglobin levels, and preventing severe postpartum complications make it a critical tool in maternal healthcare. For high-risk populations, including women with anemia and those undergoing cesarean sections, TXA offers a relatively safe and cost-effective solution to curb the high morbidity and mortality associated with PPH. As more studies continue to refine its clinical protocols, TXA is poised to become an indispensable part of PPH management strategies worldwide.

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