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The Evolving Role of Tranexamic Acid in the Prevention of Postpartum Hemorrhage Following Vaginal Delivery: An Evidence-Based Narrative Review

1. Sana Ahmad, Obstetrics and Gynaecology Department, Integral Institute of Medical Sciences and Research, Lucknow.
2. Shweta Singh, Obstetrics and Gynaecology Department, Integral Institute of Medical Sciences and Research, Lucknow.
3. Suraiya Khanam, Obstetrics and Gynaecology Department, Integral Institute of Medical Sciences and Research, Lucknow.
Corresponding author- Sana Ahmad*

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KEYWORDS

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ABSTRACT:

Postpartum hemorrhage (PPH) remains a leading cause of maternal morbidity and mortality worldwide, particularly in lowand middleincome countries where baseline anaemia and delayed access to advanced care amplify its impact. Although active management of the third stage of labor has reduced the incidence of severe bleeding, postpartum hemorrhage continues to occur unpredictably even after uncomplicated vaginal delivery. While tranexamic acid has an established role in the treatment of established PPH, its potential role as a prophylactic agent to prevent postpartum hemorrhage has gained increasing attention in recent years.

This narrative review focuses on the evolving evidence for prophylactic tranexamic acid administration following vaginal delivery, an area where data remains limited and at times, conflicting. The physiological rationale for antifibrinolytic use in the immediate postpartum period is examined, followed by a critical synthesis of randomized controlled trials and meta-analyses evaluating tranexamic acid for primary prevention of postpartum hemorrhage. Particular emphasis is placed on differences in study populations, timing of administration, baseline anaemia status, and outcome definitions, which may explain variability in trial results.

The review also discusses safety considerations, real-world applicability in resource-constrained settings, and current positions of international guidelines regarding prophylactic use. By highlighting existing evidence gaps and ongoing controversies, this review aims to clarify the potential role of tranexamic acid as an adjunct to standard preventive strategies and to identify priorities for future research before routine prophylactic use can be widely recommended.

1.Introduction

Postpartum hemorrhage (PPH) remains the leading direct cause of maternal mortality worldwide, accounting for approximately one-quarter of maternal deaths, with a disproportionately higher burden in low and middle-income countries (LMICs)[1]. In India, hemorrhage continues to be the most common cause of maternal mortality despite improvements in antenatal care, intrapartum surveillance, and institutional deliveries [2]. Importantly, postpartum hemorrhage frequently occurs even after apparently uncomplicated vaginal deliveries, underscoring its unpredictable nature[3].

Active management of the third stage of labor (AMTSL), including prophylactic uterotonic administration, has significantly reduced the incidence of severe postpartum hemorrhage. However, uterotonics primarily address uterine atony and do not influence the systemic coagulation and fibrinolytic changes that accompany placental separation. Persistent bleeding despite adequate uterine tone suggests that postpartum hemorrhage is not solely a mechanical problem, but rather a complex hemostatic phenomenon involving fibrinolysis and clot instability[4–6].

Tranexamic acid (TXA), a synthetic antifibrinolytic agent, has a well-established role in reducing bleeding

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in trauma and surgical settings[7]. Its effectiveness in reducing death due to bleeding in established postpartum hemorrhage has been conclusively demonstrated, leading to strong recommendations for therapeutic use. These findings have generated increasing interest in the prophylactic use of tranexamic acid to prevent postpartum hemorrhage, particularly following vaginal delivery[8,9].

Unlike therapeutic use, prophylactic administration of tranexamic acid aims to attenuate the physiological postpartum fibrinolytic surge before clinically significant bleeding develops, thereby stabilizing early clot formation[10–14]. Several randomized trials have explored this approach following vaginal delivery, including large multicenter studies [11,15]. However, trial results have been inconsistent, and routine prophylactic use remains controversial [9,10,12]. Differences in baseline maternal risk, prevalence of anaemia, timing of administration, and outcome definitions further complicate interpretation of the available evidence[10–12].

Given the evolving nature of evidence and the absence of consensus regarding routine prophylactic use, a focused synthesis of current literature is warranted. This narrative review critically examines the physiological rationale, clinical trial evidence, safety profile, and guideline positions regarding prophylactic tranexamic acid use following vaginal delivery, with particular emphasis on relevance to low resource settings.

2.Methodology

2.1Review Design

This article was conducted as a narrative review to evaluate the evolving evidence for the prophylactic use of tranexamic acid in the prevention of postpartum hemorrhage following vaginal delivery. A narrative approach was selected to allow critical interpretation of heterogeneous clinical data, including randomized trials, meta-analyses, and guideline statements, rather than quantitative synthesis. This approach was considered appropriate given the variability in study populations, timing of intervention, outcome definitions, and baseline risk profiles across available studies.

2.2Search Strategy

A comprehensive literature search was undertaken using electronic databases including PubMed, Scopus, Web of Science, Cochrane Library, and Google Scholar. Publications from January 2015 to June 2025 were reviewed to ensure inclusion of contemporary evidence relevant to prophylactic tranexamic acid use in obstetric practice. Search terms were used in various combinations and included: “tranexamic acid,” “postpartum hemorrhage prevention,” “prophylaxis,” “vaginal delivery,” “third stage of labor,” and “antifibrinolytic therapy.” In addition, reference lists of key articles and reviews were manually screened to identify further relevant studies.

2.3InclusionCriteria

Studies were eligible for inclusion if they evaluated prophylactic administration of tranexamic acid during or immediately after vaginal delivery, including randomized controlled trials, high-quality observational studies, and systematic reviews addressing prevention of postpartum hemorrhage. International and national clinical guidelines discussing prophylactic antifibrinolytic use were also considered.

2.4Exclusion Criteria

Studies were excluded if they focused exclusively on therapeutic use in established postpartum hemorrhage, were limited to cesarean delivery without vaginal subgroups, or consisted of case reports, conference abstracts, or animal studies.

2.5Data Extraction and Evidence Synthesis

Data extraction focused on study characteristics relevant to prevention, including obstetric population (low-risk versus high-risk), baseline maternal hemoglobin status, timing and dosage of tranexamic acid administration, and comparator interventions. Primary outcomes of interest included incidence of postpartum hemorrhage and quantified postpartum blood loss, while secondary outcomes included need for additional uterotonics, blood transfusion, and reported adverse events.

Given the narrative nature of this review, formal meta-analytic pooling and risk-of-bias assessment were not performed. Instead, findings were synthesized thematically, with emphasis on explaining differences

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between trials, identifying patterns across populations, and assessing real-world applicability, particularly in low- and middle-income settings where preventive strategies may have greater clinical impact.

2.6Ethical Considerations

As this review is based solely on previously published literature, ethical approval and informed consent were not required.

3.Physiological rationale for prophylactic tranexamic acid in the immediate postpartum period

Hemostasis following childbirth is achieved through coordinated uterine contraction, platelet aggregation, and stabilization of fibrin clots at the placental site. While uterine contraction is essential, it does not act independently, and postpartum bleeding may persist despite adequate uterine tone, highlighting the role of systemic hemostatic mechanisms[13–16].

Pregnancy is characterized by a hypercoagulable state with increased fibrinogen and clotting factors. However, placental separation triggers a marked increase in fibrinolytic activity due to release of tissue plasminogen activator, leading to accelerated fibrin degradation [17,18]. This fibrinolytic surge is most pronounced in the immediate postpartum period and may contribute to excessive bleeding, particularly when clot stability is compromised.

Tranexamic acid inhibits plasminogen activation by blocking lysine-binding sites, thereby preventing fibrin degradation and stabilizing clot formation. Unlike uterotonics, which act locally on uterine muscle, tranexamic acid provides systemic antifibrinolytic support[7,13].Prophylactic administration during or immediately after the third stage of labor may therefore mitigate early fibrinolysis before hemorrhage becomes clinically apparent[19,20].

This preventive rationale is particularly relevant in LMICs, where anaemia is prevalent and even moderate blood loss may have significant clinical consequences[15,18,21].

4.Evidence from clinical trials on prophylactic tranexamic acid following vaginal delivery

The prophylactic use of tranexamic acid following vaginal delivery has been investigated across a heterogeneous body of literature, encompassing early single-center trials, regional randomized controlled studies, large multicentre trials, and pooled analyses[9–11].Unlike therapeutic use, where benefit is consistent and guideline-endorsed, preventive use has produced variable outcomes, necessitating careful interpretation of study context rather than reliance on individual trial results alone.

4.1Early Randomized and Regional Trials

Early randomized trials evaluating prophylactic tranexamic acid after vaginal delivery were primarily conducted in Asia, the Middle East, and parts of Africa, regions characterized by a higher baseline prevalence of maternal anaemia and limited access to advanced obstetric care[19,20]. In many of these studies, tranexamic acid administered in conjunction with standard uterotonic therapy was associated with significant reductions in mean postpartum blood loss, lower declines in post-delivery hemoglobin levels, and reduced need for additional uterotonics[22].

Although these trials were generally underpowered to detect differences in severe postpartum hemorrhage or transfusion rates, their findings are clinically meaningful in contexts where even moderate blood loss may precipitate hemodynamic instability. Importantly, several studies demonstrated benefit despite routine use of active management of the third stage of labor, suggesting that antifibrinolytic prophylaxis may offer additive hemostatic support beyond uterine contraction alone[7,10].

Limitations of these early studies include variability in blood loss estimation methods, small sample sizes, and inconsistent definitions of postpartum hemorrhage. Nonetheless, collectively they provided foundational evidence supporting the biological plausibility of prophylactic antifibrinolytic therapy in the immediate postpartum period.

42Influence of Timing and Dosing on Preventive Outcomes

One of the most critical yet under-discussed contributors to heterogeneity in trial outcomes is timing of tranexamic acid administration. Several studies administered tranexamic acid prior to placental delivery, while others administered it after cord clamping or following placental expulsion. Given that fibrinolytic

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activity increases rapidly following placental separation, even minor delays in administration may attenuate the preventive effect[9].

Dosing strategies have also varied, with most trials employing a fixed 1-g intravenous dose, while others used weight-based regimens or repeat dosing[9–12]. These methodological differences complicate direct comparison across trials and may partially explain discrepancies in observed efficacy[9,10]. Few studies were specifically designed to evaluate optimal timing or dosing for prophylaxis, representing an important gap in the literature[10,12].

4.3Large Multicentre Trials in Unselected Populations

The TRAAP trial marked a significant methodological advance by evaluating prophylactic tranexamic acid in a large, multicentre cohort of women undergoing vaginal delivery in a high-resource setting. In this predominantly low-risk population with widespread use of active management of the third stage of labor, routine prophylactic tranexamic acid did not significantly reduce the incidence of postpartum hemorrhage defined by blood loss ≥500 mL[11].Although the WOMAN trial primarily evaluated tranexamic acid for the treatment rather than prevention of postpartum hemorrhage, it demonstrated a significant reduction in death due to bleeding when tranexamic acid was administered early, without an increase in thromboembolic events, thereby providing strong biological and safety justification for exploring its prophylactic use in large obstetric populations[8].

However, secondary outcomes demonstrated reductions in clinically relevant bleeding indicators, including decreased need for additional uterotonics. These findings suggest that while universal prophylaxis may not substantially alter hemorrhage incidence in low-risk women, tranexamic acid may still modulate bleeding severity and reduce escalation of care[11]. The results also highlight how baseline risk and quality of obstetric care influence the apparent effectiveness of preventive interventions.

4.4High-Risk Populations and The Role of Baseline Anaemia

Recognition that the clinical impact of postpartum bleeding is amplified in women with pre-existing anaemia prompted targeted evaluation of prophylactic tranexamic acid in high-risk populations. The WOMAN-2 trial focused on women with moderate to severe anaemia undergoing vaginal delivery, a population highly relevant to LMICs[15].

Although the trial did not demonstrate a statistically significant reduction in postpartum hemorrhage incidence using conventional thresholds, reductions in blood loss and intervention escalation were observed in certain subgroups[15]. These findings underscore the limitations of categorical blood loss definitions and suggest that prophylactic benefit may be better captured through clinically meaningful outcomes rather than rigid volume thresholds.

4.*5Evidence From Meta-Analyses and Pooled Studies*

Multiple systematic reviews and meta-analyses incorporating early and contemporary trials have evaluated prophylactic tranexamic acid following vaginal delivery. Large trials includingTRAAP trial and WOMAN-2 trial consistently report reductions in mean postpartum blood loss, decreased need for additional uterotonics, and improved post-delivery hemoglobin levels as reflected in subsequent meta-analyses[11,15].However, pooled effects on categorical postpartum hemorrhage thresholds remain inconsistent[9,15,21–23].

Importantly, across analyses, no significant increase in thromboembolic events has been observed, reinforcing the overall safety of prophylactic use[7,8,11,15]. Authors of these reviews consistently emphasize that while current evidence does not support routine prophylaxis for all women, selective use in high-risk populations may be justified[24].

5.Integrated Interpretation and Clinical Implications

When interpreted collectively, the available evidence suggests that the effectiveness of prophylactic tranexamic acid is context-dependent. In low-risk populations with optimal third-stage management and low anaemia prevalence, routine prophylaxis offers limited incremental benefit[11]. In contrast, in settings characterized by high anaemia burden, limited transfusion access, and delayed escalation of care, even

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modest reductions in blood loss may translate into meaningful clinical benefit[24].

Rather than negating the role of prophylactic tranexamic acid, heterogeneity in trial outcomes highlights the need for refined patient selection, optimized timing, and clinically relevant outcome measures. Current evidence supports a selective, risk-based approach to prophylactic tranexamic acid use following vaginal delivery, pending further trials designed to identify populations most likely to benefit.

6.Safety of prophylactic tranexamic acid following vaginal delivery

Concerns regarding the safety of tranexamic acid, particularly the risk of thromboembolic events, have historically limited enthusiasm for its prophylactic use in obstetrics. Pregnancy itself represents a hypercoagulable state, and any intervention influencing coagulation pathways warrants careful evaluation[13,14]. Nevertheless, evidence from randomized trials and pooled analyses has consistently demonstrated a reassuring safety profile for tranexamic acid when used in the obstetric setting[7,8,11].

Across randomized trials evaluating prophylactic tranexamic acid following vaginal delivery, no significant increase in venous thromboembolism, myocardial infarction, or cerebrovascular events has been observed when compared with placebo or standard care. These findings are concordant with data from therapeutic use in postpartum hemorrhage, where large-scale trials have similarly failed to demonstrate an excess thrombotic risk[11,24,25].

Adverse effects reported in prophylactic trials have generally been mild and self-limiting, most commonly including nausea, vomiting, and dizziness. Serious adverse events such as renal impairment or seizures—rarely reported with high-dose or prolonged use in non-obstetric settings—have not emerged as significant concerns in obstetric prophylaxis trials, which typically employ a single 1-g intravenous dose[7,8,24].

Regarding lactation, tranexamic acid is excreted into breast milk in minimal concentrations, and available evidence suggests no clinically significant adverse neonatal effects. Consequently, tranexamic acid is considered compatible with breastfeeding by most professional bodies[26].

Overall, current evidence supports the safety of prophylactic tranexamic acid when administered as a single dose in the immediate postpartum period. Nonetheless, ongoing pharmacovigilance and reporting of rare adverse events remain important, particularly if broader prophylactic use is contemplated in the future.

7.Current guideline positions on prophylactic tranexamic acid use

Despite growing interest in prophylactic tranexamic acid, international guidelines remain cautious, reflecting the heterogeneity and limitations of available evidence. Importantly, no major guideline currently endorses routine prophylactic use following vaginal delivery in all women.

The World Health Organization strongly recommends tranexamic acid for the treatment of established postpartum hemorrhage but does not support its routine prophylactic use, citing insufficient evidence to justify universal administration. The WHO emphasizes the need for further research, particularly among high-risk populations and in low-resource settings[25,26].

Similarly, the International Federation of Gynaecology and Obstetrics acknowledges emerging evidence suggesting potential benefit in selected populations but refrains from recommending routine prophylaxis. FIGO highlights the importance of individualized risk assessment and context-specific decision-making[24].

Guidelines from high-income settings, including NICE, ACOG, and RCOG, do not currently recommend prophylactic tranexamic acid following vaginal delivery outside research settings. These organizations emphasize the effectiveness of active management of the third stage of labor and note that the incremental benefit of antifibrinolytic prophylaxis in low-risk populations appears limited based on current evidence[27–29].

Collectively, these positions reflect a consensus that while tranexamic acid is safe and effective for treatment, its role in prevention remains selective rather than universal, pending further high-quality evidence.

8.Knowledge gaps and future research directions

The heterogeneity of existing trials highlights several important gaps in current knowledge. First, there is limited clarity regarding optimal patient selection for

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prophylactic tranexamic acid. Future research should prioritize risk-stratified approaches incorporating factors such as baseline anaemia, previous postpartum hemorrhage, prolonged labor, and operative vaginal delivery.

Second, the optimal timing of administration remains inadequately defined. Comparative trials evaluating administration before placental delivery versus immediately after placental expulsion may help identify the window during which antifibrinolytic prophylaxis is most effective.

Third, reliance on fixed blood-loss thresholds may underestimate clinically meaningful benefits, particularly in anaemic populations. Incorporating patient-centered outcomes—such as changes in postpartum hemoglobin, functional recovery, and need for escalation of care—may provide a more nuanced assessment of benefit.

Finally, cost-effectiveness analyses and implementation studies are required, especially in low-resource settings where preventive strategies may yield the greatest public health impact. Addressing these gaps will be essential before routine prophylactic use can be confidently recommended.

9.Conclusion

Postpartum hemorrhage remains an unpredictable and potentially life-threatening complication of vaginal delivery, even in the presence of effective uterotonic prophylaxis. Tranexamic acid, through its antifibrinolytic mechanism, represents a biologically plausible adjunctive strategy aimed at stabilizing hemostasis during the immediate postpartum period.

Current evidence from randomized trials and meta-analyses indicates that routine prophylactic use of tranexamic acid following vaginal delivery is not supported. However, selective use in high-risk populations—particularly in settings with a high prevalence of maternal anaemia—may offer clinically meaningful benefit. The absence of significant safety concerns further supports continued investigation of this approach.

Until additional high-quality, risk-stratified trials become available, prophylactic tranexamic acid should be viewed as an evolving strategy rather than standard practice. A targeted, context-specific approach aligned with existing preventive measures may represent the most appropriate path forward in optimizing maternal outcomes.

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Declarations

Patient Consent

Not required

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Conflict of Interest

The authors declare that they have no conflict of interest.

Ethical considerations

As this review is based solely on previously published literature, ethical approval and informed consent were not required.

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