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Systematic Review

Tranexamic Acid for the Prevention and Treatment of Postpartum Hemorrhage: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Background: Postpartum hemorrhage (PPH) is a leading cause of maternal death worldwide. Tranexamic acid (TXA), an antifibrinolytic agent, has been evaluated for both treatment and prevention of PPH in randomized controlled trials (RCTs). This systematic review summarizes its efficacy and safety.
Methods: Placebo-controlled RCTs of intravenous TXA in women giving birth, either with PPH (treatment) or at risk of PPH (prevention), were eligible. Data were extracted and synthesized without meta-analysis following the SWiM reporting guideline, with trials grouped by treatment or prevention and with qualitative risk-of-bias appraisal using RoB 2 domains.
Findings: Three RCTs (WOMAN, TRAAP, TRAAP2; 28,690 randomized women) were included. In WOMAN, TXA did not reduce death or hysterectomy (RR 0.97, 95% CI 0.87–1.09) but reduced death due to bleeding (RR 0.81, 95% CI 0.65–1.00), especially when given within 3 hours of birth (RR 0.69, 95% CI 0.52–0.91). For prevention, TXA did not significantly reduce blood loss ≥500 mL after vaginal birth (RR 0.83, 95% CI 0.68–1.01) but reduced PPH after cesarean delivery (adjusted RR 0.84, 95% CI 0.75–0.93). Nausea and vomiting were more frequent with TXA.
Conclusion: TXA given early reduces bleeding-related death in PPH, and may reduce PPH after cesarean delivery; evidence for prevention after vaginal birth is not conclusive.

INTRODUCTION

Postpartum hemorrhage (PPH) remains a major cause of maternal morbidity and mortality, particularly in low- and middle-income settings. Management relies on uterotonic drugs, procedural measures, and supportive care, and additional pharmacological options have been sought to reduce blood loss and bleeding-related death.

Tranexamic acid (TXA) is an antifibrinolytic drug that has been evaluated both as treatment of established PPH and as prophylaxis in women at risk. Three large placebo-controlled randomized controlled trials (RCTs) address this question: WOMAN, which evaluated TXA for treatment of PPH [1], and TRAAP and TRAAP2, which evaluated prophylactic TXA after vaginal birth [2] and cesarean delivery [3], respectively.

These trials address different clinical questions and use different primary outcomes. WOMAN assessed death or hysterectomy among

women with PPH, whereas the prevention trials assessed blood loss or a composite of blood loss and transfusion. Their results therefore cannot be combined simply, and a structured summary is useful.

This systematic review aims to summarize the efficacy and safety of intravenous TXA versus placebo for treatment and prevention of PPH, and to describe how the evidence differs between treatment and prevention and between modes of delivery.

METHODS

1. Design

This systematic review of RCTs was planned using the PICO framework. No protocol was prospectively registered. Results were synthesized without meta-analysis, following the principles of the SWiM reporting guideline [4].

2. Eligibility Criteria

Eligibility criteria are summarized in Table 1. RCTs published in peer-reviewed journals were eligible. Trials were grouped by clinical question: treatment of PPH (WOMAN) and prevention of PPH (TRAAP after vaginal birth and TRAAP2 after cesarean delivery).

Table 1. Eligibility Criteria (PICO)

Element	Criterion
Population	Women giving birth, with PPH (treatment) or at risk of PPH (prevention)
Intervention	Intravenous tranexamic acid
Comparator	Placebo
Outcomes	Death, hysterectomy, blood loss, transfusion, thromboembolic and other adverse events
Design	Placebo-controlled RCT in a peer-reviewed journal

3. Information Sources and Search

Peer-reviewed literature indexed in PubMed was searched in November 2026 through a web search interface, using the terms “tranexamic acid,” “postpartum hemorrhage,” and “randomized trial”. Publisher abstracts and verified secondary records were used to confirm the content of each trial report.

4. Study Selection

Records were screened against the eligibility criteria by title, abstract, and available full-text information. Selection was performed by a single reviewer.

5. Data Items

Sample size, population, TXA dose and timing, primary outcome definition and results, secondary outcomes (death due to bleeding, transfusion), and safety findings (thromboembolic events, nausea and vomiting) were extracted.

6. Risk-of-Bias Appraisal

Risk of bias was appraised qualitatively using the domains of the RoB 2 tool [5] (randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting), based on information in published abstracts and verified secondary records.

7. Effect Measures

Effect measures were reported as given by each trial, including hazard ratios, risk ratios, vaccine or treatment efficacy, absolute event rates, and mean differences, each with its 95% confidence interval where available. When a trial reported a confidence level other than 95%, this is stated in the text. Measures were not converted between scales, because conversion requires data that were not available in the records reviewed.

8. Missing and Unreported Data

When a result, confidence interval, or safety rate was not available in the records reviewed, it is stated as not available and was not estimated. Where a figure was derived by simple arithmetic from reported values, this is stated in the text and no confidence interval is given.

9. Certainty of the Evidence

A formal certainty-of-evidence rating was not performed. Instead, the consistency of results across trials, the precision of estimates, the directness of the evidence, and the potential for bias were considered narratively when interpreting the findings.

10. Ethical Considerations

This review used only published data from previously reported trials and did not involve new contact with patients. Ethical approval was therefore not required, and the original trials reported their own ethical approvals and participant consent.

11. Synthesis

Because drugs, populations, durations, comparators, and outcomes differed, a pooled estimate was not calculated. Results are reported as provided by each trial and are tabulated and described narratively.

RESULTS

1. Study Selection

The search identified three RCTs that met the eligibility criteria [1–3], with 28,690 randomized women in total. All used intravenous TXA 1 g compared with placebo.

2. Characteristics of Included Trials

WOMAN enrolled women with PPH and allowed a second dose of 1 g if bleeding continued after 30 minutes or restarted within 24 hours [1]. TRAAP randomized women planned for vaginal birth and gave TXA within 2 minutes after birth, following routine oxytocin [2]. TRAAP2 randomized women undergoing cesarean delivery at 27 centers in France and gave TXA within 3 minutes after birth, after a prophylactic uterotonic bolus [3].

Table 2. Characteristics of Included Trials

Trial	Design and population
WOMAN [1]	20,060 women with PPH (TXA n = 10,051; placebo n = 10,009); TXA 1 g IV, with a second dose if bleeding continued; primary outcome death or hysterectomy
TRAAP [2]	4,079 women planned for vaginal birth (3,891 delivered vaginally); TXA 1 g IV vs placebo after birth; primary outcome blood loss ≥500 mL
TRAAP2 [3]	4,551 women undergoing cesarean delivery (TXA n = 2,276; placebo n = 2,275); TXA 1 g IV; primary outcome blood loss >1000 mL or red-cell transfusion by day 2

3. Treatment of Established PPH

In WOMAN, death from any cause or hysterectomy occurred in 534 women (5.3%) with TXA and 546 (5.5%) with placebo (RR 0.97, 95% CI 0.87–1.09; P = 0.65). Death due to bleeding was lower with TXA (155 [1.5%] vs 191 [1.9%]; RR 0.81, 95% CI 0.65–1.00; P = 0.045), and among women treated within 3 hours of birth the risk ratio was 0.69 (95% CI 0.52–0.91; P = 0.008) [1].

Table 3. Efficacy of TXA in WOMAN

Outcome	Result
Death or hysterectomy	5.3% vs 5.5%; RR 0.97 (0.87–1.09)
Death due to bleeding	1.5% vs 1.9%; RR 0.81 (0.65–1.00)
Death due to bleeding, treated within 3 hours	RR 0.69 (0.52–0.91)

4. Prevention of PPH

4.1 After Vaginal Birth (TRAAP)

In TRAAP, blood loss ≥500 mL occurred in 156 of 1,921 women (8.1%) with TXA and 188 of 1,918 (9.8%) with placebo (RR 0.83, 95% CI 0.68–1.01; P = 0.07), which was not statistically significant [2].

4.2 After Cesarean Delivery (TRAAP2)

In TRAAP2, PPH (calculated blood loss >1000 mL or red-cell transfusion by day 2) occurred in 556 of 2,086 women (26.7%) with TXA and 653 of 2,067 (31.6%) with placebo (adjusted RR 0.84, 95% CI 0.75–0.93; P = 0.003). When missing primary-outcome data were counted as failures, the rates were 31.1% and 36.0% (P = 0.006). Transfusion (1.9% vs 1.8%), clinically significant blood loss (13.6% vs 14.8%), and gravimetric blood loss (689 vs 719 mL) did not differ significantly [3].

Table 4. Efficacy of TXA for Prevention

Trial	Result
TRAAP [2]	8.1% vs 9.8%; RR 0.83 (0.68–1.01); P = 0.07
TRAAP2 [3]	26.7% vs 31.6%; adjusted RR 0.84 (0.75–0.93); P = 0.003

5. Safety

In WOMAN, adverse events, including thromboembolic events, did not differ significantly between groups [1]. In TRAAP, thromboembolic events within 3 months occurred in 0.1% with TXA and 0.2% with placebo (RR 0.25, 95% CI 0.03–2.24), and nausea and vomiting after delivery were more frequent with TXA [2].

In TRAAP2, deep vein thrombosis or pulmonary embolism occurred in 0.4% (8 cases) with TXA and 0.1% (2 cases) with placebo, seizures occurred in 1 woman in each arm, and nausea and vomiting were more frequent with TXA (43.0% vs 36.3%; P<0.001) [3].

Table 5. Selected Safety Findings

Trial	Safety finding
WOMAN [1]	No significant difference in adverse events, including thromboembolic events
TRAAP [2]	Thromboembolic events 0.1% vs 0.2%; more nausea/vomiting with TXA
TRAAP2 [3]	DVT/PE 0.4% vs 0.1%; nausea/vomiting 43.0% vs 36.3%

6. Risk-of-Bias Appraisal

All three trials were randomized, double-blind, placebo-controlled, multicenter studies published in peer-reviewed journals. No major concerns were evident from the information reviewed. A domain-level RoB 2 judgement requires full-text and protocol review and was not completed.

Table 6. Qualitative Risk-of-Bias Summary

Trial	Appraisal
WOMAN [1]	Randomized, double-blind, placebo-controlled; no major concerns evident
TRAAP [2]	Randomized, placebo-controlled; no major concerns evident
TRAAP2 [3]	Randomized, double-blind, placebo-controlled; modified intention-to-treat analysis

DISCUSSIONS

1. Summary of Evidence

Across 28,690 women, TXA 1 g did not reduce the composite of death or hysterectomy in established PPH, but reduced death due to bleeding [1]. For prevention, the effect was not significant after vaginal birth [2] but significant after cesarean delivery under the outcome definition used [3].

2. Treatment of PPH and Importance of Timing

In WOMAN, the reduction in death due to bleeding was larger when TXA was given within 3 hours of birth (RR 0.69) than in the overall population (RR 0.81) [1], which supports early administration once PPH is diagnosed. The null result for the composite outcome of death or hysterectomy suggests that the benefit relates mainly to bleeding-related death rather than to hysterectomy.

3. Prevention after Vaginal Birth

In TRAAP, the point estimate (RR 0.83) suggested lower risk of blood loss ≥500 mL with TXA, but the confidence interval included 1 (0.68–1.01) and the result was not statistically significant [2]. The trial therefore does not exclude a modest benefit, but it does not demonstrate one either.

4. Prevention after Cesarean Delivery

In TRAAP2, TXA reduced PPH defined by calculated blood loss >1000 mL or transfusion (26.7% vs 31.6%) [3]. However, transfusion alone, clinically significant blood loss, and gravimetric blood loss did not differ significantly between groups [3], so the clinical significance of the reduction in the primary outcome is uncertain.

5. Outcome Definitions

The prevention trials used different outcome definitions (blood loss ≥500 mL versus >1000 mL or transfusion) and different populations, so their results should not be compared directly [2][3]. Differences in how

blood loss is measured may also contribute to variation between trials.

6. Safety Considerations

Nausea and vomiting were more frequent with TXA in both prevention trials [2][3]. Thromboembolic events were rare and did not differ significantly, although numerically more deep vein thrombosis or pulmonary embolism occurred with TXA in TRAAP2 (0.4% vs 0.1%) [3]. Continued attention to thromboembolic safety is warranted, particularly in women with additional risk factors.

7. Implications for Practice

The evidence supports early use of TXA in women diagnosed with PPH. Routine prophylaxis is less clear, particularly after vaginal birth. The records reviewed did not include data from Indonesia, and the availability of TXA and cost-effectiveness were not addressed; decisions should follow national guidance.

8. Implications for Research

Future research should clarify the role of prophylactic TXA after vaginal birth, examine thromboembolic safety in larger populations, and include trials in settings with high maternal mortality, including Indonesia.

9. Strengths of the Review

This review focused on randomized controlled trials published in major peer-reviewed journals, which are the strongest design for estimating intervention effects. Each trial result was cross-checked against the published abstract or a verified secondary record, and the numbers reported here are those given by the trial authors. The reporting of synthesis without meta-analysis followed a published guideline, and limitations in the methods are described openly.

10. Certainty and Consistency of the Evidence

Considered narratively, the certainty of the evidence depends on three features: the number and size of the trials, the consistency of the direction and size of effects between trials, and the precision of the estimates. Where trials agree in direction and have narrow confidence intervals, the evidence is stronger; where trials disagree or have wide confidence intervals, the evidence is weaker and conclusions should be more cautious. A formal grading of certainty was not undertaken and would be needed before the findings are used to support a guideline recommendation.

11. Generalizability

Trial participants are selected by eligibility criteria and often receive closer monitoring than patients in routine care, so effects seen in trials may differ in practice. The populations in the included trials may differ from patients in Indonesia in baseline risk, access to care, and background treatment, and the findings should be applied with attention to local circumstances.

12. Recommendations for an Updated Review

An updated review suitable for journal submission should register a protocol in a public registry before the search, search several databases such as PubMed, Embase, and the Cochrane Library with an exportable strategy, and screen records independently in duplicate. Data should be extracted from full-text reports and trial registries, risk of bias should be assessed domain by domain with RoB 2, and, where trials are sufficiently similar, a random-effects meta-analysis with an assessment of heterogeneity should be performed. The certainty of evidence for each outcome should then be graded using the GRADE approach.

13. Limitations

Several limitations should be acknowledged. Searching was performed through a web interface rather than an exportable multi-database search and no protocol was registered, so relevant trials may have been missed. Selection and extraction were performed by one reviewer, using published abstracts and verified secondary records. A formal RoB 2 assessment was not completed and no pooled estimate was computed. Only three trials were included, no pooled estimate was computed, and the trials addressed different clinical questions. The review should be repeated with a documented multi-database

search and independent duplicate review before the findings are used for clinical recommendations.

CONCLUSIONS

Evidence from three large RCTs shows that TXA 1 g given early reduces death due to bleeding in women with PPH and may reduce PPH after cesarean delivery. Evidence for prophylactic use after vaginal birth is not conclusive, and nausea and vomiting are more frequent with TXA.

Future work should include a pre-registered, multi-database systematic review with meta-analysis, formal risk-of-bias and certainty-of-evidence assessment, and attention to thromboembolic safety and to settings with high maternal mortality, including Indonesia.

Author Contribution Statement

The author performed all aspects of this study.

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