Wits Journal of Clinical Medicine, 2026, 8(1) 29–38 http://dx.doi.org/10.18772/26180197.2026.v8n1a6

Review Article

Tranexamic acid use in neonates and children: a narrative review of current evidence, and knowledge gaps

Joseline Nkhoma, Harrilene Apleni, Gontse Leballo, Palesa Motshabi Chakane, Moses Kebalepile*

Department of Anaesthesiology, School of Clinical Medicine, Faculty of Health Sciences, University of Witwatersrand

Corresponding author: *Moses.kebalepile@wits.ac.za*

ABSTRACT

Background: Neonatal anaemia is common, particularly in preterm and critically ill infants, and is frequently managed with red blood cell transfusion despite well-recognised associated morbidity. Patient blood management strategies aim to reduce transfusion exposure, and tranexamic acid (TXA) has emerged as a potential pharmacological adjunct. However, evidence supporting the use of TXA in neonates remains limited.

Methods: We conducted a comprehensive narrative review of peer-reviewed literature published between January 2015 and December 2025. Searches were performed in PubMed/MEDLINE, Scopus, and Web of Science using Medical Subject Headings and keyword combinations related to neonates, children, blood conservation strategies, and TXA. Eligible studies included systematic reviews, randomised controlled trials, observational cohort studies, and case reports evaluating TXA use in paediatric and neonatal populations across surgical, critical care, and selected medical contexts. Adult-only and animal studies were excluded. Findings were synthesised qualitatively.

Results: Seventeen studies met the inclusion criteria. Evidence consistently supports the use of TXA as part of multimodal blood-conservation strategies in elective paediatric surgery with predictable bleeding, particularly in craniosynostosis surgery, where reductions in blood loss and transfusion requirements were observed. In paediatric cardiac surgery and life-threatening haemorrhage, TXA may reduce bleeding and early mortality; however, benefits were less consistent in neonates. Evidence for TXA use in neonatal medical indications was sparse and inconclusive. Safety data suggest a dose- and context-dependent risk of seizures, with limited neonatal-specific adverse event reporting.

Conclusion: TXA shows promise as a pharmacological blood conservation strategy in selected paediatric surgical populations, but evidence supporting its routine use in neonates remains limited. The unique haemostatic physiology, immature renal clearance, and neurological vulnerability of neonates necessitate cautious use. High-quality neonatal pharmacokinetic studies and prospective trials are urgently needed to define optimal dosing, safety, and efficacy before widespread adoption in neonatal practice.

Keywords: neonatal anaemia; tranexamic acid; patient blood management; blood conservation strategies; neonatal surgery; transfusion

INTRODUCTION

Anaemia is a major global health problem, affecting nearly one-third of the world's population,(1) and is associated with a disproportionate burden of morbidity and mortality in infants and children. Approximately 29% of newborns develop anaemia, with preterm infants, particularly those with extremely low birth weight (ELBW), at substantially higher risk.(1,2) Neonatal anaemia results from blood loss, reduced red blood cell (RBC) production, or increased RBC destruction.(3) In preterm and critically ill neonates, anaemia is often more severe, compromising tissue oxygen delivery and contributing to adverse short- and long-term outcomes.(4) These vulnerable infants frequently require perioperative blood transfusion; however, transfusion exposure is consistently associated with poorer outcomes. Transfused neonates have significantly higher morbidity compared with non-transfused infants (46.2% vs. 16.2%, $p < 0.01$).(5)

Anaemia, commonly defined using a haematocrit (HcT) threshold of 40%, has been identified as an independent

predictor of in-hospital mortality.(6) Clinically, neonatal anaemia may present subtly but can progress to cerebral hypoxia and long-term neurodevelopmental impairment if severe.(7) More than 80% of ELBW infants receive at least one RBC transfusion during hospitalisation.(8,9) Blood conservation strategies have been reported to be efficacious, with a one-third reduction in blood loss and a significant decrease in transfusion requirements (41% vs. 73%; RR = 0.56; p = 0.001).(10) Therefore, optimising perioperative blood management is critical for improving neonatal outcomes.(6,11,12)

Physiological anaemia of infancy occurs in all neonates due to reduced erythropoietin (EPO) production, transition from foetal to adult haemoglobin, shortened RBC lifespan, and haemodilution with growth.(4) While this typically resolves without intervention in term neonates,(13) preterm neonates experience anaemia that is earlier, more profound, and prolonged, termed anaemia of prematurity, driven by immature erythropoiesis and bone marrow function.(14,15) Consequently, RBC transfusions are frequently required to support oxygen delivery in this population.(13)

Despite advances in transfusion medicine, neonatal transfusion practices remain highly variable, reflecting a lack of consensus on optimal thresholds and strategies.(16,17) Transfusion decisions are guided by gestational age, birth weight, haemodynamic status, and laboratory indices, with adjunctive tools such as echocardiography and near-infrared spectroscopy (NIRS) increasingly explored to refine clinical judgement.(3,18) However, transfusions carry substantial risks in neonates, including infection, transfusion-related lung injury (TRALI), circulatory overload, and associations with bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), intraventricular haemorrhage (IVH), and necrotising enterocolitis (NEC).(19–22) These risks highlight the need for safe and effective blood-conservation strategies, coupled with evidence-based practices.

Perioperative patient blood management (PBM) and blood conservation strategies aim to reduce blood loss and transfusion exposure by optimising preoperative anaemia, meticulous surgical and anaesthetic techniques, and goal-directed transfusion practices.(23–25) Many conventional blood-conservation methods are unsuitable in neonates due to limited blood volume and physiological reserve, underscoring the importance of potent pharmacological approaches.

Tranexamic acid (TXA), a synthetic lysine analogue that inhibits fibrinolysis, has emerged as a potent and key pharmacological blood-conservation strategy. TXA inhibits fibrinolysis by blocking the binding of plasminogen to fibrin, thereby preventing its conversion to plasmin and subsequent clot breakdown.(26,27) By preserving existing clots rather than promoting new clot formation, TXA enhances clot stability and reduces ongoing and excessive bleeding by targeting the final common pathway of haemorrhage.(28) While well established in paediatric and neonatal cardiac surgery,(29,30) TXA is increasingly used off-label in non-cardiac paediatric settings.(26,31) However, evidence regarding its safety, dosing, and effectiveness in neonates remains heterogeneous and incompletely synthesised.

This narrative review aims to synthesise the current evidence on the use of TXA as a pharmacological blood conservation strategy in paediatric patients, with a particular focus on neonates, and to identify key knowledge gaps to inform future research and clinical practice.

METHODS

Review design

This narrative review evaluated the perioperative and clinical application of TXA in paediatric patients, with particular emphasis on the neonatal population, highlighting current evidence and identifying existing knowledge gaps.

Literature search strategy

The review was conducted using a structured and transparent methodology by two reviewers (GL and MK). A focused search of peer-reviewed literature published between January 2015 and December 2025 was undertaken across three electronic databases: PubMed/MEDLINE, Scopus, and Web of Science. The search strategy combined Medical Subject Headings (MeSH) and relevant keywords, including *neonates*, *newborns*, *blood conservation strategies*, and *tranexamic acid*. The complete search strategy is presented in Table 1.

Eligibility criteria

EndNote 20 (Clarivate Analytics, Philadelphia, USA, 2022) was used to export study records identified across the different search engines, to identify and remove duplicate citations, and to manage the screening of titles, abstracts, and full-text articles. Peer-reviewed journal articles were included if they examined the use of TXA in children and neonates within the perioperative period, intensive care settings, or other relevant medical contexts where its use has been reported or proposed. Eligible study designs included systematic reviews, meta-analyses, narrative reviews, randomised controlled trials (RCTs), case reports, and observational cohort studies that evaluated TXA as a pharmacological blood conservation strategy. Only full-text articles published in English were included. Studies involving adult populations and animal models were excluded. Figure 1 illustrates the literature identification, screening, and study inclusion process.

Risk of bias (quality) assessment

Given the substantial heterogeneity of study designs included in this narrative review; RCTs, systematic reviews, meta-analyses, observational studies, narrative reviews,

Table 1: Search strategy: databases and key terms used

Database	MeSH Terms, Keywords, and Boolean Points
PubMed/ MEDLINE	((“infant, newborn”[MeSH Terms] OR “neonate”[Text Word]) AND (((“blood conservation strategies”[Text Word] OR “blood conservation strategies”[All Fields]) AND “tranexamic acid”[Text Word]) OR “tranexamic acid”[All Fields])) AND ((y_10[Filter]) AND (humans[Filter]) AND (english[Filter]) AND (allinfant[Filter] OR infant[Filter]))
Scopus	(TITLE-ABS-KEY(neonates AND infants) AND TITLE-ABS-KEY(tranexamic ANDacid ANDuse) AND TITLE-ABS-KEY(blood ANDconservation ANDstrategies)) AND (LIMIT-TO(SUBJAREA, “MEDI”)) AND (LIMIT-TO(EXACTKEYWORD, “Tranexamic Acid”) OR LIMIT-TO(EXACTKEYWORD, “Infant, Newborn”) OR LIMIT-TO(EXACTKEYWORD, “Newborn”) OR LIMIT-TO(EXACTKEYWORD, “Humans”)) AND (LIMIT-TO(LANGUAGE, “English”))
Web of Science	neonates OR infants (All Fields) AND blood transfusion conservation strategies (All Fields) AND tranexamic acid use (All fields)

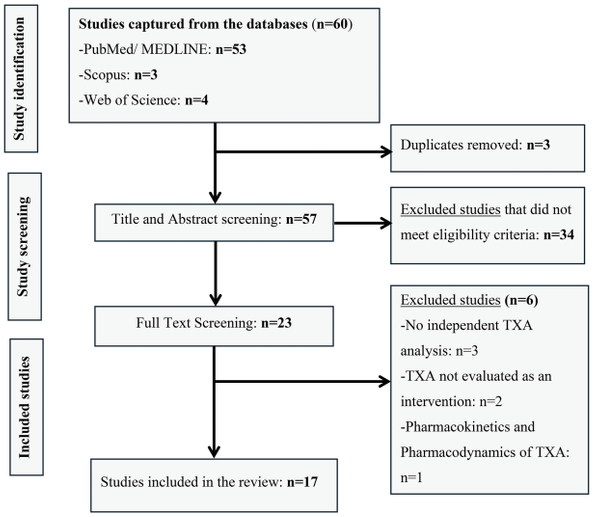

Figure 1: Flow diagram of the literature search, screening, and inclusion process.

and case reports, a single unified risk-of-bias tool was not applied. Instead, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework was used to assess the overall certainty of evidence. GRADE was selected because it allows structured appraisal across diverse evidence types by considering key domains including risk of bias, inconsistency, indirectness, imprecision, and publication bias, rather than relying on design-specific tools that are not directly comparable across heterogeneous study designs.

Data extraction and synthesis

Following study selection, a narrative synthesis was undertaken to integrate findings across heterogeneous study designs, populations, and clinical contexts. The retained evidence clustered into distinct clinical domains. These results were synthesised qualitatively, and the strength and certainty of evidence were assessed descriptively, considering study design, risk of bias, consistency of findings, and applicability to paediatric and neonatal populations.

RESULTS

A structured literature search identified 60 peer-reviewed studies, of which three were duplicates. Following title and abstract screening, 34 studies were excluded as they primarily involved adult obstetric populations and did not meet the inclusion criteria. Full-text screening of the remaining articles identified 17 studies for inclusion in the narrative synthesis (Figure 1). These studies examined TXA use across elective surgical, cardiac, trauma, and massive haemorrhage contexts, as well as selected paediatric and neonatal medical contexts, with substantial variability in the certainty of the evidence across indications and age groups. The majority of included studies demonstrated moderate certainty of evidence according to the GRADE assessment (47%), while 29% were rated as very low certainty (Table 2). No included studies were assessed as having high certainty of evidence.

Across the retained studies, the evidence on tranexamic acid can be synthesised into four key clinical domains: (i) elective surgery with predictable bleeding, (ii) efficacy of tranexamic acid in reducing bleeding and transfusion requirements and life-threatening haemorrhage, (iii) safety outcomes, including seizures, thrombotic events, and renal effects, and (iv) neonatal medical indications for tranexamic acid use. Table 3 summarises the included studies, with particular emphasis on study design and key findings.

Elective surgery and bleeding

Moderate certainty evidence across multiple study designs, as assessed using the GRADE approach, including prospective single-centre cohorts, RCTs, and systematic reviews with meta-analyses, demonstrates consistent reductions in perioperative allogeneic blood product use among neonatal and paediatric patients receiving TXA during cranial vault surgery.(32,35,47) A 2015 systematic review and meta-analysis

Table 2: GRADE assessment of the included studies

Author (year)	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall GRADE certainty
White et al., 2015 (32)	SR and Meta-analysis of RCTs	Low	Moderate (I^2 ~ 50%)	Low	Moderate	Low	Moderate
Goobie et al., 2025 (33)	Narrative review	Low	Low	Low	Moderate	Low	Moderate
Dorgalaleh et al., 2020 (34)	Case report	High	High	High	High	High	Very low
Erb et al., 2016 (35)	Narrative review	Low	Low	Low	Moderate	Low	Moderate
Faraoni et al., 2019 (36)	Narrative review	Low	Moderate	Low	Moderate	Moderate	Low
Goel et al., 2016 (37)	Narrative review	Moderate	Moderate	Low	Low	Low	Moderate
Han et al., 2016 (38)	Retrospective study	High	High	Moderate	High	Moderate	Very low
Maeda et al., 2017 (39)	Retrospective study (Nationwide)	Moderate	Low	Low	Low	Moderate	Moderate
Moynihan et al., 2024 (40)	SR and Delphi consensus	High	High	Moderate	High	Moderate	Very low
Spinella et al., 2022 (41)	Prospective observational study	High	Low	Moderate	Moderate	Moderate	Low – Moderate
Streif et al., 2020 (42)	Narrative review	Moderate	High	Moderate	High	Moderate	Very low
Tanis-Arens et al., 2023 (43)	Retrospective study	Moderate	Low	Low	Moderate	Low	Low – Moderate
Verma et al., 2009 (44)	Narrative review	Moderate	Moderate	Low	Moderate	Moderate	Low – Moderate
Wang et al., 2023 (45)	Case report	Moderate	High	Moderate	High	Moderate	Very low
Willems et al., 2019 (46)	Retrospective study	Moderate	Low	Low	Low	Low	Moderate
Wood et al., 2020 (47)	Prospective study	Moderate	Low	Low	Low	Low	Moderate
Yao et al., 2023 (48)	SR and Meta-analysis	Low	Low	Low	Moderate	Low	Moderate

SR= systematic review, RCT(s)= randomised control trial(s)
GRADE levels interpretation: High = Very confident that the true effect lies close to the estimate, Moderate = true effect is probably close to the estimate, Low = limited confidence in the estimate, Very Low = evidence is sparse, inconsistent and indirect.

of children undergoing craniosynostosis surgery, with a mean age ranging from 2 months to 4 years, reported a significant reduction in allogeneic blood transfusion volume in the TXA compared with controls (mean difference −111.6 mL, 95% CI −207.1 to −16.1 mL; I^2 = 51%; p = 0.002).(32)

In a single-centre prospective observational cohort study, Wood and colleagues evaluated 279 children aged 1 year or younger undergoing craniosynostosis surgery and demonstrated a significant reduction in intraoperative blood loss following implementation of a multimodal blood-conservation protocol.(47) This protocol included TXA administered at a loading dose of 20 mg/kg followed by an infusion of 10 mg/kg/h and was associated with substantially lower blood loss compared with standard care (6.6 mL vs. 24.8 mL, p < 0.001). However, as TXA formed part of a comprehensive strategy that also incorporated modified surgical techniques, preoperative EPO administration, local anaesthetic infiltration, and hypervolaemic haemodilution, the independent effect of TXA cannot be isolated.

Table 3: A summary and key findings of the included studies

Author (year)	Population	Clinical context	Study design	Comparator	Outcomes	Main findings
White et al., 2015 (32)	Infants & young children (mean age: 2 m–4 yrs)	Craniosynostosis surgery	SR & meta-analysis of RCTs	Placebo / no TXA	Transfusion volume	↓ transfusion volume (MD ≈ −112 mL, p=0.02)
Goobie et al., 2025 (33)	Infants & children	Multimodal PBM strategies	Narrative review	Blood products and other antifibrinolytics (EACA)	Blood loss, transfusion, TXA safety	↓ transfusion, ↓blood loss, and no thromboembolic risk
Dorgalaleh et al., 2020 (34)	Single neonate	Factor X deficiency + COVID-19	Case report	—	GI bleeding	Bleeding resolved with FFP + TXA; efficacy of TXA could not be isolated
Erb et al., 2016 (35)	Neonates and infants up to 10 months	Craniosynostosis surgery	Narrative review	Blood products	Perioperative anaesthetic and haemostatic management	Significant ↓ in blood transfusion volumes along with modified surgical technique
Faraoni et al., 2019 (36)	Neonates, infants, and children	Paediatric cardiac surgery	Narrative review	Placebo and Epsilon-aminocaproic acid	TXA efficacy	TXA ↓ perioperative bleeding and transfusion Comparable to EACA
Goel et al., 2016 (37)	Neonates, infants, children, and adolescents	Paediatric patient blood management programs	Narrative review and Expert synthesis	Placebo/ no TXA	Perioperative antifibrinolytic agent efficacy	Limited data in neonates and trauma patients Supporting evidence in paediatric cardiac, orthopaedic, and cranial remodelling surgeries
Han et al., 2016 (38)	Infants and children	Craniosynostosis surgery	Retrospective cohort	No TXA	Blood loss	Higher EBL in TXA group due to confounding (247 mL vs. 138 mL)
Maeda et al., 2017 (39)	Neonates to 12yrs (median 1 yr)	Paediatric cardiac surgery on CPB	Retrospective cohort	No TXA	Seizures, mortality, hospital stay	↑ seizures (1.6% vs 0.2%, p<0.0001); no mortality difference
Moynihan et al., 2024 (40)	Neonates	Paediatric ECMO Anticoagulation Collaborative (PEACE)	SR + Delphi consensus	—	Bleeding	TXA may reduce bleeding; evidence is sparse
Spinella et al., 2022 (41)	0–17 yrs (median 7 yrs)	Life-threatening haemorrhage	Prospective multicentre observational (secondary analysis)	No antifibrinolytic	Early mortality	↓ 6-h mortality with antifibrinolytics (TXA and EACA cohorts) No seizures with TXA AKI with EACA
Streif et al., 2020 (42)	Newborns	Haemophilia	Narrative review	—	Bleeding	Insufficient evidence for routine TXA
Tanis-Arens et al., 2023 (43)	Neonates (<30 days)	Paediatric cardiac surgery on CPB	Retrospective cohort	EACA	Seizures	No ↑ seizure risk with low-dose TXA ↑ seizures with EACA

Continued

Table 3: A summary and key findings of the included studies *Continued*

Author (year)	Population	Clinical context	Study design	Comparator	Outcomes	Main findings
Verma et al., 2009 (44)	Infants to adolescents (2 m to 14.5 yrs)	Paediatric surgery (cardiac and non-cardiac)	Narrative review	—	Bleeding, transfusion	TXA is effective in cardiac surgery and non-cardiac, ↓ blood use and comparable to EACA
Wang et al., 2023 (45)	19-day-old neonate	Pulmonary haemorrhage and thrombocytopaenia	Case report	—	Coagulation monitoring	Treatment with TXA resulted in hypercoagulability
Willems et al., 2019 (46)	0-16 yrs (mean 9.6 m)	Paediatric cardiac surgery on CPB	Retrospective cohort	Aprotinin	Blood product use	↓ Use of blood products vs aprotinin (59.8% vs 77.5%, p<0.001)
Wood et al., 2020 (47)	Neonates and infants (≤ 1 yr; mean 1 m)	Craniosynostosis surgery	Prospective observational	Standard care/ no added TXA	Bleeding	Significant ↓ in blood loss vs standard care (24.8 mL vs 6.6 mL, p<0.001)
Yao et al., 2023 (48)	Neonates	IVH prevention in premature neonates	SR and meta-analysis	No TXA	Bleeding severity	No statistically significant ↓ in bleeding severity (44% vs 40%)

yr(s) = year(s), SR = systematic review, RCT(s) = randomised control trial(s), TXA = tranexamic acid, MD = mean difference, PBM = perioperative patient blood management, EACA = epsilon-aminocaproic acid, ↓ = reduced/ decreased, ↑ = elevated/ increased, GI = gastrointestinal, FFP = fresh frozen plasma, ECMO = extra-corporeal membrane oxygenation, CPB = cardio-pulmonary bypass, AKI = acute kidney injury, IVH = intraventricular haemorrhage

In contrast, a retrospective study reported higher estimated blood loss (EBL) in patients who received TXA compared with those who did not (274 mL vs. 138 mL) in a cohort with a mean age of 3.4 ± 1.2 months.(38) This finding likely reflects confounding by indication, as TXA was preferentially administered to patients undergoing more complex or extensive procedures, highlighting the challenges of interpreting observational data in this setting.

In paediatric cardiac surgery with cardiopulmonary bypass (CPB), the results on TXA efficacy were less uniform. Observational comparative studies suggest that TXA was associated with lower overall blood product exposure when compared with historical antifibrinolytics or alternative agents.(36,44,46) These benefits were more consistently observed in infants and children beyond the immediate neonatal period. In neonates, however, transfusion requirements remained high irrespective of the antifibrinolytic agent used, including TXA or epsilon-aminocaproic acid (EACA).

Furthermore, a systematic review and Delphi consensus from the Paediatric Extracorporeal Membrane Oxygenation Anticoagulation Collaborative (PEACE) identified only a single neonatal study involving congenital heart disease in which tranexamic acid use was associated with reduced bleeding and transfusion requirements.(40) The evidence in neonates was heterogeneous, sparse, and inconclusive, highlighting the limited and low-certainty evidence in this population.

TXA efficacy in life-threatening bleeding and massive transfusion

Studies evaluating TXA efficacy in life-threatening haemorrhage, including trauma and massive transfusion scenarios, suggest a potential early benefit. A secondary analysis of a large prospective paediatric dataset demonstrated that early administration of antifibrinolytic agents, including TXA, was associated with reduced early (6-hour) mortality.(41) These results suggest a potential early survival benefit from attenuating hyperfibrinolysis during acute bleeding.

Nevertheless, TXA was administered as part of complex resuscitation bundles, and the observational nature of these analyses introduces substantial confounding by indication. Consequently, while these data support biological plausibility and align with trauma evidence, the certainty of benefit in paediatric trauma and massive haemorrhage remains low to moderate.

TXA and safety outcomes

Principal adverse effects associated with TXA include an increased risk of seizures, thromboembolic events, and renal complications. A narrative review exploring multimodal PBM strategies and antifibrinolytic profile of different pharmacotherapeutic agents reported no thromboembolic risk following TXA use.(33) A neonatal-specific study evaluating infants undergoing cardiac surgery with CPB and directly comparing TXA with EACA demonstrated no increase in seizure incidence in the low-dose TXA group.

In contrast, a higher seizure frequency was observed in the EACA cohort.(43) An increased risk of acute kidney injury (AKI) was reported in paediatric cohorts receiving EACA, whereas no associated increase in AKI was observed with TXA administration.(41)

Neonatal TXA use indications

Evidence for TXA use in neonatal medical haemorrhage remains limited and inconsistent. Reports involving conditions such as haemophilia, factor X deficiency, and thrombocytopenia have yielded conflicting findings. A single neonatal case report described an episode of hypercoagulability following TXA administration,(45) while available evidence in newborns with haemophilia has been insufficient to support routine use in this subgroup.(42) Similarly, studies investigating TXA for the prevention of IVH in ELBW neonates have demonstrated no clinically or statistically significant benefit.(48)

In contrast, a single case report of a neonate with factor X deficiency described resolution of gastrointestinal bleeding following tranexamic acid administration; however, the concurrent use of fresh frozen plasma limits attribution of efficacy to tranexamic acid alone.(34)

DISCUSSION

This narrative review evaluated the role of TXA as a pharmacological blood conservation strategy in paediatric patients, with particular emphasis on neonates. The overall body of evidence suggests that TXA has a clearly defined role in selected paediatric surgical populations, while its application in neonates remains limited by physiological complexity, inconsistent efficacy signals, and a paucity of neonatal-specific safety data.

A key finding emerging from this synthesis is that TXA appears most beneficial when used in procedural contexts with predictable, surgical bleeding and when incorporated into structured, multimodal PBM strategies. In these settings, TXA functions as an adjunct to haemostatic optimisation by attenuating surgery and CPB-triggered hyperfibrinolysis, thereby supporting early clot stability and reducing exposure to allogeneic transfusion when other contributors to bleeding (temperature, calcium, fibrinogen, platelets, surgical haemostasis) are simultaneously addressed.(49) Paediatric PBM frameworks emphasise that antifibrinolytics are most effective when combined with broader strategies such as preoperative anaemia management, minimisation of iatrogenic haemodilution, meticulous operative technique, point-of-care coagulation–guided transfusion, and targeted factor therapy, reinforcing that TXA is rarely a single-solution intervention.(33) Importantly, the more consistent benefit observed in older infants and children contrasts with the variability reported in neonates, which likely reflects developmental differences in haemostasis, circulating blood volume, and pharmacology. Neonates exhibit developmental haemostasis, including lower plasminogen concentrations at birth, age-dependent differences in fibrinolytic regulation, and immature renal clearance mechanisms.(50,51) These features may blunt the net antifibrinolytic effect achievable with TXA compared with older children in whom fibrinolysis and compensatory haemostatic mechanisms are more mature.(52) These challenges are amplified in high-complexity haemostatic environments such as CPB and ECMO where bleeding is multifactorial and not exclusively fibrinolytic. In such contexts, CPB-related bleeding in neonates is driven by a convergence of haemodilution (small circulating volume relative to prime), platelet dysfunction or consumption, inflammatory activation, and circuit-related perturbations of coagulation and fibrinolysis, alongside procedure-specific surgical bleeding risk.(53–55) Therefore, even if TXA successfully reduces fibrinolysis, the dominant haemostatic limitation may be platelet dysfunction or dilutional hypofibrinogenaemia, thereby constraining the isolated impact of TXA unless PBM elements that address these parallel pathways are implemented. Consistent with this mechanistic rationale, neonatal-focused clinical evidence has been more heterogeneous than broader paediatric datasets, and systematic reviews continue to highlight variability in effect estimates and outcomes across paediatric cardiac surgery populations.(56) This supports an interpretation that TXA's apparent benefit is context-dependent, with the strongest signal occurring where fibrinolysis is a principal driver of bleeding and where multimodal PBM reduces competing causes of haemorrhage.

The evidence base supporting TXA use outside elective surgical settings remains comparatively limited and less robust methodologically. While TXA appears biologically plausible in life-threatening haemorrhage and massive transfusion scenarios, available data are largely observational and embedded within complex resuscitation bundles.(57) The majority of supporting data in these contexts derive from adult trauma and obstetric populations, and from observational paediatric series rather than randomised neonatal trials.

As a result, causal attribution remains uncertain, and the magnitude of the TXA-specific benefit cannot be reliably quantified, particularly in neonates. Large landmark studies, such as the CRASH-2 and WOMAN trials,(58,59) demonstrated a mortality benefit with early TXA administration; however, their findings cannot be directly extrapolated to neonates given fundamental differences in haemostatic physiology, injury patterns, and competing causes of bleeding. While TXA remains a biologically rational adjunct in severe haemorrhage, the magnitude of benefit specific to TXA in non-elective neonatal settings cannot be reliably quantified with the current evidence base. This uncertainty underscores the need for prospective, context-specific studies and for cautious interpretation of observational data when TXA is used within bundled resuscitation strategies rather than as an isolated intervention

Off-label TXA use for neonatal medical haemorrhage highlights a clinically important gap between perceived need and evidentiary support. Although TXA is mechanistically attractive as an antifibrinolytic, neonatal bleeding phenotypes are heterogeneous and frequently reflect developmental haemostasis and systemic illness rather than isolated hyperfibrinolysis. In the study included in the review by Yao et al. on early IVH prevention, early randomised evidence demonstrated biochemical suppression of fibrinolysis without a corresponding reduction in haemorrhage incidence.(48) This suggests that fibrinolysis is unlikely to be the dominant modifiable driver of IVH in very preterm infants and that TXA's effect may not translate into meaningful clinical benefit in this indication. Broader syntheses of IVH prevention interventions similarly do not support TXA as an effective preventive therapy, reinforcing that routine prophylactic use in this setting is not evidence-based.

For inherited bleeding disorders and other neonatal medical haemorrhage indications, the literature remains limited and is largely composed of small series and isolated reports, typically in conjunction with concurrent haemostatic therapies.(34,42,45)In haemophilia, major international guidance positions antifibrinolytics as adjuncts, particularly for mucosal bleeding and dental/ENT procedures, rather than definitive stand-alone therapy, which further supports cautious interpretation of apparent "TXA success" in case-based neonatal reports where factor replacement or other haemostatic optimisation is occurring simultaneously.(60) Collectively, these findings support the conclusion that routine TXA use for neonatal medical haemorrhage cannot currently be recommended, and that future research should prioritise clearly defined haemorrhage phenotypes, standardised co-interventions, and prospective evaluation to isolate TXA-specific effects.

Safety considerations remain central to TXA use in neonates, particularly given the vulnerability of the developing brain and the immaturity of renal clearance pathways. Among reported adverse events, neurological complications, most notably seizures, represent the most consistent safety signal associated with TXA exposure. The available evidence suggests that seizure risk is dose-dependent and context-specific, with neonatal-specific studies using low-dose regimens not demonstrating the same risk profile observed in larger paediatric cohorts.(56) Importantly, no consistent association between TXA and thromboembolic events has been demonstrated, and renal adverse effects appear more prominent with alternative antifibrinolytic agents. Nevertheless, the absence of strong safety signals must be interpreted in light of the limited statistical power of existing neonatal studies, which are typically under-represented, heterogeneous, and not designed to detect rare adverse events.

Given that TXA is predominantly renally eliminated, and that neonatal glomerular filtration and tubular handling mature over the first weeks of life, inter-individual variability in drug exposure remains a legitimate concern, particularly in critically ill neonates or those with evolving renal dysfunction.(61)

Collectively, these considerations reinforce the view that TXA should not be regarded as a universal or benign solution for neonatal bleeding. Rather, it should be considered a context-specific adjunct, used selectively within broader blood conservation strategies, and guided by neonatal physiology, exposure-conscious dosing, and careful neurological and renal surveillance. Extrapolation from adult or older paediatric data, particularly with respect to safety, should be approached cautiously until adequately powered neonatal studies become available.

CONCLUSIONS

Neonatal anaemia and transfusion exposure remain major contributors to morbidity in preterm and critically ill infants. Pharmacological blood conservation strategies are therefore highly desirable. TXA demonstrates clear benefit in selected paediatric surgical populations; however, its role in neonates remains incompletely defined. Current evidence does not support routine neonatal use outside carefully selected surgical contexts, and significant uncertainty persists regarding optimal dosing, efficacy, and safety.

Until high-quality neonatal-specific data are available, TXA use in neonates should be cautious, individualised, and embedded within comprehensive patient blood management strategies. Addressing the identified evidence gaps is essential to ensure that TXA, if adopted more widely in neonatal care, improves outcomes without introducing avoidable harm.

FUTURE DIRECTIONS

This review identified several critical gaps that warrant prioritisation. Neonatal-specific pharmacokinetic and pharmacodynamic studies are urgently needed to define safe and effective dosing regimens. Prospective trials focusing on clinically meaningful outcomes, including transfusion exposure, neurological events, renal injury, and mortality, are essential before TXA can be routinely recommended in neonatal practice.

Author Contribution:

The following authors equally contributed to the project conceptualisation (PC), data curation (DC), results synthesis (RS), and the writing of the manuscript (WM).

- Dr Joseline Nkhoma - PC, DC, RS, WM
- Dr Harrilene Apleni - PC, DC, RS, WM
- Dr Gontse Leballo - PC, DC, RS, WM
- Professor Palesa Motshabi Chakane - PC, DC, RS, WM
- Dr Moses Kebalepile* - PC, DC, RS, WM

Funding: This research received no external funding.
Conflicts of Interest: The authors declare no conflicts of interest

REFERENCES

1. Dereje I, Etefa T, Gebremariam T, et al. Prevalence of anemia and associated factors among term newborns in Nekemte Specialised Hospital, Western Ethiopia. J Multidiscip Healthc. 2021; 14:2607–2615. doi:10.2147/JMDH.S326962.
2. Rocha G, Pereira S, Antunes-Sarmento J, et al. Early anemia and neonatal morbidity in extremely low birth-weight preterm infants. J Matern Fetal Neonatal Med. 2021; 34:3697–3703. doi:10.1080/14767058.2019.1689948.
3. Petrolini C, Chiara L, Chiara B, et al. The anemic newborn at birth: from diagnosis to treatment. Curr Pediatr Rev. 2023; 19:331–341. doi:10.2174/1573396319666221220110156.
4. German KR, Juul SE. Neonatal anemia. Curr Pediatr Rev. 2023; 19:388–394. doi:10.2174/1573396319666221121140627.
5. Dukleska K, Vinocur CD, Brenn BR, et al. Preoperative blood transfusions and morbidity in neonates undergoing surgery. Pediatrics. 2020; 146:e20193718. doi:10.1542/peds.2019-3718.
6. Goobie SM, Faraoni D, Zurakowski D, DiNardo JA. Association of preoperative anemia with postoperative mortality in neonates. JAMA Pediatr. 2016; 170:855–862. doi:10.1001/jamapediatrics.2016.1032.
7. Kalteren WS, Verhagen EA, Mintzer JP, Bos AF, Kooi EMW. Anemia and red blood cell transfusions, cerebral oxygenation, brain injury and development, and neurodevelopmental outcome in preterm infants: a systematic review. Front Pediatr. 2021; 9:644462. doi:10.3389/fped.2021.644462.
8. Lee EY, Kim SS, Park GY, Lee SH. Effect of red blood cell transfusion on short-term outcomes in very low birth weight infants. Clin Exp Pediatr. 2020; 63:56–62. doi:10.3345/kjp.2019.00990.
9. Al-Shehri H, Alghamdi GA, Alshabanat GB, et al. Neonatal red blood cell transfusion practices: a multi-national survey study. Healthcare MDPI. 2025; 13:568. doi:10.3390/healthcare13050568.
10. Balasubramanian H, Bhanushali M, Tripathi V, et al. Effect of minimization of early blood sampling losses among extremely premature neonates: a randomized clinical trial. J Pediatr. 2024; 269:114002. doi:10.1016/j.jpeds.2024.114002.
11. Fuchs A, Disma N, Virag K, et al. Peri-operative red blood cell transfusion in neonates and infants: NEonate and Children audiT of Anaesthesia pRactice IN Europe: a prospective European multicentre observational study. Eur J Anaesthesiol. 2022; 39:252–260. doi:10.1097/EJA.0000000000001646.
12. Disma N, Veyckemans F, Virag K, et al. Morbidity and mortality after anaesthesia in early life: results of the European prospective multicentre observational study, neonate and children audit of anaesthesia practice in Europe (NECTARINE). Br J Anaesth. 2021; 126:1157–1172. doi:10.1016/j.bja.2021.02.016.
13. Villeneuve A, Arsenault V, Lacroix J, Tucci M. Neonatal red blood cell transfusion. Int J Transfus Med. 2021; 116:366–378. doi:10.1111/vox.13036.
14. Cassady G. Anemia of prematurity. Medscape. Updated Dec 16, 2022. Medscape article 978238 overview. Available from: https://emedicine.medscape.com/article/978238-overview?form=fpf. [Accessed on Nov 12, 2025]
15. Strauss RG. Anaemia of prematurity: pathophysiology and treatment. Blood Rev. 2010; 24:221–225. doi:10.1016/j.blre.2010.08.001.
16. Boix H, Sanchez-Redondo MD, Cernada M, et al. Recommendations for transfusion of blood products in neonatology. An Pediatr. 2022; 97:60.e61–60.e68. doi:10.1016/j.anpede.2022.05.003.
17. Ahmed Z, Danielson L, Albeiruti R, Thomas R, Klein M. Blood transfusion in patients treated with surgery for necrotizing enterocolitis. Paediatr Anaesth. 2015; 25:196–199. doi:10.1111/pan.12485.
18. Shafique MA, Abbas SQ, Habiba U, et al. Transfusion strategies for neonates: current perspectives. Ann Med Surg. 2024; 86:1550–1562. doi:10.1097/MS9.0000000000001751.
19. Kim DH. Transfusion practice in neonates. Korean J Pediatr. 2018; 61:265–270. doi:10.3345/kjp.2018.06849.
20. Johns Hopkins All Children's Hospital. Red blood cell transfusion in the neonate: clinical pathway. Updated Aug 9, 2022. Available from: https://www.hopkinsmedicine.org/-/media/files/allchildrens/clinical-pathways/blood-product-transfusion-clinical-pathway-2022.pdf. [Accessed on Nov 18, 2025]
21. Deschmann E, Dame C, Sola-Visner MC, et al. Clinical practice guideline for red blood cell transfusion thresholds in very preterm neonates. JAMA Netw Open. 2024; 7:e2417431. doi:10.1001/jamanetworkopen.2024.17431.
22. Franz AR, Engel C, Bassler D, et al. Effects of liberal vs restrictive transfusion thresholds on survival and neurocognitive outcomes in extremely low-birth-weight infants: the ETTNO randomized clinical trial. JAMA. 2020; 324:560–570. doi:10.1001/jama.2020.10690.
23. Govender K, Kemp E, Motshabi Chakane P. Intraoperative transfusion practice and associated outcomes following neonatal surgery in a middle-income country: a 5-year single center retrospective review. Paediatr Anaesth. 2023; 33:720–727. doi:10.1111/pan.14715.
24. Eeles A, Baikady RR. Peri-operative blood management. Indian J Anaesth. 2017; 61:456–462. doi:10.4103/ija.IJA_341_17.
25. Scheffczik J. Blood sparing techniques in paediatric anaesthesia. Anaesthesia Tutorial of the Week (WFSA Resource Library). Updated Mar 13, 2015. Available from: https://resources.wfsahq.org/atotw/blood-sparing-techniques-in-paediatric-anaesthesia/?utm_source=chatgpt.com. [Accessed on Nov 12, 2025]
26. Lykissas MG, Crawford AH, Chan G, Aronson LA, Al-Sayyad MJ. The effect of tranexamic acid in blood loss and transfusion volume in adolescent idiopathic scoliosis surgery: a single-surgeon experience. J Child Orthop. 2013; 7:245–249. doi:10.1007/s11832-013-0486-7.
27. Chauncey JM, Patel P. Tranexamic acid. In: StatPearls. Treasure Island, FL: StatPearls Publishing; 2024. Updated Jul 24, 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532909/. [Accessed on Nov 12, 2025]
28. Levy JH, Koster A, Quinones QJ, Milling TJ, Key NS. Antifibrinolytic therapy and perioperative considerations. Anesthesiology. 2018; 128:657–670. doi:10.1097/ALN.0000000000001997.
29. Zou ZY, He LX, Yao YT. Tranexamic acid reduces postoperative blood loss in Chinese pediatric patients undergoing cardiac surgery: a PRISMA-compliant systematic review and meta-analysis. Medicine. 2022; 101:e28966. doi:10.1097/MD.0000000000028966.

30. Zhang Y, Zhang X, Wang Y, et al. Efficacy and safety of tranexamic acid in pediatric patients undergoing cardiac surgery: a single-center experience. Front Pediatr. 2019; 7:181. doi:10.3389/fped.2019.00181.
31. Johnson SM, Tsang D, Dansby M, Allen C. New and off-label uses of tranexamic acid. AACN Adv Crit Care. 2021; 32:237–242. doi:10.4037/aacnacc2021193.
32. White N, Bayliss S, Moore D. Systematic review of interventions for minimizing perioperative blood transfusion for surgery for craniosynostosis. J Craniofac Surg. 2015; 26:26–36. doi:10.1097/SCS.0000000000001108.
33. Goobie SM, Faraoni D. Perioperative paediatric patient blood management: a narrative review. Br J Anaesth. 2025; 134:168–179. doi:10.1097/SCS.0000000000001108.
34. Dorgalaleh A, Baghaipour MR, Tabibian S, et al. Gastrointestinal bleeding in a newborn infant with congenital factor X deficiency and COVID-19: a common clinical feature between a rare disorder and a new, common infection. Int J Lab Hematol. 2020; 42:e277–e279. doi:10.1111/ijlh.13318.
35. Erb TO, Meier PM. Surgical treatment of craniosynostosis in infants: open vs closed repair. Curr Opin Anaesthesiol. 2016; 29:345–351. doi:10.1097/ACO.0000000000000324.
36. Faraoni D, Rahe C, Cybulski KA. Use of antifibrinolytics in pediatric cardiac surgery: where are we now? Paediatr Anaesth. 2019; 29:435–440. doi:10.1111/pan.13533.
37. Goel R, Cushing MM, Tobian AA. Pediatric patient blood management programs: not just transfusing little adults. Transfus Med Rev. 2016; 30:235–241. doi:10.1016/j.tmrv.2016.07.004.
38. Han RH, Nguyen DC, Bruck BS, et al. Characterization of complications associated with open and endoscopic craniosynostosis surgery at a single institution. J Neurosurg Pediatr 2016; 17:361–370. doi:10.3171/2015.7.PEDS15187.
39. Maeda T, Sasabuchi Y, Matsui H, et al. Safety of tranexamic acid in pediatric cardiac surgery: a nationwide database study. J Cardiothorac Vasc Anesth. 2017; 31:549–553. doi:10.1053/j.jvca.2016.10.001.
40. Moynihan KM, Ryerson LM, Le J, et al. Antifibrinolytic and adjunct hemostatic agents: the pediatric extracorporeal membrane oxygenation anticoagulation collaborative consensus conference. Pediatr Crit Care Med. 2024; 25:e44–e52. doi:10.1097/PCC.0000000000003491.
41. Spinella PC, Leonard JC, Gaines BA, et al. Use of antifibrinolytics in pediatric life-threatening hemorrhage: a prospective observational multicenter study. Crit Care Med. 2022; 50:e382–e392. doi:10.1097/CCM.0000000000005383.
42. Streif W, Knofler R. Perinatal management of haemophilia. Hamostaseologie. 2020; 40:226–232. doi:10.1055/a-1141-1252.
43. Tanis-Arens CE, Mastropietro CM, Walker SG, Abbasi RK. Antifibrinolytic agents and seizure risk in neonates undergoing cardiac surgery. Paediatr Anaesth. 2023; 33:765–767. doi:10.1111/pan.14696.
44. Verma S, Eisses M, Richards M. Blood conservation strategies in pediatric anesthesia. Anesthesiol Clin. 2009; 27:337–351. doi:10.1016/j.anclin.2009.05.002.
45. Wang Y, He J, Zhang X, Zhang G. Confusion in the monitoring of coagulation function in pregnant and neonate patients with severe disease: a case reports and brief literature review. Medicine. 2023; 102:e35997. doi:10.1097/MD.0000000000035997.
46. Willems A, De Groote F, Dumoulin M, Fils JF, Van der Linden P. Aprotinin versus tranexamic acid in children undergoing cardiac surgery: an observational study. Eur J Cardiothorac Surg. 2019; 56:688–695. doi:10.1093/ejcts/ezz088.
47. Wood RJ, Stewart CN, Liljeberg K, Sylvanus TS, Lim PK. Transfusion-free cranial vault remodeling: a novel, multifaceted approach. Plast Reconst Surg. 2020; 145:167–174. doi:10.1097/PRS.0000000000006323.
48. Yao SL, Smit E, Odd D. The effectiveness of interventions to prevent intraventricular haemorrhage in premature infants: a systematic review and network meta-analysis. J Neonatal Perinatal Med. 2023; 16:5–20. doi:10.3233/NPM-221048.
49. Colomina MJ, Méndez E, Sabate A. Altered fibrinolysis during and after surgery. Semin Thromb Hemost. 2021; 47:512–519. doi:10.1055/s-0041-1722971.
50. Khizroeva J, Makatsariya A, Vorobev A, et al. The hemostatic system in newborns and the risk of neonatal thrombosis. Int J Mol Sci. 2023; 24:13864. doi:10.3390/ijms241813864.
51. Rey YFV, Barreto Mota R, Soares H. Developmental hemostasis in the neonatal period. World J Pediatr. 2022; 18:7–15. doi:10.1007/s12519-021-00492-3.
52. Andrew M. The relevance of developmental hemostasis to hemorrhagic disorders of newborns. Semin Perinatol. 1997; 21:70–85. doi:10.1016/s0146-0005(97)80022-5.
53. Jaggers J, Lawson JH. Coagulopathy and inflammation in neonatal heart surgery: mechanisms and strategies. Ann Thorac Surg. 2006; 81:S2360–S2366. doi:10.1016/S0146-0005(97)80022-5.
54. Frantzeskaki F, Konstantonis D, Rizos M, et al. Extracorporeal membrane oxygenation (ECMO)-associated coagulopathy in adults. Diagnostics. 2023; 13:3496. doi:10.3390/diagnostics13233496.
55. Singh SP. Strategies for blood conservation in pediatric cardiac surgery. Ann Card Anaesth. 2016; 19:705–716. doi:10.4103/0971-9784.191562.
56. Faraoni D, Willems A, Melot C, De Hert S, Van der Linden P. Efficacy of tranexamic acid in paediatric cardiac surgery: a systematic review and meta-analysis. Eur J Cardiothorac Surg. 2012; 42:781–786. doi:10.1093/ejcts/ezs127.
57. Neff LP, Beckwith MA, Russell RT, Cannon JW, Spinella PC. Massive transfusion in pediatric patients. Clin Lab Med. 2021; 41:35–49. doi:10.1016/j.cll.2020.10.003.
58. Roberts I, Shakur H, Coats T, et al. The CRASH-2 trial: a randomised controlled trial and economic evaluation of the effects of tranexamic acid on death, vascular occlusive events and transfusion requirement in bleeding trauma patients. Health Technol Assess. 2013; 17:1–79. doi:10.3310/hta17100.
59. Shakur H, Elbourne D, Gulmezoglu M, Alfirevic Z, et al. The WOMAN trial (world maternal antifibrinolytic trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial. Trials 2010; 11:40. doi:10.1186/1745-6215-11-40.
60. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. Haemophilia. 2013; 19:e1–e47. doi:10.1111/j.1365-2516.2012.02909.x.
61. Gertler R, Gruber M, Grassin-Delyle S, et al. Pharmacokinetics of tranexamic acid in neonates and infants undergoing cardiac surgery. Br J Clin Pharmacol. 2017; 83:1745–1757. doi:10.1111/bcp.13274.