

Tranexamic acid use in critically ill children with hemorrhage: a single-center retrospective descriptive study

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Abstract

Background

Tranexamic acid (TXA) is used to control hemorrhage in children, but evidence describing its use across heterogeneous pediatric intensive care unit (PICU) populations remains limited. We aimed to describe the indications, administration, transfusion requirements, adverse events, and clinical outcomes of children who received TXA for hemorrhage in a PICU.

Methods

In this single-center retrospective descriptive study, we reviewed 44 children who received TXA for hemorrhage in the Ankara University Faculty of Medicine PICU between March 2020 and December 2023. Demographic and clinical characteristics, TXA administration, blood component transfusion, documented adverse events, organ support, and outcomes were summarized. Exploratory univariable analyses assessed associations between selected clinical factors and mortality.

Results

The cohort included 21 female and 23 male patients with a mean age of 72.0 ± 65.3 months. Trauma accounted for 25 cases (56.8%), and intracranial bleeding was the most common bleeding site (28/44, 63.6%). TXA was initiated a mean of 6.1 ± 6.8 hours after bleeding onset and administered for 3.9 ± 2.8 days. Twenty-one patients (47.7%) received at least one blood component. The number receiving red blood cell suspension was 12 before TXA, 7 at 8 hours, and 5 at 24 hours; these descriptive within-patient counts were not adjusted for co-interventions. One patient (2.3%) developed deep vein thrombosis, and no seizures were documented. Twenty-nine patients (65.9%) survived to PICU discharge. Time to TXA initiation was not significantly associated with mortality ($p = 0.726$) or neurological sequelae ($p = 0.466$).

Conclusions

In this heterogeneous, high-acuity PICU cohort, TXA was used for both traumatic and non-traumatic hemorrhage, with one documented thrombotic event. Because the study lacked an untreated comparator and was not designed to establish causality, the findings describe practice patterns and observed outcomes rather than TXA efficacy or safety. Prospective multicenter studies are needed to define patient selection, timing, dosing, and comparative outcomes.

Background

Hemorrhage is an important cause of preventable morbidity and mortality in injured and critically ill children. Tranexamic acid (TXA) is a synthetic lysine analogue that competitively inhibits the interaction of plasminogen with fibrin and thereby attenuates fibrinolysis [1, 2]. Although TXA was initially used mainly for dental and menstrual bleeding, its clinical use has expanded to trauma, surgery, and other hemorrhagic conditions.

In adults with bleeding trauma, evidence supporting early TXA administration was shaped by the CRASH-2 trial and its exploratory analysis, which found the greatest benefit when treatment was started within 3 hours of injury and suggested potential harm from later administration [3–5]. Pediatric practice is less standardized. Published pediatric surgical studies have used widely varying loading doses and maintenance infusions, and observational trauma data remain more limited than the adult evidence base [6–9].

Critically ill children who receive TXA form a heterogeneous group: bleeding may be traumatic or non-traumatic, and outcomes are influenced by illness severity, bleeding site, organ dysfunction, transfusion, and concurrent interventions. Describing real-world PICU practice can identify the populations being treated and the outcomes that require prospective evaluation. We therefore aimed to characterize the indications, dosing approach, timing, transfusion requirements, documented adverse events, organ support, and clinical outcomes among children who received TXA for hemorrhage in a tertiary PICU.

Methods

Study design and setting

We conducted a single-center retrospective descriptive study in the Ankara University Faculty of Medicine PICU. The reporting of this study was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations. Medical records from March 2020 through December 2023 were reviewed.

Participants

Children admitted to the PICU who received TXA for clinically identified hemorrhage were eligible. Patients were excluded if their clinical records were incomplete or if they received an antifibrinolytic agent other than TXA. Because the cohort was defined by exposure to TXA and did not include an untreated comparator, the study was designed to describe treatment patterns and observed outcomes rather than estimate the comparative effectiveness or safety of TXA.

Data collection and variables

We recorded age, sex, Glasgow Coma Scale score at PICU admission, underlying chronic disease, primary reason for admission, bleeding etiology and site, time from bleeding onset to TXA initiation,

treatment duration, discontinuation method, transfusion of red blood cell suspension, fresh frozen plasma, or platelet suspension, extracorporeal therapies, respiratory and inotropic support, PICU length of stay, clinician-documented hemostatic response, documented complications, survival to PICU discharge, hemorrhage-related death, and neurological sequelae. PRISM III and PELOD scores were sought from the medical records; sufficiently complete values for analysis were not available in the source manuscript dataset and are therefore not reported.

TXA administration

TXA was prescribed at the discretion of the treating team. The usual protocol consisted of a loading dose of 10 mg/kg administered over 1 hour followed by an infusion of 10 mg/kg/hour. Duration and discontinuation were individualized. In general, dose reduction began 24 hours after bleeding and clinical evidence of hemorrhagic diathesis had resolved, with discontinuation targeted within the following 48 hours.

Outcomes

The prespecified clinical outcomes recorded for this analysis were PICU mortality and neurological sequelae. Additional descriptive outcomes included TXA timing and duration, documented complications, transfusion requirements, and clinician-documented hemostatic response. Adverse events were identified from routine clinical documentation; systematic screening for asymptomatic thrombosis was not performed.

Statistical analysis

Analyses were performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables are reported as mean $\pm$ standard deviation and median (minimum–maximum), and categorical variables as number (percentage). Continuous variables were compared using Student's t test or the Mann–Whitney U test according to distributional assumptions. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. Exploratory unadjusted associations with mortality were summarized using odds ratios (ORs) and 95% confidence intervals (CIs). For 2 $\times$ 2 tables containing zero cells, the Haldane–Anscombe continuity correction was applied. No multivariable model was fitted because of the small sample and limited number of outcome events. All tests were two-sided and $p < 0.05$ was considered statistically significant. No adjustment was made for multiple comparisons; inferential findings should therefore be interpreted as exploratory.

Ethics

The Ankara University Faculty of Medicine Clinical Research Ethics Committee approved the study (decision no. 2023/356; 22 June 2023) and waived the requirement for informed consent because the

study involved retrospective review of medical records. The study was conducted in accordance with the Declaration of Helsinki and applicable institutional requirements.

Use of generative AI-assisted technology

During manuscript preparation, the authors used ChatGPT (OpenAI) for English-language editing and organization of the manuscript. The authors reviewed and revised the output and take full responsibility for the final content.

Results

Participant characteristics and TXA administration

Forty-four children were included: 23 (52.3%) were male and 21 (47.7%) were female. Mean age was 72.0 ± 65.3 months, and mean admission Glasgow Coma Scale score was 9.5 ± 4.1 . Twenty-two patients (50.0%) had an underlying chronic condition. Trauma was the most frequent bleeding etiology (25/44, 56.8%), and intracranial bleeding was the most frequent bleeding site (28/44, 63.6%) (Table 1).

Table 1
Characteristics of the study population and TXA treatment (N = 44)

Characteristic	Value
Continuous variables	
Age, months	72.0 ± 65.3; 54 (2–204)
Time to TXA initiation, hours	6.1 ± 6.8; 3 (0–24)
Admission GCS score	9.5 ± 4.1; 9.5 (3–15)
TXA treatment duration, days	3.9 ± 2.8; 3 (0.5–14)
PICU length of stay, days	39.1 ± 51.5; 14 (1–223)
Sex	
Male	23 (52.3)
Female	21 (47.7)
Comorbidity	
Present	22 (50.0)
Absent	22 (50.0)
Neurological	7 (15.9)
Cardiological	5 (11.4)
Oncological	5 (11.4)
Other	5 (11.4)
Primary reason for admission	
Central nervous system	24 (54.5)
Infectious disease	5 (11.4)
Gastroenterology	3 (6.8)
Cardiology	3 (6.8)
Pulmonology	2 (4.5)
Hematology	2 (4.5)
Other	5 (11.4)
Bleeding etiology	
Trauma	25 (56.8)

Characteristic	Value
Continuous variables	
Gastrointestinal	4 (9.1)
Mucosal	2 (4.5)
Postoperative	2 (4.5)
Other	11 (25.0)
Bleeding site	
Intracranial	28 (63.6)
Pulmonary	9 (20.5)
Gastrointestinal	4 (9.1)
Mucosal	2 (4.5)
Extremity	1 (2.3)
TXA discontinuation	
Stopped without tapering	23 (52.3)
Tapered	21 (47.7)
Respiratory support	
No respiratory support	8 (18.2)
Any respiratory support	36 (81.8)
Mechanical ventilation	31 (70.5)
Reservoir mask	4 (9.1)
Oxygen hood	1 (2.3)
Other treatment and outcomes	
Inotropic support	17 (38.6)
Clinician-documented hemostatic response	40 (90.9)
Survived to PICU discharge	29 (65.9)
Died in PICU	15 (34.1)
CRRT	5 (11.4)
ECMO	3 (6.8)
Plasma exchange	2 (4.5)

Characteristic	Value
Continuous variables	
Transfusion during admission	
Any blood component	21 (47.7)
Red blood cell suspension	20 (45.5)
Fresh frozen plasma	17 (38.6)
Platelet suspension	11 (25.0)

Continuous variables are presented as mean $\pm$ standard deviation; median (minimum–maximum). Categorical variables are presented as n (%). CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; GCS, Glasgow Coma Scale; PICU, pediatric intensive care unit; TXA, tranexamic acid.

TXA was initiated a mean of 6.1 ± 6.8 hours after bleeding onset and continued for 3.9 ± 2.8 days. Treatment was stopped without tapering in 23 patients (52.3%) and tapered in 21 (47.7%). A clinician-documented hemostatic response was recorded in 40 patients (90.9%); because this assessment was retrospective and not based on a prespecified validated definition, it should be interpreted descriptively.

Transfusion and organ support

Twenty-one patients (47.7%) received at least one blood component. Across the admission, 20 (45.5%) received red blood cell suspension, 17 (38.6%) received fresh frozen plasma, and 11 (25.0%) received platelet suspension. Before TXA administration, 12 patients received red blood cell suspension, 12 received fresh frozen plasma, and 7 received platelet suspension. The corresponding counts at 8 hours were 7, 4, and 3, and at 24 hours were 5, 2, and 3, respectively (Fig. 1). These time-specific counts were not tested as a causal effect of TXA and may reflect bleeding control, co-interventions, survivor effects, or changes in clinical indication.

Mechanical ventilation was provided to 31 patients (70.5%) and inotropic support to 17 (38.6%). Five patients (11.4%) received continuous renal replacement therapy (CRRT), three (6.8%) received extracorporeal membrane oxygenation (ECMO), and two (4.5%) underwent plasma exchange.

Adverse events and outcomes

One patient (2.3%) had documented deep vein thrombosis. No seizures or other adverse events attributed to TXA were documented. Because adverse events were identified retrospectively and asymptomatic thrombosis was not systematically screened, this observation should not be interpreted as an incidence estimate or proof of safety.

Twenty-nine patients (65.9%) survived to PICU discharge and 15 (34.1%) died; six deaths (13.6% of the cohort) were attributed directly to hemorrhage. Time to TXA initiation did not differ significantly according to mortality ($p = 0.726$) or neurological sequelae ($p = 0.466$) (Table 2). In exploratory unadjusted analyses, mortality was associated with ECMO, CRRT, inotropic support, and mechanical ventilation (Table 3). These estimates had wide confidence intervals and reflect illness severity and treatment selection; they should not be interpreted as causal effects of the support modalities.

Table 2
Time to TXA initiation according to clinical outcomes

Outcome	Group	Time to TXA initiation, hours	p value
Mortality	Died	5.1 ± 6.2; 2 (0–24)	0.726
	Survived	6.5 ± 7.1; 3 (1–24)	
Neurological sequelae	Present	4.4 ± 3.8; 3 (1–12)	0.466
	Absent	6.8 ± 7.7; 3 (0–24)	

Values are mean ± standard deviation; median (minimum–maximum). TXA, tranexamic acid.

Table 3
Exploratory unadjusted associations with PICU mortality

Variable	Mortality with factor	Mortality without factor	OR	95% CI	p value
ECMO	3/3 (100.0)	12/41 (29.3)	16.52	0.97–344.04	0.034
CRRT	5/5 (100.0)	10/39 (25.6)	30.90	1.57–608.18	0.003
Inotropic support	14/17 (82.4)	1/27 (3.7)	121.33	11.52–1278.10	< 0.001
Mechanical ventilation	15/31 (48.4)	0/13 (0.0)	25.38	1.39–464.02	0.002
Neurological sequelae	7/13 (53.8)	8/31 (25.8)	3.35	0.87–13.00	0.092

For tables with zero cells, ORs and 95% CIs were calculated using the Haldane–Anscombe continuity correction. CI, confidence interval; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; OR, odds ratio; PICU, pediatric intensive care unit.

Discussion

This study describes TXA use in 44 critically ill children treated for heterogeneous traumatic and non-traumatic hemorrhage. More than half of the cohort had trauma, nearly two thirds had intracranial bleeding, and many required mechanical ventilation or other organ support. TXA was usually started

several hours after bleeding onset and was administered for multiple days, illustrating a practice pattern that differs from the short-course regimens studied in adult trauma. One deep vein thrombosis and no seizures were documented, while approximately one third of the cohort died, consistent with the high acuity of the population.

The adult CRASH-2 evidence supports early TXA use in bleeding trauma, particularly within 3 hours of injury [5, 11]. Pediatric evidence is less definitive. The PED-TRAX combat registry study reported associations between TXA exposure and outcomes in severely injured children, but its observational design is susceptible to confounding by indication [9]. Studies of pediatric cardiac and non-cardiac surgery support a reduction in perioperative blood loss or transfusion under selected protocols, although dosing regimens vary considerably [6, 7, 10, 12]. Our cohort extends the descriptive literature by including both traumatic and non-traumatic PICU hemorrhage, but it does not provide a comparator against which a treatment effect can be estimated.

The number of patients receiving each blood component decreased over the 24 hours after TXA initiation. This temporal pattern is clinically relevant but cannot be attributed to TXA alone. Bleeding may have abated because of surgery, interventional procedures, component therapy, correction of coagulopathy, or the natural course of illness. Moreover, the analysis used counts at selected time points rather than component volumes or a standardized transfusion outcome. Future studies should capture weight-adjusted component volumes, blood loss, laboratory markers of fibrinolysis, co-interventions, and repeated measures within patients.

Thromboembolism and seizures are recognized concerns during TXA therapy. Large adult trauma trials did not show a clear increase in vascular occlusive events [11], whereas seizures have been associated particularly with higher doses and certain surgical settings [12, 14]. The low number of documented events in this cohort is reassuring only at a descriptive level. Retrospective chart review can miss transient neurological events and clinically silent thrombosis, and the small sample cannot exclude clinically important risks.

Strengths and limitations

The study provides detailed real-world information on indications, timing, treatment duration, transfusion, organ support, and outcomes in a population for which published PICU data are limited. Its principal limitations are the retrospective single-center design, small sample, absence of an untreated comparator, heterogeneous bleeding etiologies, confounding by indication and illness severity, incomplete availability of standardized severity scores, reliance on clinician documentation for hemostatic response and adverse events, lack of systematic thrombosis screening, and absence of standardized blood-loss or weight-adjusted transfusion measurements. The exploratory analyses were unadjusted, some contingency tables contained zero cells, confidence intervals were wide, and no correction was made for multiple testing. These limitations preclude conclusions about the efficacy or safety of TXA and limit generalizability.

Conclusions

TXA was used across a broad range of traumatic and non-traumatic hemorrhagic conditions in this high-acuity PICU cohort. A single thrombotic event and no seizures were documented, but the design and sample size do not permit comparative safety conclusions. The observed decline in transfusion counts after treatment is hypothesis-generating and cannot establish efficacy. Prospective multicenter studies with standardized indications, dosing, co-intervention measurement, and active adverse-event surveillance are needed.

Abbreviations

CI

confidence interval

CRRT

continuous renal replacement therapy

ECMO

extracorporeal membrane oxygenation

FFP

fresh frozen plasma

GCS

Glasgow Coma Scale

OR

odds ratio

PELOD

Pediatric Logistic Organ Dysfunction

PICU

pediatric intensive care unit

PRISM III

Pediatric Risk of Mortality III

RBC

red blood cell

TXA

tranexamic acid.

Declarations

Ethics approval and consent to participate

The Ankara University Faculty of Medicine Clinical Research Ethics Committee approved the study (decision no. 2023/356; 22 June 2023) and waived the requirement for informed consent because the study involved retrospective review of medical records.

Consent for publication

Not applicable.

Availability of data and materials

The dataset analysed during the current study is not publicly available because it contains potentially identifiable clinical information, but de-identified data may be available from the corresponding author on reasonable request and subject to ethics committee and institutional approval.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HÖ conceptualized the study, collected data, reviewed the literature, and drafted the manuscript. GK collected data and critically reviewed the manuscript. AG contributed to clinical interpretation and critically reviewed the manuscript. BB acquired data and critically reviewed the manuscript. FK contributed to clinical interpretation and critically reviewed the manuscript. HU collected data and critically reviewed the manuscript. MH reviewed the literature and critically reviewed the manuscript. HFÇ contributed to clinical interpretation and critically reviewed the manuscript. Eİ acquired data and critically reviewed the manuscript. TK supervised the study and critically revised the manuscript. All authors read and approved the final manuscript.

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Figures

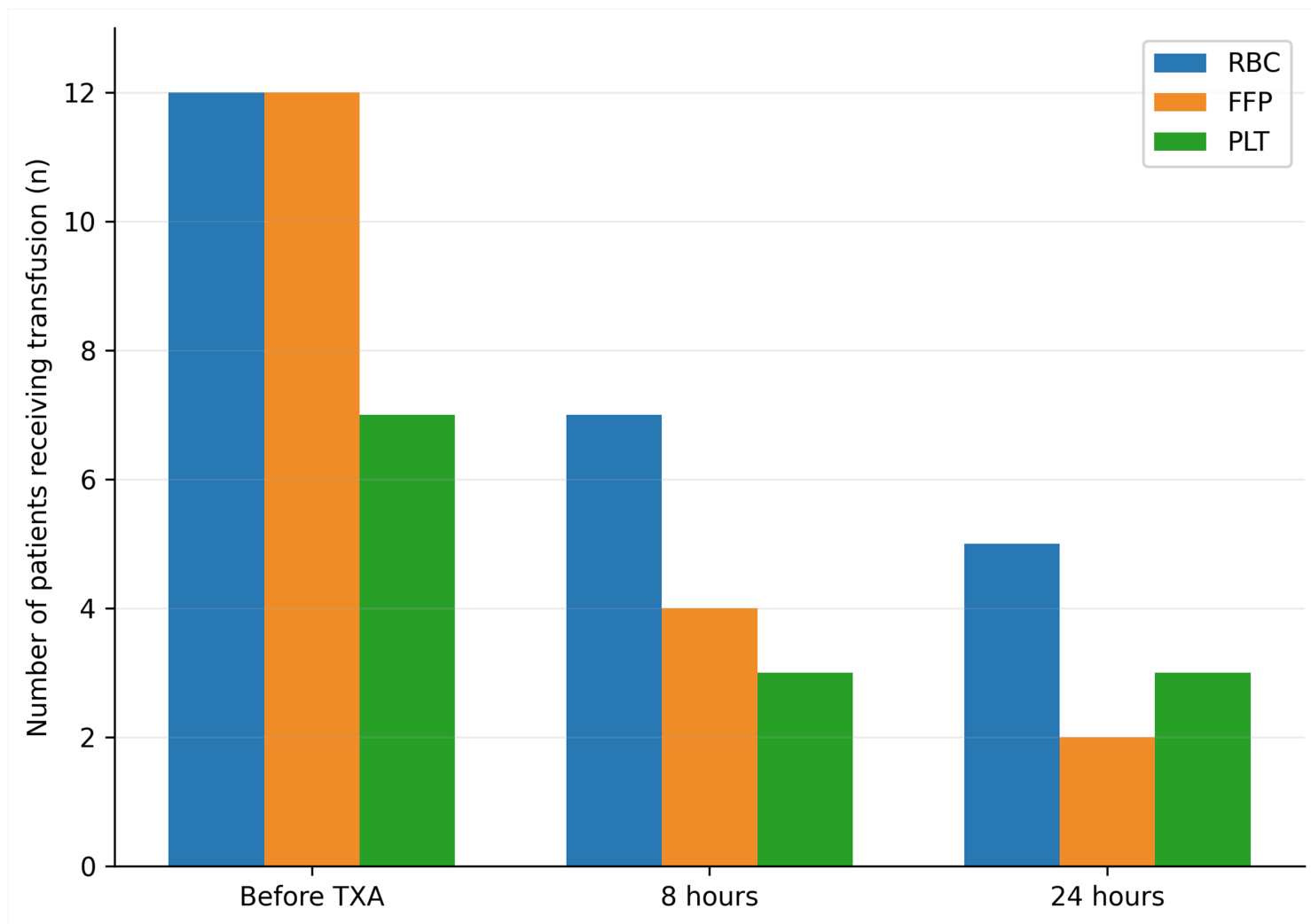


Figure 1

Number of patients receiving each blood component before TXA and at 8 and 24 hours after TXA initiation. Counts are descriptive and do not establish a causal effect of TXA. FFP, fresh frozen plasma; PLT, platelet suspension; RBC, red blood cell suspension; TXA, tranexamic acid.

Mechanical ventilation was provided to 31 patients (70.5%) and inotropic support to 17 (38.6%). Five patients (11.4%) received continuous renal replacement therapy (CRRT), three (6.8%) received extracorporeal membrane oxygenation (ECMO), and two (4.5%) underwent plasma exchange.