Inhaled Tranexamic Acid As a Novel Treatment for Pulmonary Hemorrhage in Critically Ill Pediatric Patients: An Observational Study

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Objectives: To describe the use of inhaled or endotracheally instilled tranexamic acid in critically ill pediatric patients for the treatment of pulmonary hemorrhage, which can be severe, life-threatening, and include potentially high-risk management procedures.

Design: Retrospective observational study from 2011-2018 with patients followed until hospital discharge.

Setting: Free-standing children’s hospital with an annual ICU volume of more than 3,500 yearly admissions.

Patients: Pediatric patients, ages 0 to 18 years, admitted to an ICU and who received at least one dose of inhaled or endotracheally instilled tranexamic acid were included.

Interventions: Inhaled or endotracheally instilled tranexamic acid.

Measurements and Main Results: This study described the efficacy and adverse effects of patients who received inhaled or endotracheally instilled tranexamic acid. A total of 19 patients met inclusion criteria; median age was 72 months (11–187 mo), most patients were female (11, 58%), and almost half our patients (8, 42%) had congenital heart disease. Nine of 19 encounters (47%) had diffuse alveolar hemorrhage, four (21%) had pulmonary hemorrhage related to major aortopulmonary collateral arteries, two (11%) had mucosal airway bleeding, two (11%) were iatrogenic, one had a pulmonary embolism, and one patient did not have their etiology of pulmonary hemorrhage determined. Cessation of pulmonary hemorrhage was achieved in 18 of 19 patients (95%) with inhaled tranexamic acid with no major adverse events recorded.

Conclusions and Relevance: We demonstrate that inhaled tranexamic acid may be safely used to treat pulmonary hemorrhage from varied etiologies in critically ill pediatric patients. Prospective studies are required in this vulnerable population to determine optimal dosing and delivery strategies, as well as to define any differential effect according to etiology.

Key Words: inhaled tranexamic acid; pediatric; pulmonary hemorrhage

Pulmonary hemorrhage, frequently referred to as hemoptysis, can be severe and life threatening (1). In pediatric patients, etiologies of pulmonary hemorrhage include infection, bronchiectasis, vascular disorders, parenchymal lung disease, and post-surgical complications (1–3). Duration of pulmonary hemorrhage and amount of blood loss depends on etiology and the ability to control the bleeding. Median duration of bleeding ranges between 2.9 and 7.5 days (3–5). Acute management of pulmonary hemorrhage includes stabilization of the patient, securing the airway, application of positive end-expiratory pressure ventilation to tamponade the source of hemorrhage, and repletion with blood products if necessary. Further investigation and management of hemorrhage include potentially high-risk procedures such as bronchoscopy, catheterization, or more invasive surgical interventions.

Tranexamic acid (TXA) is a lysine analog that blocks the conversion of plasminogen to plasmin and inhibits binding of plasmin to fibrin which stabilizes the fibrin matrix, thereby reducing bleeding (6, 7). The cost of IV TXA solution 1,000 mg/10 mL vial is $17.50–$86.80 (8). Multiple studies show the successful off-label use of systemic TXA in children for the treatment of hemorrhage associated with congenital heart surgery, orthopedic operations, neurosurgical procedures, trauma, and other medical diagnoses (9–11). In adults, an increasing number of studies reported the successful use of systemic TXA for hemoptysis, defined as bleeding from the lower respiratory tract (5, 12). A systematic review
concluded that the use of systemic (oral or IV) TXA for hemoptysis was associated with a significant reduction in the length of bleeding in adult patients (13). Systemic TXA, however, may be associated with serious complications including venous thromboembolism, neurotoxicity, and seizures (14–22).

In contrast, adult studies and case reports demonstrate rapid cessation of hemoptysis after one dose of TXA via the inhaled route (inhaled TXA) with no major adverse events (23–30). Wand et al (23) in the only randomized control trial using inhaled TXA for hemoptysis, showed resolution of hemoptysis in 96% of patients within 5 days and no side effects. Limited data on the use of TXA for pediatric pulmonary hemorrhage exists. Two case reports show systemic TXA controlling hemoptysis in children with cystic fibrosis-related hemoptysis (31, 32). There are no published data on the use of inhaled TXA in pediatric patients.

The antifibrinolytic properties, low side-effect profile, and low costs lend TXA to the off-label use in children, but studies and data to recommend the routine use of inhaled TXA in pulmonary hemorrhage remain insufficient. We aimed to report 1) the indications associated with inhaled TXA use in our center; 2) patient outcomes of cessation of pulmonary hemorrhage while receiving inhaled TXA and survival; and 3) associated side effects of the medication.

MATERIALS AND METHODS

Study Design
We performed a retrospective observational study in the ICUs at a free-standing quaternary care children’s hospital. Pediatric patients, ages 0 to 18 years who were admitted to an ICU from January 2011 to November 2018 and received inhaled or endotracheally instilled TXA for pulmonary hemorrhage were included. The use of inhaled TXA for pulmonary hemorrhage was determined by the primary medical team and was an off-label use of TXA. There was no protocol or guideline at our hospital recommending the use of inhaled TXA for pulmonary hemorrhage.

Data Collection and Analysis
Pharmacy medication-administration records were queried to identify patients who met inclusion criteria. A pharmacist blinded to the outcomes of the study was asked to identify patients who received inhaled or endotracheally instilled TXA. Electronic medical records (EMRs) were abstracted for demographics, clinical and laboratory data, and resource utilization including admission unit, ICU and hospital length of stay (LOS), procedures performed (bronchoscopy and catheterization), coagulation variables, and in-hospital mortality. Preexisting potentially clinical important comorbidities (congenital heart disease [CHD], malignancy, genetic mutation, respiratory disorders, preexisting liver or renal failure) were identified and were defined by International Classification of Diseases, 9th Revision (ICD-9) or International Classification of Diseases, 10th Revision (ICD-10) codes in the chart. EMR documentation was also reviewed for known adverse effects with treatment of systemic TXA: seizures, new-onset of renal failure, and new vascular occlusive event; and bronchospasm, the only reported side effect associated with the use of inhaled TXA. Ventilation (positive end-expiratory pressure, minute ventilation, use of neuromuscular blockade agents) and oxygenation (inspiratory oxygen fraction, peripheral capillary oxygen saturation (Spo2), arterial Po2, PaCO2, use of inhaled nitric oxide) variables before and after inhaled TXA treatment were reviewed. Therapeutic enteral (aspirin, coumadin) and IV systemic (unfractionated and low-molecular-weight heparin, bivalirudin) anticoagulation were extracted from the medical record. Hemoglobin and standard plasma coagulation tests (prothrombin time, partial thromboplastin time, international normalized ratio) were collected before and after TXA treatment to assess coagulopathy or hypercoagulability. The amount of blood product transfusions (RBCs, fresh frozen plasma, cryoprecipitate, and platelets) during the 48 hours prior to inhaled TXA and 48 hours after inhaled TXA were assessed to directly assess the effect of inhaled TXA. Institutional review board approval was obtained prior to initiation of the study, and consent from subjects was waived.

Key Outcome Measures
The primary outcomes were efficacy and adverse effects of patients who received inhaled or endotracheally instilled TXA. Efficacy of inhaled TXA was defined as the cessation of pulmonary hemorrhage within 48 hours of starting inhaled TXA as documented in the EMR by physicians or respiratory therapists that bloody secretions had resolved. Adverse effects evaluated included seizures, deep vein thromboses (DVTs), and renal failure after administration of inhaled TXA as documented in the notes or by an ICD-9/ICD-10 codes. Secondary outcomes included in-hospital mortality, ICU LOS, hospital LOS, additional surgical procedures performed, ventilation variables (defined above) prior to and after use of TXA, coagulation variables (defined above) number of doses of TXA, number of bleeding days, and amount of blood product transfusions (RBCs, fresh frozen plasma, cryoprecipitate, and platelets) during the 48 hours prior to and after administration of inhaled TXA.

Statistical Analysis
Statistical analyses were carried out using JMP (Version 13; SAS, Cary, NC). Categorical and dichotomous variables are expressed as exact numbers with percentages, whereas continuous variables are expressed as median with 25–75th interquartile ranges (IQRs). Fisher exact test was used to look for associations between categorical variables, whereas Wilcoxon-Mann-Whitney U test was used to compare non-normally continuous variables. Logistic regression was performed for continuous variables compared with binary outcomes and reported in odds ratios with 95% CIs. Haldane-Anscombe correction was used where applicable. Statistical significance was defined as a p value of less than 0.05.

RESULTS

Patient Demographics
A total of 19 patients met inclusion criteria (Table 1). Almost half of our patients (eight, 42%) had CHD and the second most common comorbidity was malignancy (four patients, 21%) (Table 2). Survivors, although not statistically significant, were more likely to have CHD (60% vs 22%; p = 0.17), major aortopulmonary collateral arteries (MAPCAs) (30% vs 11%; p = 0.58), less renal...
failure (30% vs 67%; \( p = 0.18 \)), and less malignancy (10% vs 33%; \( p = 0.30 \)) (Table 3). Lower FiO\(_2\) before TXA use, however, was significantly associated with survival (0.60 vs 0.93; \( p = 0.021 \)). There were no other significant differences in patient demographics between the two groups.

**Etiologies of Pulmonary Hemorrhage**

Nine of 19 encounters (47%) had diffuse alveolar hemorrhage, four (21%) had pulmonary hemorrhage associated with MAPCAs, two (11%) had mucosal airway bleeding, two (11%) were iatrogenic, one from a wire puncture of a pulmonary artery during a catheterization for pulmonary artery balloon angioplasty and one from a bronchoalveolar lavage, one had a pulmonary emboli, and one patient did not have an etiology determined (Table 2).

**TXA Administration Method**

TXA was administered via inhalation or direct endotracheal instillation using the 100 mg/mL solution designed for injection product. In intubated and mechanically ventilated patients, TXA was nebulized using Aerogen Solo nebulizer (Aerogen, Galway, Ireland) for 15–20 minutes. One patient received inhaled TXA via the Aerogen Solo nebulizer in-line with noninvasive mechanical ventilation for 15–20 minutes. One patient received endotracheally instilled TXA during a bronchoscopy. Endotracheal suctioning was performed immediately prior to administration of TXA in order to remove secretions that could limit the distribution of TXA throughout the lungs, instilled TXA was administered as three equal aliquots directly into the endotracheal tube, followed by 3–5 positive pressure breaths during manual bagging, and suctioning was avoided for at least 15 minutes after the TXA was administered. After identification of pulmonary hemorrhage, inhaled TXA was initiated at 250–500 mg every 6–24 hours. The modal frequency was every 8 hours. Subsequent administrations were not timed with episodes of bleeding in most cases. Dosing frequency was subsequently decreased based on patients’ responses.

**Inhaled TXA Efficacy**

Inhaled TXA was effective in 18 of patients (95%), achieving cessation of pulmonary hemorrhage within 48 hours of inhaled TXA (Table 2). No patient who achieved cessation of bleeding developed repeat hemorrhage during their admission. Median days of bleeding after TXA was initiated was 1.0 day (IQR, 1.0–2.0 d) (Table 2). Reported pulmonary hemorrhage improved after one dose of TXA for all patient except one, patient I, who was on systemic anticoagulation with unfractionated heparin for extracorporeal membrane oxygenation (ECMO) (Table 1). The other patients receiving

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**TABLE 1. Summary of Clinical Characteristics**

| Patient | Age/Sex | Weight (kg) | Bleeding Cause           | Comorbidity | Systemic Anticoagulation | Maximum TXA Dose | TXA Effective?* |
|---------|---------|-------------|--------------------------|-------------|--------------------------|------------------|-----------------|
| A       | 2 yr/Female | 11.8 | MAPCAs related CHD | No | 250 mg q6h | Yes |
| B       | 10 yr/Female | 31.7 | DAH Malignancy | No | 250 mg once | Yes |
| C       | 19 yr/Female | 58.6 | MAPCAs related CHD | No | 500 mg q6h | Yes |
| D       | 15 yr/Male | 92 | DAH Malignancy | No | 500 mg q12h | Yes |
| E       | 16 yr/Female | 52.3 | DAH Heart transplant | No | 500 mg q8h | Yes |
| F       | 5 yr/Female | 27.3 | DAH Malignancy | No | 250 mg q8h | Yes |
| G       | 10 yr/Male | 93.8 | MAPCAs related CHD | No | 500 mg q8h | Yes |
| H       | 6 mo/Female | 7.8 | MAPCAs related CHD | No | 250 mg q24h | Yes |
| I       | 5 mo/Female | 5.8 | DAH Genetic mutation | No | 250 mg q8h | Yes |
| J       | 3 yr/Male | 14.6 | AMB Genetic mutation | Yes | 250 mg q8h | No |
| K       | 2 mo/Male | 4.2 | AMB CHD | Yes | 250 mg q8h | Yes |
| L       | 6 yr/Male | 33.3 | iatrogenic CHD | No | 500 mg q6h | Yes |
| M       | 9 mo/Female | 9.4 | DAH Liver failure | No | 250 mg q8h | Yes |
| N       | 12 yr/Male | 28.3 | DAH Asthma | Yes | 500 mg q6h | Yes |
| O       | 19 yr/Male | 59.1 | DAH Malignancy | No | 500 mg q8h | Yes |
| P       | 17 yr/Male | 42.6 | DAH Alagille syndrome, liver failure | No | 500 mg q8h | Yes |
| Q       | 10 mo/Male | 8.5 | iatrogenic CHD | No | 250 mg q8h | Yes |
| R       | 1.5 yr/Male | 14.2 | Unknown Renal failure, coagulopathy | Yes | 250 mg q8h | Yes |
| S       | 15 yr/Female | 31.4 | Pulmonary embolism Turner syndrome | No | 500 mg q6h | Yes |

AMB = airway mucosal bleeding, CHD = congenital heart disease, DAH = diffuse alveolar hemorrhage, MAPCAs = main aortopulmonary collateral arteries, TXA = tranexamic acid.

*Efficacy defined as cessation of pulmonary hemorrhage within 48 hr of starting inhaled TXA.
systemic anticoagulation with unfractionated heparin, patients K, N, and R, achieved cessation of pulmonary hemorrhage after one dose of TXA. The most common dosing of TXA was 250 mg/dose every 8 hours (250–500 every 6–24 hr). Survivors and nonsurvivors had no significant differences in numbers of bleeding days once TXA was initiated, days of TXA therapy, or doses of TXA used (Table 3).

No Major Adverse Events With Inhaled TXA
Patients experienced no major adverse events after receiving inhaled TXA. No patient experienced a seizure, developed a DVT, nor developed renal failure after receiving TXA. One patient who received systemic TXA before receiving inhaled TXA (patient F) developed a DVT while receiving systemic TXA but no further DVTs while receiving inhaled TXA. Patients did not require increasing respiratory support nor did any experience increased difficulty ventilating nor oxygenating after receiving inhaled TXA (Table 4). Coagulation variables did not significantly change after receiving inhaled TXA. Patients did receive significantly less blood product transfusions after receiving inhaled TXA (480 vs 29.5 mL/kg; \( p = 0.034 \)) (Table 4).

DISCUSSION
TXA, an antifibrinolytic medication, has been used successfully in children to control bleeding in hemophiliacs and postoperative bleeding (8–10). In pediatric patients, oral and IV TXA has also been used successfully in some cases of hemoptysis associated with cystic fibrosis, but data are insufficient to support the routine use of TXA for pediatric pulmonary hemorrhage (31, 32). We describe 19 pediatric patients with pulmonary hemorrhage who were successfully, safely, and inexpensively treated with inhaled TXA.

Inhaled or endotracheal TXA seems to be effective and safe for pulmonary hemorrhage in our case series as well as five other smaller case series involving adult patients (23–30) and a recent randomized controlled trial (23). Segrelles Calvo et al (27) reported the successful use of inhaled TXA in four patients, three with malignancy. Patel et al (30) achieved cessation of hemoptysis within 72 hours of initiating inhaled TXA. In the largest case series, Márquez-Martín et al (25) prospectively showed efficacy of endotracheally administered TXA in 31 of 48 adult patients. Wand et al (23), in the only randomized controlled trial of inhaled TXA, reported cessation of hemoptysis in 24 of 25 adult patients (96%) within 5 days of use, with significant reduction in hemoptysis starting on the second day. We found TXA to be effective in the treatment of pulmonary hemorrhage in pediatric patients after just one dose, with rapid control of bleeding in 18 of 19 encounters. The only patient who did not have cessation of pulmonary hemorrhage with inhaled TXA was a patient on systemic anticoagulation while on ECMO. The efficacy of inhaled TXA while on ECMO has never been described. The use of inhaled TXA may allow for the benefit of greater local

| Characteristics | \( n \) (\%) or Median (IQR) |
|-----------------|-----------------------------|
| Demographics    |                             |
| Age, mo         | 72 (11–187)                 |
| Male            | 8 (42)                      |
| Weight, kg      | 28.3 (9.4–52.3)             |
| Comorbidities   |                             |
| Congenital heart disease | 8 (42)               |
| Malignancy      | 4 (21)                      |
| Cause of bleeding |                          |
| Main aortopulmonary collateral arteries related | 4 (21)  |
| Diffuse alveolar hemorrhage | 9 (47)     |
| Airway mucosal bleeding | 2 (11)       |
| Iatrogenic      | 2 (11)                      |
| Pulmonary embolism | 1 (5)                    |
| No source identified | 1 (5)                |
| Organ failure   |                             |
| Liver failure   | 4 (21)                      |
| Renal failure   | 9 (47)                      |
| Length of stay, d|                             |
| ICU             | 25 (15–37)                  |
| Hospital        | 32 (25–49)                  |
| Mechanical support |                            |
| Invasive mechanical ventilation | 18 (95)  |
| Positive end-expiratory pressure (cm H\(_2\)O) | 10.0 (8.0–14.5) |
| Neuromuscular blockade | 9 (47)    |
| Inhaled nitric oxide | 8 (42)    |
| Procedures      |                             |
| Bronchoscopy    | 10 (53)                     |
| Catheterization | 3 (16)                      |
| Autopsy         | 4/9 (45)                    |
| Tranexamic acid therapy |                     |
| Total days of bleeding | 1.0 (1.0–2.0)   |
| Days of TXA therapy | 3.0 (2.0–6.0)   |
| Total doses of TXA | 7 (4–15)        |
| Cumulative dose TXA, mg | 2,500 (1,500–4,750) |
| Outcomes        |                             |
| Cessation of bleeding | 18 (95)      |
| Adverse events  | 0                           |
| Deaths          | 9 (47)                      |

IQR = interquartile range, TXA = tranexamic acid.
concentration of the medication and more rapid onset while minimizing the risks associated with systemic use.

No patients in our case series experienced major adverse events from the use of inhaled TXA. The few other case series on inhaled TXA and one randomized control trial also reported no adverse events with the use of inhaled TXA for hemoptysis (23–29). Side effects such as seizures and renal failure have been reported with systemic TXA (10, 14, 18, 19). In our case series, no patients

| TABLE 3. Characteristics in Survivors Versus Nonsurvivors |
|----------------------------------------------------------|
| **Characteristics**                                     | **Survivors (n = 10),** | **Nonsurvivors (n = 9),** | **OR (95% CI)** | **p** |
| Demographics                                             | n (%) or Median (IQR)   | n (%) or Median (IQR)   |                |      |
| Age, mo                                                  | 48 (11–162)             | 123 (21–192)            | 1.00 (0.99–1.02) | 0.43 |
| Male                                                     | 5 (50)                  | 3 (33)                  | 0.5 (0.08–3.21)  | 0.65 |
| Weight, kg                                               | 21.3 (9.2–46.8)         | 31.4 (10.2–55.5)        | 1.01 (0.97–1.04) | 0.72 |
| Comorbidities                                            |                         |                        |                |      |
| Congenital heart disease                                 | 6 (60)                  | 2 (22)                  | 0.2 (0.03–1.43)  | 0.17 |
| Malignancy                                               | 1 (10)                  | 3 (33)                  | 4.5 (0.37–54.16) | 0.30 |
| Cause of bleeding                                        |                         |                        |                |      |
| Main aortopulmonary collateral arteries related          | 3 (30)                  | 1 (11)                  | 0.3 (0.02–3.48)  | 0.58 |
| Diffuse alveolar hemorrhage                              | 4 (40)                  | 5 (56)                  | 1.8 (0.30–11.63) | 0.66 |
| Airway mucosal bleeding                                  | 0                       | 2 (22)                  | 7.0 (0.29–16794) | 0.21 |
| Iatrogenic                                               | 2 (20)                  | 0                       | 0.18 (0.01–4.28) | 0.35 |
| Organ failure                                            |                         |                        |                |      |
| Liver failure                                            | 2 (20)                  | 2 (22)                  | 1.14 (0.13–10.39)| > 0.99|
| Renal failure                                            | 3 (30)                  | 6 (67)                  | 4.67 (0.67–32.36)| 0.18 |
| Length of stay, d                                        |                         |                        |                |      |
| ICU                                                      | 20.5 (11.8–79.8)        | 28.0 (24.5–35.0)        | 0.99 (0.97–1.01) | 0.39 |
| Hospital                                                 | 32.0 (12.0–82.5)        | 29.0 (25.0–51.0)        | 0.99 (0.97–1.01) | 0.36 |
| Mechanical support                                       |                         |                        |                |      |
| Invasive mechanical ventilation                         | 10 (100)                | 8 (89)                  | 0.27 (0.01–751)  | 0.47 |
| Positive end-expiratory pressure, cm H₂O               | 11 (73–15.0)            | 10 (8.0–140)            | 0.99 (0.74–1.32) | 0.94 |
| Neuromuscular blockade                                   | 3 (30)                  | 6 (67)                  | 4.67 (0.67–32.36)| 0.18 |
| Inhaled nitric oxide                                     | 3 (30)                  | 5 (56)                  | 2.92 (0.44–19.23)| 0.37 |
| Fio₂ prior to TXA                                        | 0.60 (0.50–0.68)        | 0.93 (0.80–1.00)        | 1.13 (1.02–1.26) | **0.021**|
| Procedures                                               |                         |                        |                |      |
| Bronchoscopy                                             | 4 (40)                  | 6 (67)                  | 3.00 (0.45–19.59)| 0.37 |
| Catheterization                                          | 2 (20)                  | 1 (11)                  | 0.50 (0.04–6.68) | > 0.99|
| Tranexamic acid                                          |                         |                        |                |      |
| Total days of bleeding                                   | 1.0 (1.0–1.3)           | 1.0 (1.0–3.5)           | 1.44 (0.72–2.89) | 0.30 |
| Days of TXA therapy                                      | 3.0 (2.8–3.8)           | 5.0 (2.0–75)            | 1.40 (0.89–2.20) | 0.15 |
| Total doses of TXA                                       | 4.5 (3.0–9.3)           | 11.0 (6.5–170)          | 1.11 (0.96–1.30) | 0.17 |
| Cumulative dose TXA, mg                                   | 1,875 (938–2,875)       | 3,500 (2,375–8,750)     | 1.00 (0.99–1.00) | 0.21 |
| Outcomes                                                 |                         |                        |                |      |
| Adverse events                                           | 0 (0)                   | 0 (0)                   |                |      |

IQR = interquartile range, OR = odds ratio, TXA = tranexamic acid.
Boldface value indicates a statistically significant variable.
developed new-onset renal failure nor experienced seizures or clinical DVTs after receiving inhaled TXA. One patient in our study (patient F) developed a subclavian DVT near a peripherally inserted central catheter after receiving two 48-hour courses of systemic TXA and two doses of systemic recombinant factor seven for pulmonary hemorrhage. This prompted the conversion to inhaled TXA to manage the pulmonary hemorrhage, which resolved within 48 hours of initiation of inhaled TXA. The patient did not experience further DVTs after the conversion to inhaled TXA.

In addition, no patients in our study experienced minor side effects, such as bronchospasm. Only one study reports the minor side effect of bronchospasm with inhaled TXA, highlighting the safety of a targeted therapy compared with systemic use (27). Just as in a previous study, the use of inhaled TXA did not affect ventilatory settings during mechanical ventilation (25). Other variables such as oxygenation and coagulation were not affected by the use of inhaled TXA in our study. We did find, however, that patients received significantly less blood product after receiving inhaled TXA.

The median cumulative dose of inhaled TXA in our study was 2,500 mg of the IV formulation via nebulization. With the cost of IV TXA solution 1,000 mg/10 mL vial of $17.50–$86.80 (8), the total cost of inhaled TXA per patient in our study was inexpensive, ranging from $43.75 to $217.00. With the hopes of achieving more rapid onset of action locally and minimizing systemic side effects, the development of an aerosolized form of TXA designed specifically for use in patients with hemoptysis is being investigated (34).

We recognize limitations to our study. We were unable to provide a control group of patients with pulmonary hemorrhage who did not receive inhaled TXA due to the low prevalence of this disease process in pediatric patients and limitations in our EMR. Our patient population was heterogeneous, and transfusion goals and variables were not standardized for all patients. The small number of patients studied did not allow us to determine if the use of inhaled TXA had a significant impact on mortality, bleeding time, and specific blood product transfusion needs. The retrospective nature of the study required the efficacy of inhaled TXA to be determined by documentation in the medical record of cessation of pulmonary hemorrhage or blood in the endotracheal tube, instead of an objective bleeding score.

**CONCLUSIONS**

Inhaled TXA may be a safe, well-tolerated, inexpensive, and effective therapy for pulmonary hemorrhage in critically ill pediatric patients. At our institution, we created a protocol using TXA injection via nebulization at 250–500 mg/dose every 6 to 12 hours until improvement in pulmonary hemorrhage as a temporizing or palliative measure. Prospective studies are required in this vulnerable population to determine optimal dosing and delivery strategies, evaluate mortality benefit, as well as to define any differential effect according to etiology.

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