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ORIGINAL ARTICLE

Effect of tranexamic acid on blood loss in pediatric cardiac surgery: a randomized trial

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Abstract
Purpose The benefit of tranexamic acid (TXA) in pediatric cardiac surgery on postoperative bleeding has varied among studies. It is also unclear whether the effects of TXA differ between cyanotic patients and acyanotic patients. The aim of this study was to test the benefit of TXA in pediatric cardiac surgery in a well-balanced study population of cyanotic and acyanotic patients.
Methods A total of 160 pediatric patients undergoing cardiac surgery with cardiopulmonary bypass (81 cyanotic, 79 acyanotic) were included in this single-blinded, randomized trial at a tertiary care university-affiliated teaching hospital. Eighty-one children (41 cyanotic, 40 acyanotic) were randomly assigned to a TXA group, in which they received 50 mg/kg of TXA as a bolus followed by 15 mg/kg/h infusion and another 50 mg/kg into the bypass circuit. The other 79 patients were randomly assigned to a placebo group. The primary end point was the amount of 24-h blood loss.
Results The amount of 24-h blood loss was significantly less in the TXA group than in the placebo group [mean (95% confidence interval): 18.6 (15.8–21.4) vs. 23.5 (19.4–27.5) ml/kg, respectively; mean difference −4.9 (−9.7 to −0.01) ml/kg; $p = 0.049$]. This effect of TXA was already significant at 6 h [9.5 (7.5–11.5) vs. 13.2 (10.6–15.9) ml/kg, respectively; mean difference −3.47 (−7.0 to −0.4) ml/kg; $p = 0.027$]. However, there was no significant difference in the amount of blood transfusion between the groups. There was also no statistical difference in the effect of TXA in each cyanotic and acyanotic subgroup.
Conclusion TXA can reduce blood loss in pediatric cardiac surgery but not the transfusion requirement (http://ClinicalTrials.gov number NCT00994994).

Keywords Tranexamic acid · Children · Cardiac surgery · Blood loss · Cyanosis

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Introduction

Excessive bleeding leads to increases in morbidity and mortality in adults [1] and children [2] after cardiac surgery with cardiopulmonary bypass (CPB). Excessive bleeding in children can be as large as 110 ml/kg/24 h [3], which necessitates blood transfusion, and allogeneic blood transfusion may increase mortality [4]. Although major causes of postoperative bleeding in pediatric cardiac surgery are thrombocytopenia, platelet dysfunction, and hemodilution, one possible cause is increased fibrinolysis during CPB [5, 6], which occurs in about 16% of patients [7]. Moreover, congenital heart disease itself in pediatric patients has been shown to be associated with fibrinolysis [8, 9].

Tranexamic acid (TXA), an analog of the amino acid lysine, is an antifibrinolytic agent that competes with

plasminogen for binding sites on fibrin and also prevents plasmin-induced platelet activation [10]. To date, there have been seven randomized control trials to assess the effect of TXA in pediatric cardiac surgery [11–17]. Four of those studies showed a significant reduction in postoperative blood loss by TXA [11, 12, 14, 16], whereas two studies showed no significant effect of TXA [15, 17], and one study showed mixed results depending on dose [13]. Although the presence of cyanosis would be associated with more bleeding episodes due to collateral vessel formation and platelet dysfunction caused by erythrocytosis [18], it is unclear whether there is a difference in the effects of TXA in cyanotic and acyanotic patients.

Accordingly, we conducted a randomized control study involving a well-balanced study population of cyanotic and acyanotic patients in order to determine the effect of TXA on blood loss in pediatric cardiac surgery patients.

Materials and methods

Our Institutional Review Board approved the study protocol. Written informed consent was obtained from the legal guardian of each patient because all participants were younger than 18 years of age.

Patient selection

Children younger than 18 years of age who were scheduled to undergo elective cardiac surgery with CPB between January 2006 and July 2007 were considered potentially eligible for inclusion in the study. Neonates of less than 1 month of age, children on mechanical ventilation preoperatively, and children on inotropic support before surgery were excluded from the study. Other exclusion criteria included a preexisting coagulation disorder, re-operation within 48 h, obvious kidney or liver disease, and known allergy to TXA. Preoperative anticoagulation therapy, such as administration of warfarin, aspirin, or ticlopidine, was considered acceptable for inclusion.

Group allocation

After informed consent had been obtained, participants were divided into a cyanotic congenital heart disease (CCHD) cohort and an acyanotic congenital heart disease (ACHD) cohort according to the presence of a right-to-left shunt region (oxygen saturation of <90%). The patients in each cohort were then randomly assigned to a TXA group or placebo group (1:1) in each cyanotic and acyanotic cohort. Randomization was stratified with the use of computer-based random-number generator lists provided by one of the co-investigators (HM) who was not involved in the determination of eligibility, administration of study drugs, patient's treatment, or assessment of outcomes.

Study protocol

In the TXA group, 50 mg/kg of intravenous TXA (100 mg/ml solution) was administered before skin incision; this was followed by 15 mg/kg/h of continuous infusion. Another 50 mg/kg of TXA was injected into a CPB circuit prior to commencement of the CPB. Continuous infusion was ceased with skin closure. Patients in the placebo group received an equivalent volume of normal saline, including continuous infusion and injection into the CPB circuit.

Perioperative management of patients

Management of general anesthesia was standardized. A blood sample was taken after the induction of anesthesia to check hemoglobin, platelet count, prothrombin time, and activated partial thromboplastin time (APTT).

Heparin (300 units/kg) was given for anticoagulation prior to aortic cannulation to maintain activated clotting time (ACT) (Hemochron 401 or 801; SOMA Technology, Bloomfield, CT) at more than 400 s. Priming volumes in CPB circuits were approximately 400, 600, 1200, and 1500 ml for patients with body weights of approximately <15, 15–25, 25–35, and >35 kg, respectively. The CPB circuit was primed with 25% albumin, mannnitol, sodium bicarbonate, and acetate Ringer's solution, with the ratio of amounts of acetate Ringer's fluid and albumin being maintained at approximately 5:1. Packed red blood cells were also added to the prime to achieve a hematocrit level of >25% if the body weight was <10 kg. Protamine at the dose of 3 mg/kg was injected after termination of CPB. If ACT was still more than 130 s, additional protamine was administered. If the surgeon considered that hemostasis was not achieved after protamine administration, fresh frozen plasma (FFP) was given to the patient. Although the anesthesiologists were responsible for intraoperative fluid management, including blood transfusion, platelet transfusion was performed after consultation with the responsible cardiac surgeon because of the cost issue. Our approximate targets for hemoglobin were 12 g/dl in patients with acyanotic status and 15 g/dl in patients with cyanotic status, although a clear-cut trigger of transfusion was not defined in this trial. We basically tried not to give any blood product to patients whose CPB circuit was filled without red cells. Left atrial pressure or central venous pressure was maintained at 5–10 mmHg to keep preload.

The patients were transferred to the intensive care unit (ICU) after confirming chest X-rays, and another blood sample was taken following the same protocol as used for the intraoperative collection. Postoperative management,

including blood product transfusion, was performed by attending physicians in the ICU, who were blinded to the study group. FFP was given if the physician considered that the patients required clotting factors based on the results of coagulation tests. Similarly, permission by the responsible surgeon was required for platelet transfusion while the patient was in the ICU.

Since this was a single-blinded randomized trial, anesthesiologists who cared for the participants were aware of the group allocation, but surgeons, intensive care physicians, operating and intensive care nurses, and perfusionists did not know the group assignment.

Outcomes

Our hypothesis was that TXA would reduce the amount of blood loss in pediatric cardiac surgery patients. The primary end point in this study was 24-h blood loss. Blood loss was defined as the total amount of pericardial and mediastinal tube drainage after admission to the ICU. The amount of drainage was noted in the medical chart recorded by ICU nurses who were not aware of group allocation. As secondary end points, 6-h blood loss, amount of transfusion required, chest closure time (from the time of protamine injection to skin closure), re-exploration of the chest for bleeding within 24 h, duration of mechanical ventilation, duration of ICU stay, and episodes of thrombotic complication were also recorded.

Power calculation

To calculate the sample size for the current trial, we considered a 50% reduction of blood loss during the first 24 h post-surgery to be satisfactory. Assuming an average blood loss of 35 ml/kg, a standard deviation of 25 ml/kg, a power of 0.80, and an alpha level of 0.05, 33 participants were required in each group. We increased the sample size to 40 to allow for loss to follow-up in each of the four groups. Therefore, the aim was to investigate 160 patients in the study.

Statistical analysis

Statistical analyses were performed by JMP ver. 7.0 (SAS Institute, Cary, NC). Data were expressed as the mean and 95% confidence interval (95% CI). Student's t test or Wilcoxon's test was used for statistical analysis where applicable. Fisher's exact test or the chi-square test was used for categorical data. A p value <0.05 was considered to be statistically significant.

Results

We studied 160 children undergoing cardiac surgery with CPB. Eighty-one patients (41 cyanotic and 40 acyanotic patients) were assigned to the TXA group and 79 patients (40 cyanotic and 39 acyanotic patients) were assigned to the placebo group. All patients received a full-predefined dose of TXA, and none of the patients were lost to follow-up. Thus, we included data for all 160 patients in our final analyses (Fig. 1). The mean age of the patients was 32.5 (range 1–170) months and mean body weight was 10.6 (range 3.2–50.6) kg. There were 54 infants (33.8%) younger than 12 months. Although 56 (35%) of the children received anticoagulants prior to surgery, there was no association between anticoagulant therapy and preoperative APTT or PT. The patients

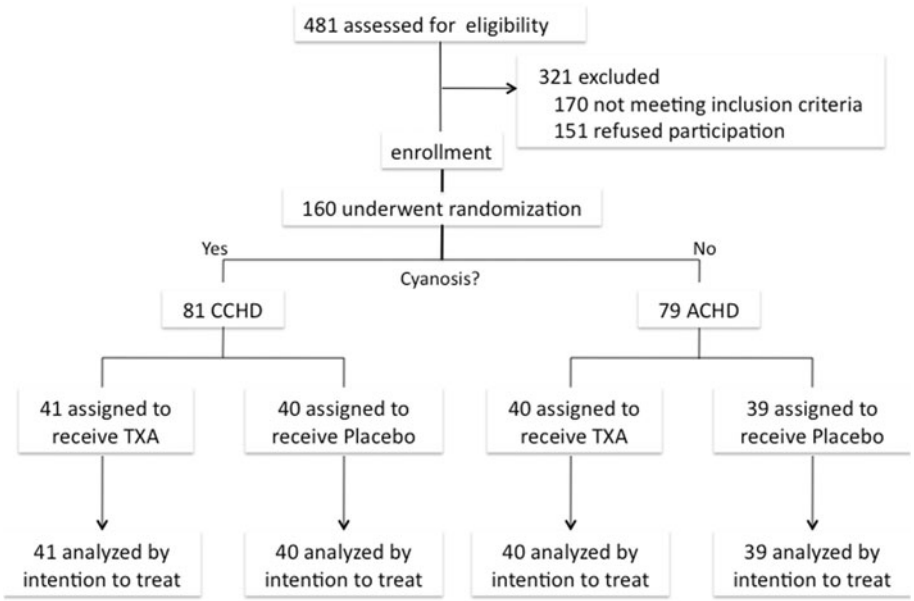

Fig. 1 Flow diagram of the study. None of the participants were lost to follow-up. *TXA* Tranexamic acid, *CCHD* cyanotic congenital heart disease, *ACHD* acyanotic congenital heart disease

received various types of operations, and 135 (84.4%) of the patients were in Risk Adjustment in Congenital Heart Surgery (RACHS-1) category [19] 2 or 3. Sixty-one (38.2%) of the patients had received previous sternotomy. The mean CPB time was 102.5 (95% CI 92.0–113.0) min and mean aortic cross clamp time was 64.5 (95% CI 59.2–69.9) min. All of these pre- and intra-operative variables were well balanced between the TXA and placebo groups, except number of patients whose APTT was above the normal limit (Table 1). There were 24 (29.6%) children in the TXA group compared with 41 (52.6%) children in the placebo group with supranormal APTT ($p = 0.004$).

Primary and secondary endpoints

The mean amount of drainage at 24 h post-surgery was 18.6 (95% CI 15.8–21.4) ml/kg in the TXA group and 23.5 (19.4–27.5) ml/kg in the placebo group; the difference between the groups was statistically significant [mean difference −4.9 (−9.7 to −0.01) ml/kg; $p = 0.049$]. This effect of TXA on the amount of bleeding was already significant at 6 h after the operation [9.5 (7.5–11.5) ml/kg in the TXA group vs. 13.2 (10.6–15.9) ml/kg in the placebo group; mean difference −3.7 (−7.0 to −0.4) ml/kg; $p = 0.027$] (Fig. 2).

Table 1 Characteristics of patients and surgery

Characteristics of patients/surgery	Total	TXA	Placebo	*p* value
Age (months)	32.5 (26.1–36.3)	31.2 (24.5–37.9)	31.3 (23.5–39.1)	0.99
Age in CCHD (months)		27.9 (22.6–33.2)	36.6 (25.0–48.0)	0.18
Infants (<12 month)	54	28 (34.6%)	26 (32.9%)	0.87
Gender (male)	84 (52.5%)	42 (51.9%)	42 (53.2%)	0.99
Height (cm)	80.9 (77.7–84.2)	81.8 (77.3–86.4)	80.0 (75.4–84.7)	0.58
Weight (kg)	10.6 (9.5–11.7)	10.9 (9.4–12.3)	10.3 (8.7–12.0)	0.63
Preoperative anticoagulation		28	29	0.87
Aspirin	23	14	9	
Warfarin	22	10	12	
Ticlopidine	18	7	11	
Repeat sternotomy	61 (38.1%)	25 (30.9%)	36 (45.6%)	0.10
Surgeon A/B/C	87/46/27	48/22/11	39/24/16	0.41
Preoperative laboratory data				
Hemoglobin (Hb) (g/dl)	12.8 (12.5–13.2)	12.9 (12.3–13.4)	12.8 (12.3–13.4)	0.86
Hb in CCHD (g/dl)		14.3 (13.6–15.0)	14.3 (13.6–15.0)	0.97
Platelets ($\times 10^3$/ml)	300 (284–315)	287 (266–309)	312 (291–334)	0.11
Prothrombin time (%)	94.2 (92.0–96.4)	93.5 (90.4–96.6)	94.9 (91.8–98.1)	0.53
APTT (s)	41.7 (36.8–46.5)	39.6 (32.8–46.4)	43.9 (36.9–50.7)	0.39
Creatinine (mg/dl)	0.29 (0.27–0.30)	0.29 (0.27–0.31)	0.28 (0.26–0.30)	0.77
Procedures				0.65
ASD/VSD closure	54 (33.8%)	27 (33.3%)	27 (34.2%)	1.0
TCPC	29 (18.1%)	15 (18.5%)	14 (17.7%)	1.0
TOF repair	23 (14.4%)	11 (13.6%)	12 (15.2%)	1.0
AVSD repair	10 (6.3%)	6 (7.4%)	4 (5.1%)	1.0
BDG	9 (5.6%)	4 (4.9%)	5 (6.3%)	0.74
Rastelli	7 (4.4%)	4 (4.9%)	3 (3.8%)	1.0
CPB time (min)	102.5 (92.0–113.0)	97.2 (87.0–107.4)	107.9 (89.2–126.7)	0.31
ACC time (min)	64.5 (59.2–69.9)	65.5 (58.5–72.6)	63.5 (55.4–71.7)	0.71
Temp during CPB (°C)	29.9 (29.3–30.4)	29.9 (29.1–30.7)	29.8 (29.1–30.6)	0.92
Blood prime	76 (47.5%)	40 (49.4%)	36 (45.6%)	0.64

Data are expressed as the mean with the 95% confidence interval (95% CI) in parentheses, or as the number of patients with the percentage in parentheses

TXA Tranexamic acid, *CCHD* cyanotic congenital heart disease, *APTT* activated partial thromboplastin time, *ASD* atrial septal defect, *VSD* ventricular septal defect, *TCPC* total cavo-pulmonary connection, *TOF* tetralogy of fallot, *AVSD* atrioventricular septal defect, *BDG* bidirectional Glenn, *CPB* cardiopulmonary bypass, *ACC* aortic cross clamp, *Temp* temperature

There were only two patients requiring re-exploration of the chest for bleeding in both groups. Transfusions of blood products were required by 59 (72.8%) of the patients in the TXA group and 66 (83.5%) of the patients in the placebo group ($p = 0.13$). There were no significant differences between the groups in terms of the amount of blood products administered during the operation and for 24 h post-surgery and of the number of patient donor exposures. Mechanical ventilation in the ICU was required by 58 (72.5%) of the patients in the TXA group and 63 (78.8%) of the patients in the placebo group, and there was no significant difference in the mean duration of mechanical ventilation between the groups. The mean duration of ICU stay was not different between the groups ($p = 0.32$), and chest closure time was also not different between the groups (Table 2). Only one patient in the TXA group suffered from cerebral infarction at approximately 2 weeks post-surgery. Although the cause of infarction was not proven, it was considered to be a thrombotic complication. However, the neurological status of this patient gradually improved on an outpatient clinic basis. Although TXA is eliminated by urinary excretion, there were no significant differences in pre- and postoperative creatinine values between the TXA and placebo groups (Tables 1, 2).

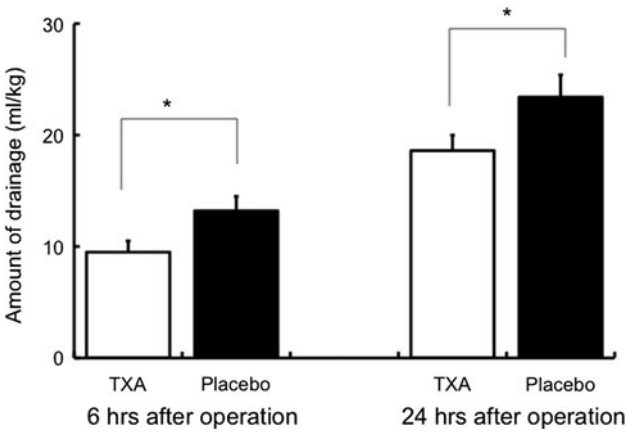

Fig. 2 Blood loss in patients assigned to the TXA and placebo groups at 6 and 24 h post-surgery. *White bar* TXA, *black bar* placebo. *Vertical line above bars* Standard error (SE). *$p < 0.05$

Subgroup analysis

Based on our protocol definition, we included 81 cyanotic and 79 acyanotic patients. The mean amount of 24-h drainage was significantly greater in the cyanotic patients than in the acyanotic patients [24.9 (21.3–28.6) vs. 17.0 (13.9–20.1) ml/kg, respectively; mean difference 7.9 (3.2–12.7) ml/kg; $p = 0.0012$]. There was no interaction between cyanotic status and TXA treatment ($p = 0.66$). There was a similar difference between the cyanotic and acyanotic patients in amount of drainage at 6 h post-surgery [13.0 (10.6–15.4) vs. 9.6 (7.3–11.9) ml/kg; mean difference 3.4 (0.1–6.7) ml/kg; $p = 0.045$]. Although there were trends for a benefit of TXA in both the cyanotic and acyanotic patients, there were no statistical differences in any subgroups (Fig. 3).

For the 61 children who underwent repeat sternotomy, there were also no significant differences in blood loss at 6

Table 2 Amounts of blood products administered during the operation and for 24 h after the operation and other outcomes

Use of blood products	TXA	Placebo	Mean difference (95% CI)	*p* value
Re-exploration of chest	2	2		0.99
Transfusion	59 (72.8%)	66 (83.5%)		0.13
PRBC (ml/kg)	54 (66.7%)	58 (73.4%)		0.35
OR	14.4 (10.2–18.5)	21.4 (13.4–29.3)	−7.0 (−15.6 to 1.6)	0.12
ICU	13.2 (10.5–15.9)	15.6 (11.8–19.4)	−2.4 (−7.0 to 2.2)	0.3
Total	21.9 (18.0–25.7)	26.3 (20.1–32.6)	−4.5 (−11.9 to 2.9)	0.23
FFP (ml/kg)	56 (69.1%)	61 (77.2%)		0.25
OR	13.3 (10.6–16.0)	15.2 (11.9–18.6)	−1.9 (−6.2 to 2.3)	0.36
ICU	13.8 (11.1–16.6)	13.2 (10.4–16.0)	0.6 (−3.3 to 4.5)	0.76
Total	24.9 (21.2–28.6)	26.3 (22.4–30.3)	−1.5 (−6.8 to 3.9)	0.59
PC (ml/kg)	24 (29.6%)	20 (25.3%)		0.54
OR	12.9 (9.6–16.1)	15.3 (10.4–20.3)	−2.5 (−7.9 to 3.0)	0.36
ICU	14.6 (8.4–20.8)	11.0 (4.3–17.8)	3.6 (−5.2 to 2.3)	0.41
Total	18.7 (14.6–22.9)	16.4 (11.8–20.9)	2.4 (−3.6 to 8.3)	0.43
Chest closure time (min)	58.3 (52.6–64.1)	58.8 (53.7–63.9)	−4.6 (−8.1 to 7.2)	0.90
MV in the ICU	58 (71.6%)	63 (79.7%)		0.37
Duration of MV (h)	35.9 (9.0–62.9)	66.9 (4.3–129.5)	−31.0 (−98.8 to 36.9)	0.37
ICU stay (days)	5.6 (3.9–7.2)	7.4 (4.1–10.7)	−1.8 (−5.5 to 1.8)	0.32
Postope creatinine (mg/dl)	0.30 (0.29–0.32)	0.30 (0.29–0.33)	0.30 (0.27 to 0.31)	0.34

Data are expressed as the mean with the 95% CI in parentheses, or as the number of patients with the percentage in parentheses

PRBC packed red blood cells, *OR* operating room, *ICU* intensive care unit, *FFP* fresh frozen plasma, *PC* apheresis platelet concentrate, *MV* mechanical ventilation

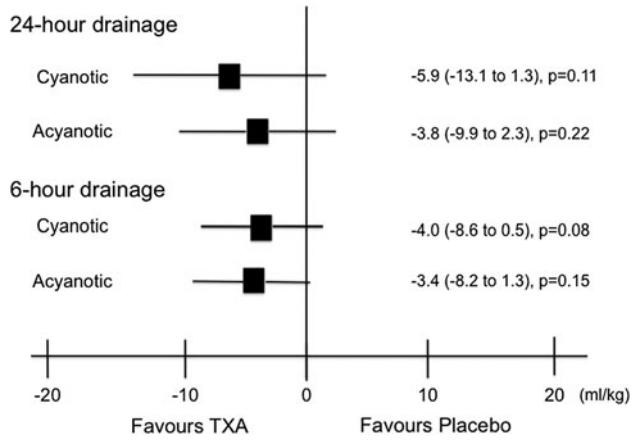

Fig. 3 Differences in blood loss with TXA and placebo. *X*-axis represents units in milliliters per kilogram. *Black squares* Mean, *bars* 95% confidence interval (95% CI). Data are given as the mean differences (95% CI)

and 24 h post-surgery between the TXA and placebo groups [20.0 (14.0–25.9) vs. 25.1 (19.9–30.2) ml/kg at 24 h, $p = 0.201$; 11.0 (7.2–14.7) vs. 13.0 (9.8–16.2) ml/kg at 6 h, $p = 0.404$]. There was also no significant difference in blood loss between patients with repeat sternotomy and those with non-repeat sternotomy [22.9 (19.0–26.9) vs. 19.8 (16.7–22.9) ml/kg/24 h, respectively, $p = 0.227$; 12.1 (9.4–14.8) vs 10.8 (8.7–13.0) ml/kg/6 h, respectively, $p = 0.454$].

Discussion

We conducted a randomized control trial to assess the benefit of TXA in pediatric cardiac surgery cohorts, in which cyanotic and acyanotic patients were well balanced (1:1 ratio). In this study, TXA significantly reduced blood loss, but it did not alter the amount of blood products administered.

Our study included a larger number of participants than the seven previously reported studies. It also included equal numbers of patients with CCHD and ACHD, which is in contrast to most of the previous studies in which the respective patient populations were not well balanced with respect to CCHD/ACHD. All previous studies were single-center studies as was our study. Of these seven earlier studies, two were double-blinded studies that showed negative effects of TXA on both bleeding and amount of transfusion products required [15, 17]. A recent study by Bulutcu et al. [11] that included 50 children and in which anesthesiologist and perfusionists were not blinded to patients allocation showed that TXA was effective in terms of both blood loss and transfusion. Three studies conducted by the same group showed desirable effects of TXA [12–14]. However, these studies appear to be non-blind studies and the method of randomization is unclear. Nevertheless, they included relatively large numbers of patients, while other studies had fewer than 100 participants. The proportion of cyanotic patients varied among these earlier studies. Three studies included both patients with CCHD and patients with ACHD [15–17]. However, two of these studies failed to show any benefit of TXA [15, 17]. On the other hand, four recent studies in which the participants were all cyanotic patients did show beneficial effects of TXA [11–14]. Since it is not clear whether the benefits of TXA in patients with CCHD differ from those in patients with ACHD, a randomized control trial including equal numbers of patients with and without cyanosis might be desirable. Our results of just such a trial in which relatively equal numbers of cyanotic and acyanotic patients were enrolled demonstrate that TXA has similar effects among these two patient populations.

There is a large variation (10–100 mg/kg) in the recommended dose in pediatric cardiac surgery [11–17]. A single bolus of 50 mg/kg showed no benefit on blood loss in three trials [13, 15, 17], but a larger dose of 100 mg/kg followed by continuous infusion or an additional dose of TXA did show effects [11, 16]. Dowd et al. [20] reported that plasma concentration rapidly fell after the initiation of CPB in adult patients and continued to fall over time despite infusion at 1 mg/kg/h. Thus, our protocol using continuous infusion following a bolus may be adequate to maintain the plasma concentration of TXA in pediatric patients. A possible risk of using a high dose of TXA is the occurrence of seizures seen in adult cardiac surgery [21, 22]. We had one case of cerebral infarction, but there were no other neurological complications. Thus, further investigation is needed to determine the appropriate doses of TXA in both adults and children.

The amount of blood transfusion was not significantly different in the TXA group and placebo group in our study. This is consistent with the results of another study showing that there was no significant difference in transfusion despite the fact that blood loss was significantly different [16]. On the other hand, the blood transfusion requirement was lower in cyanotic patients in the TXA treatment group in previous studies [11–14]. However, we did not find any statistical difference in the amount of blood transfusion between the TXA groups and the placebo groups in the CCHD cohort and ACHD cohort. However, the fact that we did not implement a detailed transfusion protocol in the current trial might be a confounding factor. Standard practice at our hospital is not to encourage blood transfusion when CPB circuits are primed without red cells. We also encountered the situation in which patients required

intravascular volumes even if there was no bleeding. Intraoperative transfusion practice was determined by individual anesthesiologists. Both of these practices can also be confounding factors. Moreover, the amount of blood loss could be affected by the amount of platelets and/or FFP given during and after surgery because these would promote the coagulation cascade [23]. However, the amount of such products was not different between the groups. Significant but only small differences in blood loss could be a reason why the amount of blood transfusion did not reach statistical significance.

Since bleeding leads to increased morbidity and mortality in children [2], our results show possible benefits of TXA. However, there are several limitations to our study. First, this was a single-center trial. Thus, our findings may not be applicable to other pediatric cardiac centers. Second, the assessment of results was not blinded and this can be a bias. Although anesthesiologists knew about group allocation, the decision to give blood products was made by many physicians. Thus, this effect might not be strong. Third, neonates of less than 1 month of age were excluded from this study because, compared to other age groups, coagulation disorders in this age group are known to be much stronger [24, 25], and the amount of blood loss in neonates has been shown to be much larger [7, 26]. Since TXA showed a minimal clinical effect on blood loss in our study population, whether it can benefit neonates or other patients at high risk for bleeding is unknown.

Prior sternotomy would be one of the risk factors for postoperative bleeding in this cohort. Although it did not reach statistical significance, the number of patients with repeat sternotomy was greater in the placebo group than in the TXA group in our study. However, the amount of blood loss was not different between repeat sternotomy patients and non-repeat sternotomy patients.

We allowed patients who were taking anticoagulant medicine prior to surgery to enroll in our study. In our basic strategy, patients are requested to cease all anticoagulants 7 days before surgery. Thus, APTT or PT after anesthetic induction was normalized in most patients. Although the number of children whose APTT was above normal was greater in the placebo group than in the TXA group, there was no difference in blood loss between patients with normal APTT and those with supranormal APTT. Thus, these effects could be negligible.

In conclusion, we have shown a small beneficial effect of TXA in reducing blood loss in pediatric cardiac surgery patients who are not at high risk for bleeding. There was no difference in the effects of TXA to reduce blood loss between cyanotic and acyanotic patients. Routine use of this medication for these patients should be entrusted to each institution.

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