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Different Dosing Regimen of Tranexamic Acid in Adeloscent Idiopathic Scoliosis Surgery: A Retrospective Study

Adölesan İdiopatik Skolyoz Cerrahisinde Traneksamik Asidin Farklı Doz Uygulaması: Retrospektif Bir Çalışma

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ABSTRACT Objective: We aimed to retrospectively evaluate perioperative blood loss and allogeneic blood transfusion in child and adolescent patients who were given different doses of tranexamic acid (TXA) for adolescent idiopathic scoliosis surgery between 2011 and 2018. **Material and Methods:** After obtaining hospital's ethic committee approval, retrospective data were evaluated from anesthesia and medical files. **Results:** Ninety patients were included in the study. Two groups were identified: Group I (n=49) received intravenous TXA with 10 $mgkg^{-1}$ bolus dose and 1 $mgkg^{-1}h^{-1}$ maintenance. Group II (n=41) received 20 $mgkg^{-1}$ bolus and 2 $mgkg^{-1}h^{-1}$ maintenance. Mean estimated blood loss (EBL) and EBL per body weight were higher in Group I than Group II (933.8±161.2 vs. 846.3±94.1 ml; p=0.019) and (21.2±10.3 vs. 14.7±8.8 $mlkg^{-1}$; p=0.011). More patients in Group I were transfused packed red blood cell (28.6% vs. 17.0%, p=0.036; 2.0±0.9 vs. 1.6±0.7 U; p=0.041) and fresh frozen plasma than Group II (12.2% vs. 7.3%; p=0.021, 1.6±0. vs. 1.0±0.4 U; p=0.033). Four patients in Group I and 3 in Group II (p=0.101) were admitted in the intensive care unit (ICU) for 12.0±3.3 hours. Major complications were not observed. Hospital discharge time was similar (3.5±1.2 vs. 3.2±0.9 days; p=0.801). **Conclusion:** A bolus TXA dose of 20 $mgkg^{-1}$ and 2 $mlkg^{-1}h^{-1}$ maintenance was more effective in reducing blood loss and blood transfusion compared to a bolus dose of 10 $mgkg^{-1}$ and 1 $mlkg^{-1}h^{-1}$ maintenance. ICU admission rate, complications, and discharge time were similar between groups.

Keywords: :Scoliosis; general anesthesia; tranexamic acid

ÖZET Amaç: Bu çalışmanın amacı 2011 ve 2018 yılları arasında adölesan idiopatik skolyoz cerrahisi uygulanan çocuk ve adölesan hastalarda farklı dozlarda traneksamik asit (TXA) uygulanmasının perioperatif kanama miktarı ve kan transfüzyonu üzerine etkisinin geriye dönük olarak incelenmesidir. **Gereç ve Yöntemler:** Hastane etik komite onayının alınmasını takiben, hastane veri tabanı, anestezi kayıtları ve hasta dosyaları incelendi. **Bulgular:** Çalışmaya 90 hasta dahil oldu ve iki grup tanımlandı: Grup I (n=49)'e intravenöz TXA 10 $mgkg^{-1}$ bolus ve 1 $mgkg^{-1}sa^{-1}$ idame dozlarında, Grup II (n=41)'ye ise 20 $mgkg^{-1}$ bolus ve 2 $mgkg^{-1}sa^{-1}$ idame dozlarında uygulanmıştı. Ortalama tahmini kan kaybı (ml) ve vücut ağırlığına göre kan kaybı ($mlkg^{-1}$) Grup I'de Grup II'den fazlaydı. (933,8±161,2'ye karşı 846,3±94,1 ml; p=0,019) ve (21,2±10,3'e karşı 14,7±8,8 $mlkg^{-1}$; p=0,011). Eritrosit süspansiyonu ve taze donmuş plazma transfüzyonu uygulanan hasta sayısı ve miktarı Grup I'de Grup II'den fazlaydı (%28,6'ya karşı %17,0; p=0,036 ve 2,0±0,9'a karşı 1,6±0,7 ünite; p=0,041); (%12,2'e karşı %7,3; p=0,021 ve 1,6±0,5'e karşı 1,0±0,4 ünite; p=0,033). Grup I'den 4 ve Grup II'den 3 hasta (p=0,101) yoğun bakım ünitesinde (YBÜ) 12,0±3,3 saat takip edildiler. Önemli bir komplikasyon gözlenmedi. Hastaneden taburcu edilme süreleri her iki grup arasında benzerdi (3,5±1,2'e karşı 3,2±0,9 gün; p=0,801). **Sonuç:** TXA'in 20 $mgkg^{-1}$ bolus ve 2 $mlkg^{-1}sa^{-1}$ idame dozlarında uygulanmasının 10 $mgkg^{-1}$ bolus ve 1 $mlkg^{-1}sa^{-1}$ idame dozlarına kıyasla kanama miktarı ve kan ürünleri transfüzyonu uygulanmasının azaltılmasında daha etkilidir. YBÜ'ne hasta alınma oranı, komplikasyonlar ve hastaneden taburcu edilme süreleri bakımından gruplar arasında farklılık gözlenmemiştir.

Anahtar Kelimeler: Skolyoz; genel anestezi; traneksamik asit

Posterior spinal fusion (PSF) is one of the most complex surgical procedures in patients with scoliosis that makes every surgery a challenge for anesthesiologists. The procedure causes significant blood loss and often necessiates allogenic blood transfusion due to the larger surgical incision, longer

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duration of the surgery, and surgical exposure of the vertebral body, venous plexus, and paraspinal muscles.[1] Intraoperative bleeding may be highly variable ranging between 600-4500 ml and lead to complications including hypotension, end-organ damage, metabolic disturbances, coagulopathy, and a need for significant blood transfusion which may increase the risk for morbidity and mortality on their own.[2] Studies in the literature suggested that extension of instrumentation levels, scoliosis curve angle, duration of the surgery, and type of the underlying disease are main factors that precipitate perioperative bleeding.[3] There were many interventions developed to limit perioperative bleeding including controlled hypotensive anesthesia, blood cell salvage techniques, acute normovolemic hemodilution, and perioperative administration of pharmacologic agents including tranexamic acid (TXA) and epsilon amino caproic acid.[4] Among them, controlled hypotensive anesthesia and TXA became widely popular due to their efficacy and safety.[4]

TXA is a synthetic lysine analog which acts as an antifibrinolytic by binding receptor sites on plasma and plasminogen. This inhibits plasminogen activation which results in a decrease of bleeding during surgery.[5] TXA is widely used in surgery, and its efficacy has been reported in spine surgery. A single bolus dose may be used between 10 and 100 $mgkg^{-1}$ and a maintenance dose between 1 and 10 $mgkg^{-1}h^{-1}$. [5,6] We have been using TXA in scoliosis surgery for 9 years, and have increased the loading dose from 10 $mgkg^{-1}$ to 20 $mgkg^{-1}$ and maintenance dose from 1 $mgkg^{-1}h^{-1}$ to 2 $mgkg^{-1}h^{-1}$ since 2016.

In this retrospective study, we aimed to evaluate blood loss in patients who received different doses of the TXA (10 $mgkg^{-1}$ bolus and 1 $mgkg^{-1}h^{-1}$ maintenance or 20 $mgkg^{-1}$ bolus and 2 $mgkg^{-1}h^{-1}$ maintenance) during posterior spinal fusion for adeloscent idiopathic scoliosis (AIS) under general anesthesia between May 2011 and April 2018. The primary outcome measure was to determine perioperative bleeding and blood transfusion. The secondary aim was to find out whether the blood loss and transfusion did have an effect on the complication rate and hospitalization times.

MATERIAL AND METHODS

The study was approved by the instutional review board and ethics committee of University of Health Sciences, Gülhane Training and Research Hospital with a protocol no: 18/101 at 22 May 2018. Data were retrospectively collected from the hospital's computerized data base, medical files, anesthesia and intensive care unit (ICU) charts between 2011 and 2018. ASA status 1 and 2 patients, aged between 6-18 years were included in the study who underwent elective posterior spinal fusion surgery for AIS by a single surgeon. Exclusion criteria were previous scoliosis surgery, growing rod instrumentation, a procedure that involved an anterior approach, a fusion of lower than 6 vertebral levels, missing data, and lost to follow-up in the postoperative period.The study has been performed in accordance with ethical standards of Helsinki Declaration and was designed in accordance with STROBE criteria (Strengthening the Reporting of Observational Studies in Epidemiology).

ANESTHETIC TECHNIQUE

The routine anesthetic protocol for the posterior fusion in scoliosis surgery in our clinic was as follows: All patients were evaluated before the surgery and given oral or intravenous (IV) midazolam for premedication. Intravenous propofol (2.5 $mgkg^{-1}$), rocuronium (0.6 $mgkg^{-1}$), and fentanyl (1 μgkg^{-1}) were used to induce general anesthesia. Propofol (3-6 $mgkg^{-1}h^{-1}$) and remifentanil (1-2 $\mu gkg^{-1}h^{-1}$) infusions were used for the maintenance. Patients were monitored continuously with ECG, peripheral oxygen saturation, invasive and non-invasive arterial blood pressure, urine output with bladder catheterization, central venous pressure, end-tidal CO_2, and body temperature. Arterial blood gas analyses were repeated with regular intervals. Neuromonitorization was used to detect any neurological injury in the intraoperative period. A balanced hypotensive anesthetic technique was induced using a nitroglycerine infusion to keep the mean arterial blood pressure between 55-60 mmHg. TXA was given as an antifibrinolytic agent with a bolus dose of 10 $mgkg^{-1}$ with a 1 $mgkg^{-1}h^{-1}$ maintenance or 20 $mgkg^{-1}$ bolus with 2 $mgkg^{-1}h^{-1}$ maintenance. Blood loss was estimated by collecting,

counting gauzes saturated with blood and measuring the blood mixed with other liquids in the aspirator. A packed red blood cell (PRBC) was transfused when estimated blood loss (EBL) exceeded 30% of total blood volume (TBV) or hemoglobin count was lower than 7 gdL^{-1} on the arterial blood gas analysis. TBV was calculated according to the conventional formula: TBV = actual body weight × fixed 70 $mlkg^{-1}$. If two or more unit of packed red blood cell (PRBC) were transfused, fresh frozen plasma (FFP) was given in an 1:1 ratio. At the end of the surgery, a local anesthetic mixture containing 2% lidocaine (max. 5 $mgkg^{-1}$) with 0.5% bupivacaine (max. 2 $mgkg^{-1}$) was infiltrated into the wound. Intravenous tramadol (1 $mgkg^{-1}$) and paracetamol (15 $mgkg^{-1}$) were used for postoperative pain relief. After the surgery, the TIVA infusion was discontinued. The patients were extubated according to the following criteria: Respiratory rate: 10-20 min^{-1}, tidal volume >5 $mlkg^{-1}$, paO_2>80 mmHg, $paCO_2$ 25-40 mmHg, hemoglobin >7 gdL^{-1}, normothermia, and stable hemodynamic parameters including MAP>65 mmHg, heart rate 60-120 $beatmin^{-1}$. The patients with EBL > 50% of TBV, deep metabolic or respiratory acidosis (pH<7.30), lactate level > 5 $mmolL^{-1}$, hemodynamic disturbances, insufficient respiration, and arrhythmias were transferred into ICU.

POSTOPERATIVE FOLLOW-UP PERIOD

A multimodal analgesic regimen was used for postoperative pain relief including paracetamol (10 $mgkg^{-1}$IV; 8 hours intervals), ibuprofen (10 $mgkg^{-1}$ oral; 12 hours intervals), and a IV tramadol patient-controlled analgesia (4 mgh^{-1}, 5 mg bolus, 30 min. lock-out, with a max.50 mg for 4 h). A Visual Analogue Scale (VAS; 0-10 cm) was used to measure postoperative pain. Pethidine was given intravenously in a dose of 0.5 $mgkg^{-1}$ when VAS score was more than 3. The patients were discharged from the hospital when hemodynamic parameters and laboratory results were stable within normal limits, VAS score <3, and basic physiotherapy exercises were completed under the supervision of a physiotherapist.

DATA COLLECTION

All medical data were reviewed in detail to obtain: a) demographic characteristics including age (years), gender, ASA status, comorbidities, body weight (kg), body height (cm), b) estimated blood loss (EBL; ml), d) EBL per kg of body weight ($mlkg^{-1}$), e) EBL per level ($mllevel^{-1}$), f) instrumentation level (n), g) number of vertebra osteotomized (n), h) operative time (min), i) ICU admission (n, %), j) duration of the ICU care (h), k) hospital discharge time (day), l) intraoperative and postoperative transfusion of blood products (PRBC, FFP, and thrombocyte (unit) m) postoperative drainage (ml) n) postoperative rescueanalgesic requirement, o) postoperative complications (n), p) ICU re-admission (n, %)

STATISTICAL ANALYSIS

IBM SPSS Statistics (version 21; IBM SPSS Inc., Chicago;IL,USA) was used to analyse perioperative data. Kolmogorov-Smirnov test was used when the distribution of the continuous data was normal. Mann-Whitney U test was used when continuous data was abnormal distributed. Mean and standard deviation (mean±SD) were used to describe continuous data and frequency and percentage (n, %) were used to describe catecorigal data. A *p* value lower than 0.05 was considered statistically significant.

RESULTS

DEMOGRAPHIC CHARACTERISTICS

One hundred and twelve patient's files were included in the study and 12 files were excluded due to the missing data (Figure 1). Of the remaining 90 files, two groups were identified according to the dose of TXA: Group I consisted of 49 patients who

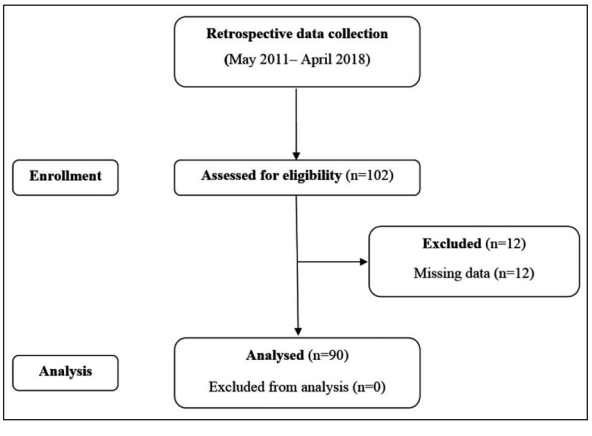

FIGURE 1: Study flow diagram.

TABLE 1: Demographic characteristics and preoperative hemoglobin, hematocrit, and platelet counts in study groups.

	Group I (n=49)	Group II (n=41)	p
Age (mean)	12.9±4.5 (8-17)	13.1±2.2 (8-16)	0.701
Gender (female/male)	27/22 (55.1% / 44.9%)	22/19 (53.6% / 46.4%)	0.827
ASA physical status (I/II)	46/3 (93.8% / 6.2%)	39/2 (95.1% / 4.9%)	0.314
Height (cm)	143.6±18.1	146.6±18.2	0.840
Weight (kg)	45.6±11.5	47.7±10.6	0.213
Preoperative hemoglobin level (gdL^{-1})	13.4±1.3	13.2±1.4	0.719
Preoperative hematocrit level (%)	40.2±3.8	39.6±4.1	0.972
Preoperative platelet level (μL^{-1})	293960±69041	283054.05±63782	0.456

Values are presented as mean±standard deviation or numbers and percentage with min-max values. p <0.05 was considered as statistically significant.

received a bolus TXA (10 $mgkg^{-1}$) and a 1$mgkg^{-1}h^{-1}$maintenance. Group II consisted of 41 patients who received with a bolus TXA (20 $mgkg^{-1}$) and a 2 $mgkg^{-1}h^{-1}$ maintenance.

Table 1 shows the demographic data in the study groups. The patients were aged 13.0±3.3 (8-17) years. Forty nine patients (54.4%) were female and 41 patients (45.6%) were male. (p=0.7). Mean age, gender distribution, and ASA physical status were similar (p>0.05). Two patients (one in each group) had diabetes mellitus and three patients (two in Group I and one in Group II) had mild asthma. Mean body weight and height were similar (45.6±11.5 kg vs. 47.7±10.6 kg; p=0.213 and 143.6±18.1 cm vs. 146.6±18.2 cm; p=0.840). Preoperative mean hemoglobin, hematocrit, and platelet levels were within normal limits and similar between groups (p>0.05).

THE SURGICAL PROCEDURE

Posterior fusion procedures involved similar vertebrae levels in the Group I and II [9.9±1.1 (8-14) vs. 10.3±0.7 (8-14); p=0.133]. Osteotomy was performed in 14 patients (8 patients of Group I and 6 patients in Group II; p=0.565). Similar number of vertebra was osteotomized in groups [2.3±0.6 (1-3) vs. 2.6±0.9 (1-4); p=0.344]. Mean operative time was not different between groups [206.2±51.6 (150-290) min; vs. 200.1±40.8 (145-275) min; p=0.202].

ESTIMATED BLOOD LOSS

Estimated blood loss (EBL) was higher in Group I than in Group II [933.8±161.2 (230-2060) ml vs. 846.3±94.1 (330-1910) ml; p=0.019] (Table 2). Mean EBL per kg of body weight ($mlkg^{-1}$) was increased in Group I compared to Group II [21.2±10.3 (7.2-35.4) $mlkg^{-1}$ vs. 14.7±8.8 (6.3-30.8) $mlkg^{-1}$; p=0.011] (Table 2). Mean EBL per instrumentation level ($mllevel^{-1}$) was lower in Group II (79.3±9.1 vs. 94.4±16.5; p=0.033) (Table 2). The ratio and number of patients whose EBL/TBV was between 30%-50% of TBV and >50% of TBV were found to be increased in Group I [20.4% (10) vs. 14.6% (6); p=0.012 and 8.2% (4) vs. 2.4% (1); p=0.027, respectively]. EBL/TBV was lower than 30% in 35 patients (71.4%) of Group I and in 30 patients (83.0%) of Group AIS (p=0.036).

INTRAOPERATIVE TRANSFUSION OF BLOOD PRODUCTS

More patients in Group I received PRBC compared to the patients in Group II [28.6% (14) vs. 17.0% (7); p=0.036] and the amount of PRBC was also higher [2.0±0.9 (0-4) U vs. 1.6±0.7 (1-3) U; p=0.041] (Table 2). Similarly, FFP was transfused in more patients of Group I in comparison to the patients of Group II [6 (12.2%) vs. 3 (7.3%); p=0.021 and (1.6 ±0.5 (1-3) U vs. 1.0±0.4 (1-3) U; p=0.033] (Table 2).

POSTOPERATIVE TRANSFUSION OF BLOOD PRODUCTS

Six patients (12.2%) in Group I and 3 patients (7.3%) in Group II received PRBC (p=0.027) with a higher amount of PRBC transfused [1.4±0.6 (0-2) U vs. 1.0±0.0 (0-1) U; p=0.011] (Table 2). Similarly, more patients in Group I were transfused FFP compared to Group II [4 (8.2%) vs. 1 (2.4%); p=0.009 and (1.5±0.5 (0-2) U vs. 1.0±0.0 (0-1) U; p=0.017]. Postoperative drainage was similar between two

TABLE 2: Comparing perioperative characteristics between study groups.

	Group I (n=49)	Group II (n=41)	p
Instrumentation level (n)	9.9 ±1.1 (8-14)	10.3±0.7 (8-14)	0.133
Osteotomy (yes/no)	8/41 (16.3% / 83.7%)	6/35 (14.6% / 85.4%)	0.565
Osteotomy level (n)	2.3±0.6 (1-3)	2.6±0.9 (1-4)	0.344
Operative time (min)	206.2±51.6 (150-290)	200.1±40.8 (145-275)	0.202
Estimated blood loss (EBL) (ml)	933.8±161.2 (230-2060)	846.3±94.1 (330-1910)	0.019
EBL per kg body weight (ml/kg)	21.2±10.3 (7.2-35.4)	14.7±8.8 (6.3-30.8)	0.011
EBL per instrumentation level (ml/level)	94.4± 16.5	79.3±9.1	0.033
EBL between 30-50% of Total Blood Volume	10 (20.4%)	6 (14.6%)	0.012
EBL> 50% of total blood volume	4 (8.2%)	1 (2.4%)	0.027
EBL< 30% of total blood volume	35 (71.4%)	34 (83.0%)	0.036
Intraoperative transfusion-PRBC (yes/no)	14/35 (28.6%/71.4%)	7/34 (17.0% / 83.0%)	0.036
Intraoperative transfusion-PRBC (unit)	2.0±0.9 (1-4)	1.6±0.7 (1-3)	0.041
Intraoperative transfusion-FFP (yes/no))	6/43 (12.2% / 87.8%)	3/38 (7.3% / 92.7%)	0.021
Intraoperative transfusion-FFP (unit)	1.6±0.5 (1-3)	1.0±0.4 (1-3)	0.033
Drainage (ml)	403.1±151.5	398.2±160.0	0.608
Postoperative transfusion-PRBC (yes/no)	6/43 (12.2% / 87.8%)	3/38 (7.9% / 92.1%)	0.027
Postoperative transfusion-PRBC (unit)	1.4 ±0.6 (0-2)	1.0±0.0 (0-1)	0.011
Postoperative transfusion-FFP (yes/no)	4/45 (8.2% / 91.8%)	1/40 (2.4% / 97.6%)	0.009
Postoperative transfusion-FFP (unit)	1.5±0.5 (0-2)	1.0±0.0 (0-1)	0.017

Values are presented as mean±standard deviation or numbers and percentage with min-max values. p <0.05 was considered as statistically significant.
PRBC: Packed red blood cell, FFP: Fresh frozen plasma.

groups (403.1±151.5 ml vs. 398.2.2± 160.0 ml; p=0.608) (Table 2).

ICU ADMISSION

A total of 7 patients (4 in Group I and 3 in Group II; p=0.101) were admitted in the ICU after the surgery due to the significant EBL (EBL > 50% TBV) or a lactate level higher than 5 $mmolL^{-1}$ (Table 3). Among those patients, all patients were extubated as they were transferred into the ICU. Mean discharge time from the ICU was 12.0±3.3 (8-23) hours and similar between groups (12.2±4.8 vs. 11.9±5.5; p=0.739) (Table 3).

POSTOPERATIVE COMPLICATIONS AND HOSPITAL DISCHARGE

There was not a major complication observed related to the surgery or to the anesthetic management including hemodynamic disturbance, respiratory insufficiency, transfusion complications, or neuro- logical injury. Pain was the major complaint in all patients followed by nausea and vomiting (PONV). Rescue analgesic was required in all patients (100%) in the postoperative period. Twenty five patients (27.7%) suffered from PONV and the incidence was not different [14 (28.5%) vs.

TABLE 3: Comparing postoperative course between study groups.

	Group I (n=49)	Group II (n=41)	p
Intensive care unit admission (yes/no)	4/45 (8.2% / 91.8 %)	3/38 (7.3% / 92.7%)	0.101
Intubated at ICU admission (yes/no)	0/49	0/41	1.00
Discharge from the intensive care unit (hour)	12.2±4.8	11.9±5.5	0.739
Hospital discharge time (day)	3.5±1.2	3.2±0.9	0.801
Complications			
Postoperative pain requiring rescue analgesic	49 (100%)	41 (%100)	1.00
Postoperative nausea and vomiting	14 (28.5%)	11 (26.8%)	0.055

Values are presented as mean±standard deviation or numbers and percentage with min-max values. p <0.05 was considered as statistically significant. ICU: Intensive care unit.

11 (26.8%); p=0.055]. Mean hospital discharge time was similar in both groups (3.5±1.2 vs. 3.2±0.9 days; p=0.801).

DISCUSSION

This retrospective study indicated that administration of TXA in a 20 $mgkg^{-1}$ bolus dose with a 2 $mgkg^{-1}h^{-1}$ maintenance decreased perioperative bleeding and the need for blood transfusion in both intraoperative and postoperative periods compared to 10 $mgkg^{-1}$ bolus dose with a 1 $mgkg^{-1}h^{-1}$ maintenance in healthy pediatric and adolescent patients who were diagnosed with AIS and underwent posterior spinal fusion for scoliosis surgery. Our results are consistent with previous studies which have reported the efficacy of high-dose TXA on perioperative bleeding in AIS surgery.[5,6] In a recent study, it was reported that TXA more than 20 mg/kg was more effective than the dose of lower than 20 mg/kg to reduce perioperative bleeding. In a retrospective cohort study by Johnson et al., high dose of TXA (50 $mgkg^{-1}$ bolus and a 5 $mgkg^{-1}h^{-1}$ maintenance) was compared to the low dose (10 $mgkg^{-1}$ bolus and 1 $mgkg^{-1}h^{-1}$ maintenance) and it was reported that high dose TXA reduced EBL, intraoperative and postoperative PRBC transfusion requirements in AIS.[8] In a review by Goobie and Faraoni, the use of TXA with a bolus 10-30 $mgkg^{-1}$ and 5-10 $mgkg^{-1}h^{-1}$ maintenance was recommended for trauma and surgery in pediatric patients.[9]

Absolute contraindications of TXA are history of allergy, thromboembolism, and fibrinolysis. Also, TXA should be cautiously used or not used in renal dysfunction, thrombosis disorders, and preexisting coagulopathy or oral anticoagulant use. Adverse events are rare (1/1000-1/10000) which included allergic skin reactions anaphylaxis, hypotension due to fast IV injection, nausea, vomiting, diarrhea, convulsion with high doses, and thromboembolic event due to stabilization of clot.[5-9]

Scoliosis surgery is related with massive blood loss and need for transfusion of blood products. Posterior instrumentation and fusion is one of the most performed single-stage surgeries for correction of AIS which included bilateral pedicle screw fixation, rod placement and derotation with or without osteotomy.[2,10] Many factors have been found to be associated with perioperative significant blood loss in posterior fusion surgery including more than 6 vertebrae, preoperative Cobb angle more than 50°, osteotomy, and neuromuscular disease.[11] Patients with neuromuscular diseases have generally osteopenia or several genetic defects which results in excessive blood loss. For example, the lack of dystrophin gene in Duchenne muscular dystrophy causes a poor vascular smooth muscle which inhibits vasoconstrictive response.[12] Massive transfusion increases the risk for development of severe complications including coagulopathy, end organ failure and even mortality, as well as ICU admission rate and duration of hospitalization.[1,4,9,11,12] Therefore, interventions to reduce blood loss are essential to reduce mortality and morbidity.

Several strategies are used to reduce blood loss including deliberate hypotensive anesthesia, antifibrinolytic agents such as epsilon-aminocaproic acid and TXA, cell salvage techniques, acute normovolemic hemodilution, and permissive fluid resuscitation.[1,2,4,13] Controlled hypotension is a well-known technique which decreases perioperative bleeding in many surgeries. But, excessive hypotension may have impact on the blood supply of the spinal cord which have a potential to develop neural injury. Interventions to keep the mean arterial blood pressure between 50 and 60 mmHg plays an important role to protect the spinal cord under the supervision of neurological monitoring.[14]

The effectiveness of using cell savage techniques remains unclear. Although numerous studies have found that the use of cell salvage techniques reduced allogeneic blood transfusion, it was also reported that the hospital discharge rate was not reduced and the technique was not cost-effective.[15,16]

Acute normovolemic hemodilution (ANH) is another option to reduce blood loss which includes removing and storing the patient's blood and replacing with crystalloid or colloid solutions.[17] We did not use this technique because there are limited number of studies supporting the efficacy of the use

of ANH in pediatric or adolescent population undergoing scoliosis surgery.

But, the discharge time, ICU admission rate, and complication rate did not differ between groups. A retrospective cohort study including 16992 cases of AIS obtained from a pediatric health information database reported that ICU admission rates, need for blood transfusion, and complication rates were highly variable between hospitals and the incidence is associated with underlying neuromuscular disease, anterior fusion, combined fusion, developmental delay, preoperative comorbidities, preoperative cardio-respiratory status, intraoperative excessive blood loss and allogenic blood transfusion, higher Cobb angle, and perioperative complications.[18] Hospital discharge times were lower in centers with higher rate of ICU admission.[18,19] We think that the similarities in discharge time, ICU admission rate, and complication rate between two groups in our study were caused by the reduced blood loss and blood transfusion, preoperative good health status of the patients, and lack of intraoperative adverse events and complications. Seven patients (7.7%) were transferred into the ICU after the surgery for a potential complication of significant blood loss. Those patients were safely extubated immediately after surgery in the operating room. The discharge time of those patients were also not different compared to the other patients.

This study has several limitations. The study may have selection and recall bias due to the retrospective nature. But, the same inclusion and exclusion criteria and multiple data sources including medical records database, patient files, and anesthesia charts were used. The second limitation was that the study included immediate postoperative period until the discharge from the hospital. Long term follow-up results might provide valuable information including development of postoperative infection, development of chronic pain, satisfaction of patients and their relatives.

CONCLUSION

We retrospectively evaluated perioperative bleeding and blood transfusion in posterior fusion surgery for adolescent idiopathic scoliosis who were given different dosing regimen of TXA. It is concluded that TXA in a bolus dose of 20 $mgkg^{-1}$ with a 2 $mlkg^{-1}h^{-1}$ maintenance may be more effective in reducing blood loss and transfusion in both intraoperative and postoperative periods compared to a bolus dose of 10 $mgkg^{-1}$ with a 1 $mlkg^{-1}h^{-1}$ maintenance. But, the difference in the TXA dose did not have an effect on the complications rate, ICU admission, and hospital discharge time. Prospective and randomized studies are required to find out the optimal dose of TXA to reduce intraoperative blood loss.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Mehmet Özgür Özhan, Mehmet Anıl Süzer;* ***Design:*** *Mehmet Özgür Özhan, Mehmet Anıl Süzer;* ***Control/Supervision:*** *Mehmet Özgür Özhan;* ***Data Collection and/or Processing:*** *Mehmet Burak Eşkin, Hasan Kamburoğlu;* ***Analysis and/or Interpretation:*** *Bülent Atik, Hasan Kamburoğlu;* ***Literature Review:*** *Bülent Atik, Hasan Kamburoğlu;* ***Writing the Article:*** *Mehmet Özgür Özhan;* ***Critical Review:*** *Mehmet Özgür Özhan;* ***References and Fundings:*** *Bülent Atik, Hasan Kamburoğlu;* ***Materials:*** *Hasan Kamburoğlu, Bülent Atik.*

REFERENCES

1. Entwistle MA, Patel D. Scoliosis surgery in children. Continuing Education in Anaesthesia Critical Care & Pain. 2006;6(1):13-6.[Crossref]
2. Shapiro F, Sethna N. Blood loss in pediatric spine surgery. Eur Spine J. 2004;13 Suppl 1(Suppl 1):S6-17.[Crossref] [PubMed] [PMC]
3. Cristante AF, Borges PA, Barbosa AR, Letaif OB, Marcon RM, Barros Filho TE. Predictive factors for perioperative blood transfusion in surgeries for correction of idiopathic, neuromuscular or congenital scoliosis. Clinics (Sao Paulo). 2014;69(10):672-6.[Crossref] [PubMed] [PMC]
4. Fletcher ND, Marks MC, Asghar JK, Hwang SW, Sponseller PD, Newton PO. Development of consensus based best practice guidelines for perioperative management of blood loss in patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis. Spine Deform. 2018;6(4):424-9.[Crossref] [PubMed]
5. 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(3):245-9.[Crossref] [PubMed] [PMC]
6. Sui WY, Ye F, Yang JL. Efficacy of tranexamic acid in reducing allogeneic blood products in adolescent idiopathic scoliosis surgery. BMC Musculoskelet Disord. 2016;17:187.[Crossref] [PubMed] [PMC]
7. Yuan QM, Zhao ZH, Xu BS. Efficacy and safety of tranexamic acid in reducing blood loss in scoliosis surgery: a systematic review and meta-analysis. Eur Spine J. 2017;26(1):131-9.[Crossref] [PubMed]
8. Johnson DJ, Johnson CC, Goobie SM, Nami N, Wetzler JA, Sponseller PD, et al. High-dose versus low-dose tranexamic acid to reduce transfusion requirements in pediatric scoliosis surgery. J Pediatr Orthop. 2017;37(8):e552-7.[Crossref] [PubMed]
9. Goobie SM, Faraoni D. Tranexamic acid and perioperative bleeding in children: what do we still need to know? Curr Opin Anaesthesiol. 2019;32(3):343-52.[Crossref] [PubMed]
10. Szpalski M, Gunzburg R, Sztern B. An overview of blood-sparing techniques used in spine surgery during the perioperative period. Eur Spine J. 2004;13 Suppl 1(Suppl 1):S18-27.[Crossref] [PubMed] [PMC]
11. Yu X, Xiao H, Wang R, Huang Y. Prediction of massive blood loss in scoliosis surgery from preoperative variables. Spine (Phila Pa 1976). 2013;38(4):350-5.[Crossref] [PubMed]
12. Cristante AF, Borges PA, Barbosa AR, Letaif OB, Marcon RM, Barros Filho TE. Predictive factors for perioperative blood transfusion in surgeries for correction of idiopathic, neuromuscular or congenital scoliosis. Clinics (Sao Paulo). 2014;69(10):672-6. [Crossref] [PubMed] [PMC]
13. Bible JE, Mirza M, Knaub MA. Blood-loss management in spine surgery. J Am Acad Orthop Surg. 2018;26(2):35-44.[Crossref] [PubMed]
14. Jiang J, Zhou R, Li B, Xue F. Is deliberate hypotension a safe technique for orthopedic surgery?: a systematic review and meta-analysis of parallel randomized controlled trials. J Orthop Surg Res. 2019;14(1):409.[Crossref] [PubMed] [PMC]
15. Başaran SH, Bayrak A, Sayit E, Öneş HN, Gözügöl K, Kural C. Efficacy and cost-effectiveness of the cell saver system in instrumented posterior fusion with thoracic and lumbar vertebral fractures. Ulus Travma Acil Cerrahi Derg. 2019;25(1):66-70.[Crossref] [PubMed]
16. Liu JM, Fu BQ, Chen WZ, Chen JW, Huang SH, Liu ZL. Cell salvage used in scoliosis surgery: is it really effective? World Neurosurg. 2017;101:568-76.[Crossref] [PubMed]
17. Wong ECC. Acute Normovolemic hemodilution: a critical evaluation of its safety and utility in pediatric patients. Tranfusion Alternatives in Transfusion Medicine. 2004;6(2):10-21.[Crossref]
18. Malik AT, Yu E, Kim J, Khan SN. Intensive care unit admission following surgery for pediatric spinal deformity: an analysis of the ACS-NSQIP pediatric spinal fusion procedure targeted dataset. Global Spine J. 2020;10(2):177-82. [Crossref] [PubMed] [PMC]
19. Workman JK, Wilkes J, Presson AP, Xu Y, Heflin JA, Smith JT. Variation in adolescent idiopathic scoliosis surgery: implications for improving healthcare value. J Pediatr. 2018;195:213-9.[Crossref] [PubMed]