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Research Article

Assessment of the effect of tranexamic acid on perioperative bleeding in pediatric patients undergoing tonsillectomy

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KEYWORDS

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Abstract *Background:* Tonsillectomy is one of the most common surgery in pediatric and bleeding is one of the most serious complications related to tonsillectomy. Tranexamic acid is a plasminogen inhibitor which has been successfully used to control bleeding in a variety of surgeries.
Aim: The aim of the present study was to assess the effect of tranexamic acid on bleeding in pediatric patients undergoing elective tonsillectomy.
Materials and methods: The present study included 225 patients classified into three groups: (n = 75): Group A: The tranexamic acid was given after induction intravenously as 15 mg/kg over 10 min. Group B: The tranexamic acid was given after induction intravenously as 15 mg/kg over 10 min and continued infusion as 5 mg/kg/h during surgery. Group C (control group): The patients did not receive tranexamic acid. The bleeding was assessed by the extent of blood loss using the Boezaart blood grading scale, measuring blood in the suction jar, and by visual estimation of 4×4 gauze pads.
Results: The comparison of Boezaart blood grading scale and amount of blood loss was insignificant between the three groups ($p > 0.05$).
Conclusion: The present study showed no effect of tranexamic acid in decreasing the tonsillectomy-related bleeding and there is no complication related to tranexamic acid. We are recommending other studies to measure the fibrinolytic activity during tonsillectomy and its inhibition by tranexamic acid.

1. Introduction

Tonsillectomy is one of the most common surgical procedures performed in otolaryngology practice. Tonsillectomy-related hemorrhage may occur intraoperatively or postoperatively.

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The latter is subdivided into primary hemorrhage (within 24 h of surgery) and secondary hemorrhage (more than 24 h after surgery, typically one week postoperative). Intraoperatively bleeding is controlled at the time of surgery. Primary hemorrhage usually requires return to theater (80% of cases), while the return to theater rate is less for secondary hemorrhage (17%) [1].

Tranexamic acid is a synthetic lysine analogue, producing an antifibrinolytic effect by the reversible blockade of lysine binding sites on plasminogen molecules. This inhibits the conversion of plasminogen to plasmin on the surface of the fibrin [2,3]. It has been used in cardiac, orthopedic and urological surgery to reduce perioperative blood loss [4], and to reduce the need for blood transfusion with no increased risk of thromboembolic complications [5]. It has also been used topically as a mouth wash following dental and oral surgery [6].

The aim of the present study was to assess the role of tranexamic acid in pediatric patients undergoing elective tonsillectomy. The primary outcome was measuring the amount of blood loss and the extent of blood loss.

2. Methods and patients

After approval from the local ethics committee and obtaining written informed parental consent in King Fahad military hospital, Khamis Mushait, Saudi Arabia, we studied 225 children (ASA physical status I–II) undergoing elective tonsillectomy without adenoidectomy. The indications of tonsillectomy were recurrent acute tonsillitis.

Exclusion criteria included patients with liver or kidney dysfunction or patients with inherited coagulopathy or preoperative use of anticoagulant therapy or abnormal coagulation profiles or allergy to tranexamic acid or neurologic or psychiatric disease. The present study included 225 patients classified into three groups (each = 75):

Group A: The tranexamic acid was given after induction intravenously as 15 mg/kg (single bolus dose) over 10 min.
Group B: The tranexamic acid was given after induction intravenously as 15 mg/kg over 10 min and continued infusion as 5 mg/kg/h during surgery.
Group C (control group): The patients did not receive tranexamic acid.

2.1. Anesthetic technique

After attaching the monitors to patients, the anesthetic induction was started either inhalationally (sevoflurane) or intravenously (ketamine) in addition to fentanyl (2 μg/kg) and rocuronium (0.6 mg/kg) and after tracheal intubation, the patients were ventilated mechanically and the anesthesia was maintained with sevoflurane (2–3%) and oxygen/air mixture (50%). At the end of surgery, the muscle relaxant was reversed and the patients were extubated.

2.2. Surgical technique

The techniques of tonsillectomy can be broadly divided into two major categories: extracapsular (total tonsillectomy, subcapsular) and intracapsular (partial tonsillectomy). Extracapsular tonsillectomy involves dissecting lateral to the tonsil in the plane between the tonsillar capsule and the pharyngeal musculature, and the tonsil is generally removed as a single unit. The most common extracapsular techniques use a "cold" knife (sharp dissection), bipolar cautery (or bipolar scissors). Extracapsular techniques are used for patients undergoing tonsillectomy as a result of tonsillitis or peritonsillar abscess [7]. In the present study, extracapsular technique is used for all cases.

2.3. Monitoring of patients

Heart rate, noninvasive arterial blood pressure, arterial oxygen saturation, end-tidal carbon dioxide, and body temperature were recorded every 5 min during surgery. At the end of each procedure, the extent of blood loss was assessed using the Boezaart blood grading scale (Table 1) [8].

2.4. Calculation of blood loss

For measuring blood in the suction jar, the fluid in the suction jar was poured into a measuring cylinder and the quantity of fluid present before the surgery was subtracted. The lower edge of the fluid meniscus after the foam had settled, was considered for the readings, also by visual estimation of 4×4 gauze pads, if mildly moist from 8 ml, moderately moist from 10 ml and completely moist from 12 ml blood [9–11].

2.5. Sample size calculation

Power analysis was performed using Chi square test for independent samples on frequency of patients complaining of tonsillectomy-related hemorrhage because it was the main outcome variable in the present study. A pilot study was done before starting this study because there are no clear data in the literature for the incidence of tonsillectomy-related hemorrhage with tranexamic acid administration. The results of the pilot study showed incidence of postoperative agitation of 10% in tranexamic acid group, and 30% in control group. Taking power 0.8 and alpha error 0.05, a minimum sample size of 72 patients was calculated for each group. A total of patients in each group 75 were included to compensate for possible dropouts.

2.6. The statistical analysis

Data were statistically described in terms of mean ± standard deviation (±SD), and frequencies (number of cases). Comparison of numerical variables between the study groups was done using one-way analysis of variance (ANOVA) test with post hoc multiple 2-group comparisons. Exact test was used instead when the expected frequency is less than 5. p values less than 0.05 were considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

3. Results

The study included 225 patients randomized to three groups and all patients had completed the study (Fig. 1). There were

Table 1 Quality of surgical field Boezaart et al. [8].

Grade	Assessment
0	No bleeding, cadaveric conditions
1	Slight bleeding, no suctioning required
2	Slight bleeding, occasional suctioning required
3	Slight bleeding, frequent suctioning required. Bleeding threatens surgical field a few seconds after the suction is removed
4	Moderate bleeding, frequent suctioning required, and bleeding that threatens surgical field directly after suction is removed
5	Severe bleeding, constant suctioning required. Bleeding appears faster than can be removed by the suction; surgical field severely threatened, and surgery usually not possible

no significant differences regarding the demographic data, heart rate, mean arterial blood pressure, temperature and duration of surgery ($p > 0.05$) (Table 2).

The comparison of blood loss between the three groups is insignificant and the mean was 46.56 ± 5.92 in Group A patients, 47.07 ± 5.96 in Group B patients and 47.17 ± 5.36 in Group C patients ($p = 0.691$).

The comparison of blood grading scale (grades 1, 2, 3, 4, and 5) between the three group is insignificant ($p > 0.05$) (Table 2). The incidence of primary bleeding (< 24 h after surgery), between the three groups was insignificant ($p > 0.05$) (Table 2). There was no secondary bleeding in the present study.

4. Discussion

The present study showed no effect of single intravenous dose or infusion of tranexamic acid to decrease the incidence of bleeding and blood loss during tonsillectomy in comparison with the control group and the cause is not clear in spite of many papers showed the effectiveness of tranexamic acid in decreasing surgical bleeding.

There are some studies supporting our results. Brum et al., found in a double-blind, randomized placebo-controlled trial included ninety-five children who underwent adenotonsillectomy, that there is no benefit of using the tranexamic acid

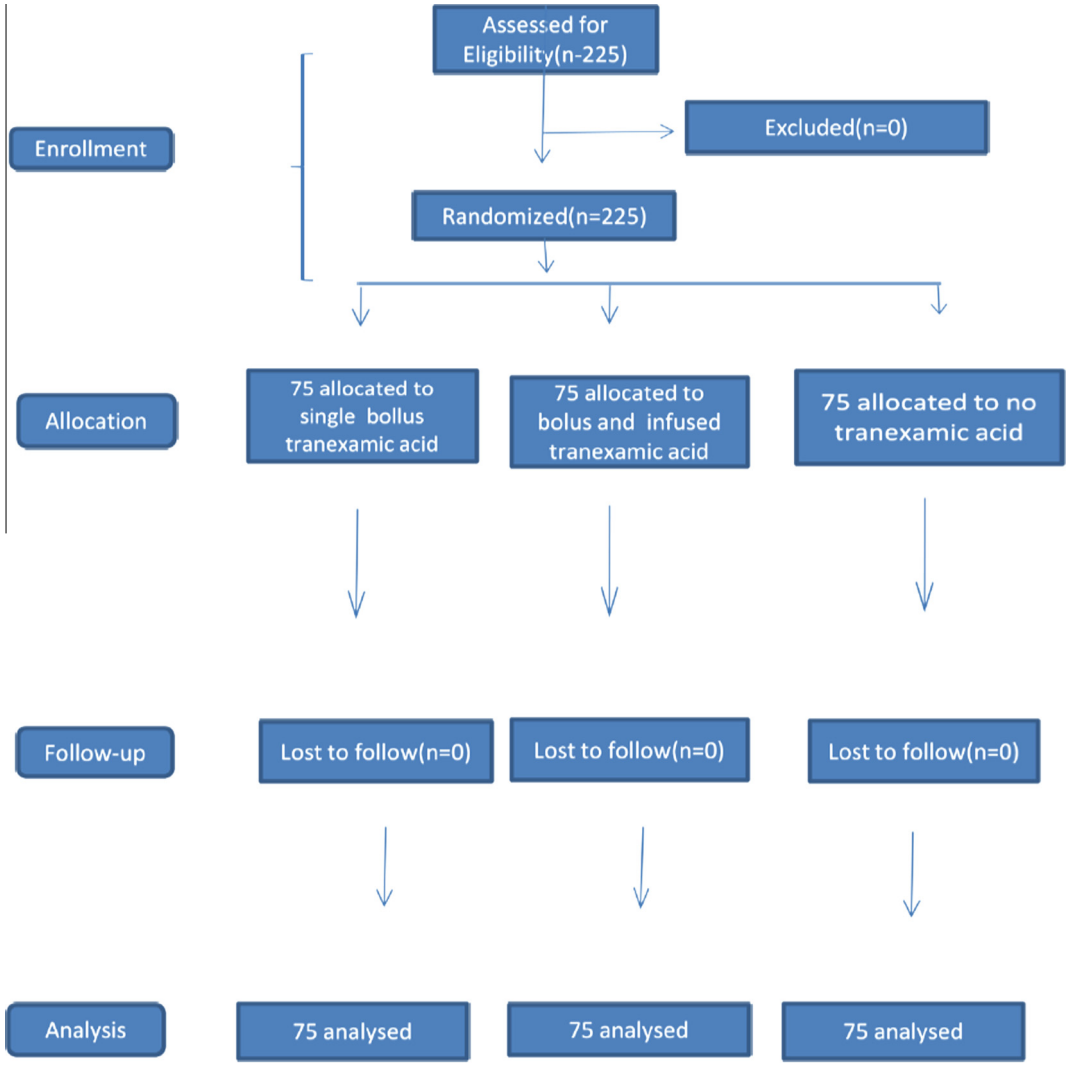

Figure 1 Flow diagram of the progress through the phases of a parallel randomised three groups (that is, enrollment, intervention allocation, follow-up, and data analysis).

Table 2 Data of patients (data are presented as mean ± SD, number).

Variable		Group A (n = 75)	Group B (n = 75)	Group C (n = 75)	p-value
Age (year)		7.14 ± 2.35	7.00 ± 2.32	7.10 ± 2.45	0.346
Weight (kg)		17.05 ± 3.92	17.00 ± 3.84	16.96 ± 3.97	0.557
Gender (number of patients)	Male	36	40	38	0.870
	Female	39	35	37	0.765
Heart rate (bpm)		84.10 ± 11.56	82.,00 ± 11.30	83.15 ± 12.04	0.954
MAP (mmHg)		76.04 ± 6.46	77.07 ± 6.34	78.27 ± 6.25	0.969
Temperature (°C)		36.76 ± 0.36	36.45 ± 0.73	36.57 ± 0.53	0.484
Duration (min)		39.01 ± 7.58	39.18 ± 7.34	38.87 ± 7.28	0.895
Blood loss (ml)		46.56 ± 5.92	47.07 ± 5.96	47.17 ± 5.36	0.691
Blood grading scale	Grade 0	–	–	–	
	Grade 1	35	32	36	0.844
	Grade 2	24	27	25	0.546
	Grade 3	10	8	7	0.308
	Grade 4	4	5	6	0.356
	Grade 5	2	3	1	0.245
Primary bleeding (number of patients)		1	2	1	0.649
Secondary bleeding (number of patients)		–	–	–	

for reducing bleeding during the adenotonsillectomy in children [12].

Other two results documented that tranexamic acid is not effective in decreasing the bleeding associated with surgery but one study was done in hip surgery [13], and one study done for third molar extraction [14]. Another study showed no significant benefit from the routine use of tranexamic acid during tonsillectomy but this study was done in adult patients [15].

A systemic review and meta-analysis of the tranexamic acid for tonsillectomy included 1670 patients and concluded that tranexamic acid did not reduce the number of patients with post-tonsillectomy hemorrhage significantly (p = 0.08) [16], but the authors noted that these studies varied enormously in the age range, dosage, schedule and duration of tranexamic acid administration, including one paper reporting topical application of tranexamic acid paste, resulting in a higher bleeding rate than the placebo group [17].

Against our result, there are two studies showed that the preoperative intravenous tranexamic acid is effective and significantly decreased the tonsillectomy bleeding [18,19]. In a randomized controlled trial, a single dose of intravenous perioperative tranexamic acid at l0 mg/kg produced a mean blood loss of 56.61 ml compared with 66.52 ml in the control group during tonsillectomy using conventional dissection techniques [20]. An observational study done by Robb PJ and his colleague in pediatric found that tranexamic acid has a potential benefits to decrease bleeding after tonsillectomy, therefore they recommended a large, prospective, multicentre, randomized controlled trial [21].

In another study done by Robb PJ and his colleague, they found that tranexamic acid decreased the frequency and severity of postoperative bleeding following tonsillectomy but this study was done in adult patients [22]. In a double-blinded control study included forty patients, 9–18 yrs of age, and randomized to either tranexamic acid (initial dose of 10 mg/kg and infusion of 1 mg/kg/h) or placebo (isotonic saline). Tranexamic acid reduced significantly the total blood loss and the total amount of blood transfused in the perioperative period (p = 0.045), but this study was done in pediatric scoliosis surgery [23].

The present study and the other studies are showing different results regarding the effect of tranexamic acid in decreasing the bleeding associated with tonsillectomy as some authors found that tranexamic acid is effective in decreasing tonsillectomy, while others showing no benefits from tranexamic acid and this may be related to many factors such as age of patients, route, dose, duration of administration, surgical techniques of tonsillectomy and number of patients in the studies. Other studies documented the effectiveness of tranexamic acid in the presence of fibrinolysis during cardiac surgery and cardiopulmonary bypass [24,25], neurosurgery [26,27], prostatectomy [28,29], and other surgeries, while there are no studies measured the fibrinolytic activity during tonsillectomy. This means that the tranexamic acid may be more effective to decrease the bleeding due to fibrinolysis, while it is not effective in other surgery without fibrinolysis.

There are limitations to the present study. First, small study populations of the present study, and second the fibrinolytic activity during tonsillectomy were not measured as the kits for measurement were not available in the laboratory.

5. Conclusion

The present study showed no effect of tranexamic acid in decreasing the tonsillectomy-related bleeding and there is no complication related to tranexamic acid. Other studies are recommended to measure the fibrinolytic activity during tonsillectomy and its inhibition by tranexamic acid.

Disclosures

The authors declare that they have no competing interests.

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