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The Effect of Tranexamic Acid on the Control of Postoperative Bleeding in Children Undergoing Adenotonsillectomy

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ABSTRACT

Background and Objective: Post-tonsillectomy bleeding is a significant concern in otolaryngological surgeries. Tranexamic acid has been extensively studied for its role in reducing bleeding, particularly in surgical settings. This study aimed to evaluate the efficacy of tranexamic acid in controlling bleeding in patients undergoing adenotonsillectomy.

Methods: A randomized clinical trial was conducted on 160 patients aged 6 to 14 years, who were candidates for tonsillectomy at the Ear, Nose, and Throat Clinic of Khatam Al-Anbiya Hospital in Zahedan in 2017. Patients were randomly divided into two groups of 80 each (case and control). The intervention group received intravenous tranexamic acid (TXA; 10 mg/kg, TRANEXIP®) administered as follows: an initial dose 5 minutes prior to surgical incision, followed by subsequent doses every 6 hours for 48 hours postoperatively. The volume of bleeding during surgery, as well as 24 hours and two weeks post-surgery, was recorded for all patients.

Findings: The mean volume of intraoperative bleeding in the case group (receiving tranexamic acid) was 44.18± 11.67 ml, compared to 55.62±20.93 ml in the control group. This difference was statistically significant ($p<0.001$). Postoperative bleeding was reported in only two cases, both in the control group. The mean heart rate in the case group was 92.82±12.15, and in the control group, it was 96.12±13.42, but this difference was not statistically significant ($p=0.105$).

Conclusion: The findings of this study indicate that tranexamic acid significantly reduces the volume of intraoperative bleeding in patients undergoing adenotonsillectomy.

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Introduction

Chronic adenotonsillar hypertrophy is indeed a significant cause of upper airway obstruction in children, often leading to obstructive sleep apnea (OSA). In severe cases, the chronic upper airway obstruction can result in increased pulmonary vascular resistance, leading to pulmonary hypertension. This pathogenesis stems from recurrent hypoxia and hypercapnia, which induce pulmonary arterial vasoconstriction and, with chronicity, promote structural remodeling of the pulmonary vasculature [1- 3]. The primary cause of mortality related to tonsillectomy is hemorrhage, particularly when treatment is delayed [4]. According to the Royal College of Surgeons, in 2005, 3.5% of tonsillectomy surgeries were associated with bleeding [5]. Tranexamic acid (TXA) is an antifibrinolytic agent with over four decades of clinical use across various surgical specialties. Its applications span obstetrics and gynecology, neurosurgery, cardiothoracic surgery, liver transplantation, hematology, and the management of gastrointestinal, respiratory, and even cutaneous hemorrhage. As an antifibrinolytic agent, TXA has demonstrated efficacy in multiple surgical specialties involving significant hemorrhage. However, its application in otorhinolaryngology remains relatively limited. Given the potential for life-threatening bleeding in ENT procedures-particularly tonsillectomy, judicious use of TXA in this surgical domain warrants careful consideration [6]. Extensive clinical research has established the efficacy of TXA in hemorrhage control, particularly in surgical settings. Multiple studies have demonstrated that TXA administration significantly reduces both intraoperative blood loss and the requirement for blood transfusions across various surgical procedures [7-12]. Despite robust evidence demonstrating tranexamic acid's (TXA) efficacy in hemorrhage reduction across numerous clinical studies [8-17], nevertheless, considerable uncertainty persists regarding TXA's effectiveness in controlling post-tonsillectomy hemorrhage [13-22]. Numerous systematic studies, meta-analyses, and clinical trials have been performed on the role of TXA [14-17]. Although TXA has been used for about 40 years, it is still associated with some side effects, such as the increased risk of kidney damage [9]. This study aims to evaluate the efficacy of tranexamic acid (TXA) in hemorrhage control among patients undergoing adenotonsillectomy. The investigation is prompted by two key gaps in current evidence: (1) the indeterminate role of TXA in post-tonsillectomy bleeding management, and (2) insufficient data regarding its potential benefits, especially in pediatric populations. As TXA represents a non-invasive, cost-effective hemostatic intervention, this study seeks to generate robust clinical evidence supporting its use in adenotonsillectomy procedures. The primary objective is to determine whether TXA administration significantly reduces perioperative blood loss, potentially establishing it as a safer and more economical alternative to conventional hemostatic measures.

Methods

This randomized clinical trial study was performed on 160 patients aged 6 to 14 years who were candidates for tonsillectomy referred to the Ear, Nose, and Throat (ENT) Clinic of Khatam Al-Anbiya Hospital in Zahedan in 2017. Taking into account similar studies [23, 24], 80 patients in each group and a total of 160 patients were selected. Based on whether or not they received tranexamic acid before surgery, Participants were randomized into two equally sized cohorts. The study population comprised patients with: recurrent tonsillitis, chronic tonsillitis, obstructive sleep apnea (OSA), tonsillar hypertrophy, or dysphagia requiring surgical intervention. Exclusion criteria included: (1) known hypersensitivity to tranexamic acid, (2) personal history of hematuria or coagulopathy, (3) hepatic dysfunction, (4) family history of bleeding disorders in first-degree relatives, and (5) current use of anticoagulant or antiplatelet medications. Patients were randomized using a block randomization method and allocated into two study groups. All participants underwent standard preoperative laboratory testing, including complete blood count (CBC), coagulation studies (prothrombin time [PT], activated partial thromboplastin time [aPTT], bleeding time [BT]), and electrolyte panels (sodium [Na], potassium [K]). The intervention group

received intravenous tranexamic acid (TXA; 10 mg/kg, TRANEXIP®) administered as follows: an initial dose 5 minutes prior to surgical incision, followed by subsequent doses every 6 hours for 48 hours postoperatively. However, the patients in the other group did not receive this injection before the operation, and routine procedures were performed similarly for both groups. Patients in both groups received 5 ml/kg crystalloid solution, 0.05 mg/kg midazolam, and 1 µg / kg remifentanil. General anesthesia was performed using 5 mg/kg thiopental sodium, and atracurium (0.6 mg/kg) was used to facilitate endotracheal intubation. Patients were given intravenous dexamethasone 0.2 mg/kg to reduce postoperative nausea and vomiting. Neuromuscular blockade reversal was achieved using intravenous neostigmine (0.05 mg/kg) co-administered with atropine (0.2 mg/kg). Intraoperative local bleeding was managed with monopolar electrocautery as needed. All procedures were performed by a consistent surgical and anesthesia team adhering to a standardized protocol. Patients were extubated following complete neuromuscular recovery and transferred to the post-anesthesia care unit (PACU) after achieving full consciousnessHemostasis was achieved using monopolar electrocautery. Patients were discharged to the ward only after meeting all postoperative stability criteria, including: (1) full return of consciousness, (2) adequate pain control, (3) absence of active bleeding, and (4) no nausea or vomiting. All participants underwent continuous postoperative monitoring in the ward for a minimum of 24 hours. Notably, no patients in either study group required blood transfusion during the observation period. Quantification of intraoperative blood loss was performed by measuring the total volume of blood-suction fluid collected during the procedure. The net blood volume was calculated by subtracting the known volume of irrigation saline used during surgery from the total suction output. This method allowed for the determination of the actual hemorrhage volume while accounting for fluid dilution [25].

Postoperative hemorrhage in the first 24 hours after surgery and two weeks later was recorded only as clear bleeding, and its volume was not measured.

Finally, all patient information was recorded in information forms.

Statistical data were described using descriptive tests, including mean and standard deviation, frequency, and percentage. To analyze the qualitative data between the two groups, the chi-square test and comparison of mean bleeding or other quantitative variables between the two groups, independent t-test, and comparison of bleeding intensity between the two groups, Mann-Whitney U test were used. SPSS 19 was used for statistical analysis, and the significance level of the tests was considered less than 0.05.

Results

In this study, 160 patients who underwent adenotonsillectomy were evaluated. In each group, 50% (n=40) were female patients and 50% were male patients. The mean age of patients in the case group was 8.35±3.35 years and in the control group was 7.76±3.28 years. There was no significant difference between the two groups in terms of mean age (p=0.265) and frequency distribution of gender (p=1.000).

Table 1 shows the mean bleeding in the two study groups.

As can be seen in Table 1, the mean volume of intraoperative bleeding in the case group (receiving tranexamic acid) was 44.18±11.67 ml, and in the control group (not receiving tranexamic acid) was 55.62±20.93.

Based on statistical analysis, this difference was significant between the two groups (p<0.001), so the mean bleeding was lower in the group receiving tranexamic acid.

During the present study, bleeding was examined 24 hours after surgery, as well as two weeks after surgery, as clear bleeding.

No cases of re-bleeding were reported in the tranexamic acid group within 24 hours and 2 weeks after surgery (0%). Bleeding cases in the group not receiving tranexamic acid were obtained in the first 24 hours after surgery, 2 cases (2.5%), and two weeks after surgery, 1 case (1.25%). Fisher's accuracy was not significant (p> 0.05).

Table 1 shows the mean heart rate in the two study groups. As can be seen, this means was 92.82±12.15 in the case group and 96.12±13.42 in the control group. Based on statistical analysis, this difference did not show a significant difference between the two groups (p=0.105).

Table 1. Mean bleeding volume and heart rate in the two groups

Group		Number	Average	Standard deviation	P-value
Bleeding volume (milliliter)	case	80	44.18	11.67	0.001
	control	80	55.62	20.93	
heart beat (Number per minute)	case	80	92.82	12.15	0.105
	control	80	96.12	13.42	

Discussion

This study aimed to evaluate the effect of tranexamic acid in controlling bleeding in patients undergoing adenotonsillectomy. Based on the results of the present study, it was observed that tranexamic acid significantly reduced the amount of intraoperative bleeding in the case group. In our study, none of the patients had side effects thus therefore, the effectiveness of tranexamic acid in controlling bleeding in children undergoing tonsillectomy surgery is discussed.

TXA is indeed a cost-effective antifibrinolytic agent widely used in various surgical settings to reduce bleeding and the need for blood transfusions. However, its efficacy and safety in pediatric populations have not been as thoroughly studied or conclusively established as in adults [26].

Despite the effectiveness of TXA in significantly reducing bleeding in many studies [13-22], there is still ambiguity about the role of TXA in reducing bleeding after tonsillectomy. Administration of TXA after tonsillectomy or adenectomy has been reviewed in several studies [23, 27]. However, there are no clear results regarding the role of TXA in bleeding after tonsillectomy.

The results of the study showed that the difference between the mean bleeding between the two groups was significant (p<0.001), so the mean bleeding in the group receiving tranexamic acid was significantly lower.

The study by George et al. (2011) in India aligns with the findings of the present study regarding the effectiveness of TXA in reducing postoperative bleeding in tonsillectomy patients. In their research, 100 patients undergoing tonsillectomy were divided into two groups, with one group receiving 10 mg/kg of intravenous TXA preoperatively. The results demonstrated that TXA significantly reduced bleeding after the procedure, supporting its utility as an effective intervention to minimize blood loss during and after surgery [28], which is consistent with the results obtained in the present study.

In another similar study by Castelli et al. In Germany, 80 patients were enrolled, 40 of whom received TXA. Bleeding was milder in the TXA group than in the control group. The authors concluded at the end of the study that TXA is a suitable factor for reducing bleeding after tonsillectomy [27], which is in line with the results obtained in the present study.

The study by Brum et al. (2012) in Brazil highlights an important point in medical research: the variability in outcomes when evaluating the efficacy of interventions like TXA in different clinical settings. In this case, the study found that TXA did not significantly reduce bleeding during or after adenotonsillectomy in children, which contrasts with findings from other studies that have reported beneficial effects of TXA in similar or different surgical contexts [24].

Soliman et al. in 2014, Saudi Arabia, evaluated the efficacy of TXA in bleeding during tonsillectomy. In this study, 225 patients were divided into 3 groups. The authors concluded that TXA had no role in reducing tonsillectomy-related bleeding and that TXA was not associated with any side effects. In this study, further studies on the effect of TXA on reducing bleeding due to tonsillectomy were suggested [29].

In this regard, some studies have investigated the effect of topical tranexamic acid. In 2013, for example, Albirmawy et al. in Egypt examined the

topical effect of TXA on reducing post-adenectomy bleeding in 400 children. In this study, it was concluded that topical application of TXA before adenectomy significantly reduces intraoperative and postoperative bleeding [25]. Although this result is similar to the finding in the present study on the reducing effect of tranexamic acid on intraoperative bleeding, some other studies that have examined the local effect of tranexamic acid have yielded different findings

For example, a 2014 study by Hinder et al. In Switzerland found that topical TXA did not reduce bleeding after tonsillectomy. However, in patients older than 12 years, there was a slight reduction in postoperative bleeding [30].

Finally, the study showed that tranexamic acid has an effective role in controlling bleeding in patients undergoing tonsillectomy, but similar studies are needed.

Conclusion

Based on the results of the present study, it was observed that tranexamic acid significantly reduced the volume of intraoperative bleeding in the case group. However, no difference was observed in the bleeding reported at 24 hours and 2 weeks postoperatively, or in heart rate. It is recommended to perform similar studies on patients who are candidates for other surgeries who are at risk of postoperative bleeding, and also to conduct similar studies with more statistical communities in other geographical areas.

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Ethical consideration

This study was approved by the Ethics Committee of Zahedan University of Medical Sciences, Iran (with ethics code IR.ZAUMS.REC.1396.344) and IRCT code (IRCT20180404039191N1).

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Conflict of interest

None of the authors involved in the preparation of this article declares any conflict of interest.

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