

Use of Topical Tranexamic Acid to Reduce Drainage Output After Thyroidectomy

Fadlullah Aksoy¹ , Alper Yenigün¹ , Vildan Betül Yenigün² , Seda Sezen Göktaş³ , Abdullah Özdem¹ , Remzi Doğan¹ , Orhan Özturan¹ 

¹Department of Otorhinolaryngology, Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

²Department of Medical Biochemistry, Bezmialem Vakıf University, Faculty of Medicine, İstanbul, Turkey

³Boyabat 75th Year State Hospital, Otolaryngology Clinic, Sinop, Turkey

Cite this article as: Aksoy F, Yenigün A, Betül Yenigün V, *et al.* Use of topical tranexamic acid to reduce drainage output after thyroidectomy. 2022;18(2):99-102.

ABSTRACT

Objective: Thyroid surgery is one of the frequent surgeries in daily operation schedules more often since the thyroid gland is very vascular. Hematomas after thyroidectomy may cause airway obstruction, which is life-threatening and requires immediate surgical intervention. Therefore, many hemostatic devices and methods have been developed. Tranexamic acid is a synthetic lysine analog with low molecular weight. This study was planned to demonstrate the effect of intraoperative topical tranexamic acid on postoperative drainage output for thyroid surgery.

Methods: This study was conducted in a tertiary referral center as a case-control study. In this case-control study, 57 patients were included. The patients were classified into 2 groups: those with intraoperative tranexamic acid (Group 1) and those without tranexamic acid (Group 2). The drainage output of patients after surgery was compared between the 2 groups. In Group 1, 1 ampoule of tranexamic acid was applied intraoperatively to the thyroid bed using a syringe after total thyroidectomy for 5 minutes. All the patients were followed up for the first 24 hours.

Results: The mean value of postoperative drainage output in Group 1 was 28.55 mL (21.9 mL-35.1 mL); in Group 2 it was 51.75 mL (46-57.4 mL). We observed a statistically significant difference between the two groups in terms of postoperative drainage ($P < .05$).

Conclusion: In our study, intraoperative topical tranexamic acid administration to the surgical bed after total thyroidectomy showed a significant decrease in postoperative drainage output.

Keywords: Thyroidectomy, tranexamic acid, drainage, methods

Introduction

In recent years, thyroid surgery is being performed increasingly. In the United States, 97,231 thyroid surgeries were recorded in 2006, but in 2011 this number reached 130,126.¹ Major complications following thyroid surgery include bleeding, nerve injury, vocal cord paralysis, infection, and hypoparathyroidism.² The thyroid gland is very vascular. Because of its location, postthyroidectomy hemorrhage can cause airway obstruction, which is life-threatening and requires immediate surgical intervention.³ Postoperative bleeding rates were reported between 0.4% and 4%.^{4,5} However, in the majority of studies, this rate is less than 2%.⁶ Many hemostatic devices and methods have been developed other than classical hemostasis methods such as compress, clamp ligation, suture ligation, and electrocautery. In addition, local hemostatic agents that reduce bleeding have

been developed and the clinical use of these local hemostatic agents is increasing.⁷

The tranexamic acid (TXA) is a synthetic lysine analog with low molecular weight found in 1960. It is linked reversibly to plasminogen lysine-binding sites. So that fibrinolysis is inhibited because the plasmin cannot form and bind to the fibrin.⁸ It also protects platelet function by inhibiting plasmin-dependent platelet glycoprotein 1b receptors.⁹ In many studies, topical TXA has been shown to significantly reduce both intraoperative bleeding and the need for postoperative blood transfusion compared to placebo.¹⁰ However, in our review, we did not find any publication in the English literature about topical use of TXA in thyroid surgery. The aim of this study was to evaluate the effect of intraoperative topical TXA on postoperative drainage output in the thyroid surgery.

Corresponding Author: Alper Yenigün, alperyenigun@gmail.com

Received: August 12, 2021 **Accepted:** January 24, 2022

Available online at www.b-ent.be



CC BY 4.0: Copyright@Author(s), "Content of this journal is licensed under a Creative Commons Attribution 4.0 International License."

Methods

This study was planned prospectively and was approved by the Clinical Research Ethics Committee of Bezmialem Vakif University Faculty of Medicine (02/12/2020; decision number 14/7). All of the patients underwent total thyroidectomy due to a suspicious or malignant result after thyroid fine needle biopsy. Patients who had undergone thyroid and neck surgery were excluded from this study. In addition, the history of pulmonary thromboembolism or deep vein thrombosis, hypercoagulability, use of anticoagulant drugs, and abnormal coagulation tests were accepted as exclusion criteria. Information on informed consent was obtained from all patients participating in the study.

Total thyroidectomy was performed by the same surgeon following the same surgical principles for all patients. No other additional surgery was done. Bleeding control was performed by ligation with clamping during all operations. The study was planned as 2 groups, patients who used intraoperative TXA (Group 1) and patients who did not use TXA (Group 2). Patients were randomly selected for 2 groups. The bleeding through the hemovac drainage findings in patients after the surgery were compared between the groups with TXA and without TXA. In Group 1, 1 ampoule TXA (Transamine 10% 2.5 mL 250 mg ampoule, Actavis Corp.) was applied intraoperatively to the thyroid bed using a syringe after total thyroidectomy and it was left for 5 minutes. All patients' incisions were closed in the same manner by placing hemovac drains. All patients were followed up for the first 24 hours. The amount of blood drained for 24 hours was measured.

We planned the number of individuals to be surveyed before starting the research as 75 by performing power analysis. For 95% confidence level, 80% power, 130 units of the mean difference, and 185 units for the standard deviation based on the result of power analysis, it is calculated that minimum of 32 cases are appropriate for both groups. Estimated blood loss variability was taken as reference value. In our study, we performed the statistical evaluation using the SPSS version 24.0 program (SPSS Inc, Chicago, Ill, USA). We calculated descriptive statistics as a mean and standard deviation. We used Student's *t*-test for comparisons between groups. We considered a value of $P < .05$ to be significant.

Main Points

- Hematomas seen after thyroidectomy can cause airway obstruction, which is life-threatening and requires urgent surgical intervention.
- Topical application of tranexamic acid during surgery has been shown to significantly reduce the need for intraoperative and postoperative blood transfusions.
- The aim of this study is to show that the use of intraoperative topical tranexamic acid in thyroid surgery reduces the risk of hematoma formation by reducing the postoperative drainage output.
- According to our study, we observed a significant decrease in postoperative drainage output with the application of topical tranexamic acid intraoperatively during thyroidectomy.

Results

We included 57 patients in our study. There were 27 patients in the TXA group, of which 20 were female (74.1%) and 7 were male (25.9%). The age range was 12–78, the mean age was 47 years. The control group included 30 patients, 24 (80%) women, and 6 (20%) men. The age range was 21–71 and the mean age was 45.38.

The mean value of postoperative drainage output in Group 1 was 28.55 mL (21.9–35.1 mL), whereas in Group 2 it was 51.75 mL (46–57.4 mL). The difference between the 2 groups was statistically significant ($P < .001$). The drainage in the TXA group was statistically lower than the control group ($P < .0001$).

Discussion

Postoperative bleeding in thyroid surgery is a life-threatening complication, causing acute airway problems and even cardiac arrest. The airway obstruction may develop with hematoma behind the strap muscles. This obstruction is due to both the pressure of the hematoma on the trachea and, more importantly, the development of laryngopharyngeal edema caused by the obstruction of venous and lymphatic drainage.^{11,12}

The classic symptoms of hematoma include swelling, increased pressure in the middle of the neck, difficulty in breathing and suffocation, dysphagia, and difficulty in speaking. Physical examination showed significant swelling and ecchymosis that become visible with palpation. Radiological examinations are often unnecessary and lead to time loss.¹³

Risk factors for postoperative hematoma include advanced age, male gender, tumor size, additional neck dissection, presence of Graves' disease, and systolic blood pressure above 150 mmHg.^{5,14} Advanced age and male gender have been defined as independent risk factors for hemorrhage.¹⁵ A study reported that bleeding risk was significantly increased in patients older 45 years of age, while the risk was 40% lower in females.¹⁶ Another risk factor is previous thyroid surgery, because the scar tissue located in the surgical area causes adhesions and deterioration of normal anatomy.¹⁷ In addition, vasoconstriction of small vessels is not sufficient postoperatively due to scar tissue blocking the collapsed dead space.¹⁸

In another study, multinodular goiter, malignancy, and Graves' disease were compared and only increased risk of hematomas in Graves' disease was identified.¹⁹ Zhang et al showed that the risk significantly increased in patients with Body Mass Index (BMI) >30 .²⁰ Although the experience of the surgeon seems to be effective, recent studies have

Table 1. The Age and Gender Information of Patients Is Shown in the Table.

	Age (years)			Gender	
	Minimum	Maximum	Mean	Female	Male
Group 1 (n=27)	12	78	47	74.1% (n=20)	25.9% (n=7)
Group 2 (n=30)	21	71	45.38	80% (n=24)	20% (n=6)

Table 2. Postoperative Drain Output Values Are in the Table. The Tranexamic Acid Group Was Statistically Lower than the Control Group ($P < .0001$)

	Postoperative Drain Output Values (mL)			
	P-Value	Mean Difference	95% Confidence Interval of the Difference	
			Lower	Upper
Tranexamic acid group	<.0001	28.55556 mL	21.9741 mL	35.1370 mL
Control group	<.0001	51.75000 mL	46.0395 mL	57.4605 mL

found similar rates of hemorrhage between seniors and less experienced surgeons.²¹⁻²³

Careful hemostasis during thyroidectomy is important for the prevention of hemorrhage postoperatively. A bleeding focus has been defined in about 55-90% of all cases.^{24,25}

Schwartz et al reported that 94 bleeding-related deaths in 100,000 cases could be prevented by extending the postoperative follow-up period from 6 hours to 1 day after thyroidectomy.²⁶ Lang et al also found this number as 194 in 100,000 cases.¹⁸ It may be possible to discharge on the same day only in selected low-risk cases.²³ In our study, patients were followed up for at least 24 hours postoperatively.

The traditional hemostasis method is a ligation with clamping and is still considered to be the gold standard.²⁷ There are many studies on the intraoperative use of topical hemostatic agents in major surgeries.²⁸ These agents can be divided into 2 groups, synthetic and biological agents. TachoSil, one of the biological agents, is a ready-to-use collagen patch with one surface coated with human fibrinogen and thrombin.⁷ In one study, TachoSil was administered to the thyroid bed after total thyroidectomy, but no significant reduction was reported for hemorrhage rates.²⁹ In another study, adrenaline spray was applied to the thyroid bed after total thyroidectomy and it was shown to decrease the hemorrhage rates significantly.³⁰ In our study, for the first time in the literature, we applied topical TXA to the thyroid bed using a syringe and waited for 5 minutes before serum irrigation.

There is no standardized dose for the topical TXA usage. When we look at the studies in the literature, it is seen that they are used at rates ranging from 1 to 100 mg/mL. In this study, we used 100 mg/mL doses. Tranexamic acid rapidly reaches its peak conformation in intravenous use and has about 100% bioavailability. The bioavailability of oral TXA is 35-45% and takes about 3 hours for the required plasma concentration.³¹ In one study, systemic absorption was reported below 30% in intra-articular administration.³² Topical and pericardial administration did not show systemic absorption.³³

Gilbody et al. reported that topical TXA is safe in terms of thromboembolic side effects such as pulmonary embolism, stroke, deep vein thrombosis, and myocardial infarction and can be used safely in patients with renal failure.^{10,34}

One study concluded that topical TXA reduced the blood transfusion requirement by 71% when compared with a placebo.¹⁰ In another study, it was shown that with the topical use of TXA in many surgeries, blood loss was reduced by 29% and the need for blood transfusion by 45%.³⁵ Recent studies have shown that the topical use of TXA in knee and hip arthroplasties results in

successful postoperative bleeding control and the blood transfusion requirements are less.^{36,37} The topical use of TXA in spinal surgery has been shown to reduce total blood loss, drainage volume, and length of hospital stay.³⁸ In epistaxis control, topical TXA was found to be more successful in bleeding control compared to standard anterior nasal packing.³⁹ In our study, TXA, which we applied to the thyroid bed after total thyroidectomy, resulted in a significant decrease in the amount of postoperative drainage output.

We demonstrated that drainage output was decreased after thyroidectomy with the use of TXA. We believe that the removal of the drain might be earlier with the use of TXA after thyroidectomy. It has been reported that seroma and infection were not observed in the long-term follow-up of patients who were applied with topical TXA. Wound healing was not adversely affected by TXA. Therefore, we do not think that TXA is partially or completely blocks the drain.

The limitations of our study are the small number of patients and the fact that factors that may affect the bleeding rate such as tumor size, BMI, and malignancy were not taken into account.

Conclusion

The postoperative hemorrhage is important because it can cause a life-threatening airway obstruction. Various methods have been tried to prevent post-thyroidectomy hemorrhage. One of these methods is TXA which is active when administered topically and has no systemic side effects. According to our study, when topical TXA was administered intraoperatively to the thyroid bed after total thyroidectomy, postoperative drainage output was reduced significantly, allowing earlier discharge of the patients from the hospital.

Ethics Committee Approval: This study was approved by Ethics committee of Bezmialem Vakif University, (Approval No: 02/12/2020; 14/7).

Informed Consent: Verbal and written informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.A.; Design – F.A., A.Y.; Resources – V.B.Y.; Data Collection and/or Processing – A.Ö., R.D.; Analysis and/or Interpretation – O.Ö.; Literature Search – S.S.G.; Writing Manuscript – A.Y.; Critical Review – F.A.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

References

- Sun GH, DeMonner S, Davis MM. Epidemiological and economic trends in inpatient and outpatient thyroidectomy in the United States, 1996-2006. *Thyroid*. 2013;23(6):727-733. [\[CrossRef\]](#)
- Samona S, Hagglund K, Edhayan E. Case cohort study of risk factors for post-thyroidectomy hemorrhage. *Am J Surg*. 2016;211(3):537-540. [\[CrossRef\]](#)
- Tian J, Li L, Liu P, Wang X. Comparison of drain versus no-drain thyroidectomy: a meta-analysis. *Eur Arch Otorhinolaryngol*. 2017;274(1):567-577. [\[CrossRef\]](#)
- Lee HS, Lee BJ, Kim SW, et al. Patterns of post-thyroidectomy hemorrhage. *Clin Exp Otorhinolaryngol*. 2009;2(2):72-77. [\[CrossRef\]](#)
- Chen E, Cai Y, Li Q, et al. Risk factors target in patients with post-thyroidectomy bleeding. *Int J Clin Exp Med*. 2014;7(7):1837-1844.
- Liu J, Sun W, Dong W, et al. Risk factors for post-thyroidectomy haemorrhage: a meta-analysis. *Eur J Endocrinol*. 2017;176(5):591-602. [\[CrossRef\]](#)
- Haas S. The use of a surgical patch coated With human coagulation factors in surgical routine: a multicenter postauthorization surveillance. *Clin Appl Thromb Hemost*. 2006;12(4):445-450. [\[CrossRef\]](#)
- Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. *Drugs*. 1999;57(6):1005-1032. [\[CrossRef\]](#)
- Hardy JF, Desroches J. Natural and synthetic antifibrinolytics in cardiac surgery. *Can J Anaesth*. 1992;39(4):353-365. [\[CrossRef\]](#)
- Montroy J, Hutton B, Moodley P, et al. The efficacy and safety of topical tranexamic acid: a systematic review and meta-analysis. *Transfus Med Rev*. 2018;S0887-7963:30151-30157. [\[CrossRef\]](#)
- Savargaonkar AP. Post-Thyroidectomy haematoma causing total airway obstruction -A case report. *Indian J Anaesth*. 2004;48:483-485.
- Mittendorf EA, McHenry CR. Complications and sequelae of thyroidectomy and an analysis of surgeon experience and outcome. *Surg Technol Int*. 2004;12:152-157.
- Dixon JL, Snyder SK, Lairmore TC, Jupiter D, Govednik C, Hendricks JC. A novel method for the management of post-thyroidectomy or parathyroidectomy hematoma: a single-institution experience after over 4,000 central neck operations. *World J Surg*. 2014;38(6):1262-1267. [\[CrossRef\]](#)
- Calò PG, Erdas E, Medas F, et al. Late Bleeding after Total thyroidectomy: report of Two Cases occurring 13 days after Operation. *Clin Med Insights Case Rep*. 2013;6:165-170. [\[CrossRef\]](#)
- Promberger R, Ott J, Kober F, et al. Risk factors for postoperative bleeding after thyroid surgery. *Br J Surg*. 2012;99(3):373-379. [\[CrossRef\]](#)
- Weiss A, Lee KC, Brumund KT, Chang DC, Bouvet M. Risk factors for hematoma after thyroidectomy: results from the nationwide inpatient sample. *Surgery*. 2014;156(2):399-404. [\[CrossRef\]](#)
- Shaha AR. Revision thyroid surgery - technical considerations. *Otolaryngol Clin North Am*. 2008;41(6):1169-83, x. [\[CrossRef\]](#)
- Lang BH-H, Yih PC-L, Lo CY. A review of risk factors and timing for postoperative hematoma after thyroidectomy: is outpatient thyroidectomy really safe? *World J Surg*. 2012;36(10):2497-2502. [\[CrossRef\]](#)
- Quimby AE, Wells ST, Hearn M, Javidnia H, Johnson-Obaseki S. Is there a group of patients at greater risk for hematoma following thyroidectomy? A systematic review and meta-analysis. *Laryngoscope*. 2017;127(6):1483-1490. [\[CrossRef\]](#)
- Zhang X, Du W, Fang Q. Risk factors for postoperative haemorrhage after total thyroidectomy: clinical results based on 2,678 patients. *Sci Rep*. 2017;7(1):7075. [\[CrossRef\]](#)
- Emre AU, Cakmak GK, Tascilar O, et al. Complications of total thyroidectomy performed by surgical residents versus specialist surgeons. *Surg Today*. 2008;38(10):879-885. [\[CrossRef\]](#)
- Manolidis S, Takashima M, Kirby M, Scarlett M. Thyroid surgery: a comparison of outcomes between experts and surgeons in training. *Otolaryngol Head Neck Surg*. 2001;125(1):30-33. [\[CrossRef\]](#)
- Perera M, Anabell L, Page D, Harding T, Gnanaswaran N, Chan S. Risk factors for post-thyroidectomy haematoma. *J Laryngol Otol*. 2016;130(suppl 1):S20-S25. [\[CrossRef\]](#)
- Burkey SH, van Heerden JA, Thompson GB, Grant CS, Schleck CD, Farley DR. Reexploration for symptomatic hematomas after cervical exploration. *Surgery*. 2001;130(6):914-920. [\[CrossRef\]](#)
- Rosenbaum MA, Haridas M, McHenry CR. Life-threatening neck hematoma complicating thyroid and parathyroid surgery. *Am J Surg*. 2008;195(3):339-343. [\[CrossRef\]](#)
- Schwartz DL, Lobo MJ, Ang KK, et al. Postoperative external beam radiotherapy for differentiated thyroid cancer: outcomes and morbidity with conformal treatment. *Int J Radiat Oncol Biol Phys*. 2009;74(4):1083-1091. [\[CrossRef\]](#)
- Lachanas VA, Prokopakis EP, Mpenakis AA, Karatzanis AD, Velegarakis GA. The use of LigaSure Vessel Sealing System in thyroid surgery. *Otolaryngol Head Neck Surg*. 2005;132(3):487-489. [\[CrossRef\]](#)
- Wright JD, Ananth CV, Lewin SN, et al. Patterns of use of hemostatic agents in patients undergoing major surgery. *J Surg Res*. 2014;186(1):458-466. [\[CrossRef\]](#)
- Erdas E, Medas F, Podda F, et al. The use of a biologic topical haemostatic agent (TachoSil®) for the prevention of postoperative bleeding in patients on antithrombotic therapy undergoing thyroid surgery: a randomised controlled pilot trial. *Int J Surg*. 2015;20:95-100. [\[CrossRef\]](#)
- Ersoy YE, Aysan E, Meric A, et al. Does adrenaline spraying over thyroidectomy area reduce bleeding? *Int J Clin Exp Med*. 2014;7(1):274-279.
- Pilbrant A, Schannong M, Vessman J. Pharmacokinetics and bioavailability of tranexamic acid. *Eur J Clin Pharmacol*. 1981;20(1):65-72. [\[CrossRef\]](#)
- Wong J, Abrishami A, El Beheiry H, et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. *J Bone Joint Surg Am*. 2010;92(15):2503-2513. [\[CrossRef\]](#)
- De Bonis M, Cavaliere F, Alessandrini F, et al. Topical use of tranexamic acid in coronary artery bypass operations: a double-blind, prospective, randomized, placebo-controlled study. *J Thorac Cardiovasc Surg*. 2000;119(3):575-580. [\[CrossRef\]](#)
- Gilbody J, Dhotar HS, Perruccio AV, Davey JR. Topical tranexamic acid reduces transfusion rates in total hip and knee arthroplasty. *J Arthroplasty*. 2014;29(4):681-684. [\[CrossRef\]](#)
- Ker K, Beecher D, Roberts I. Topical application of tranexamic acid for the reduction of bleeding. In: Ker K, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2013:CD010562. [\[CrossRef\]](#)
- Chen Y, Chen Z, Cui S, Li Z, Yuan Z. Topical versus systemic tranexamic acid after total knee and hip arthroplasty: a meta-analysis of randomized controlled trials. *Med (Baltim)*. 2016;95(41):e4656. [\[CrossRef\]](#)
- Chen TP, Chen YM, Jiao JB, et al. Comparison of the effectiveness and safety of topical versus intravenous tranexamic acid in primary total knee arthroplasty: a meta-analysis of randomized controlled trials. *J Orthop Surg Res*. 2017;12(1):11. [\[CrossRef\]](#)
- Luo Y, Li X, Dong J, Sun W. A comparison of surgical outcomes and complications between hemostatic devices for thyroid surgery: a network meta-analysis. *Eur Arch Otorhinolaryngol*. 2017;274(3):1269-1278. [\[CrossRef\]](#)
- Morgenstern J, Rangarajan S, Heitz C, Bond C, Milne WK. Hot off the press: topical tranexamic acid compared with anterior nasal packing for treatment of epistaxis in patients taking antiplatelet drugs. *Acad Emerg Med*. 2018;25(9):1062-1064. [\[CrossRef\]](#)