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Role of Tranexamic Acid in Reducing Blood Loss in Head and Neck Cancer Surgery - A systematic Review

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KEYWORDS

Tranexamic acid, Malignancy, Perioperative Blood loss, Blood transfusion, Postoperative drain volume, Innovation

ABSTRACT:

Introduction: Tranexamic acid (TXA) has been demonstrated in studies to lessen blood loss and the requirement for transfusions in patients with head and neck malignancies. But no single trial has been sufficiently large to conclude with certainty whether the medication is safe and effective. The objective of this study was to methodically examine randomised controlled trials assessing TXA's safety and effectiveness in lowering blood loss and transfusion in patients with head and neck cancer.

Materials and Methods: This systematic review of randomised controlled trials of different doses of TXA or TXA with control group in patients undergoing surgeries for head and neck cancer. A literature search of PubMed, Web of Science, Cochrane, Lilacs etc were performed. Two authors independently reviewed the articles and screened on the basis of the study design; the inclusion and exclusion criteria; the primary outcomes; the findings; the number of participants; the age and sex of the participants; the participant characteristics; the main study outcomes. Data extraction and risk of bias was performed with ROB II tool.

Results: After thorough screening, four studies were included in the review. Three out of four included studies had normal saline as control group and one group had no intervention as control group. One of the included study had different does of TXA. Comparing all 4 studies, 10 mg/kg of TXA was enough dose to control blood loss compared to normal saline. Also ROB assessment resulted that one included study had low of ROB and other 3 studies had medium ROB

Conclusion: Tranexamic acid is both effective and affordable, it can be used as a strategic tool in the surgeon's toolbox as healthcare systems struggle to balance the demands of managing resource constraints with optimizing patient outcomes.

1. Introduction

Head and neck cancers (HNCs) are the sixth most prevalent malignancy worldwide, however they are more predominant in the Indian subcontinent. In India, the prevalence of malignant diseases of the body might reach 30–40%. HNC in India is distinct due to its etiology, clinical presentation, and patient features [1]. It has been acknowledged that radical neck dissection and wide local excision are key components of HNC surgical techniques. Surgeons and anesthesiologists find it difficult to treat bleeding, and frequently transfusions of blood and blood products are necessary. On the other hand, the administration of blood and blood products carries multiple risks and adverse effects [2].

Allogenic blood transfusions are expensive, but more significantly, there is an unacceptably high risk of major side effects, such as infection, immunosuppression, and cardiovascular dysfunction, which could have a fatal consequence for the patient [3].

A broad spectrum of interventions, such as the use of energy-saving devices, tourniquets, pharmaceutical agents, and barbed sutures, are available to minimize blood loss[4]. In terms of medication use, recommendations have been made for intravenous oxytocin infusion, vaginal or rectal misoprostol, and intramyometrial vasopressin injection to reduce intraoperative blood loss and, in certain situations, transfusion rates. Vasopressin was prohibited from being used during myomectomy in many countries due to

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safety concerns. Then, additional agents were used to help surgeons safely perform myomectomy [5].

Antifibrinolytic agents like tranexamic acid (TXA) are one of them. In 1962, Shosuke and Utako Okamoto, two Japanese researchers, made the first batch of tranexamic acid. Application of tranexamic acid (TXA) started with first usage to treat menorrhagia in 1968 [6]. By postponing the plasminogen-to-plasmin conversion, TXA reduces fibrinolysis and stabilizes the blood clot. It prevents plasminogen, plasmin, and tissue plasminogen activator from attaching to fibrin by competitively blocking their lysine-binding sites. As a result, plasminogen to plasmin conversion is inhibited, and plasmin's proteolytic action on fibrinogen and fibrin monomers is stopped [7].

In a variety of hemorrhagic conditions (such as menorrheagia, hemophilia, postpartum hemorrhage, and hereditary angioneurotic edema) and surgical procedures (such as multiple, cardiac, obstetric, orthopedic, and trauma surgeries), It has been demonstrated that TXA is a useful hemostatic agent [8]. According to these studies, administering TXA is generally safe and can greatly lower the need for transfusion, blood loss, and mortality from bleeding. In order to reduce postoperative pain, swelling, and patient satisfaction, TXA has been demonstrated to reduce the inflammatory response. Due to shortened hospital stays and fewer transfusions, TXA can also lower overall healthcare costs [9]. When it comes to lowering the transfusion rate following some major surgeries, topical application of TXA is just as effective as IV administration. It is included in the List of Essential Medicines by the World Health Organization. After which TXA has become widely used in various medical specialties, such as hematology, surgery, and—perhaps surprisingly—trauma, because of its ability to lower both bleeding and death rates [10].

One of the widest use of TXA is in head and neck (H&N) surgeries. In order to reduce the risk of multiple postoperative complications, including hematoma, seroma, space-occupying structural compression, surgical site infection, delayed wound healing, surgeons performing head and neck trauma and surgeries most frequently use drainage tubes [11,12]. The closed-suction mechanism of these drainage tubes eliminates surplus body fluids, saturates large dead spaces, and approximates skin flaps. However, in the H&N region, a longer duration of drainage tube in situ is associated with longer hospital stays, higher health accessibility costs, a higher incidence of surgical wound infections, and significantly delayed wound healing [13,14]. Therefore, in order to reduce postoperative morbidity and speed recovery following H&N procedures, TRA interventions to forego the insertion of drainage tubes or expedite their removal are essential [15].

Further research is needed to create management plans for patients with bleeding disease risk factors, such as anticoagulated patients having more extensive dental work done or head and neck surgeries, as well as those with underlying chronic medical conditions. The purpose of this systematic review was to assess high-grade evidence supporting the administration of the antifibrinolytic tranexamic acid in lowering complications related to bleeding after surgery.

2. Materials and Methods

Protocol

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 Statement and the Cochrane Handbook were followed in the preparation of the review's protocol [16,17]. This review's main question was: How does tranexamic acid affect patients with head and neck cancer in terms of lessening their post-operative blood loss during surgery?

Eligibility Criteria

A PICOS criterion was developed to help with the search strategy and ascertain which studies should be included in the present systematic review [18]. The following is the PICOS formula:

- Population (P) - Patients diagnosed with Head and Neck Cancer
- Intervention (I) - Tranexamic acid.
- Comparison (C) - Normal Saline.
- Outcome (O) - Blood loss
- Study Design (S): Original research investigating the effects of Tranexamic acid in patients undergoing head and neck surgery (randomized controlled trials) was included; overviews, narrative reviews, letters to the editor, brief

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communications, case reports, and case series were not.

For this review, only articles that were published were reviewed. The English translation attached to the article or its publication status determined whether or not it was included in the review process.

Information Sources and Search Strategy

To find all peer-reviewed studies relevant to the review's question, a comprehensive search of PubMed, Google Scholar, Cochrane CENTRAL, Scopus, Web of Science, and LILACS was conducted for all the articles which were published. When developing thorough search strategies, each database's unique vocabulary and syntactical restrictions were taken into account.

The following MeSH terms were used in search strategy. ((head and neck cancer) OR (head and neck surgery) OR (head and neck surgery) OR (cancer surgery) AND (Tranexamic acid) OR (TXA) OR (Antifibrinolytic) OR (Antifibrinolytics) AND (bleeding) OR (blood loss) OR (post operative blood loss) OR (peri operative blood loss) OR (blood tranfusion)). Table 1 displays the search strategy that was employed in the databases. A manual search of several journals, including the American Journal of Oral Surgery, BMC Oral Health, Oral Oncology, and Oral Surgery Oral Medicine, covering oral surgery and oncology was also conducted.

To find more studies that could be included in the review, a search for grey literature was done using the databases Open Grey and GreyNet International. In order to find any studies that might be added to the review process, references to the studies that were part of the review were also examined.

Two authors carried out the search on their own. First, the eligibility of the article titles that the investigation had found was ascertained through a screening process. In order to conduct the qualitative analysis, we searched for and assessed relevant full-text studies. To find out if there were any additional studies that were overlooked during the first search, references of the included studies were examined. Throughout the search and review process, a third reviewer was consulted on several occasions to resolve disagreements that arose between the primary reviewers.

Data extraction

Two reviewers carried out the data extraction. The following information was taken from the studies that satisfied the requirements for inclusion and eligibility and entered into a Microsoft Excel spreadsheet that was predetermined (Microsoft Corp., Redmond, WA, USA): the level of evidence; sample size; anesthesia measured; the route and dose of TXA administration; the intervention and control group; the first author, the year the study was published, the country; the study design; the inclusion and exclusion criteria; the primary outcomes; the findings; the number of participants; the age and sex of the participants; the participant characteristics; the main study outcomes (blood volume loss, operative time, adverse events, pain score, hospital length of stay, thromboembolic events, and mortality). Figure 1 shows the stages of article selection schematically as shown in the PRISMA flow diagram [19].

Assessment of Risk of Bias

The ROB-II tool which is revised in August 2019 was the tool used for assessment of risk of bias in randomized trials. This is also approved by Cochrane Handbook. First the data was entered in ROB2 excel sheet. Then the Robvis application was used to visualize risk of bias assessments. The scale has five main domains (randomisation, deviation from intended intervention, missing data, outcome measurement, and selection of reported results) and assigns one point for each of the following three judgements: high, moderate, and low [20,21]. Egger's test was used to assess the publication bias [22].

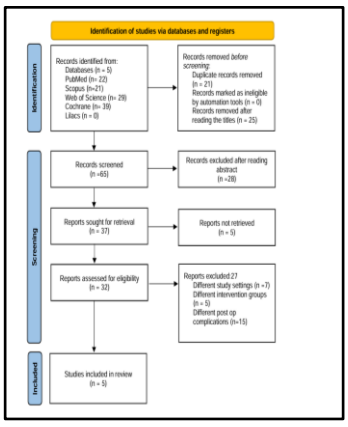

Figure 1. PRISMA flowchart

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3. Results

The present systematic literature search generated 566 publications from various databases and registers. Two hundred and seven articles were removed for duplications. Discussions were used to settle disagreements over the studies' inclusion. Three hundred and fifty seven articles titles were identified from the search after reading the titles. Abstracts of selected articles were reviewed independently. Three hundred and fourteen were excluded after reading the abstract. Forty three full text articles were retrieved for relevant studies. Thirty one articles were excluded for being non randomised trials. Eight articles were excluded after reading the complete article because they had different study settings or different intervention groups. Following separate reviews of the articles, four were ultimately chosen in accordance with the eligibility requirements. Numerous factors, including the study location, study design, study setting, year of publication, comparison groups, TXA dosage, and outcome variables, were taken into consideration when characterizing the studies. The general features and data of all the included studies are described in Table 1.

In the selected studies, all were conducted in India except for one and all were randomised controlled trials. One of the most distinguishing feature of the selected studies is that one study (Anand S et al; 2020) had administration of TXA through topical method and others had intravenously administrated. This is the main reason for the heterogeneity in the review. All the studies had similar sample size except one study conducted in 2016 had 240 participants (Atul P Kulkarni et al). Age and gender distribution were similar in all the studies however in the study conducted by Anand S, the mean age of TXA group was 58.2±11.48 and the control group was 60.71±12.27.

Another most salient distinguishing feature of the selected studies is, there was only one study which has 2 intervention group of different doses of TXA and one control group which only received normal saline (Mittapalli J Babu et al). In the other hand, all the other studies had one intervention group which received TXA and one control group which received either nothing or a normal saline as a placebo drug.

The dosage of intravenous TXA was 10 -15mg/kg in two studies and in two studies it was 20 mg/kg. In the study done by Atul P Kulkarni et al, 2016, it was revealed that even when there was a significant difference between control and TXA (10mg/kg) group post 24 hours, there was no significant difference in need for blood tranfusion. But contrastingly in the study done by Mittapalli J Babu et al, control group and 10 mg/kg TXA had significant difference in blood loss. The study also revealed that 10mg/kg and 15 mg/kg doses did not have significant differences so they concluded that 10mg/kg TXA is an effective way to reduce blood loss and blodd transfusion during the head and neck surgeries. On the other hand, Anand S et al; 2020 proved that 20 ml of 25 mg/ml TXA also produced similar results when applied topically.

The main concern of TXA was if it caused any post operative complications. Mittipalli J Babu et and Arjun Das et al studies did not mention about any post operative complications. But the other two studies had an extensive report on it.

In the study Atul P Kulkarni et al, In each group, two patients had necrosis of the skin flap, and three each had more than 50% necrosis of the reconstruction flap. On the day of surgery, one patient (placebo group) required a second examination of the wound to check for bleeding. Three patients in the placebo group and two patients in the TA group both experienced a similar incidence of oro-cutaneous fistula. In neither group did thromboembolic complications arise. The author concluded that none of the complications was significantly higher in TXA group.

Similarly, in the study done by Anand S et al, post operative infection, flap necrosis, secondary procedure incidence was higher in standard closure group than the TXA group but again it was not statistically significant.

The quality assessment of the studies were summarised in figure 2. Study conducted by Mittapalli J Babu et al and Alipour et al had the low overall risk and the other studies had moderate overall risk. Table 2 explains the characteristics of the excluded studies that was eliminated during the search process.

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Table 1: Data extraction table with baseline characteristics of the included studies

Study	Country	Study design	Sample size	Intervention groups	Comparison group	Age (Mean ± SD)	Sex (M:F)	Administration	Parameter	Outcome
Mittapalli J Babu et al, 2021 [23]	India	RCT	84	Group I - TXA 10mg/kg Group II - TXA 15mg/kg	Control group - Normal saline	Group I- 47.21 ± 9.30 Group II - 49.00 ± 9.08 Control - 44.29 ± 11.74	Group I - 24:4 Group II - 21:7 Control - 20:8	Intravenously 10minbefore surgery	Surgical time, blood loss, transfusion using colorimetric method	Median blood loss in control group was significantly higher than Group I and II. But there is no significant differences between Group I and II.
Arjun Das et al, 2015 [24]	India	RCT	80	TXA 20 mg/kg diluted to 25 cc with normal saline	Equal volume of normal saline	TXA - 43.95土 10.62 Control - 44土10.55	TXA - 32:8 Control - 33:7	Intravenously 15 min before surgery	Hemoglobin (Hb) concentration, platelet count, packed cell volume, fibrinogen level, D-dimer level were measured pre- and post-operatively	Compared to the TXA group, the Saline (C) group needed more blood, colloid, and crystalloid for blood loss. Hb% in Group C after 6 and 24 hours was significantly lower than in Group T, even after multiple transfusions.
Atul P Kulkarni et al, 2016 [25]	India	RCT	240	TXA (10 mg/kg)	Equal volume of normal saline	TXA - 51.26土 11.3 Control - 50.67土 11.68	TXA - 79:27 Control 87:23	Intravenously 15 mins after GA and 10 mins before the surgery	Perioperative (up to 24 h) blood loss, need for transfusion and fluid therapy was recorded using gravimetry	No difference in intra operative blood loss. Post-operative blood loss was significantly higher in the Control group at 24 h. But need for blood transfusion was similar in both groups.
Anand S et al; 2020 [26]	India	RCT	99	20 ml of 25 mg/ml topical TXA	Neck closure without any Antifibrinolytics	TXA - 58.2 土11.48 Control - 60.71土 12.27	TXA - 43:8 Control 33:15	Prior to the placement of the neck drains and at the end of the procedure, topical TXA was used to the	postoperative drain volume for the first five days and the day of removal of the drains.	When comparing the TXA group to the standard closure group, there was a significant reduction in blood loss. In comparison to

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Study	Country	Study design	Sample size	Interventi on groups	Comparison group	Age (Mean ± SD)	Sex (M:F)	Administration	Parameter	Outcome
								intervention group.		the standard closure group, the tranexamic acid group underwent drain removal earlier.
Alipour, et al. 2020	Iran	RCT	83	20 mg/kg of TXA	Equal volume of normal saline	TXA group 46.16±11.3, Control group - 47.85±14.1	20:63	A 20 mg/kg dose of TA, diluted to 20 cc with normal saline, was administered intravenously for five minutes, fifteen minutes prior to surgery	Based on the volume of blood collected in the Hemovac drain, BL was calculated.	Blood loss during and post-op surgery in the TXA receiving group was significantly lower than in the control group.

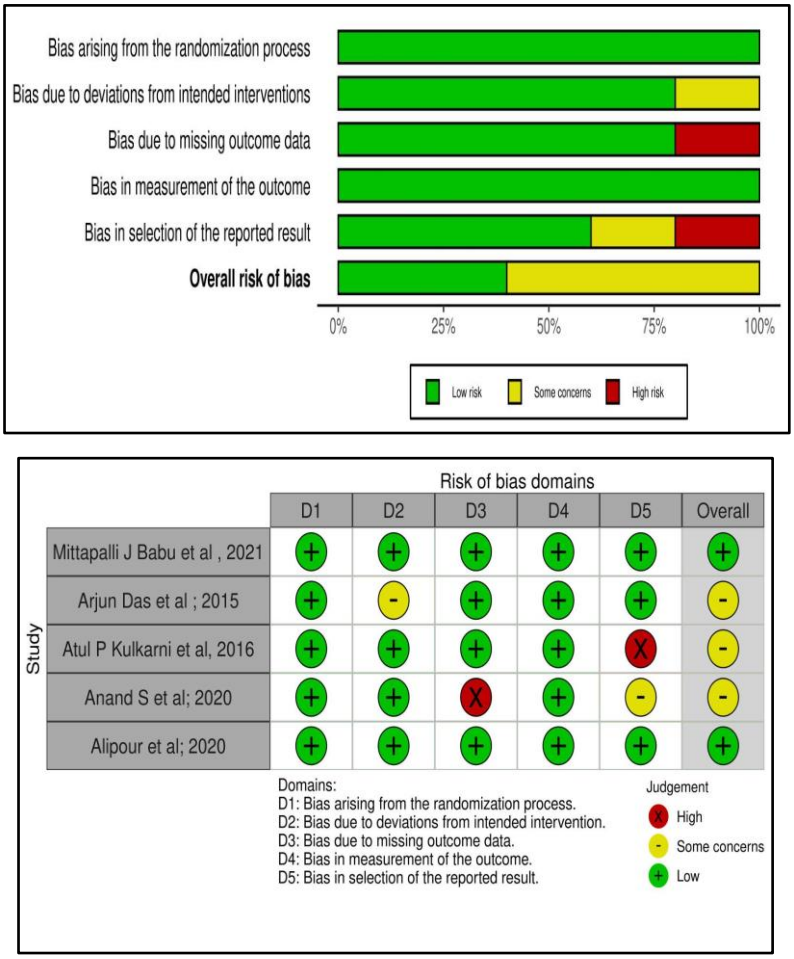

Figure 2a and 2b. Risk of bias chart - Study-by-study bias evaluation using a traffic light plot. A weighted summary plot illustrating the overall type of bias found in every study

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Table 2: Characteristics of excluded studies

S.No.	Article	Reason for exclusion
1	Chen CC, Wang CC, Wang CP, et al. Prospective, randomized, controlled trial of tranexamic acid in patients who undergo head and neck procedures. Otolaryngol Head Neck Surg 2008;138: 762–767	Study was done in head and neck surrey patients but reasons not involving malignancy
2	Wing Chan Choi et al. The Effect of Tranexamic Acid on Blood Loss During Orthognathic Surgery: A Randomized Controlled Trial. 2009; 67(1): 125-133	Study was done in patients undergoing orthognathic surgery
3	Mohammed Ali Ghavimi et al. Efficacy of tranexamic acid on side effects of rhinoplasty: A randomized double-blind study. 2017; 45(6): 897-902	Study was done in patients undergoing rhinoplasty
4	Guilherme C. Arantes et al. Effectiveness of tranexamic acid for reducing intraoperative bleeding in palatoplasties: A randomized clinical trial. 2017; 45(5):642-648	Study was done in patients undergoing palatoplasty
5	Raven Spencer. Efficacy of tranexamic acid (TXA) for post-tonsillectomy hemorrhage. 2022; 45(3): 103582	TXA was given to patients who have undergone tonsillectomy and faced hemorrhage post surgery

4. Discussion

In the present systematic review and meta-analysis, the efficacy of TXA on bleeding-related outcomes among patients undergoing H&N procedures was assessed. Four studies was included, comprising standalone RCTs and a total of 503 patients: 267 and 236 patients were allocated to the TXA and control groups, respectively. Most of the studies favoured the TXA group as an effective drug to reduce blood loss.

TXA is a synthetic antifibrinolytic agent that was brought to the clinical setting with the goal of minimizing intra- and postoperative blood loss. As a result, TXA has been used in many types of surgery more and more in recent years. A large number of high-quality studies involving RCTs and meta-analyses have since been published, proving its efficacy in lowering blood loss and, as a result, the requirement for postoperative transfusions [27]. Among these, Wu et al. conducted a meta-analysis on 34 studies in 2015 and found that, although not lowering intraoperative blood loss, the use of TXA via IV or IA significantly decreased postoperative blood loss, hemoglobin decrease, and transfusion rate following primary total knee arthroplasty [28].

Similarly, Wei and Liu examined 39 trials that year and found that TXA administration significantly lowered blood loss and the requirement for allogeneic blood transfusion. Positive outcomes have also been observed for these indications, including a noteworthy decrease in hemarthrosis and suction drainage blood volume, enhanced range of motion and quadriceps strength, and a decreased incidence of fever in the first two weeks following surgery [29].

Not only in orthopedic surgeries, Nikolaos Kathopoulis et al concluded that when administered intravenously, TXA has been shown to significantly lower intraoperative blood loss in myomectomy patients. Furthermore, in this patient group, this agent may predispose to shorter operating times [30].

In the present study, topical TXA had significantly reduced blood loss and need for blood transfusion than the placebo group. Similarly, in a meta analysis comprising of 71 trials conducted by Teoh et al, topical TXA decreased the incidence of blood transfusion without any significant side effects linked to TXA, involving 7539 patients [31]. Other than these, TXA has been used in spine surgeries [32], coronary artery

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surgeries [33], non cardiac surgeries, [34] emergency surgeries [35] and minor oral procedures [36]

TXA application is helpful for critically injured patients who are in shock and need large blood transfusions. Since TXA is a stand-alone risk factor for a thromboembolic event and D-dimers are nearly always elevated in trauma patients, patients receiving TXA treatment should be closely watched for clinical signs of thromboembolism [37].

But in a meta analysis conducted by Davide Reale et al, he concluded that no differences in terms of thromboembolic complications were detected between the TXA and control groups [38]. Also in a meta analysis, there is no evidence to support a link between TXA and any major thromboembolic or nonthromboembolic complication. This includes multiple recent studies involving topical and intravenous (IV) administration that were left out of earlier meta-analyses [39]. It is also proven to be one of the most cost effective method in surgeries [40].

The present provided thorough literature searches that incorporated pertinent randomized controlled trials. When the study with the biggest effect size was taken out to examine how local tranexamic acid affected postoperative bleeding, the results were also favorable to intervention. The moderate number of trials conducted in this study was one of its limitations, and the overall quality of the evidence might be regarded as moderate. Furthermore, even though antifibrinolytic therapy has been shown to be effective, its advantages over alternative methods of local hemostasis are not entirely clear.

5. Conclusion

The evidence summarized in this systematic review highlights the important role tranexamic acid plays in head and neck cancer surgeries. It does this by synthesizing results from four carefully conducted randomized controlled trials. There is a strong case to be made for tranexamic acid's inclusion in the perioperative management of these procedures given the majority of studies' consistent support for its ability to reduce blood loss during and after surgery.

Beyond its hemostatic effectiveness, this review reveals another important aspect: tranexamic acid's cost-effectiveness in treating blood loss during a variety of surgical procedures. When used in appropriate dosages, tranexamic acid has economic benefits that further enhance its appeal as a useful and effective tool in the larger context of surgical procedures. This cost effective feature increases the viability and practicality of incorporating tranexamic acid into standard surgical procedures.

Because tranexamic acid is both effective and affordable, it can be used as a strategic tool in the surgeon's toolbox as healthcare systems struggle to balance the demands of managing resource constraints with optimizing patient outcomes. These findings have implications not only for head and neck cancer surgeries but also for other surgical specialties, indicating a wider applicability.

It is critical to recognize the complexity of individual trials and the possibility of variation in patient characteristics and surgical methods. Future studies should keep improving our knowledge of the best dosage, patient selection standards, and long-term effects of using tranexamic acid in various surgical contexts. In conclusion, the evidence compiled in this systematic review makes a strong case for the routine inclusion of tranexamic acid in head and neck cancer surgeries, as it can both improve patient outcomes and maximize cost-effectiveness. Tranexamic acid is a cost-effective and clinically useful intervention that can be used to minimize blood loss during a wide range of surgical procedures as we work to improve surgical care.

References:

1. Moawad MHED, Shalaby MM, Sadeq MA, Al-Jafari M, A'amar JW, Alsayed O, et al. Insights into head and neck cancer research in Egypt: A scoping review. Cancer Treat Res Commun 2023; 37:100782.
2. Yen C-C, Ho C-F, Wu C-C, Tsao Y-N, Chaou C-H, Chen S-Y, et al. In-Hospital and Long-Term Outcomes in Patients with Head and Neck Cancer Bleeding. Medicina 2022;58. https://doi.org/10.3390/medicina58020177.
3. Guerado E, Medina A, Mata MI, Galvan JM, Bertrand ML. Protocols for massive blood transfusion: when and why, and potential complications. Eur J Trauma Emerg Surg 2016; 42:283–95.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(5), 721-730 | ISSN:2251-6727

4. Butcher A, Richards T. Cornerstones of patient blood management in surgery. Transfus Med 2018; 28:150–7.
5. Lee EJ, Park SJ, Kim Y, Lim H, Lee S, Yim GW, et al. Effect and safety of diluted vasopressin injection on bleeding during robot-assisted laparoscopic myomectomy: a protocol for a randomised controlled pilot trial. BMJ Open 2022; 12:e056145.
6. Forbat E, Al-Niaimi F, Ali FR. The emerging importance of tranexamic acid in dermatology. Clin Exp Dermatol 2020; 45:445–9.
7. Roberts I, Prieto-Merino D, Manno D. Mechanism of action of tranexamic acid in bleeding trauma patients: an exploratory analysis of data from the CRASH-2 trial. Crit Care 2014; 18:685.
8. Wright JD, Ananth CV, Lewin SN, Burke WM, Siddiq Z, Neugut AI, et al. Patterns of use of hemostatic agents in patients undergoing major surgery. J Surg Res 2014; 186:458–66.
9. Suter T, McRae S, Zhang Y, MacDonald PB, Woodmass JM, Mutter TC, et al. The Effect of Intravenous Tranexamic Acid On Visual Clarity in Arthroscopic Shoulder Surgery Compared to Epinephrine and a Placebo: A Double-blinded, Randomized Controlled Trial. J Shoulder Elbow Surg 2023. https://doi.org/10.1016/j.jse.2023.10.001.
10. Cai J, Ribkoff J, Olson S, Raghunathan V, Al-Samkari H, DeLoughery TG, et al. The many roles of tranexamic acid: An overview of the clinical indications for TXA in medical and surgical patients. Eur J Haematol 2020; 104:79–87.
11. Tripathi V, Rai O, Shaykh N, Patel F, Reddy P. Role of Tranexamic Acid in Palliative Control of Bleeding in End-Stage Head and Neck Cancer: A Case Report. Cureus 2023;15:e45534.
12. Jamshaid W, Jamshaid M, Coulson C, Sharma N, Muzaffar J, Nieto H. A systematic review on the efficacy of tranexamic acid in head and neck surgery. Clin Otolaryngol 2023; 48:527–39.
13. Christison-Lagay E. Complications in head and neck surgery. Semin Pediatr Surg 2016; 25:338–46.
14. Ziegler A, Carollo E, Adams W, Bier-Laning C. The total amount of fluid administered is associated with postoperative complications in head and neck cancer surgery. World J Otorhinolaryngol Head Neck Surg 2023; 9:288–94.
15. Alsubaie HM, Abu-Zaid A, Sayed SI, Pathak KA, Almayouf MA, Albarrak M, et al. Tranexamic acid in head and neck procedures: a systematic review and meta-analysis of randomized controlled trials. Eur Arch Otorhinolaryngol 2022; 279:2231–8.
16. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343:d5928.
17. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71.
18. Patole S. Principles and Practice of Systematic Reviews and Meta-Analysis. Springer Nature; 2021.
19. Haddaway NR, Page MJ, Pritchard CC, McGuinness LA. PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis. Campbell Syst Rev 2022;18:e1230.
20. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Wiley; 2008.
21. Higgins JP, Savović J, Page MJ, Elbers RG, Sterne JA. Assessing risk of bias in a randomized trial. Cochrane Handb Syst Rev Interv [Internet] 2019.
22. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997; 315:629–34.
23. Babu MJ, Neema PK, Reazaul Karim HM, Dey S, Arora R. Effect of Two Different Tranexamic Acid Doses on Blood Loss in Head and Neck Cancer Surgery: A Randomized, Double-Blind, Controlled Study. Cureus 2021;13:e20190.
24. Das A, Chattopadhyay S, Mandal D, Chhaule S, Mitra T, Mukherjee A, et al. Does the preoperative administration of tranexamic acid reduce perioperative blood loss and transfusion requirements after head neck cancer surgery? A randomized, controlled trial. Anesth Essays Res 2015; 9:384–90.
25. Kulkarni AP, Chaukar DA, Patil VP, Metgudmath RB, Hawaldar RW, Divatia JV. Does tranexamic acid reduce blood loss during head and neck cancer surgery? Indian J Anaesth 2016; 60:19–24.
26. Anand S, Singh V, Sahu PK. Evaluating the role of topical tranexamic acid in cancers of the head-and-

neck: A single-center randomized controlled trial. Cancer Research, Statistics, and Treatment 2020;3:461.
27. Bolliger D, Tanaka KA. Tranexamic acid in vascular surgery: antifibrinolytic or clot-stabilising activity. Br J Anaesth 2020; 124:4–6.
28. Wu Q, Zhang H-A, Liu S-L, Meng T, Zhou X, Wang P. Is tranexamic acid clinically effective and safe to prevent blood loss in total knee arthroplasty? A meta-analysis of 34 randomized controlled trials. Eur J Orthop Surg Traumatol 2015; 25:525–41.
29. Wei Z, Liu M. The effectiveness and safety of tranexamic acid in total hip or knee arthroplasty: a meta-analysis of 2720 cases. Transfus Med 2015; 25:151–62.
30. Kathopoulis N, Prodromidou A, Zacharakis D, Chatzipapas I, Diakosavvas M, Kypriotis K, et al. The Effect of Intravenous Tranexamic Acid on Myomectomy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. J Pers Med 2022;12. https://doi.org/10.3390/jpm12091492.
31. Teoh WY, Tan TG, Ng KT, Ong KX, Chan XL, Hung Tsan SE, et al. Prophylactic Topical Tranexamic Acid Versus Placebo in Surgical Patients: A Systematic Review and Meta-analysis∗. Ann Surg 2021; 273:676–83.
32. Cheriyan T, Maier SP 2nd, Bianco K, Slobodyanyuk K, Rattenni RN, Lafage V, et al. Efficacy of tranexamic acid on surgical bleeding in spine surgery: a meta-analysis. Spine J 2015; 15:752–61.
33. Myles PS, Smith JA, Painter T. Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery. N Engl J Med 2017; 376:1893.
34. Devereaux PJ, Marcucci M, Painter TW, Conen D, Lomivorotov V, Sessler DI, et al. Tranexamic Acid in Patients Undergoing Noncardiac Surgery. N Engl J Med 2022; 386:1986–97.
35. Perel P, Ker K, Morales Uribe CH, Roberts I. Tranexamic acid for reducing mortality in emergency and urgent surgery. Cochrane Database Syst Rev 2013;2013:CD010245.
36. Zaib A, Shaheryar M, Shakil M, Sarfraz A, Sarfraz Z, Cherrez-Ojeda I. Local Tranexamic Acid for Preventing Hemorrhage in Anticoagulated Patients Undergoing Dental and Minor Oral Procedures: A Systematic Review and Meta-Analysis. Healthcare (Basel) 2022;10. https://doi.org/10.3390/healthcare10122523.
37. Al-Jeabory M, Szarpak L, Attila K, Simpson M, Smereka A, Gasecka A, et al. Efficacy and Safety of Tranexamic Acid in Emergency Trauma: A Systematic Review and Meta-Analysis. J Clin Med Res 2021;10. https://doi.org/10.3390/jcm10051030.
38. Reale D, Andriolo L, Gursoy S, Bozkurt M, Filardo G, Zaffagnini S. Complications of Tranexamic Acid in Orthopedic Lower Limb Surgery: A Meta-Analysis of Randomized Controlled Trials. Biomed Res Int 2021; 2021:6961540.
39. Lin ZX, Woolf SK. Safety, Efficacy, and Cost-effectiveness of Tranexamic Acid in Orthopedic Surgery. Orthopedics 2016; 39:119–30.
40. Merchán-Galvis A, Posso M, Canovas E, Jordán M, Aguilera X, Martinez-Zapata MJ. Quality of life and cost-effectiveness analysis of topical tranexamic acid and fibrin glue in femur fracture surgery. BMC Musculoskelet Disord 2022; 23:827.