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Effect Of Intravenous Vs Topical Tranexamic Acid On Bleeding During Endoscopic Sinus Surgery

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ABSTRACT

Tranexamic acid functions as a hemostatic agent by impeding the degradation of fibrin, potentially offering advantages in the management of surgical bleeding. A search yielded 47 randomised controlled studies. We excluded 24 studies that did not meet our criteria. Our systematic review manuscript included 23 eligible studies. The retrieved, excluded, and included studies were all randomised controlled. 16 of 23 randomised controlled trials, most of which were double-blind controlled versus placebo trials, examined tranexamic acid administration (topical or intravenous). The combined and intravenous administration of tranexamic acid showed a difference. With moderate certainty, tranexamic acid is likely to significantly reduce surgical field bleeding score compared to placebo in 16 studies. Tranexamic acid administered intravenously, topically, locally, or in a dual-administration formulation may improve intraoperative bleeding and the operative field in nasal surgery patients. Additional studies are needed to confirm the results of this study.

Keywords: Effect size; Intravenous Versus Topical; Tranexamic Acid; Bleeding; Endoscopic Sinus Surgery; systematic review

1 INTRODUCTION

Significant bleeding may result from chronic rhinosinusitis (CRS), which is caused by the development of new blood vessels in the sinonasal mucous membrane. The nasal mucosa is supplied by the anterior cranial base artery, which is an anatomical junction of the internal and external carotid arteries. [1] Bleeding uncontrollably during and following surgery causes complications and patient illness. Bleeding may be exacerbated by tissue edoema, surgical blood vessel disruption, loss of mucous membrane homeostatic function, or withdrawal of aspirin or NSAIDs. [2]

Platelet function reduction, viral transmission, and allergic reaction can all result from blood transfusions. It has not been demonstrated that preoperative autologous or allogeneic blood donation benefits patients, and there is no consensus regarding the timing or duration of discontinuing aspirin or NSAIDs. [3] During endoscopic sinus surgery (ESS), minor tissue damage and subsequent haemorrhage are frequently observed, and significant bleeding during the procedure is a possibility; this could obstruct the surgeon's field of vision and pose a patient risk. Both intraoperative and postoperative bleeding have been linked to increased morbidity and complications during ESS, according to research. [4]

Aspiration of blood clots during endoscopic sinus surgery may increase the risk of airway obstruction; therefore, general anaesthesia should be utilised during nasal procedures. However, during surgery, general anaesthesia can decrease the resistance of small vessels and exacerbate the propensity for haemorrhaging. Undoubtedly, heightened intraoperative haemorrhaging can impede the attainment of a lucid surgical field, thereby extending the duration of the operation and augmenting the likelihood of complications including dural injury and damage to adjacent anatomical components. [5] Hematoma formation may result from postoperative bleeding; hematomas may develop a secondary infection, thereby inducing delayed bleeding. Patients who experience delayed bleeding may develop symptomatic anaemia, which would necessitate the administration of a blood transfusion. A blood transfusion for sinusitis during ESS carries a relative risk of postoperative infection of up to 2.75. [6]

In an effort to reduce endoscopic sinus surgery haemorrhage, roughly 83% of otolaryngologists pursued the development of dual pharmacotherapeutic and non-pharmacological strategies. Applying pressure to the affected area, utilising a vasoconstrictor prior to closing the lesion, and employing oxidised cellulose or gelatin foam as a local hemostatic agent are all methods for controlling bleeding. [7] In fact, the most effective methods for mitigating sinonasal bleeding are topical vasoconstrictors and hemostatic treatments such as oxidised cellulose and gel foam. However, their effectiveness is generally short-lived, and they can potentially impair cardiovascular and renal function. In order to improve visibility of the surgical field, intraoperative bleeding loss has been reduced using a variety of techniques, including controlled hypotension, preoperative steroid administration, bipolar diathermy, laser, and tranexamic acid (TXA) administration. [8] Tranexamic acid reduces intraoperative bleeding by acting as an anti-fibrinolytic agent through the inhibition of tissue plasminogen activator. It can be administered systemically or topically. [9] Recent research examining the effectiveness of tranexamic acid applied topically during endoscopic sinus surgery to treat intraoperative bleeding and other pathological conditions has produced encouraging results. [10] Notwithstanding the limited number of reported complications, TXA remains an unprofitable venture for pharmaceutical companies on account of its patent expiration and limited marketing efforts since its inception in the 1960s. [11] In addition, it has been demonstrated that high doses of intravenous tranexamic acid increase the risk of intraoperative seizure, whereas low doses may be ineffective. The utilisation of topical tranexamic acid for otolaryngologic procedures is prevalent owing to its time-efficient and dependable characteristics. [12]

However, a direct comparison between topical and intravenous administration during ESS has not been thoroughly conducted. The main objective of this systematic review study was to answer the critical question regarding the effect of intravenous administration of tranexamic acid versus localized application of tranexamic acid in mitigation bleeding risk, intensity, and duration during endoscopic sinus surgery. Of important this study was pursued to provide evidence of the effectiveness of TXA by demonstrating a decrease in surgical bleeding. We wanted to see if tranexamic acid, a medicine used to improve blood clotting, could be effective during endoscopic sinus surgery by reducing bleeding, which then potentially reduces the risk of complications. Less bleeding means that surgeons have a better view of the sinuses when they are operating.

2 METHODS

We searched for studies comparing tranexamic acid (given intravenously or directly in the nose) to a placebo or no treatment. Our focus was on adults aged ≥18. We compared and summarised the studies and rated our confidence in the evidence based on study methods and sizes. Concepts and trial designs related to intravenous, local, dual intravenous and local TXA, or placebo in functional endoscopic sinus surgery (FESS) patients were used to determine the methods, select participants, assign them to intervention and control groups, measure outcomes, and collect data.

Dosage comparison studies for tranexamic acid (TXA) may vary. This study included a few studies that compared the administration of TXA orally and intravenously. Some studies comparing TXA and its analogue Epsilon Aminocaproic Acid (EACA) were included in our analysis. A few studies comparing TXA IV to dexmedetomidine IV and nitroglycerine IV were approved. Few studies have used TXA irrigation solutions to compare irrigated normal saline with and without TXA.

We searched for and selected English-language randomised controlled trials from January 2010 to March 2024 for our systematic review manuscripting. We searched for research articles on "Effect size," "Intravenous versus topical," "tranexamic acid," "bleeding," and "endoscopic sinus surgery" in reputable indexed journals like "Medline," "SCOPUS," "Embase," "Web of Science," "Google Scholar," and "Cochrane library." We also sequentially selected generated randomised based on relevance (not date) to pre-determined researchable keywords.

However, at least two of our authors independently reviewed the titles, abstracts, and keywords of the articles of interest that could be researched. This study excluded studies that did not involve proactive intravenous TXA, TXA-soaked gauzes, or other possible TXA-related studies for intra or per-sinus endoscopic bleeding. The pledgets soaked in TXA were mostly 5% with or without 0.5% phenylephrine. Most retrievable randomised controlled studies applied pre-operative TXA-soaked gauze for 10 minutes.

We also examined the medical histories of the excluded participants, including their previous clotting disorder or coagulopathy, personal or familial history of thrombotic events like stroke or acute myocardial infarction, known hypersensitivity or negative response to tranexamic acid, renal failure, dialysis, or kidney transplant, and use of antiplatelet and/or anticoagulant medications. The retrievable studies included adults over 18 who had elective bilateral endoscopic sinus surgery.

This study excluded studies on patients with known coagulopathies, previous sino-nasal surgery (such as turbinoplasty and adenoidectomy), significant blood loss disorders, dual anticoagulant/antiplatelet medications, and pregnancy. Our study also excluded studies that included multiple reports derived from the same test data, missing or incomplete data, attempted to obtain more detailed information directly from the author, did not clearly present the results of interest as

quantifiable data, or could not identify the appropriate data. Excluded studies were removed from our study. However, if the abstract alone does not determine inclusion, we can obtain the full research text that may be relevant to this systematic review/metanalysis pre-determined standards.

In this study, specific outcomes from eligible retrievable studies were examined. However, surgical field view or quality, surgeon satisfaction, average peri and post-operative blood losses with or without averaged measured blood pressures, need for adjunctive antihypertensive medications, cumulated volume or rate of intraoperative bleeding, surgery duration, post-operative coagulation profile including thrombitic incidences, intra and post-operative complications, especially in the first 90 minutes post-anesthetic weaning, total fentanyl and esmolol consumption, recovery time, hematocrit or haemoglobin level, post-operative nausea and vomiting incidence, pain level, hemodynamics' indices, pharmacotherapeutics adverse outcomes or safety profile, overall cost, platelet function and fibrin . Sino-Nasal Outcome Test (SNOT-22) at 3-month, post-operative Modified Lund-Mackay score (MLMES) at 3 months, mean self-reported time to return to work, oxygen saturation, pressure, and D-dimer levels were recorded, Based on the variables of the eligible studies.

Surgical field view or quality was assessed using the five-point Boezaart scale. The amount of bleeding and the quality of the surgical field were evaluated at 15, 30, and 45 minutes after the surgery using Boezaart grading. Alternatively, some of the retrievable eligible studies used the Wormald grading scale or the van de Merwe grading scale to assess the intraoperative surgical field viewing. clinical profile was compared using Lund and Mackay symptom scores and radiological staging. A 10-in. visual analog scale (VAS) was used to query patients about postoperative bleeding each day for 1 week. The medical record was examined to determine the need for additional evaluations or interventions for epistaxis. The hemodynamics of interest in our study were heart rate and mean arterial pressure, or systolic blood pressure. Nevertheless, the Cochrane Risks of Bias tool was used to evaluate the potential bias in each eligible trial. In the retrievable studies comparing the administration strategies of tranexamic acid, either intravenous or localised application, with a control group, we ensure that the control group is treated with either normal saline as an ideal placebo intervention or occasionally phenylephrine 5% as a standard vasoconstrictor, rather than relying on pharmacotherapeutic hemostatic agents such as anti-fibrin agents.

3 RESULTS

3.1 DESCRIPTION OF STUDIES

3.1.1 Results of the search filtering

A total of 47 randomised controlled studies were retrieved by the search. We eliminated 24 studies that did not satisfy our predetermined inclusion criteria. We conducted 23 eligible studies for our systematic review manuscript. All of the studies that were retrieved, excluded, and included were randomised controlled studies. **Figure 1** depicted the flow chart outlining the process of shifting search results and selecting studies for inclusion.

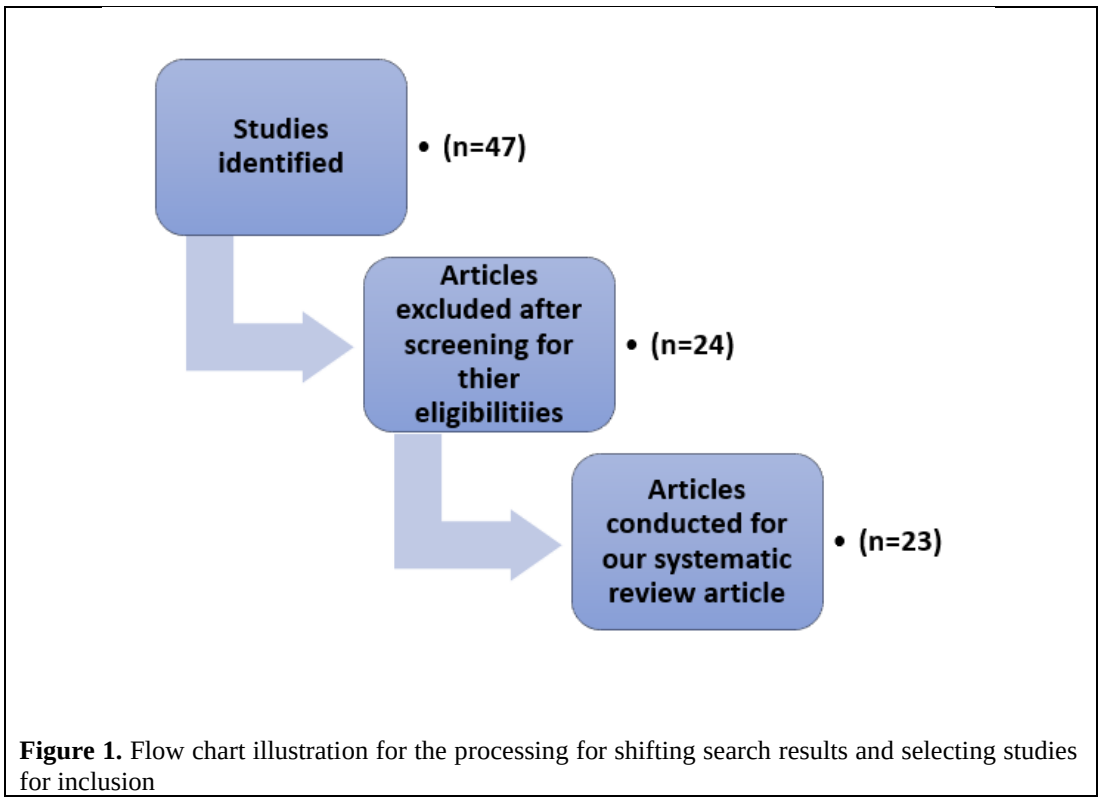

Figure 1. Flow chart illustration for the processing for shifting search results and selecting studies for inclusion

3.1.2 Included studies

Finally, we included 23 randomized controlled studies (Alimian 2011, Langille 2013, Nuhi 2015, Pannersel 2019, Sahar 2015, Beikaei 2015, Yang 2021, Padhy 2019, Khanwalkar 2023, Zaman 2019, Ahmadi 2023, Modir 2021, Abdelaziz 2024, Baradaranfar 2017, Kang 2020, Jahanshahi 2014, Achour 2023, Husain 2023, Kumar 2022, Eftekharian 2015 Jan, El-Ozairy 2021, Ratnayake Kumar 2022, and Eftekharian 2016). All of the aforementioned studies were double-blinded except 1 which was non-blinded (Langille 2013) and one was single-blinded (Ratnayake Kumar 2022).

3.1.3 Sample size, participants, and setting

The studies included in the analysis varied in sample size, ranging from 26 participants (Husain, 2023) to 177 participants (Ratnayake Kumar, 2022). Total sample size was set at 1921 participants. Every participant underwent endoscopic sinus surgery to treat chronic rhinosinusitis. All the studies included in the analysis had participants who were 18 years of age or older. The studies were conducted in single centres located in secondary or tertiary care clinics of Anesthesiology or Otorhinolaryngology departments, predominantly in Asian countries.

3.1.4 Interventions

All studies were conducted using a placebo-controlled design, with the exception of two studies. In one study by Langille (2013), the intravenous administration of TXA was compared to standard measures instead of a placebo group. In another study by Abdelaziz (2024), the intravenous administration of TXA was compared to standard measures, as well as an additional group receiving oral TXA. The majority of the studies included in the analysis consisted of two arms, while a few had three arms (Pannersel 2019, Sahar 2015, Modir 2021, Abdelaziz 2024). Only one study had four arms (El-Ozairy 2021). Both studies involving participants with 3 arms and studies involving participants with 4 arms were excluded from the analysis. The 2019 Pannersel study conducted a comparison between a higher intravenous dose of TXA, a lower intravenous dose of TXA, and a placebo saline solution. Each of the studies conducted by Sahar in 2015, Modir in 2021, and Abdelaziz in 2024 compared the intravenous administration of TXA with epsilon-aminocaproic acid, a synthetic inhibitor of the plasmin-plasminogen system. Sahar's study compared TXA IV with dexmedetomidine IV and nitroglycerine IV, while Modir's study compared TXA IV with oral TXA and standard measures. The El-Ozairy 2021 study was unique in that it encompassed four distinct groups: intravenous (IV) administration of TXA versus oral administration of TXA versus a combination of IV and oral administration of TXA, as well as a control group receiving a placebo saline solution. The Eftekharian 2016 and Ahmadi 2023 studies were excluded from our analysis eventhough they were belonged to 2 arms categories. The Eftekharian 2016 study compared oral TXA against oral placebo and the Ahmadi 2023 study compared TXA IV against dexmedetomidine IV.

Our analysis included eight studies on TXA IV (Alimian 2011, Langille 2013, Nuhi 2015, Beikaei 2015, Yang 2021, Padhy 2019, Khanwalkar 2023, and Zaman 2019) and seven studies on localised TXA (Baradaranfar 2017, Kang 2020, Jahanshahi 2014, Achour 2023, Husain 2023, Kumar 2022, Eftekharian 2015 Jan). The majority of studies on intravenous tranexamic acid (TXA) used placebo saline as the comparator, with the exception of two studies (Alimian 2011 and Langille 2013) which used sterile water and standard measures as the reference comparators. Four of the localised studies on tranexamic acid (TXA) (Baradaranfar 2017, Kang 2020, Kumar 2022, and Eftekharian 2015) employed an irrigation strategy, while three studies (Jahanshahi 2014, Achour 2023, and Husain 2023) utilised a soaked gauze strategy. The majority of studies on TXA irrigation solutions and soaked gauzes used saline irrigation as the standard comparison, with the exception of two studies (Kang 2020 and Husain 2023) which used phenylephrine 0.5% solution and Moffett/saline solutions, respectively.

Table 1 summarises the included randomised controlled studies' number, ID, interventional method, and size.

Table 1. Eligible studies characteristics

Study #	Study ID	Interventional method	Size
1	**Alimian 2011**	Double blinded, TXA IV vs Placebo sterile water	84
2	**Langille 2013**	Non-blinded, TXA IV vs Standard measures	28
3	**Nuhi 2015**	Double blinded, TXA IV vs Placebo saline	170
4	**Pannersel 2019**	Double blinded, Higher dose XA IV vs low-dose TXA IV vs Placebo saline	84
5	**Sahar 2015**	Double blinded, TXA IV vs EACA IV Placebo saline	90
6	**Beikaei 2015**	Double blinded, TXA IV vs Placebo saline	100
7	**Yang 2021**	Double blinded, TXA IV vs Placebo saline	60
8	**Padhy 2019**	Double blinded, TXA IV vs Placebo saline	30
9	**Khanwalkar 2023**	Double blinded, TXA IV vs Placebo saline	50
10	**Zaman 2019**	Double blinded, Single dose TXA IV vs placebo (normal saline)	176
11	**Ahmadi 2023**	Double blinded, TXA IV vs Dex IV	72
12	**Modir 2021**	Double blinded, TXA IV vs Dex IV vs Nitro IV	105
13	**Abdelaziz 2024**	Double blinded, TXA IV vs oral TXA vs Standard measures	159
14	**Baradaranfar 2017**	Double blinded, localized TXA irrigation vs placebo (normal saline)	60
15	**Kang 2020**	Double blinded, localized TXA 5%+ Phenylephrine 0.5% soaked gauzes vs placebo (Phenylephrine 0.5%)	60
16	**Jahanshahi 2014**	Double blinded, localized TXA 5% soaked gauzes vs placebo (normal saline)	60
17	**Achour 2023**	Double blinded, localized TXA 5% soaked gauzes vs placebo (normal saline)	74
18	**Husain 2023**	Double blinded localized TXA 5% soaked gauzes vs placebo (moffett's and normal saline solution)	26
19	**Kumar 2022**	Double blinded, Localized TXA irrigation vs placebo (normal saline)	30
20	**Eftekharian 2015 Jan**	Double blinded, Localized TXA irrigation vs placebo (normal saline)	56
21	**El-Ozairy 2021**	Double blinded, TXA IV vs localized TXA 5% irrigation solution vs dual TXA IV+localized TXA vs placebo (normal saline)	120
22	**Ratnayake Kumar 2022**	Single blinded, TXA IV + localized TXA 5% irrigation solution vs TXA IV	177

23	**Eftekharian 2016**	Double blinded, Oral TXA vs oral placebo	50

3.2 OUTCOMES

The 2011 Alimian study examined how intravenous tranexamic acid affected blood loss and surgical field quality during functional endoscopic sinus surgery. A double-blind, randomised trial was conducted on 84 consecutive adult FESS patients. IV tranexamic acid 10 mg/kg (TA group) or sterile water 0.1 mL/kg (placebo group) was given as a bolus dose after anaesthesia induction. The study found that the TA group had significantly lower blood loss (184 ± 64 mL) than the placebo group. In addition, the TA surgeon was happier with the surgical field. The study found that intravenous tranexamic acid reduces bleeding and improves FESS surgical field. [15]

Langille 2013 study examined how adjunctive intravenous tranexamic acid affected intraoperative bleeding and surgical field quality during endoscopic sinus surgery. Tranexamic acid was compared to standard blood loss-reduction measures in 28 chronic rhinosinusitis patients with or without polyposis. Tranexamic acid did not reduce estimated blood loss or improve surgical field visibility during ESS. The study included 28 patients with a median age of 45. No adverse events or complications were found in the intraoperative surgical field using the Wormald grading scale. Adjunctive intravenous tranexamic acid does not reduce blood loss or improve surgical field visibility during ESS. [17]

Nuhi 2015 examined the effects of intravenous tranexamic acid (TA) on haemorrhage in elective endoscopic sinus surgery patients. The study comprised 170 patients (90 male, 80 female) with a mean age of 30.54±4.14 years. The TA group had significantly less bleeding than the placebo group. The TA group had no significant difference in pre- and postoperative hematocrit or haemoglobin. We found no significant difference in postoperative hematocrit and haemoglobin between TA and control groups. Vomiting and nausea were higher in the control group, but not significantly. No significant coagulation changes were seen in TA. The study found that TA reduced haemorrhage without increasing side effects like coagulation changes, hemodynamic changes, vomiting, and nausea. ESS blood loss can be reduced without antihypertensive drugs with TA. [19]

Beikaei 2015 examined whether intravenous tranexamic acid (TA) reduces intraoperative bleeding during elective open rhinoplasty. Imam Khomeini Hospital, affiliated with Ahvaz Jundishapur University of Medical Sciences, conducted a single-center double-blind randomised controlled trial The study randomly assigned 100 elective rhinoplasty candidates to a treatment arm receiving a bolus 10mg/kg dose of TA and a placebo group receiving normal saline. The same surgical team performed open rhinoplasty under general anaesthesia on all subjects using standard technique. Estimated intraoperative bleeding volume was the main outcome. After controlling for age, gender, weight, and surgery duration, TA reduced intraoperative bleeding by 15.6 mL. A single bolus dose of TA (10mg/kg) upon anaesthesia induction provides adequate hemostasis in healthy open rhinoplasty candidates, according to the study. [25]

The Yang 2021 study examined how tranexamic acid (TXA) affects endoscopic sinus surgery (ESS) for high-grade rhinosinusitis surgical visualisation. 60 high-grade chronic rhinosinusitis patients were divided into control (Group C) and TXA (Group T) groups. Participants in Group T received intravenous TXA, while Group C received normal saline. Total blood loss, whole blood coagulation, and fibrinolysis were assessed, as was the Boezaart score. BS scores differed significantly between Group T and Group C. During surgery, platelet function and fibrin degradation time increased. Complications were similar between groups. The study found that a 15 mg/kg intravenous TXA bolus before surgery improves ESS visualisation for high-grade chronic rhinosinusitis without side effects. [26]

Tranexamic acid was tested for its ability to reduce intraoperative bleeding during endoscopic sinus surgery (ESS) in Padhy 2019. 30 patients were enrolled and compared using Lund and Mackay symptom score and radiological staging. A blinded surgeon and Boezaart and van de Merwe grading scale assessed the intraoperative surgical field. Tranexamic acid reduced blood loss, with a statistically significant difference in surgical field grading. The surgical field was more important in surgery completion and success. Patients taking tranexamic acid had 80% grade 2 scale scores, compared to 26.7% without the drug. Tranexamic acid can cause nausea, vomiting, and arterial or venous thrombosis, but none of the study patients experienced any side effects. Hospital stay after surgery was uneventful. Conclusion, intravenous tranexamic acid significantly reduced intraoperative bleeding and improved the operative field. [27]

Khanwalkar 2023 examined the clinical efficacy of Tranexamic acid (TXA) to reduce postoperative bleeding after endoscopic sinus or nasal surgery. April to November 2021 saw the randomised, double-blind placebo-controlled trial. Patients were randomised to receive 1 g TXA or saline intraoperatively before extubation. Patients were asked about postoperative bleeding daily for a week using a 10-inch VAS. We reviewed the medical record to determine if epistaxis needed further evaluation or treatment. Forty patients finished the study. The TXA group had a similar mean ± SD postoperative bleeding VAS to the saline group on the day of surgery. No significant differences were found between treatment arms on any postoperative day through day 7 or in VAS reduction compared to surgery baseline. Additional interventions did not differ significantly. In conclusion, TXA reduces intraoperative bleeding during sinonasal surgery, but not when postoperative bleeding is already low. [28]

A single dose of intravenous Tranexamic acid (TXA) is tested for septoplasty-related nasal bleeding by Zaman 2019. In the study, 176 patients aged 18–55 underwent septoplasty for symptomatic deviated nasal septum. One shot of intravenous TXA 10 mg/kg was given to 88 patients, while 88 received normal saline. Nasal bleeding was monitored for two weeks

after surgery. Patients receiving TXA had significantly less postoperative nasal bleeding than controls. In the placebo group, bleeding was more extensive. Seven control group patients needed nasal packing to stop bleeding, compared to one TXA patient. TXA side effects were mild and manageable. In conclusion, a single intravenous dose of TXA prevents postoperative nasal bleeding after septoplasty without nasal packing, intranasal splint, or trans-septal suturing. [31]
Baradaranfar 2017 examined how topical tranexamic acid reduced intraoperative bleeding in functional endoscopic sinus surgery. FESS was performed on 60 chronic rhinosinusitis with polyposis patients. Patients received tranexamic or saline. Regular saline or tranexamic acid was used for irrigation and suctioning during surgery. Field of view and intraoperative blood loss were recorded by surgeons. The tranexamic group lost 254.13 mL, while the saline group lost 235.6 mL. No significant differences were found in surgical field quality, surgeon satisfaction, or surgery duration. The study found that washing the nasal mucosa with tranexamic acid during FESS did not reduce blood loss or improve surgical field of view. More studies with larger samples and higher drug concentrations are advised. [13]
Kang 2020 examined how tranexamic acid (TXA) affected bleeding and surgical field improvement during functional endoscopic sinus surgery (FESS) in chronic sinusitis patients. From April to November 2013, 60 patients at Hamadan's Beasat Hospital participated in the trial. Thirty intervention patients received three pledgets soaked in TXA 5% and phenylephrine 0.5% for 10 minutes before surgery, while thirty control patients received 0.5%. Boezaart grading assessed bleeding and surgical field quality at 15, 30, and 45 minutes after surgery. The intervention group had significantly better surgical field quality in the first and second quarters but not the third. Significantly less bleeding occurred in the intervention group. [16]
Tranexamic acid (TXA) was tested for its effects on bleeding and surgical field improvement during functional endoscopic sinus surgery (FESS) in chronic sinusitis patients by Jahanshahi in 2014. From April to November 2013, 60 patients at Hamadan's Beasat Hospital participated in the trial. Thirty intervention patients received three pledgets soaked in TXA 5% and phenylephrine 0.5% for 10 minutes before surgery, while thirty control patients received 0.5%. Boezaart grading assessed surgical field quality at 15, 30, and 45 minutes after surgery. The intervention group had significantly better surgical field quality in the first and second quarters but not the third. Significantly less bleeding occurred in the intervention group. The study found that topical TXA reduces bleeding and improves surgical fields in FESS rhinosinusitis patients. [18]

Achour 2023 examined how topical tranexamic acid (TA) affected bleeding and surgical quality in functional endoscopic sinus surgery (FESS) for chronic rhinosinusitis. 74 patients were divided into TA (37 patients) and placebo (37 patients). TA had a significant effect over placebo in the first grade of the Boezaart scale at 35 minutes, but not in higher grades. There was 359 ml of blood loss in the TA group and 441 in the placebo group. Serious side effects or blood parameters were not observed. Despite its safety and low cost, TA had little effect on surgical field quality after 35 minutes of FESS in chronic rhinosinusitis patients. [24]

The Husain 2023 study examined whether topical tranexamic acid (TXA) reduced intraoperative and postoperative bleeding in functional endoscopic sinus surgery (FESS) for chronic rhinosinusitis with nasal polyposis (CRSwNP). In the trial, 26 patients received FESS for failed medical treatment. Ribbon gauze soaked in 500 mg/5 ml TXA was used in the intervention nostril, while Moffett's solution was used in the control nostril. In the first 30 minutes after surgery, intraoperative bleeding was recorded and the mean score calculated. The intervention nostril was packed with Merocel® soaked in 500 mg/5 ml TXA after surgery, while the control nostril was packed in normal saline. Intraoperative bleeding was similar for intervention and control nostrils. However, the intervention nostril significantly reduced postoperative bleeding compared to saline. TXA nasal packing reduced intraoperative and immediate postoperative bleeding, making it a safe, effective, and cost-effective alternative to Moffett's solution during FESS and normal saline post-surgery. [29]
Kumar 2022 examined how topical tranexamic acid (TXA) affected endoscopic sinus surgery (ESS) recovery in 30 patients. The study revealed that TXA reduced SNOT-22 and MLMES scores at 3 months, while NS had a mean bleeding score of 3.64 ± 2.76. Participants reported a mean return to work time of 4.67 ± 2.22 days for TXA and 6.87 ± 4.42 days for NS. No confirmed thromboembolism occurred. The findings indicate that a larger study on topical TXA after ESS may require a different formulation and increased exposure. [30]

Tranexamic acid (TXA) irrigation was tested for its effect on orthognathic surgery perioperative haemorrhage by Eftekharian in 2015. The study included 56 patients divided into two groups: one receiving TXA irrigation with normal saline and the other using it. Study variables included age, gender, operation duration, irrigation solution, preoperative haemoglobin, hematocrit, and weight. The two groups had similar variable distributions, except for operation duration. TXA reduced intraoperative blood loss. [35]

Table 2-5 summarised all eligible randomised controlled studies' IDs and aims, Methods, results, conclusion, and references based on the interventional hemostatic agent of investigation (TXA) were administered intravenously or applied locally.

Table 2. Summary of studies including intravenous tranexamic acid (TXA IV)

Study ID	Aim	Methods	Results	Conclusion	Ref
Double-blind RCT, TXA IV vs placebo (sterile water) on 84 patients					
Alimian 2011	The study aimed to assess the impact of intravenous tranexamic acid on blood loss and surgical field quality during functional endoscopic sinus surgery (FESS).	A randomized, double-blind, controlled trial was conducted on 84 consecutive adult patients undergoing FESS. Patients were randomized to receive either IV tranexamic acid 10 mg/kg (TA group) or sterile water 0.1 mL/kg (placebo group) as a bolus dose immediately after induction of anesthesia.	The results showed that the TA group experienced an average blood loss of 184 ± 64 mL, significantly lower than the placebo group. Additionally, the surgeon was more satisfied with the surgical field in the TA group.	The study concluded that intravenous tranexamic acid effectively reduces bleeding and improves the surgical field during FESS.	**15**
Single-blind RCT, TXA IV vs standard measures on 28 patients					
Langille 2013	A study aimed to evaluate the impact of adjunctive intravenous tranexamic acid on intraoperative bleeding and the surgical field quality during endoscopic sinus surgery (ESS).	The study included 28 patients with chronic rhinosinusitis with or without polyposis, and the use of tranexamic acid was compared to standard measures to minimize blood loss. The study included 28 patients, with a median age of 45 years. The Wormald grading scale was used to assess the intraoperative surgical field,	The results showed that the use of tranexamic acid did not significantly decrease estimated blood loss or improve visualization of the surgical field during ESS and the study found no adverse events or complications	The conclusion is that adjunctive intravenous tranexamic acid does not seem to result in a clinically meaningful reduction in blood loss or improve the visualization of the surgical field during ESS.	17
Double-blind RCT, TXA IV vs placebo (normal saline) on 170 patients					
Nuhi 2015	The study evaluated the efficacy of intravenous tranexamic acid (TA) on hemorrhage in patients undergoing elective endoscopic sinus surgery (ESS).	The study involved 170 patients, with 90 male and 80 female, and a mean age of 30.54±4.14 years.	The results showed a significantly lower bleeding volume in the TA group compared to the placebo group. There was no significant difference between pre- and postoperative hematocrit or hemoglobin levels in the TA group. The difference between the TA and control groups regarding postoperative hematocrit and hemoglobin levels was not significant. The control group experienced greater vomiting and nausea, but the difference was not significant. There were no significant coagulation alterations in the TA group.	The study concluded that TA significantly decreased hemorrhage without increasing side effects such as alteration in coagulation parameters, hemodynamic changes, and vomiting and nausea. The use of TA can avoid the need for antihypertensive agents to reduce blood loss in ESS.	19
Double-blind RCT, higher-dose TXA IV vs lower-dose TXA IV vs placebo (normal saline) on 84 patients					
Pannersel 2019	The study aimed to compare two different intravenous doses of tranexamic acid with a placebo on surgical field quality, surgical time, and blood loss in Functional Endoscopic Sinus Surgeries (FESS) surgeries.	The study involved 84 patients aged 18-60 years who underwent FESS surgery. Patients were randomly assigned to Group A receiving 15 mg.kg-1 tranexamic acid, Group B receiving 5 mg.kg-1 tranexamic acid, and Group C as a placebo receiving normal saline. The primary outcome was surgical field quality, while the secondary outcome was blood loss and surgical time.	The results showed that intravenous administration of tranexamic acid reduced total blood loss in FESS surgery do by 64% in group A (15 mg.kg-1) and 31% in group B (5 mg.kg-1) compared to the placebo. The reduction in bleeding also led to improved surgical field quality. The surgical field improvement by using tranexamic acid also resulted in a prominent reduction in the total time taken to complete the surgery.	In conclusion, tranexamic acid 15 mg/kg dose effectively reduces blood loss, improves surgical field quality, and reduces surgical time in FESS surgeries.	20

			Administration of 5 mg.kg-1 drug led to a 7% reduction, and 15 mg.kg-1 led to about 15% reduction in time taken for FESS surgery.		
Double-blind RCT, TXA IV vs EACA IV vs placebo (normal saline) on 90 patients					
Sahar 2015	This study aimed to evaluate the efficacy of tranexamic acid and Epsilon Aminocaproic Acid (EACA) in reducing mucosal bleeding during FESS for chronic sinusitis.	A total of 90 patients aged 18 to 50 years were enrolled in the study, which involved three equal groups: TXA group, EACA group, and control group. The study recorded the duration of surgery, volume of blood loss, pre and postoperative hemoglobin, MAP and HR, surgical field quality, surgeon satisfaction, and side effects.	The results showed that TXA and EACA groups had significantly less surgery duration, volume of blood loss, and postoperative hemoglobin compared to the control group. Both groups had comparable improved quality of the surgical field, with most patients classified as grade 1 and 2 according to the Boezaart scale. Surgeon satisfaction was significantly higher in TXA and EACA groups compared to the control group. No significant difference in side effects was found between all groups.	In conclusion, intravenous tranexamic acid and Epsilon Aminocaproic Acid effectively reduce bleeding during FESS and improve visualization of the surgical field, increasing surgeon satisfaction without significant differences between the two drugs.	23
Double-blind RCT, TXA IV vs placebo (normal saline) on 100 patients					
Beikaei 2015	This study aimed to evaluate the role of intravenous tranexamic acid (TA) in reducing intraoperative bleeding during elective open rhinoplasty.	A single-center double blind randomized controlled trial was conducted at Imam Khomeini Hospital, affiliated to Ahvaz Jundishapur University of Medical Sciences. The study involved 100 elective rhinoplasty candidates, who were randomly assigned to one treatment arm receiving a bolus 10mg/kg dose of TA and one control group receiving normal saline as a placebo. All subjects underwent open rhinoplasty under general anesthesia with the same surgical team using standard technique. The primary outcome measure was the estimated volume of intraoperative bleeding.	After controlling for age, gender, weight, and surgery duration, TA was associated with a 15.6 mL decrease in intraoperative bleeding.	The study recommends a single bolus dose of TA (10mg/kg) upon anesthesia induction for satisfactory hemostasis in healthy candidates of open rhinoplasty.	25
Double-blind RCT, TXA IV vs placebo (normal saline) on 60 patients					
Yang 2021	This study aimed to evaluate the effect of tranexamic acid (TXA) on the surgical visualization of endoscopic sinus surgery (ESS) for high-grade rhinosinusitis.	60 patients with high-grade chronic rhinosinusitis were divided into two groups: the control group (Group C) and the TXA group (Group T). Patients in Group T received intravenous TXA, while those in Group C received normal saline. The Boezaart grading scale (BS) score was assessed, and total blood loss, whole blood coagulation, and fibrinolysis were assessed.	The results showed a significant difference in the BS score between Group T and Group C. Increases in platelet function and fibrin degradation time were also observed during the operation. No difference in complications was found between the two groups.	The study concluded that a 15 mg/kg bolus of intravenous TXA before surgery can improve the surgical visualization of ESS for high-grade chronic rhinosinusitis without significant adverse effects.	26

Double-blind RCT, TXA IV vs placebo (normal saline) on 30 patients					
Padhy 2019	The study aimed to evaluate the efficacy of tranexamic acid in reducing intraoperative bleeding during endoscopic sinus surgery (ESS).	30 patients were enrolled, and the clinical profile was compared using Lund and Mackay symptom score and radiological staging. The surgical field was assessed by a blinded surgeon, and the intraoperative surgical field was assessed using Boezaart and van de Merwe grading scale.	Results showed that the arm receiving tranexamic acid experienced less blood loss, with a statistically significant difference in the surgical field grading scale. The surgical field was a more important factor in determining the completion and satisfactory outcomes of the surgery. 80% of patients who received tranexamic acid had a grade 2 scale score compared to 26.7% in patients not receiving the drug. Side effects of tranexamic acid included nausea, vomiting, and possibly arterial or venous thrombosis, but none of the patients in the study experienced any side effects. Post-operative stay in the hospital was uneventful.	In conclusion, intravenous tranexamic acid significantly reduced intraoperative bleeding and improved the operative field.	27
Double-blind RCT, TXA IV vs placebo (normal saline) on 50 patients					
Khanwalkar 2023	This study evaluated the clinical efficacy of Tranexamic acid (TXA) when given at the end of endoscopic sinus or nasal surgery to reduce postoperative bleeding.	The randomized, double-blind placebo-controlled trial was conducted from April to November 2021. Patients were randomized to receive an intravenous dose of 1 g TXA or saline intraoperatively prior to extubation. A 10-in. visual analog scale (VAS) was used to query patients about postoperative bleeding each day for 1 week. The medical record was examined to determine the need for additional evaluations or interventions for epistaxis.	Forty patients completed the study. The mean ± SD postoperative bleeding VAS for the TXA group on the day of surgery was not significantly different from the saline group. There were no significant differences between treatment arms on any postoperative day through day 7 or in the reduction in VAS compared to the respective baseline on the day of surgery. There were no significant differences in terms of additional interventions.	In conclusion, TXA has demonstrated efficacy to reduce intraoperative bleeding during sinonasal surgery, but it does not significantly reduce it further when postoperative bleeding is already minimal at baseline.	28
Double-blind RCT, Single dose TXA IV vs placebo (normal saline) on 176 patients					
Zaman 2019	This study investigates the effect of a single dose of intravenous Tranexamic acid (TXA) on postoperative nasal bleeding associated with septoplasty.	The study involved 176 patients aged 18-55 years who underwent septoplasty for symptomatic deviated nasal septum. The patients were divided into two groups: 88 patients were given normal saline and 88 were given a single shot of intravenous TXA 10 mg/kg. Nasal bleeding was monitored after surgery and up to two weeks postoperatively.	Results showed that patients receiving TXA showed significantly less postoperative nasal bleeding compared to controls. Extensive bleeding was also higher in the placebo group. Seven patients required nasal packing in the control group to stop bleeding compared to one patient in the TXA group. Adverse reactions to TXA were minimal and easily managed conservatively.	In conclusion, a single intravenous dose of TXA is shown to be effective and safe in preventing postoperative nasal bleeding after septoplasty, avoiding additional techniques such as nasal packing, intranasal splint, or trans-septal suturing during surgery.	31
Double-blind RCT, TXA IV vs Dexmedetomidine IV on 72 patients					

Ahmadi 2023	This study compared the effect of tranexamic acid and dexmedetomidine on the rate of bleeding during endoscopic sinus surgery (ESS).	72 patients with chronic rhinosinusitis were randomly assigned to two groups: group A received dexmedetomidine at a dose of 1µg/kg, and group B received tranexamic acid at a dose of 10mg/kg immediately after induction of anesthesia intravenously within 15 minutes. The two groups were evaluated and compared regarding the quality of the surgery field, volume of intraoperative bleeding, hemodynamic changes, and complications up to 90 minutes after the surgery.	The results showed that group A had a significantly higher mean volume of intraoperative bleeding than group B. The quality of the surgical field in group B was better than group A at 15, 30, and 60 minutes, but no significant difference was found at 90 minutes. The mean arterial pressure in group A was higher at 15 minutes, lower at 60 and 90 minutes, and no significant difference was found between the average surgery time and the frequency of complications.		32
Double-blind RCT, TXA IV vs Dexmedetomidine IV vs Nitroglycerine IV on 105 patients					
Modir 2021	A blinded clinical trial compared the efficacy and safety of tranexamic acid, dexmedetomidine, and nitroglycerin in preventing intraoperative bleeding and improving surgical field quality during septorhinoplasty under general anesthesia.	A blinded clinical trial compared the efficacy and safety of tranexamic acid, dexmedetomidine, and nitroglycerin in preventing intraoperative bleeding and improving surgical field quality during septorhinoplasty under general anesthesia. 105 patients were divided into three groups: dexmedetomidine, tranexamic acid, and nitroglycerin.	Results showed no significant differences in oxygen saturation, pressure, heart rate, bleeding rate, duration of surgery, or surgeon satisfaction.	However, dexmedetomidine reduced propofol dose and increased extubation and recovery time. All three drugs reduced intraoperative bleeding and improved surgical field quality, but the decision lies with the anesthesiologist's judgment and patient conditions.	34
Double-blind RCT, TXA IV vs oral TXA vs Standard measures on 159 patients					
Abdelaziz 2024	The study aimed to compare the effectiveness of oral versus intravenous Tranexamic acid (TXA) on surgical field bleeding in functional endoscopic sinus surgery (FESS).	159 participants were divided into three groups: Group O received 2gm of TXA orally 2 hours before surgery, Group I received 15mg/kg of IV TXA slowly after induction of anesthesia, and Group C did not receive any. Intraoperative surgical field bleeding was assessed using the Wormald grading scale and surgeon satisfaction. Post-operatively, the incidence of nasal bleeding, PONV, and D-dimer level were recorded.	Results showed significantly higher surgical field score, duration of surgery, recovery time, and postoperative D-dimer in group-C, while surgeon satisfaction was significantly lower in group-C. No differences were found regarding hemodynamic parameters, postoperative bleeding, pain, and PONV.	The study concluded that oral TXA was safe, cheap, and as effective as IV TXA in terms of surgical field visualization, surgeon satisfaction, and operative time during FESS, with limited adverse effects and no evidence of thromboembolic complications.	21
The primary focus of our systematic review's/metanalysis's search strategy and study selection was on randomised controlled trials published in English since Jan 2010 up to Mar 2024. We utilised specific and searchable terms, including "Effect size", "Intravenous versus topical", "tranexamic acid", "Bleeding", and "Endoscopic sinus surgery", to gather research articles from reputable indexed journals such as "Medline," "SCOPUS," "Embase," "Web of Science," "Google Scholar," and "Cochrane library.". Additionally, we sequentially selected the generated randomised based on their relevance (not on their corresponding dates) to the pre-determined researchable key-words.					

Table 3. Summary of studies including localized tranexamic acid (TXA) application

Study ID	Aim	Methods	Results	Conclusion	Ref
Double-blind RCT, localized TXA irrigation vs placebo (normal saline) on 60 patients					
Baradaranfar 2017	This study investigated the effectiveness of topical tranexamic acid in reducing intraoperative bleeding during functional endoscopic sinus surgery (FESS).	The study involved 60 patients with chronic rhinosinusitis with polyposis who underwent FES. Patients were divided into two groups: tranexamic or saline treatment. During surgery, normal saline or tranexamic acid was used for irrigation and suctioning. The surgeons'	The results showed that the tranexamic group had a mean blood loss of 254.13 mL, while the saline group had a mean blood loss of 235.6 mL. No significant differences were found in other variables, such as surgical field quality, surgeon satisfaction, or surgery duration.	The study concluded that using tranexamic acid through washing the nasal mucosa during FESS did not significantly reduce blood loss or improve the surgical field of view. Further studies with larger sample sizes and higher drug	**13**

		assessment of field of view and intraoperative blood loss were recorded.		concentrations are recommended.	
Double-blind RCT, localized TXA 5%+ Phenylephrine 0.5% soaked gauzes vs placebo (Phenylephrine 0.5%) on 60 patients					
Kang 2020	The study aimed to investigate the effect of tranexamic acid (TXA) on bleeding and surgical field improvement during functional endoscopic sinus surgery (FESS) in patients with chronic sinusitis.	The trial involved 60 patients at Beasat Hospital in Hamadan, Iran, from April to November 2013. Thirty patients in the intervention group received three pledgets soaked with TXA 5% and phenylephrine 0.5% for 10 minutes before surgery, while thirty patients in the control group received phenylephrine 0.5%. The amount of bleeding and the quality of the surgical field were evaluated at 15, 30, and 45 minutes after the surgery using Boezaart grading.	Results showed that the intervention group had significantly better surgical field quality in the first and second quarters, but not in the third quarter. Additionally, the amount of bleeding was significantly less in the intervention group.		16
Double-blind RCT, localized TXA 5% soaked gauzes vs placebo (normal saline) on 60 patients					
Jahanshahi 2014	The study aimed to investigate the impact of tranexamic acid (TXA) on bleeding and surgical field improvement during functional endoscopic sinus surgery (FESS) in patients with chronic sinusitis.	The trial involved 60 patients at Beasat Hospital in Hamadan, Iran, from April to November 2013. Thirty patients in the intervention group received three pledgets soaked with TXA 5% for 10 minutes before surgery, while thirty patients in the control group received normal saline. The quality of the surgical field was evaluated at 15, 30, and 45 minutes after surgery using Boezaart grading.	Results showed that the intervention group had significantly better surgical field quality in the first and second quarters, but not in the third quarter. Additionally, the amount of bleeding was significantly less in the intervention group.	The study concluded that topical TXA can effectively reduce bleeding and improve the surgical field in FESS patients with rhinosinusitis.	18
Double-blind RCT, localized TXA 5% soaked gauzes vs placebo (normal saline) on 74 patients					
Achour 2023	The study aimed to assess the impact of topical tranexamic acid (TA) on bleeding and surgical quality in functional endoscopic sinus surgery (FESS) in patients with chronic rhinosinusitis.	74 patients were divided into two groups: TA group (37 patients) and placebo (37 patients). The results showed a significant effect for the TA group compared to the placebo group in the first grade of the Boezaart scale at 35 minutes, but not for higher grades.	Blood loss was 359 ml in the TA group versus 441 ml in the placebo group. No significant changes were observed in blood parameters or side effects.	The study concluded that despite TA's safety and low cost, it had limited effect on the surgical field quality after 35 minutes of FESS in patients with chronic rhinosinusitis.	24
Double-blind RCT, localized TXA 5% soaked gauzes vs placebo (moffett's and normal saline solution) on 26 patients					

usain 2023	The study evaluated the effectiveness of topical tranexamic acid (TXA) in reducing intraoperative and postoperative bleeding during functional endoscopic sinus surgery (FESS) for patients with chronic rhinosinusitis with nasal polyposis (CRSwNP).	The trial involved 26 patients who underwent FESS for failed medical therapy. The intervention nostril was packed with ribbon gauze soaked in 500 mg/5 ml TXA, while the control nostril was packed with ribbon gauze soaked in Moffett's solution. Intraoperative bleeding was recorded in the initial 30 minutes after surgery, and the mean score was calculated. At the end of the surgery, the intervention nostril was packed with Merocel® soaked in 500 mg/5 ml TXA, and the control nostril was packed with Merocel® soaked in normal saline.	The results showed no significant difference in intraoperative bleeding between the intervention and control nostrils. However, the intervention nostril significantly reduced postoperative bleeding compared to the control nostril saline.	The study concluded that TXA nasal packing reduced intraoperative and immediate postoperative bleeding, making it a safe, efficacious, and cost-effective alternative to Moffett's solution during FESS and normal saline post-surgery.	29
Double-blind RCT, localized TXA 5% irrigation solution vs placebo (normal saline) on 30 patients					
Kumar 2022	A pilot study examining the effects of topical tranexamic acid (TXA) on recovery after endoscopic sinus surgery (ESS) was conducted in 30 patients.		The study found that TXA had a mean reduction in the SNOT-22 score and Modified Lund-Mackay Post-operative Endoscopic (MLMES) score at 3 months, while NS had a mean bleeding score of 3.64 ± 2.76. The mean self-reported time to return to work for TXA was 4.67 ± 2.22 days, while NS had 6.87 ± 4.42 days. No cases of confirmed thromboembolism were observed.	The results suggest that a larger study is needed to further assess the effects of topical TXA following ESS and may involve increasing exposure to TXA via a different formulation.	30
Double-blind RCT, localized TXA 5% irrigation solution vs placebo (normal saline) on 56 patients					
Eftekharian 2015 Jan	This study aimed to evaluate the impact of tranexamic acid (TXA) irrigation on perioperative hemorrhage during orthognathic surgery.	The study involved 56 patients divided into two groups, with the first group receiving TXA irrigation with normal saline and the second group using normal saline. Variables such as age, gender, operation duration, irrigation solution, and preoperative hemoglobin, hematocrit, and weight were studied.	Results showed no significant difference in the distribution of variables between the two groups, except for the duration of the operation.	TXA was found to be effective in reducing intraoperative blood loss.	35
The primary focus of our systematic review's/metanalysis's search strategy and study selection was on randomised controlled trials published in English since Jan 2010 up to Mar 2024. We utilised specific and searchable terms, including "Effect size", "Intravenous versus topical", "tranexamic acid", "Bleeding", and "Endoscopic sinus surgery", to gather research articles from reputable indexed journals such as "Medline," "SCOPUS," "Embase," "Web of Science," "Google Scholar," and "Cochrane library.". Additionally, we sequentially selected the generated randomised based on their relevance (not on their corresponding dates) to the pre-determined researchable key-words.					

Table 4. Summary of studies including intravenous tranexamic acid (TXA IV) and localized tranexamic acid (TXA) application

Study ID	Aim	Methods	Results	Conclusion	Ref
Double-blind RCT, TXA IV vs localized TXA 5% irrigation solution vs dual TXA IV + localized TXA vs placebo (normal saline) on 120 patients					
El-Ozairy 2021	This study aimed to evaluate the effectiveness of local, intravenous, and combined use of tranexamic acid (TA) in improving surgical field quality during functional endoscopic sinus surgery (FESS).	A randomized controlled double-blind prospective trial was conducted on 120 patients scheduled for elective FESS. Patients were randomly assigned to one of four groups: IV TA, local TA, both IV and local TA, and placebo. Surgical field was assessed using the five-point Boezaart scale, and total fentanyl and esmolol consumption, operative time, recovery time,	The results showed that the IV and local TA group had the best surgical field quality score, shorter operative time, lower total fentanyl consumption, shorter recovery time, and no significant differences in mean arterial pressure and heart rate decline in all groups. No significant differences were found in changes in hemoglobin, hematocrit, prothrombin time,	In conclusion, the combined use of topical and intravenous TA provided the best surgical field in FESS, less fentanyl consumption, and less recovery time without causing significant side effects.	**14**

		and postoperative complications were recorded.	and partial thromboplastin time over time in all groups.		
Double-blind RCT, TXA IV + localized TXA 5% irrigation solution vs TXA IV on 177 patients					
Ratnayake Kumar 2022	This study aimed to evaluate the safety of using both intravenous (IV) and topical Tranexamic acid (TXA) in endoscopic sinus surgery (ESS).	A scoping review was conducted on 177 comprehensive ESS cases from January 2017 to December 2019.	The study found that respiratory epithelia could withstand varying TXA concentrations without causing morphological issues. Topical TXA may have positive effects on wound healing and inflammation. The study also found no thromboembolic complications attributable to TXA in the 28 days after ESS. Only 1.3% of patients who received TXA experienced post-operative bleeding.	The use of IV and topical TXA is safe for its effect on respiratory epithelium and thromboembolic disease. Topical TXA may have more positive effects than just bleeding reduction.	22
The primary focus of our systematic review's/metanalysis's search strategy and study selection was on randomised controlled trials published in English since Jan 2010 up to Mar 2024. We utilised specific and searchable terms, including "Effect size", "Intravenous versus topical", "tranexamic acid", "Bleeding", and "Endoscopic sinus surgery", to gather research articles from reputable indexed journals such as "Medline," "SCOPUS," "Embase," "Web of Science," "Google Scholar," and "Cochrane library.". Additionally, we sequentially selected the generated randomised based on their relevance (not on their corresponding dates) to the pre-determined researchable key-words.					

Table 5. Summary of studies including oral tranexamic acid (oral TXA)

Study ID	Aim	Methods	Results	Conclusion	Ref
Double-blind RCT, oral TXA vs oral placebo on 50 patients					
Eftekharian 2016	This study aimed to evaluate the efficacy of oral tranexamic acid (TXA) on blood loss during rhinoplasty.	50 participants underwent rhinoplastic surgery and were divided into two groups: one group received 1 g of TXA tablets, and the other received a placebo two hours before surgery.	The results showed no statistical difference in the distribution of variables between the two groups, except for blood loss, duration of operation, and surgeon's satisfaction. The mean total blood loss was 144.6 ± 60.28 mL in the TXA group and 199.6 ± 73.05 mL in the placebo group.	The study concluded that TXA significantly decreased blood loss in patients undergoing rhinoplastic surgery without significant adverse effects.	33
The primary focus of our systematic review's/metanalysis's search strategy and study selection was on randomised controlled trials published in English since Jan 2010 up to Mar 2024. We utilised specific and searchable terms, including "Effect size", "Intravenous versus topical", "tranexamic acid", "Bleeding", and "Endoscopic sinus surgery", to gather research articles from reputable indexed journals such as "Medline," "SCOPUS," "Embase," "Web of Science," "Google Scholar," and "Cochrane library.". Additionally, we sequentially selected the generated randomised based on their relevance (not on their corresponding dates) to the pre-determined researchable key-words.					

4 DISCUSSION

It has been demonstrated that tranexamic acid, a synthetic derivative of the amino acid lysine, can improve the quality of the surgical field and decrease intraoperative blood loss during endoscopic sinus surgery. It has been applied topically or intravenously in response to bleeding diatheses and other surgical or clinical situations. Nevertheless, the administration of tranexamic acid systemically primarily results in gastrointestinal complications, such as postoperative nausea and vomiting, which occur between 10% and 20% of the time. Prolonged administration of an intravenous bolus can induce substantial hypotension. The potential for thromboembolism has historically been a source of concern regarding its application. A lower dose requirement and anticipated reduction in systemic absorption may benefit the local application of tranexamic acid topically, thereby possibly mitigating the risk of systemic adverse effects. This research examined studies that utilised perioperative topical administration techniques during sinus surgeries performed under general anaesthesia. Surgeon satisfaction, surgical field view or quality, surgical field bleeding score, and intraoperative blood loss volume constituted the primary outcome measures. [36-39]

The primary subgroup analysis of interest in 16 of 23 randomised controlled studies, the majority of which were double-blind controlled versus placebo trials, was the route of tranexamic acid administration (topical or intravenous). An observed disparity in favour of tranexamic acid was attributed to the two routes of administration: combined and intravenous. The analysis of 16 studies that assessed surgical field bleeding score as an outcome revealed evidence with moderate certainty that tranexamic acid is likely to significantly reduce surgical field bleeding score in comparison to placebo. Subgroup analysis revealed that adjunctive use of phenylephrine 0.05% may have a greater impact on the desired clinical outcome, and that the combination of TXA IV and localised TXA application may have a greater effect than TXA IV alone of altering the direction of the overall treatment effect in the desired direction. There was a marginally

insignificant variation in the duration of functional endoscopic sinus surgeries across the sixteen studies that were examined. Specifically, tranexamic acid was likely to have a marginal impact on the duration of the surgery when compared to the placebo. The study refrained from discussing surgical complications and the extent of surgical completion due to the limited amount of data that was collected.

The objective of this research endeavour was to examine the efficacy of tranexamic acid applied topically in regulating intraoperative bleeding and enhancing visual field visibility among patients undergoing nasal surgery. In comparison to the placebo group, the treatment group demonstrated significantly reduced intraoperative bleeding and enhanced visual field visibility, according to the findings. Ensuring successful surgical outcomes is of the utmost importance, given that even a slight haemorrhage can significantly impair the endoscope's visibility, leading to substantial structural harm, extended operation duration, or incomplete surgery. Prior meta-analyses have demonstrated that tranexamic acid, whether applied topically or systemically, decreases postoperative bleeding and enhances the overall condition of the surgical site. Nevertheless, there was no substantial reduction in operative time observed in the treatment group.

In theory, intra-operative bleeding would necessitate numerous packing and suctioning interruptions, thereby extending the duration of the operation. Although topical application may be efficacious when in contact with clot surfaces, the beneficial impact of tranexamic acid on bleeding and the surgical field generally diminishes over time as a result of local concentration reduction. Consequently, these time-dependent changes would have a greater impact on operative time than on overall operative bleeding or surgical field quality. [40-41]

Additionally, the research identified two significant methodological flaws in the prior evaluation conducted by Pundir et al.: whereas two studies examined the effectiveness of topical application, three of the five studies incorporated in the review examined the impact of systemic application. Gastrointestinal adverse effects, such as postoperative nausea and vomiting, are the most frequent adverse effects of tranexamic acid. Systemic administration may result in severe hypotension. The potential for thromboembolism has also historically been a source of concern regarding its application. Comparing the control group to the tranexamic acid-administered topical group, neither intraoperative blood pressure nor the incidence of postoperative emetic effects were significantly altered. The reduced likelihood of adverse effects can be primarily attributed to the direct and local contact with the working field, which prevented any systemic absorption. Similar to the control group, the treatment group exhibited a coagulation profile, which may corroborate prior findings and substantiate the incidence observed in this investigation.

However, there were some limitations to the study. Few studies were enrolled, indicating that further research is required in order to more accurately estimate the effects and outcomes of the treatment. Furthermore, the research employed a broad spectrum of dosages and varied application techniques, potentially accounting for a portion of the observed variability. Subsequent investigations ought to prioritise the development of a control group to facilitate a comparative analysis of tranexamic acid application in intraoperative bleeding control with other established methodologies.

5 Conclusion

In patients undergoing nasal surgery, the authors concluded that intraoperative bleeding and the operative field may be enhanced in a number of ways when tranexamic acid is administered intravenously, topically, locally, or in a dual-administration formulation.

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