The Journal of Laryngology & Otology

cambridge.org/jlo

Tranexamic acid in sinus and nasal surgery: an up-to-date meta-analysis

D Yap, A Shakir and A Hunt

Department of Otorhinolaryngology, Milton Keynes University Hospital, Milton Keynes, UK

Abstract

Objective. There are gaps within current meta-analyses looking at the effects of tranexamic acid on sino-nasal surgery. This study aimed to update and summarise all current available evidence on the use of tranexamic acid in sino-nasal surgery.

Method. A literature search was performed using four medical databases, Cochrane Library, Embase, Medline and PubMed. Data analysis was performed using dedicated meta-analysis software Review Manager (Revman).

Results. Thirteen studies were included in the meta-analysis. The amount of blood loss and duration of surgery in tranexamic acid groups was statistically lower than placebo for both sinus and nasal surgery. Tranexamic acid improves the surgical field quality in sinus surgery but worsens the field in nasal surgery. Topical or intravenous administration of tranexamic acid in sinus surgery reduces blood loss, duration of surgery and improves the quality of the surgical field.

Conclusion. This study suggests that the use of tranexamic acid in sinus surgery reduces blood loss, decreases surgical duration and improves surgical field quality.

Main Article

Dr D Yap takes responsibility for the integrity of the content of the paper

Cite this article: Yap D, Shakir A, Hunt A. Tranexamic acid in sinus and nasal surgery: an up-to-date meta-analysis. *J Laryngol Otol* 2022;**136**:692–702. https://doi.org/10.1017/S0022215121003170

Accepted: 22 April 2021
First published online: 27 October 2021

Key words:
Tranexamic Acid;
Tissue Plasminogen Activator;
Nasal Surgical Procedures;
Blood Loss, Surgical; Rhinoplasty;
Otolaryngology; Nose

Author for correspondence:
Dr D Yap, Department of Otorhinolaryngology, Milton Keynes University Hospital, Standing Way, Eaglestone, Milton Keynes MK6 5LD, UK
E-mail: darrenyap.jx@gmail.com

Introduction

There are four meta-analyses currently published in the English literature on the use of tranexamic acid in sinonasal surgery.[1–4] However, each meta-analysis did not fully include all available studies within the literature for their quantitative analyses. The purpose of this study was to summarise and update information on efficacy of tranexamic acid use in sinus and nasal surgery.

The objectives of this study were: (1) to assess the effect of using tranexamic acid on sinus and nasal surgery; (2) to assess primary outcome measures of intra-operative blood loss, quality of the surgical field and duration of surgery; (3) to determine if there is a difference between topical or intravenous administration of tranexamic acid in sinus surgery on the primary outcomes described above; and (4) to determine whether oral or intravenous tranexamic acid has any effect on nasal surgery (i.e. rhinoplasty or septoplasty).

Materials and methods

Search strategy

A literature search was performed on four medical databases: Cochrane Library, Embase, Medline and PubMed on 31 October 2019. The Embase search was a combination of Medical Subject Heading ('MeSH') terms *'"TRANEXAMIC ACID"/ AND *OTORHINOLARYNGOLOGY/ whereas the Medline search was *'"TRANEXAMIC ACID"/ AND *OTOLARYNGOLOGY/, the PubMed search was (Tranexamic acid).ti,ab AND (ENT).ti,ab OR (Otology).ti,ab OR (Rhinology).ti,ab OR (Laryngology).ti,ab OR (Otorhinolaryngology).ti,ab, and the Cochrane Library search was *Tranexamic Acid*. The initial results were reviewed by the first author (DY) and relevant articles were selected to review in full.

There was no use of human participants or animals in this study. All ethical policy and key considerations were carefully adhered to. No data contain any patient identifiable or shared data.

Study selection

Only randomised, placebo-controlled trials with results published as mean with or without standard deviation were included for quantitative analysis. Articles that were not published in English, non-randomised, controlled trials and trials without appropriate published outcome measures for quantitative analysis were excluded. Full articles were obtained and reviewed for all randomised, placebo-controlled trials of tranexamic acid use in sinus or nasal surgery. We used the revised risk of bias in randomised trials ('RoB 2') tool to assess the quality of studies included in the quantitative analysis.

Data collection

From included studies, we analysed the amount of intra-operative blood loss, quality of the surgical field and duration of surgery. Data were extracted only from papers with specific published results (i.e. mean and standard deviation). In studies where the quality of the surgical field was published using multiple time intervals, a combined mean and standard deviation was calculated.

Papers with results published in terms of charts or graphs without attached numerical values were excluded. All corresponding authors from excluded studies were contacted to obtain appropriate data for meta-analysis; unfortunately, we were not able to obtain any additional results.

Analysis

Data from the included studies were extracted by the first author (DY). Data analysis was performed using dedicated meta-analysis software (Review manager (Revman), version 5.0; the Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Standardised mean differences and 95 per cent confidence intervals (CIs) were calculated using a fixed effect model.

Results

Search results

A total of 75 studies were identified, with duplicates removed, on initial searches of Cochrane Library, Medline, Embase and PubMed. Titles and abstracts were reviewed, and 23 studies were identified for review.

Following a review of the 23 identified studies, 6 studies were excluded for the following reasons: (1) 1 study had no direct comparison with a placebo; (2) 4 studies did not have appropriate published numerical data to be included in the quantitative analysis; and (3) 1 study was an abstract publication with no appropriate numerical data published to be included in the quantitative analysis.

A further four papers had previously conducted meta-analyses on the use of tranexamic acid in nasal or sinus surgery.[1–4] All excluded studies are summarised in Appendix 1 and the Preferred Reporting Items for Systematic Reviews flow diagram is shown in Appendix 2.

Using the risk of bias 2 tool, the remaining 13 papers were assessed for risk of bias.[5] Following quality assessment, 7 papers were graded as having some concerns, 1 paper was graded as high risk of bias and the other 5 papers were considered low risk. Table 1 summarises the risk assessments of individual studies. Ten papers studied the effects of tranexamic acid on sinus surgery, and 3 papers were on nasal surgery.[6–18]

The study by Athanasiadis *et al.* was the only 'intra-individual study design' in the quantitative analysis,[17] and the remaining 12 studies allocated individuals to an intervention or placebo-controlled arm.[6–16,18] Eldaba *et al.* was the only study involving a paediatric population.[14]

The study by Athanasiadis *et al.* was a 3-arm randomised, controlled trial (100 mg tranexamic acid, 1 g tranexamic acid and saline).[17] We have only included the results for the 100 mg group for quantitative analysis because the 1 g group did not have appropriate published data to be included.

Concentration of tranexamic acid varied between all the included studies as shown in Table 2; therefore we were not able to obtain a meaningful meta-analysis regarding a specific dose of tranexamic acid.

Blood loss

Twelve studies were included in the quantitative analysis of intra-operative surgical blood loss (nine sinus surgery and three rhinoplasty studies). In comparison with placebo, the tranexamic acid group had less blood loss (standard mean difference, −58.45; 95 per cent CI = −59.20 to −57.70) in both sinus surgery (standard mean difference, −58.45; 95 per cent CI = −59.20 to −57.70) and nasal surgery (standard mean difference, −55.05; 95 per cent CI, −72.45 to −37.66). The measure of heterogeneity was $chi^2 = 188.30$, df = 8 ($p < 0.00001$) and (I^2) = 96 per cent in the sinus surgery group and the measure of heterogeneity was $chi^2 = 1.34$, df = 2 ($p < 0.51$) and (I^2) = 0 per cent in the nasal surgery group (Figure 1).

Surgical field quality

Eight sinus surgery and one nasal surgery study rated the quality of the surgical field. Overall results favoured the intervention group (standard mean difference, −0.17; 95 per cent CI = −0.28 to −0.05). When compared with placebo, the tranexamic acid intervention group was superior in comparison to the placebo group for sinus surgery (standard mean difference, −0.53; 95 per cent CI = −0.66 to −0.40). In contrast, tranexamic acid worsens the surgical field for nasal surgery as demonstrated in Figure 2 (standard mean difference, 1.60; 95 per cent CI, 1.32 to 1.88). Sinus surgery standard mean difference was −0.53 (95 per cent CI = −0.66 to −0.40) and measure of heterogeneity was $chi^2 = 66.87$, df = 7 ($p < 0.00001$) and I^2 = 90 per cent, while nasal surgery standard mean difference was 1.60 (95 per cent CI = 1.32 to 1.88 and measure of heterogeneity was $chi^2 = 102.11$ df = 4 ($p < 0.00001$), $I^2 = 96$ per cent). There is currently no available study that shows the effect of intravenous tranexamic acid on nasal surgery.

Duration of surgery

Figure 3 shows that the tranexamic acid intervention group had a shorter duration of surgery in comparison with placebo (standard mean difference = −0.68; 95per cent CI = −0.97 to −0.39) in both sinus surgery (5 studies) and nasal surgery (2 studies). Standard mean difference in sinus surgery was −19.17 (95 per cent CI = −21.54 to −16.80) and measure of heterogeneity was $chi^2 = 25.11$ (df = 4 ($p < 0.0001$), $I^2 = 84$ per cent), while nasal surgery had a standard mean difference of −0.39 (95 per cent CI = −0.69 to −0.09) and measure of heterogeneity of $chi^2 = 262.88$ (df = 6, $I^2 = 98$ per cent).

Subgroup analysis

We found that in sinus surgery, topical or intravenous administration of tranexamic acid had lower blood loss, improved surgical field quality and had shorter duration of surgery compared with placebo (Figures 4, 5 and 6). As for nasal surgery, both oral and intravenous administration of tranexamic acid reduced intra-operative blood loss (Figure 7). There was only one study that concluded using oral tranexamic acid worsened the surgical field quality for nasal surgery (Figure 8); however, it reduced duration of surgery (Figure 9). Intravenous tranexamic acid provided no additional benefit in duration of nasal surgery (Figure 9).

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

Table 1. Risk of bias 2 tool quality assessment

Study	Randomisation process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Dongare & Saundattikar[6]	?	+	+	+	+	?
Ghavimi *et al.*[7]	+	+	+	+	+	+
Eftekharian & Rajabzadeh[8]	+	?	+	+	+	?
Sakallioğlu *et al.*[9]	?	?	+	?	+	?
El Shal & Hasanein[10]	+	+	+	+	+	+
Nuhi *et al.*[11]	+	+	?	+	+	+
Shehata *et al.*[12]	?	+	+	+	+	+
Jahanshahi *et al.*[13]	+	+	+	+	+	+
Eldaba *et al.*[14]	+	+	+	+	+	+
Langille *et al.*[15]	+	+	+	+	+	+
Alimian & Mohseni[16]	?	+	+	+	+	?
Athanasiadis *et al.*[17]	+	+	+	−	−	−
Jabalameli & Zakeri[18]	?	+	+	?	+	?

Green circle with plus symbol = low risk; yellow circle with question mark = some concerns; red circle with minus sign = high risk

Table 2. Tranexamic acid doses

Study	Year	Operation	Route of administration	Dose	Administration period	Population
Dongare & Saundattikar[6]	2018	FESS	Intravenous	15 mg/kg	Pre-operative	Adult
Ghavimi *et al.*[7]	2017	Rhinoplasty	Intravenous	10 mg/kg	Pre-operative	Adult
Eftekharian & Rajabzadeh[8]	2016	Rhinoplasty	Oral	1 g	Pre-operative	Adult
Sakallioğlu *et al.*[9]	2015	Rhinoplasty	Oral	1 g	Pre-operative	Adult
El Shal & Hasanein[10]	2015	FESS	Intravenous	10 mg/kg	Pre-operative	Adult
Nuhi *et al.*[11]	2015	FESS	Intravenous	15 mg/kg	Not mentioned (assumption of pre-operative)	Adult
Shehata *et al.*[12]	2014	FESS	Topical	1 g in 20 ml saline	Intra-operative packing and irrigation	Adult
Jahanshahi *et al.*[13]	2014	FESS	Topical	5% solution	Pre-operative packing for 10 minutes	Adult
Eldaba *et al.*[14]	2013	FESS	Intravenous	25 mg/kg	Pre-operative	Paediatric
Langille *et al.*[15]	2012	FESS	Intravenous	15 mg/kg 1 mg/kg per hour	Pre-operative bolus. Intra-operative infusion	Adult
Alimian & Mohseni[16]	2011	FESS	Intravenous	10 mg/kg	Pre-operative	Adult
Athanasiadis *et al.*[17]	2007	FESS	Topical	100 mg	Topical spray using microatomiser	Adult
Jabalameli & Zakeri[18]	2006	FESS	Topical	1 g in 20 ml saline	Topical pre-operative	Adult

FESS = functional endoscopic sinus surgery

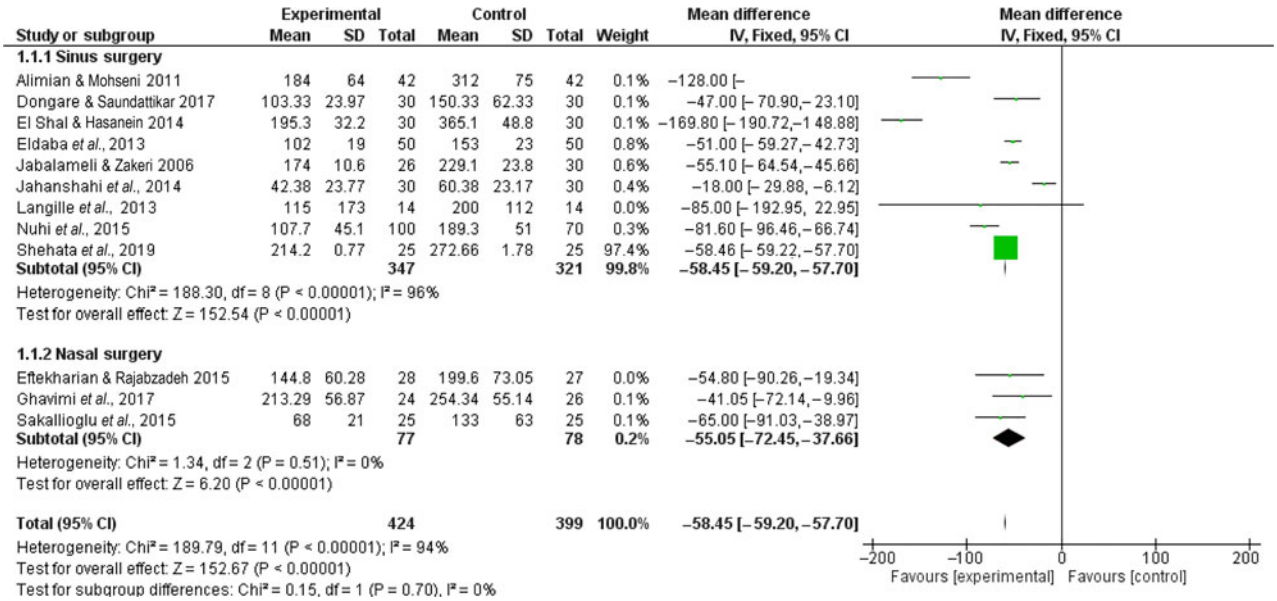


Fig. 1. Tranexamic acid compared with placebo blood loss forest plot. SD = standard deviation; IV = inverse variance; CI = confidence interval

Discussion

Background

Because of the narrow space and rich blood supply within the nasal cavity, intra-operative bleeding causes significant reduction in visual acuity, subsequently increasing the risk of surgical complications, poorer surgical outcomes, duration of surgery and even preventing completion of the procedure on some occasions.[1–3]

Multiple methods have been described to reduce intra-operative bleeding to obtain better visualisation of the surgical field, such as controlled hypotension, use of a topical vasoconstrictor, pre-operative steroid administration, patient positioning, bipolar cautery and infiltration into the pterygopalatine fossa amongst many other methods.[1,3,4]

The Wormald and Boezaart grading scales are two validated scoring systems for surgical field quality; the scoring principles are incremental changes from a clear to a vague surgical field.[2] We only included studies that used these grading scales in our quantitative analysis.

Mode of action of tranexamic acid

Surgical trauma, hypothermia, administration of crystalloid fluids during and after surgery, and consumption of

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

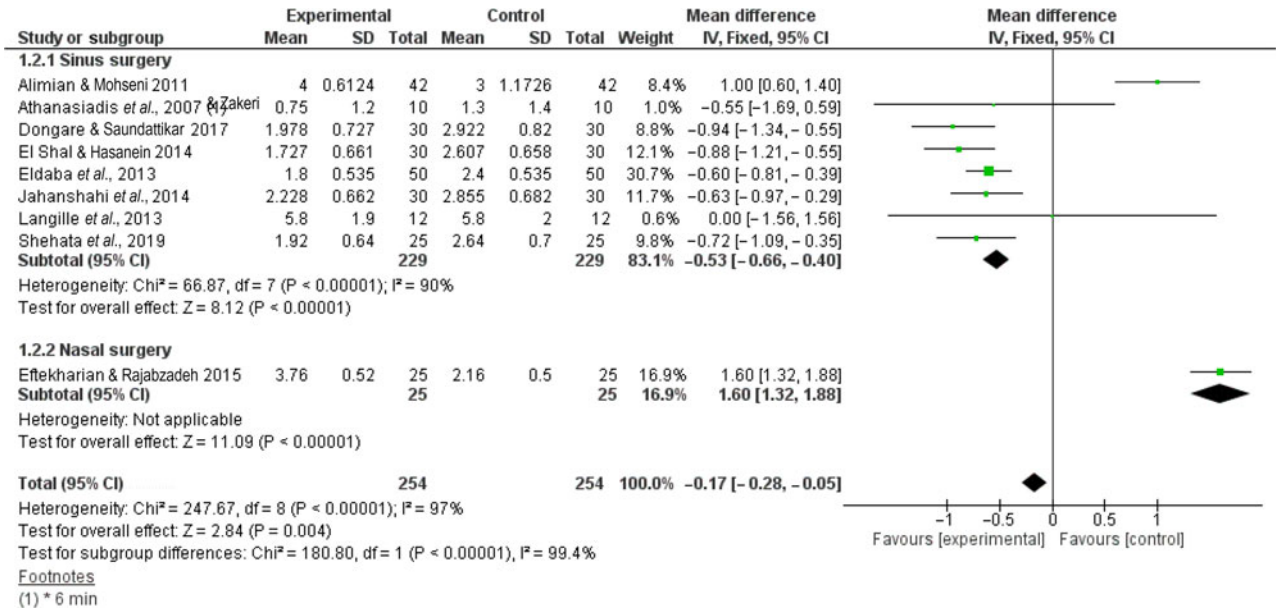


Fig. 2. Tranexamic acid compared to placebo surgical field quality forest plot. SD = standard deviation; IV = inverse variance; CI = confidence interval

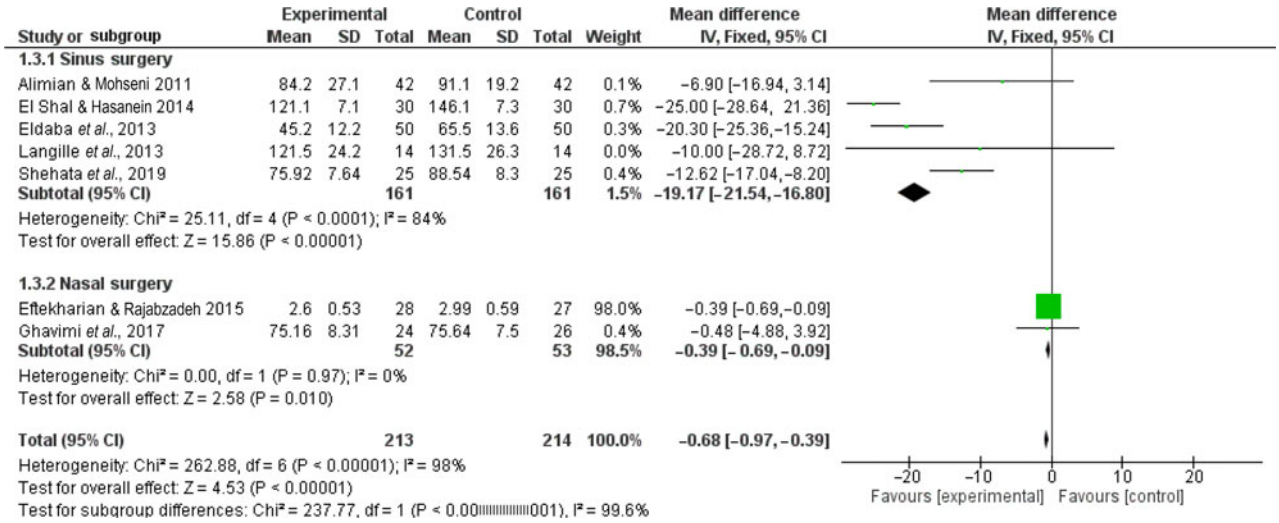


Fig. 3. Tranexamic acid compared to placebo duration of surgery forest plot. SD = standard deviation; IV = inverse variance; CI = confidence interval

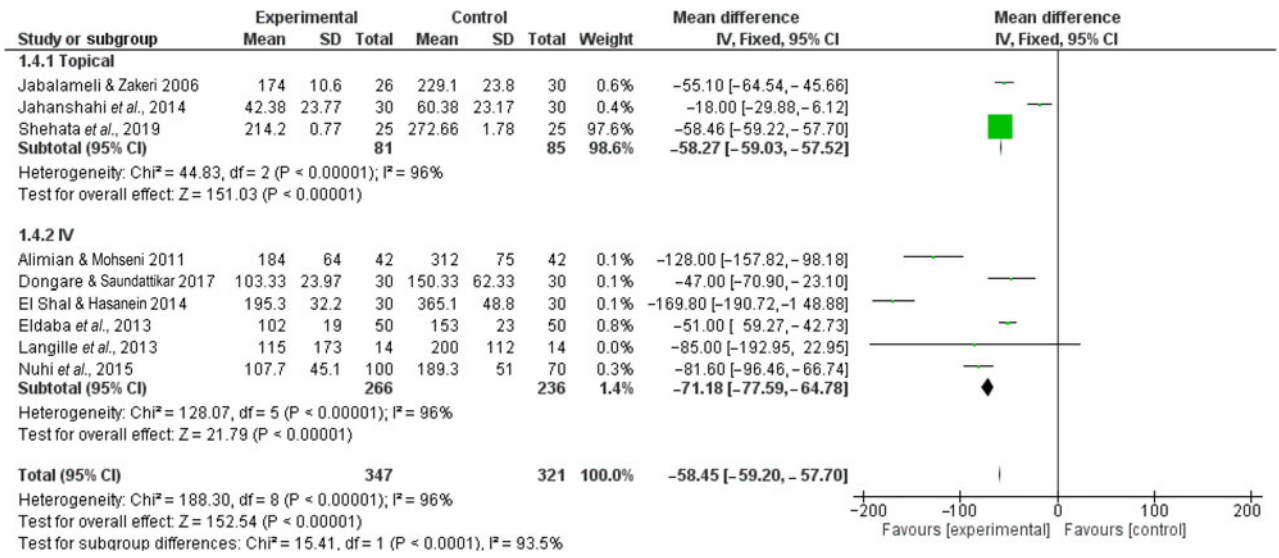


Fig. 4. Subgroup analysis: topical versus intravenous tranexamic acid on blood loss in sinus surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

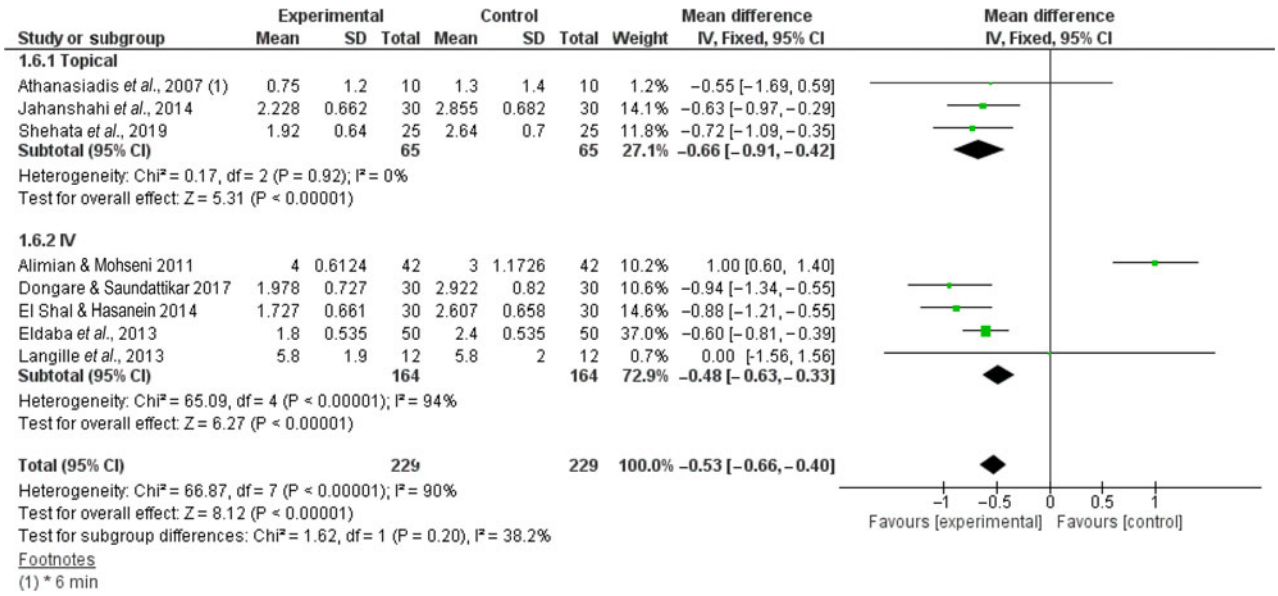


Fig. 5. Subgroup analysis: topical versus intravenous tranexamic acid on surgical field quality in sinus surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

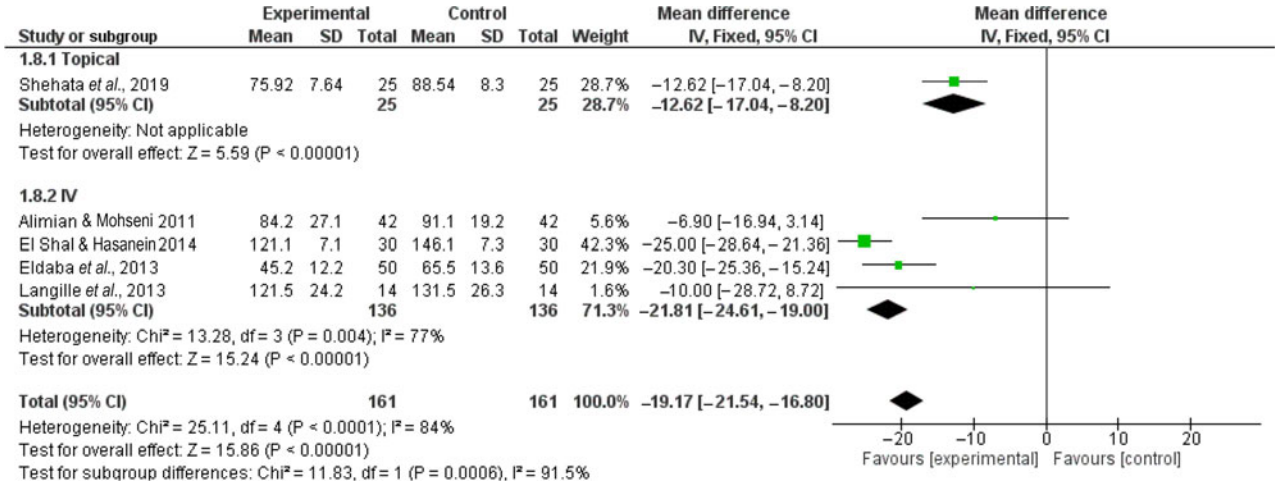


Fig. 6. Subgroup analysis: topical versus intravenous tranexamic acid on duration of surgery in sinus surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

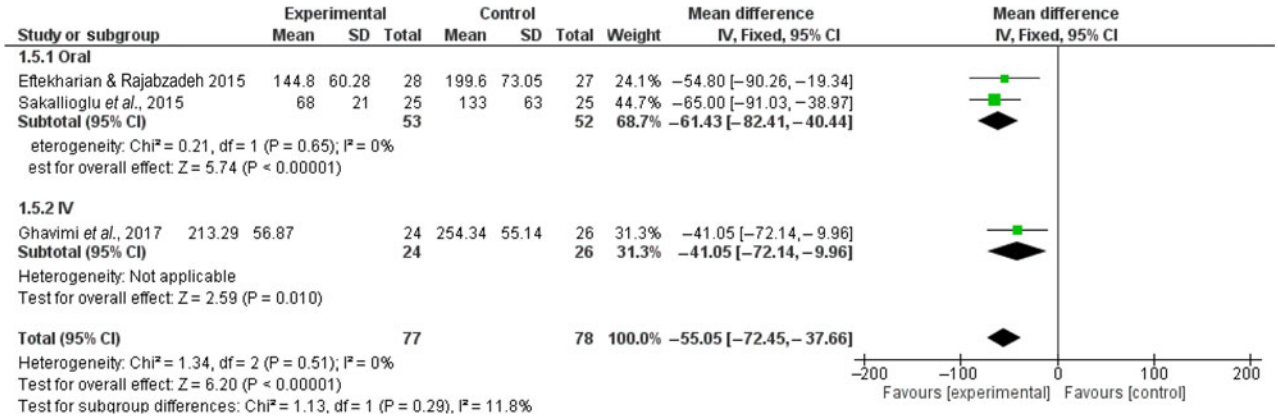


Fig. 7. Subgroup analysis: oral versus intravenous tranexamic acid on blood loss in nasal surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

coagulation factors and platelets have been known to activate fibrinolysis during surgery.[3] Tranexamic acid is a synthetic anti-fibrinolytic agent that acts as a competitive antagonist to the lysine site of plasminogen, inhibiting the tissue plasminogen activator.[12,18] This action will inhibit fibrin binding to plasminogen. In the clotting cascade, tranexamic acid

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

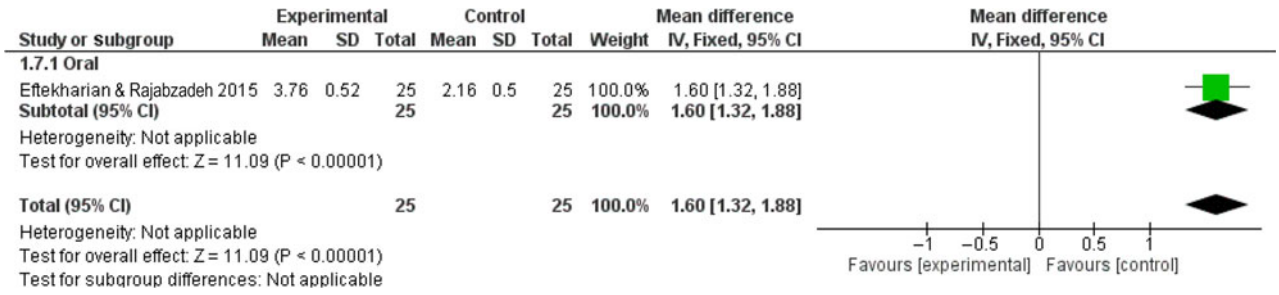


Fig. 8. Subgroup analysis: oral tranexamic acid on surgical field quality in nasal surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

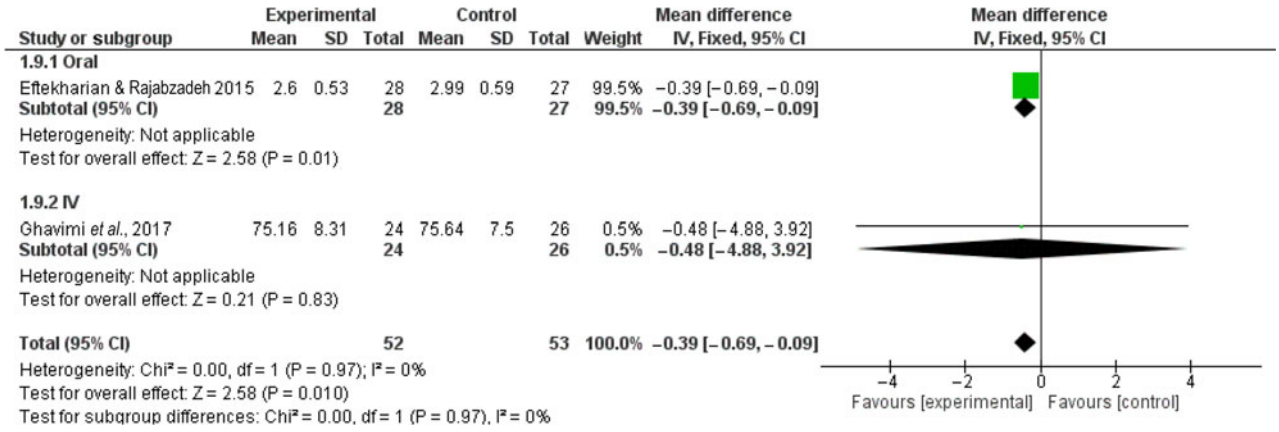


Fig. 9. Subgroup analysis: oral versus intravenous tranexamic acid on duration of surgery in nasal surgery. SD = standard deviation; IV = inverse variance; CI = confidence interval

prevents fibrinolysis and stabilises blood clot formation, which results in a reduction in bleeding.[3,12]

Generally tranexamic acid is well tolerated and considered a safe medication at the appropriate dosage. Nausea and vomiting are known as the commonest side effects, and hypotension has been observed if administered rapidly.[19] Meta-analysis by Pundir *et al.* showed no significant difference in occurrence of nausea and vomiting in patients taking tranexamic acid in comparison with placebo.[4]

The risk of a thromboembolic event secondary to tranexamic acid use has always been a concern. However, studies have shown that there is no increased risk of thromboembolic events in tranexamic acid treatment groups in comparison with controls.[20,21]

Comparison with other meta-analyses

Compared to the Kang and Hwang[1] meta-analysis studying the effects of topical tranexamic acid in functional endoscopic sinus surgery, the study by Baradaranfar *et al.*[22] did not contain results that were appropriate to be included in the quantitative meta-analysis and therefore this study was excluded. However, we included an additional study by Athanasiadis *et al.*[17] Ping *et al.*[2] had 11 studies included in their meta-analysis, while our review included 13 studies. We excluded Mehdizadeh[23] *et al.* and Sakallioğlu *et al.*[9] from our review as their primary outcomes were oedema and ecchymosis, which are not our primary outcomes. All other appropriate studies within the quantitative analysis of Ping *et al.*[2] have been included in our review.

Kim *et al.*[3] (2018) included 7 studies in their quantitative analysis, compared with this review which included 10 studies. The study results published by Chhapola *et al.*[24] and Moise *et al.*[25] were not suitable for quantitative analysis; therefore they were excluded in our review.

Lastly, Pundir *et al.*[4] included five studies in their quantitative analysis published prior to 2013. Our review included studies published after 2013, and a summary of a comparison of these is shown in Appendix 3.

Limitations

Heterogeneity is the variation in effect estimates beyond chance. Statistical heterogeneity almost always occurs in meta-analysis because of clinical and methodological diversity; however, it is important to consider the extent of consistency of the studies' results. I^2 describes the percentage of variability in effect estimates that is a result of heterogeneity rather than sampling error (chance). The interpretation of I^2 must be taken with caution as the threshold can be misleading because the importance of inconsistencies depends on several factors, such as strength of evidence for heterogeneity, magnitude and direction of effects.[26]

We acknowledge that the I^2 within our meta-analysis varied between 0 and 96 per cent, which represents substantial to considerable heterogeneity. The use of different scoring systems for the quality of surgical fields may have contributed to the heterogeneity of our analyses. Therefore, those results would need to be interpreted with caution.

Subgroup analyses should also be interpreted with caution as there are few studies included in the quantitative analysis. Further studies are required to provide more statistically significant results.

All included studies have a variation in the dose and administration of tranexamic acid. This reflects the current clinical diversity in our practice. Unfortunately, because of

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

this variation, quantitative analysis on the individual route of administration and dosage of tranexamic acid is not possible.

Implication for research

Ideally a larger multi-centred randomised, blinded, prospective controlled trial should be conducted to provide further conclusive evidence on the use of tranexamic acid in sinus and nasal surgery. It would also be clinically relevant to investigate the most efficacious mode of administration and dose of tranexamic acid use in nasal or sinus surgical procedures.

We attempted to contact corresponding authors from excluded studies to obtain appropriate data for meta-analysis; unfortunately, we were not able to obtain any additional results. Most authors did not respond to our request and of those who responded, they no longer had original data for further interpretation because of the passage of time.

Generally, all studies included were small, with the largest study containing 170 adults.[11] All data included in this meta-analysis were from studies that published raw numerical data for analysis. A further updated meta-analysis could be performed if authors of the excluded studies provided specific numerical data such as the mean with or without the standard difference.

- Tranexamic acid reduces blood loss and surgical duration and improves surgical field quality in sinus surgery
- In nasal surgery, tranexamic acid has been shown to improve surgical time and reduce blood loss but does not improve surgical field quality
- There was no difference between blood loss, surgical field quality and surgical duration between topical or intravenous administration of tranexamic acid in sinus surgery
- Due to variation in concentration and mode of administration, a standard technique cannot be recommended from this meta-analysis
- Due to the limited number of studies, future randomised, controlled trials on the efficacy of tranexamic acid in rhinology cases are recommended

Presently, there are no randomised, controlled trials studying the effect of intravenous tranexamic acid on the quality of the surgical field in nasal surgery.

Conclusion

Our review strongly suggests that tranexamic acid reduces blood loss, decreases surgical duration and improves surgical field quality in sinus surgery. For nasal surgery however, it was shown to reduce blood loss and surgical duration but does not improve surgical field quality. Given the number of studies included in the quantitative analysis, a larger multi-centred randomised, controlled trial is recommended.

Competing interests. None declared

References

1 Kang H, Hwang S. Does topical application of tranexamic acid reduce intraoperative bleeding in sinus surgery during general anesthesia? *Braz J Otorhinolaryngol* 2020;**86**:111–18
2 Ping W, Zhao Q, Sun H, Lu H, Li F. Role of tranexamic acid in nasal surgery – a systematic review and meta-analysis of randomized control trial. *Medicine* 2019;**98**:e15202
3 Kim D, Kim S, Kang H, Jin H, Hwang S. Efficacy of tranexamic acid on operative bleeding in endoscopic sinus surgery: a meta-analysis and systematic review. *Laryngoscope* 2018;**129**:800–7
4 Pundir V, Pundir J, Georgalas C, Fokkens W. Role of tranexamic acid in endoscopic sinus surgery – a systematic review and meta-analysis. *Rhinology* 201;**51**:291–7
5 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I *et al.* RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898
6 Dongare D, Saundattikar G. Comparison of intraoperative bleeding and surgical fields with and without tranexamic acid in functional endoscopic sinus surgery. *Ind J Clin Anaesth* 2018;**5**:233–6
7 Ghavimi M, Taheri Talesh K, Ghoreishizadeh A, Chavoshzadeh M, Zarandi A. Efficacy of tranexamic acid on side effects of rhinoplasty: a randomized double-blind study. *J Craniomaxillofac Surg* 2017;**45**:897–902
8 Eftekharian H, Rajabzadeh Z. The efficacy of preoperative oral tranexamic acid on intraoperative bleeding during rhinoplasty. *J Craniofac Surg* 2016;**27**:97–100
9 Sakallioğlu Ö, Polat C, Soylu E, Düzer S, Orhan İ, Akyiğit A. The efficacy of tranexamic acid and corticosteroid on edema and ecchymosis in septorhinoplasty. *Ann Plast Surg* 2015;**74**:392–6
10 El Shal S, Hasanein R. Effect of intravenous tranexamic acid and epsilon aminocaproic acid on bleeding and surgical field quality during functional endoscopic sinus surgery (FESS). *Egypt J* 2015;**31**:1–7
11 Nuhi S, Tabrizi A, Zarkhah L, Ashrafi B. Impact of intravenous tranexamic acid on hemorrhage during endoscopic sinus surgery. *Iran J Otorhinolaryngol* 2015;**27**:349–34
12 Shehata A, Ibrahim M, Abd-El-Fattah M. Topical tranexamic acid versus hot saline for field quality during endoscopic sinus surgery. *Egypt J Otolaryngol* 2014;**30**:327
13 Jahanshahi J, Hashemian F, Pazira S, Bakhshaei M, Farahani F, Abasi R *et al.* Effect of topical tranexamic acid on bleeding and quality of surgical field during functional endoscopic sinus surgery in patients with chronic rhinosinusitis: a triple blind randomized clinical trial. *PloS ONE* 2014;**9**:e104477
14 Eldaba A, Amr Y, Albirmawy O. Effects of tranexamic acid during endoscopic sinsus surgery in children. *Saudi J Anaesth* 2013;**7**:229
15 Langille M, Chiarella A, Côté D, Mulholland G, Sowerby L, Dziegielewski P *et al.* Intravenous tranexamic acid and intraoperative visualization during functional endoscopic sinus surgery: a double-blind randomized controlled trial. *Int Forum Allergy Rhinol* 2012;**3**:315–18
16 Alimian M, Mohseni M. The effect of intravenous tranexamic acid on blood loss and surgical field quality during endoscopic sinus surgery: a placebo-controlled clinical trial. *J Clin Anesth* 2011;**23**:611–15
17 Athanasiadis T, Beule A, Wormald P. Effects of topical antifibrinolytics in endoscopic sinus surgery: a pilot randomized controlled trial. *Am J Rhinol* 2007;**21**:737–42
18 Jabalameli M, Zakeri K. Evaluation of topical tranexamic acid on intraoperative bleeding in endoscopic sinus surgery. *Iran J Med Sci* 2006;**31**:221–3
19 Dunn CJ, Goa KL. Tranexamic acid: a review of its use in surgery and other indications. *Drugs* 1999;**57**:1005–32
20 Franchini M, Mengoli C, Marietta M, Marano G, Vaglio S, Pupella S *et al.* Safety of intravenous tranexamic acid in patients undergoing major orthopaedic surgery: a meta-analysis of randomised controlled trials. *Blood Transfus* 2018;**16**:36–43
21 Kim Y, Park J, Kim J, Seo D. Does Tranexamic acid increase the risk of thromboembolism after bilateral simultaneous total knee arthroplasties in Asian population? *Arch Orthop Trauma Surg* 2018;**138**:83–9
22 Baradaranfar M, Dadgarnia M, Mahmoudi H, Behniafard N, Atighechi S, Zand V *et al.* The effect of topical tranexamic acid on bleeding reduction during functional endoscopic sinus surgery. *Iran J Otorhinolaryngol* 2017;**29**:69–74
23 Mehdizadeh M, Ghassemi A, Khakzad M, Mir M, Nekoohesh L, Moghadamnia A *et al.* Comparison of the effect of dexamethasone and tranexamic acid, separately or in combination on post-rhinoplasty edema and ecchymosis. *Aesthetic Plast Surg* 2018;**42**:246–52
24 Chhapola S, Matta I. Short-term use of tranexamic acid to reduce blood loss in endoscopic nasal surgeries. *Int J Clin Rhinol* 2011;**4**:79–81
25 Moise A, Agachi L, Dragulin E, Mincu N, Stelea G. Tranexamic acid reduces with 50% the total nasal bleeding of patients that underwent functional endoscopic sinus surgery. *Eur J Anaesthesiol* 2010;**27**:115
26 Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ *et al.* Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane 2019. In: www.training.cochrane.org/handbook [31 December 2021]

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

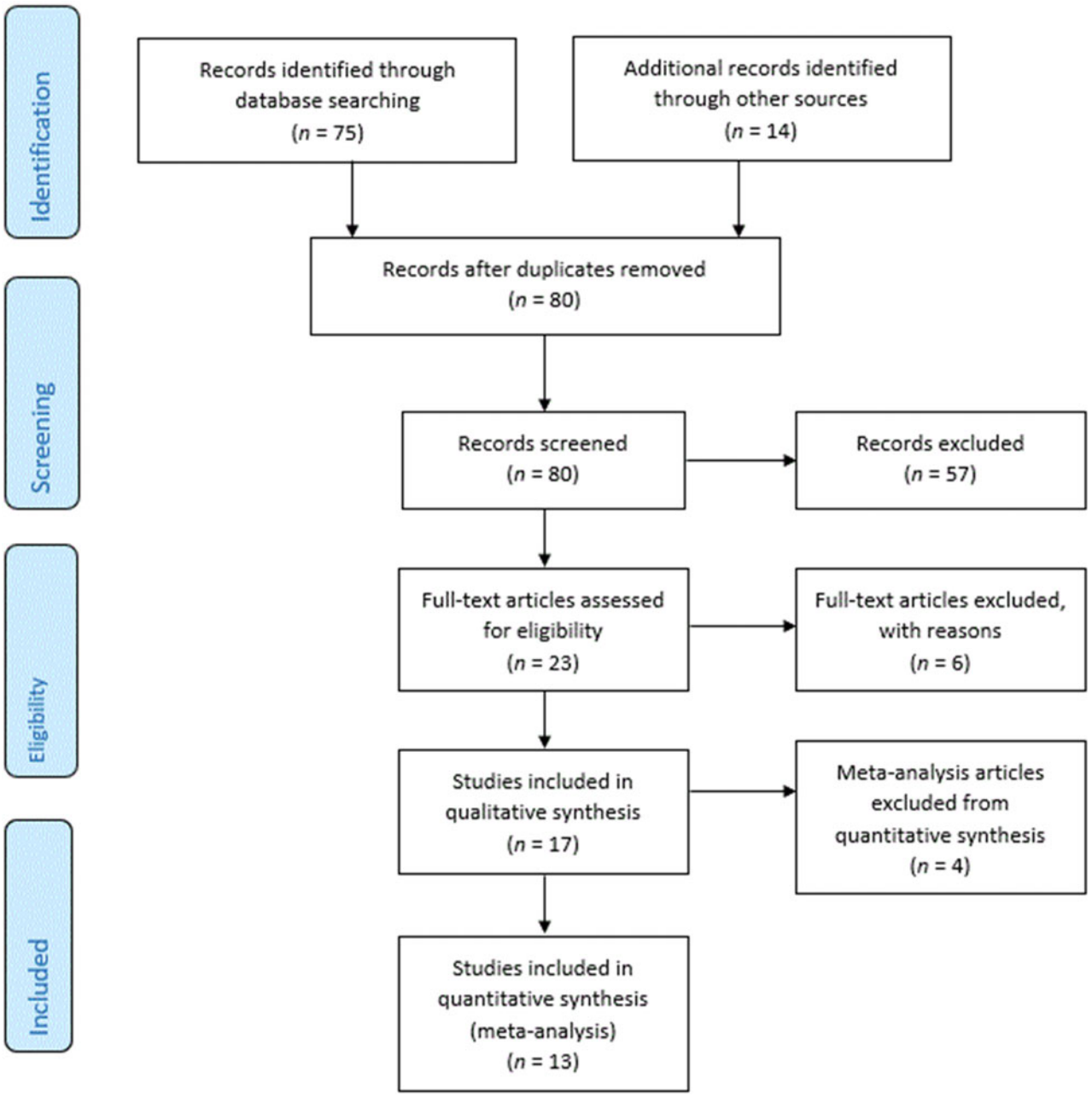
Appendix 1. Excluded studies

Author	Year	Reason for exclusion
Zaman *et al*.	2019	Published data not suitable for quantitative analysis
Ghorbani *et al*.	2018	Study had no direct comparison with placebo
Baradaranfar *et al*.	2017	Published data not suitable for quantitative analysis
Chhapola *et al*.	2011	Published data not suitable for quantitative analysis
Moise *et al*.	2010	Abstract publication; published data not suitable for quantitative analysis
Yaniv *et al*.	2006	Published data not suitable for quantitative analysis

1 Zaman S, Zakir I, Faraz Q, Akhtar S, Nawaz A, Adeel M. Effect of single-dose intravenous tranexamic acid on postoperative nasal bleed in septoplasty. *Eur Ann Otorhinolaryngol Head Neck Dis* 2019;**136**:435–8
2 Ghorbani J, Arastou S, Naeini A, Raad N, Galougahi, Jahangirifard A *et al*. Comparing the effect of oral clonidine and tranexamic acid on bleeding and surgical field quality during functional endoscopic sinus surgery. *Iran J Otorhinolaryngol* 2018;**30**:255–60
3 Baradaranfar M, Dadgarnia M, Mahmoudi H, Behniafard N, Atighechi S, Zand V *et al*. The effect of topical tranexamic acid on bleeding reduction during functional endoscopic sinus surgery. *Iran J Otorhinolaryngol* 2017;**29**:69–74
4 Chhapola S, Matta I. Short-term use of tranexamic acid to reduce blood loss in endoscopic nasal surgeries. *Int J Clin Rhinol* 2011;**4**:79–81
5 Moise A, Agachi L, Dragulin E, Mincu N, Stelea G. Tranexamic acid reduces with 50% the total nasal bleeding of patients that underwent functional endoscopic sinus surgery. *Eur J Anaesthesiol* 2010;**27**:115
6 Yaniv E, Shvero J, Hadar T. Hemostatic effect of tranexamic acid in elective nasal surgery. *Am J Rhinol* 2006;**20**:227–9

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

Appendix 2. Preferred Reporting Items for Systematic Reviews (PRISMA) 2009 flow diagram



https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press

Appendix 3. Comparison with other meta-analyses

Parameter	Yap *et al.* (this study)	Kang & Hwang[1]	Ping *et al.*[2]	Kim *et al.*[3]	Pundir *et al.*[4]
Amount of blood loss	12 studies 9 sinus surgery 3 nasal surgery	4 studies 4 sinus surgery	9 studies 6 sinus surgery 3 nasal surgery	4 studies 4 sinus surgery	4 studies 4 sinus surgery
Duration of surgery	7 studies 5 sinus surgery 2 nasal surgery	2 studies 2 sinus surgery			2 studies 2 sinus surgery
Quality of surgical field	9 studies 8 sinus surgery 1 nasal surgery	4 studies 4 sinus surgery	4 studies 4 sinus surgery	7 studies 7 sinus surgery	4 studies 4 sinus surgery

https://doi.org/10.1017/S0022215121003170 Published online by Cambridge University Press