Comparison of the efficacy of hot saline irrigation and tranexamic acid on Boezaart score, intraoperative blood loss, and duration of surgery in functional endoscopic sinus surgery: a systematic review and meta-analysis

Timmy Wibisono¹, Budi Sutikno¹*, Titiek Hidayati Ahadiah¹, Budi Utomo², Citrawati Dyah Kenconowungu³

**ABSTRACT**

**Background:** Hot saline irrigation and tranexamic acid are techniques used to control bleeding during functional endoscopic sinus surgery (FESS). Hot saline irrigation and tranexamic acid can help control bleeding originating from microvascular located in the nasal cavity and paranasal sinuses. This study aims to compare the efficacy of these two techniques on Boezaart score, intraoperative blood loss, and duration of surgery in functional endoscopic sinus surgery.

**Methods:** This study is an intervention meta-analysis, the research formulated based on the population, intervention, comparison, outcome, and study design (PICOS). Articles were searched from five databases, including PubMed Central and publisher websites, Cochrane Library, ResearchGate, SAGE Journals, and Web of Science. There were no publication year or publication status restrictions on the selected research articles, and the date of the last search was up to February 2023. The efficacy of hot saline irrigation as a bleeding control method compared to tranexamic acid was assessed based on Boezaart surgical field score, intraoperative bleeding, and duration of surgery in functional endoscopic sinus surgery (FESS).

**Results:** A total of 532 research articles were identified, and fifteen articles that met the inclusion and exclusion criteria were selected. Hot saline irrigation p-value p=0.0002 and for tranexamic acid p=0.00001 based on Boezaart score. Hot saline irrigation p=0.001 and tranexamic acid had a p=0.0002 based on the Intraoperative blood loss, but the standardized mean difference in the hot saline irrigation group was smaller compared to the tranexamic acid topical group. Hot saline irrigation p=0.06 and tranexamic acid p=0.13 for duration of surgery.

**Conclusion:** This meta-analysis showed that the administration of tranexamic acid or hot saline irrigation could significantly reduce duration of surgery, intraoperative bleeding loss and improved surgical field quality compared with room temperature saline irrigation. There is no statistically significant difference between tranexamic acid topical and hot saline irrigation.

**Keywords:** hot saline irrigation, tranexamic acid, bleeding control, endoscopic sinus surgery.


**INTRODUCTION**

Chronic rhinosinusitis (CRS) is one of the most common chronic diseases in the world, in which approximately 5-15% of the world’s population suffers from CRS. CRS can be defined as inflammation of the nose and paranasal sinuses and is characterized by two or more symptoms, one of which should be nasal obstruction or rhinorrhea, facial pain and/or hyposmia/anosmia.¹ Functional endoscopic sinus surgery (FESS) is the preferred surgical option for patients with chronic rhinosinusitis (CRS) who do not show clinical improvement after topical intranasal corticosteroid therapy and optimal nasal irrigation, as well as for CRS patients who have direct indications for surgery without appropriate medical treatment (AMT).²,³ A clear surgical field of view is crucial as it is the success factor in endoscopic surgery. An optimal surgical field of view in endoscopic surgery provides a detailed visual surface of the operative area, allowing the operator to evaluate and make decisions on maneuvers to be applied during the surgery. This helps the operator achieve the surgical goals efficiently and prevent complications.⁴,⁵

Bleeding during functional endoscopic sinus surgery can originate from both macrovascular and microvascular sources within the nasal cavity and paranasal sinuses. A study conducted by Stankiewicz on complications in patients undergoing FESS concluded that out of the total patients who experienced complications during FESS, 105 patients had complications, with bleeding being...
the most common complication in 41 patients. Bleeding during surgery can complicate the procedure for the operator, making accurate assessment of the source of bleeding, anatomy knowledge of operator’s, and adequate hemostasis techniques crucial in controlling bleeding during FESS.6

Warm saline irrigation can control bleeding originating from microvascular sources in the mucosa within the nasal cavity and paranasal sinuses. The mechanism of action of warm saline irrigation in controlling bleeding involves causing tissue edema around the microvascular bleeding sites in the nasal cavity and paranasal sinuses, which can assist in the cascade of blood clotting, stopping the oozing of blood from the mucosa, and providing a clearer surgical field of view.7

A study by Shehata A compared hot saline irrigation, room temperature saline irrigation, and topical tranexamic acid as methods to control mucosal bleeding during FESS. The study reported that the hot saline irrigation and topical tranexamic acid groups were superior in controlling bleeding compared to the room temperature saline irrigation group, as assessed by the Boezaart scoring system for intraoperative bleeding. Operator satisfaction levels were also reported to be higher in the hot saline irrigation group compared to the room temperature saline irrigation group. There was no significant difference in outcomes between the hot saline irrigation and topical tranexamic acid groups.8

A study by Gan EC comparing hot saline irrigation with room temperature saline irrigation as methods to control mucosal bleeding during FESS reported no significant difference in the efficacy of hot saline irrigation compared to room temperature saline irrigation in controlling bleeding. The study assessed Boezaart surgical field score, duration of surgery, and intraoperative blood loss.9 The objective of this meta-analysis is to compare the efficacy of hot saline irrigation as a method to control bleeding and tranexamic acid, based on Boezaart scoring, intraoperative blood loss, and duration of surgery in FESS. This meta-analysis will be conducted using a registered protocol in Prospero.

METHODS

Literature search and selection

We conducted systematic searches for randomized controlled trials (RCTs). There were no publication year or publication status restrictions. The date of the last search was up to February 2023. We searched Web of Science, Pubmed Central and publisher websites, Cochrane Library, Research Gate, SAGE Journal. Two authors independently conducted the literature search using the search terms combination of MeSH and text words (“endoscopic sinus surgery” OR “functional endoscopic sinus surgery”) AND (“bleeding” OR “hemorrhage” OR “intra operative blood loss”) AND (“tranexamic acid” OR “saline” OR “isotonic saline” OR “warm” OR “hot” OR “room temperature”) AND (“Boezaart score” OR “total time” OR “total blood lost”). The reference lists of all known primary and review articles were hand searched to identify cited articles not captured by electronic searches. The searches were conducted independently by two reviewers TW and BS.

The full texts of studies that were potentially relevant to the topic were obtained if a decision for inclusion could not be made from the abstract alone. Randomized controlled trials that met the following inclusion criteria were eligible for review: the trials studied adult patients receiving endoscopic sinus surgery with the preoperative or perioperative (during the surgery) administration of tranexamic acid or hot saline irrigation and room temperature saline as a control group. Studies were excluded if, in addition to sinus surgery, patients underwent procedures, such as turbinate surgery or adenoidectomy, or if multiple reports were based on the same trial data. In cases with missing or incomplete data, attempts were made to obtain further details directly from the authors. Studies were excluded from the analysis if the outcomes of interest were not clearly reported with quantifiable data or if it was not possible to extract and calculate the appropriate data from the published results.

Data extraction and quality assessment

The measured outcomes were intraoperative blood loss, surgical field score, duration of surgery. These results were compared between the tranexamic acid group (tranexamic acid treated and the control group treated with default saline) and hot saline irrigation group (hot saline irrigation treated and the control group treated with default saline). The number of patients, intra-operative results, and measured p-values were abstracted to compare the effect of intervention groups. Quality of the studies was assessed utilizing the Critical Appraisal Skill Programme (CASP) randomized controlled trial standard checklist.

Statistical analysis

Meta-analysis were performed using Review Manager 5 software (RevMan 5.4, The Cochrane Collaboration, Oxford, UK). Continuous variables were analyzed using standardized mean differences (SMD), with 95% confidence intervals (CIs). The results were pooled using either a fixed effect or random effect model as appropriate. Heterogeneity of the exposure effects was evaluated statistically using the I² statistic to quantify heterogeneity across studies. A I² value of >50% was taken as evidence of substantial heterogeneity and in such cases a random effect model was used. A chi-squared test for heterogeneity was also performed and the ‘p’ values are presented. The meta-analysis was performed using the standardized mean difference (SMD). This value suggests that a larger effect size indicates that a treatment is more clinically effective.10 This method was chosen to compare effect sizes due to the absence of a standardized scale for use across all studies to assess duration of surgery, intraoperative blood loss and Boezaart surgical field score.11

RESULTS

The article screening process continued with inclusion and exclusion criteria, resulting in 15 remaining articles.

Study characteristics description of fifteen included studies is summarized in Table 1.

The publication timeline of articles included in this research ranges from the oldest article published in 2006 to the most recent in 2021. The demographic characteristics of the articles in this research encompass various ethnicities,
The basic data recorded in this research includes the sample size based on gender in each research article. The distribution of sample size in the research articles based on gender is shown in Table 2. The total sample size in the fifteen research articles is 1011 patients. There are 553 male patients (54.70%) and 408 female patients (40.36%) based on the distribution in Table 2. Two articles did not provide detailed distribution based on gender, and the total sample size in these two articles is 50 patients (4.95%). Based on the available data, the male-to-female ratio is 5:4. The study with the largest sample size is Nuhi et al., 2015, with 170 patients (16.82%), of which 90 patients (52.94%) are male and 80 patients (47.06%) are female.18 The study with the smallest sample size is Athanasiadis et al., 2007, with 20 patients (1.98%), but the researchers did not provide detailed distribution based on gender.19

**Boezaart surgical field score**

The results of the hot saline irrigation analysis showed significant heterogeneity among the research articles ($\chi^2 = 4.21$, df = 2, I² = 52%), indicating the use of a random effects model. The Test for overall effect showed a standardized mean difference (SMD) of -0.78, 95% CI [-1.20, -0.36], p = 0.0002, as shown in Figure 2. The interpretation of the results indicates that the use of hot saline irrigation as a control for bleeding is more effective than placebo, based on the Boezaart surgical field score.

The overall analysis of tranexamic acid showed low heterogeneity among the research articles ($\chi^2 = 3.79$, df = 7, I² = 0%), indicating the use of a fixed effects model. The Test for overall effect showed a standardized mean difference (SMD) of -1.09, 95% CI [-1.29, -0.88], p < 0.00001. Topical tranexamic acid had an SMD of -0.99, 95% CI [-1.30, -0.68], p < 0.00001, while intravenous tranexamic acid had an SMD of -1.17, 95% CI [-1.45, -0.89], p < 0.00001, as shown in Figure 3. The interpretation of the results indicates that both topical tranexamic acid and hot saline irrigation have a significantly better effect size compared to topical tranexamic acid.

**Intraoperative blood loss**

The results of the analysis show that the use of hot saline irrigation as a method to control intraoperative blood loss is significantly better than placebo, with a standardized mean difference (SMD) of -7.55 and a 95% confidence interval ranging from -11.45 to -3.66. However, there is high heterogeneity among the studies included in the analysis of hot saline irrigation ($\chi^2 = 124.05$, df = 2, I² = 98%), which necessitates the use of a random effect method.

Furthermore, the overall analysis of tranexamic acid also indicates high heterogeneity among the studies included in the analysis of hot saline irrigation ($\chi^2 = 124.05$, df = 2, I² = 98%), which necessitates the use of a random effect method. The Test for overall effect shows a non-significant standardized mean difference (SMD) of -0.70 with a 95% confidence interval ranging from -1.40 to 0.02.
Table 1. Characteristics of the studies included in the review

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample number</th>
<th>Route of administration</th>
<th>Comparison protocol</th>
<th>Outcomes</th>
</tr>
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<tbody>
<tr>
<td>Jabalameli et al., 2006</td>
<td>56</td>
<td>Topical</td>
<td>Tranexamic acid (1000 mg diluted in 20 ml normal saline) vs. saline</td>
<td>Intraoperative blood loss Boezaart surgical field score</td>
</tr>
<tr>
<td>Athanasiadis et al., 2007</td>
<td>20</td>
<td>Topical</td>
<td>Tranexamic acid 100 mg vs. saline</td>
<td>Boezaart surgical field score</td>
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<tr>
<td>Alimian et al., 2011</td>
<td>84</td>
<td>Intravenous</td>
<td>Tranexamic acid 10 mg/kg of IV bolus vs. saline</td>
<td>Intraoperative blood loss Boezaart surgical field score</td>
</tr>
<tr>
<td>Langille et al., 2013</td>
<td>28</td>
<td>Intravenous</td>
<td>Tranexamic acid bolus (15mg/kg) followed by infusion (1mg/kg/hr) vs. saline</td>
<td>Intraoperative blood loss Wormald intraoperative Boezaart surgical field score Duration of surgery</td>
</tr>
<tr>
<td>Gan et al., 2014</td>
<td>62</td>
<td>Topical</td>
<td>Hot saline irrigation (49°C) vs. saline</td>
<td>Intraoperative blood loss Boezaart surgical field score Duration of surgery</td>
</tr>
<tr>
<td>Shehata et al., 2014</td>
<td>50</td>
<td>Topical</td>
<td>Tranexamic acid (1000 mg diluted in 20 ml normal saline) vs. warm saline (50°C) vs. saline</td>
<td>Boezaart surgical field score Intraoperative blood loss Duration of surgery</td>
</tr>
<tr>
<td>Jahansahi et al., 2014</td>
<td>60</td>
<td>Topical</td>
<td>Three pledgets soaked with tranexamic acid 5% and phenylephrine 0.5% for 10 minutes in each nasal cavity vs. saline</td>
<td>Boezaart surgical field score Intraoperative blood loss Duration of surgery</td>
</tr>
<tr>
<td>El Shal et al., 2014</td>
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<td>Tranexamic acid (10 mg/kg diluted in 100 ml saline) vs. saline</td>
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<td>Tranexamic acid (Single bolus dose, 15 mg/kg) vs saline</td>
<td>Intraoperative blood loss</td>
</tr>
<tr>
<td>Al-issis et al., 2016</td>
<td>100</td>
<td>Topical</td>
<td>Hot saline irrigation (48°C) vs. saline</td>
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</tr>
<tr>
<td>Dongare et al., 2017</td>
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<td>Single slow bolus dose of tranexamic acid 15 mg/kg intravenously vs. saline</td>
<td>Intraoperative blood loss Boezaart surgical field score</td>
</tr>
<tr>
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<td>30</td>
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<td>Intravenous and topical</td>
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<tr>
<td>Yang et al., 2021</td>
<td>60</td>
<td>Intravenous</td>
<td>Tranexamic acid 15 mg/kg dose vs. saline</td>
<td>Duration of surgery</td>
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</table>

interval ranging from -1.44 to -0.03, and a p-value of 0.06, for the duration of surgery outcome when hot saline irrigation is used as a method to control bleeding, compared to placebo (Figure 6).

Similarly, the overall analysis of tranexamic acid also indicates high heterogeneity among the studies ($\chi^2 = 99.47$, df = 9, I² = 91%), warranting the use of a random effect method. The Test for overall effect shows a significant SMD of -0.97 with a 95% confidence interval ranging from -1.53 to -0.42, and a p-value of 0.0006, for tranexamic acid overall, indicating a significant effect in reducing duration of surgery compared to placebo. However, when comparing topical tranexamic acid (SMD = -0.93, 95% CI [-2.13, -0.26], p = 0.13) and hot saline irrigation, both show nonsignificant results for duration of surgery outcome compared to placebo (Figure 7), with a slightly better effect size observed for topical tranexamic acid. On the other hand, intravenous tranexamic acid (SMD = -0.99, 95% CI [-1.65, -0.32], p = 0.004) shows significant effectiveness in reducing duration of surgery compared to placebo. Sensitivity analysis repeated the meta-analysis, omitting different studies each time, to assess the differences in the combined estimates. All results match the above results.

**DISCUSSION**

The results of this meta-analysis indicate that the use of hot saline irrigation and topical tranexamic acid as bleeding control methods in FESS can minimize bleeding, resulting in improved surgical field visibility assessed by the Boezaart score compared to the placebo group. The analysis showed significant results in both groups. The standardized mean difference in effect size between the
Topical tranexamic acid group and the hot saline irrigation group favored the use of topical tranexamic acid. Tranexamic acid is a hydrophilic drug belonging to the anti-fibrinolytic group, which competitively antagonizes lysine on plasminogen, inhibiting plasminogen activators. Tranexamic acid inhibits fibrinolysis, thereby promoting better blood clot formation and minimizing bleeding. However, the potential side effect of tranexamic acid use is the risk of deep vein thrombosis. A study conducted in Iran in 2014 comparing topical tranexamic acid use with no tranexamic acid use in FESS showed improved surgical field visibility, especially in the first 30 minutes, and reduced total bleeding volume in the tranexamic acid group.

Tranexamic acid can be administered topically or parenterally. Subgroup analysis of intravenous tranexamic acid administration was also conducted in this meta-analysis, with four articles included. The results showed that the intravenous tranexamic acid group had better outcomes compared to the topical tranexamic acid group and the hot saline irrigation group.

The results of the analysis on intraoperative blood loss outcome showed that the group treated with topical tranexamic acid had slightly better outcomes compared to the group treated with hot saline irrigation, although both groups were significantly better than the placebo group. Interestingly, in this study, the topical tranexamic acid group outperformed the intravenous tranexamic acid group. Several studies have reported the effectiveness of topical tranexamic acid in various surgeries, not limited to FESS. Other types of surgeries that have been studied include total knee arthroplasty, rhinoplasty, and even the use of topical tranexamic acid as an enema to stop rectal bleeding.

The mechanism of action of topical tranexamic acid is believed to involve inhibiting tissue plasminogen activators. The tissue plasminogen activator enzyme converts plasminogen into plasmin, which promotes fibrinolysis and activates the fibrinolytic system. This fibrinolytic response occurs until the early postoperative phase. Tranexamic acid is known to inhibit tissue plasminogen activators, thereby preventing fibrinolysis,

### Table 2. Characteristics of studies.

<table>
<thead>
<tr>
<th>No</th>
<th>Study</th>
<th>Year</th>
<th>Sex</th>
<th>Male n (%)</th>
<th>Female n (%)</th>
<th>Total sample n (%)</th>
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<tr>
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<td>2.</td>
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<td>2007</td>
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<td>20 1.98</td>
<td></td>
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<tr>
<td>3.</td>
<td>Alimian et al.,14</td>
<td>2011</td>
<td></td>
<td>49 58.33</td>
<td>35 41.67</td>
<td>84 8.31</td>
</tr>
<tr>
<td>4.</td>
<td>Langille et al.,15</td>
<td>2013</td>
<td></td>
<td>17 60.71</td>
<td>11 39.29</td>
<td>28 2.77</td>
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<tr>
<td>5.</td>
<td>Gan et al.,16</td>
<td>2014</td>
<td></td>
<td>38 61.29</td>
<td>24 38.71</td>
<td>62 6.13</td>
</tr>
<tr>
<td>6.</td>
<td>Shehata et al.,17</td>
<td>2014</td>
<td></td>
<td>45 60.00</td>
<td>30 40.00</td>
<td>75 7.42</td>
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<tr>
<td>7.</td>
<td>Jahansahi et al.,18</td>
<td>2014</td>
<td></td>
<td>36 60.00</td>
<td>24 40.00</td>
<td>60 5.93</td>
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<tr>
<td>8.</td>
<td>El Shal et al.,19</td>
<td>2014</td>
<td></td>
<td>45 75.00</td>
<td>15 25.00</td>
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<td>9.</td>
<td>Nahi et al.,16</td>
<td>2015</td>
<td></td>
<td>50 52.94</td>
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<td>2016</td>
<td></td>
<td>54 54.00</td>
<td>46 46.00</td>
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<td>11.</td>
<td>Dongare et al.,20</td>
<td>2017</td>
<td></td>
<td>28 46.67</td>
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<td>12.</td>
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<td>13.</td>
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<td>2019</td>
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<td>37 66.07</td>
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<td>14.</td>
<td>El-Ozairy et al.,23</td>
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<td>15.</td>
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<td>2021</td>
<td></td>
<td>28 46.67</td>
<td>32 53.33</td>
<td>60 5.93</td>
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<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td>553 54.70</td>
<td>408 40.36</td>
<td>1011 100</td>
</tr>
</tbody>
</table>

### Figures

**Figure 2.** Forest plot of the efficacy of hot saline irrigation as a bleeding control method compared to placebo based on Boezaart surgical field score.

**Figure 3.** Forest plot of the efficacy of tranexamic acid as a bleeding control method compared to placebo based on Boezaart surgical field score.

**Figure 4.** Forest plot of the efficacy of hot saline irrigation as a bleeding control method compared to control based on intraoperative blood loss in FESS.
The histopathological effects of hot saline irrigation were observed in a temperature range of 40-60°C in the study. The results showed that temperatures between 40-46°C did not cause mucosal changes, while temperatures above 46°C caused vasodilation and mucosal swelling. Drastic changes, such as epithelial necrosis, were observed at temperatures above 52°C.7

Another advantage of hot saline irrigation is that it allows for cleaning of endoscope lenses from steam and debris.7

The duration of surgery outcome showed significantly different results compared to previous outcomes. Both the hot saline irrigation group and the topical tranexamic acid group did not show significant results. However, the intravenous tranexamic acid group continued to show significant results, with a faster duration of surgery in this group. Non-significant results in duration of surgery can be influenced by various factors, including not only bleeding but also factors related to the operating room environment, supporting instruments, non-uniform patient conditions, and the surgeon's technique and experience. Good surgical technique plays an important role in controlling the course of surgery and minimizing complications, especially bleeding.26-30 A good technique can prevent unintended mucosal damage. Precise strategies for endoscope placement, instrument selection, and control are crucial factors in bloodless surgery with endoscopic functional sinus surgery. Proper instrument selection, such as a suction cannula with an atraumatic tip, can prevent unnecessary mucosal damage. The use of sharp cutting instruments can also avoid unnecessary mucosal stripping. The operator's speed and precision during tissue debulking of inflammation will minimize bleeding.27,29

This systematic review has the following limitations namely the regimen or dosage of the drug is not fixed; this also improved the heterogeneity of the results. It is believed that all of these factors have the ability to change the efficacy of tranexamic acid during sinus surgeries. Only fifteen RCTs were selected in our meta-analysis; if more studies were included, statistical efficacy would increase. Risk of bias cannot be avoided in this meta-analysis because...
only English and Indonesian publications were included.

CONCLUSION
This meta-analysis showed that the administration of tranexamic acid or hot saline irrigation could significantly reduce duration of surgery, blood loss intraoperatively and improved surgical field quality compared with room temperature saline irrigation. There is no statistically significant difference between tranexamic acid topical and hot saline irrigation. Larger RCTs studies are required to confirm the results of this study. More head to head RCTs comparison between tranexamic acid and hot saline irrigation are needed to get better results.

CONFLICT OF INTEREST
There have been no competing interests regarding this manuscript.

FUNDING
The authors declared that no financial support or funding was obtained for this study.

ETHICAL STATEMENT
This manuscript has followed Committee on Publication Ethics (COPE) and International Committee of Medical Journal Editors (ICMJE) guidelines regarding publication ethics.

AUTHOR CONTRIBUTION
Design, intelligent content description, literature quest, data collection, data processing, manuscript writing, manuscript editing, and manuscript review are contributed by all authors. The corresponding author is the guarantor and constructs the concept of the manuscript.

REFERENCES