Does Oral or Topical Tranexamic Acid Control Bleeding From Epistaxis?

TAKE-HOME MESSAGE

Compared with usual care, either oral or topical tranexamic acid reduces the risk of rebleeding within 7 to 10 days among adults with epistaxis. A higher proportion of patients demonstrate bleeding cessation within 10 minutes with topical tranexamic acid compared with other topical hemostatic agents.

METHODS

DATA SOURCES

An information specialist searched the Cochrane ENT Register, the Cochrane Central Register of Controlled Trials, PubMed, Ovid EMBASE, the Cumulative Index of Nursing and Allied Health, Web of Science, ClinicalTrials.gov, http://www.who.int/ictrp, and the gray literature with Google Scholar. The Cochrane review authors then evaluated reference lists of identified publications.

STUDY SELECTION

Two authors independently assessed studies for relevance and resolved disagreements through consensus. Investigators included randomized controlled trials of children or adults with epistaxis who received tranexamic acid plus standard of care compared with placebo or a different hemostatic agent plus standard of care.

DATA EXTRACTION AND SYNTHESIS

Two investigators independently extracted data from included studies. The primary outcomes included epistaxis control, as

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Results

Effect of tranexamic acid for patients with epistaxis.

Outcome	No. of Studies (Patients)	Comparator to TXA	RR (95% CI)	Evidence Quality (GRADE)	Heterogeneity (I^2), %
Hemostasis in <10 min (topical only)	3 (460)	Other hemostatic agents	2.35 (1.90–2.92)	Moderate	0
Rebleeding within 7–10 days (topical or oral)	3 (225)	Placebo	0.71 (0.56–0.94)	Moderate	0

TXA, Tranexamic acid; *RR*, relative risk; *CI*, confidence interval; *GRADE*, Grading of Recommendations Assessment, Development and Evaluation.

defined by the number of patients who experienced rebleeding within 5 to 10 days, and significant adverse effects (eg, thromboembolic events, seizures). Secondary outcomes included time to stop initial epistaxis, as defined by proportions of patients whose bleeding was controlled within a 30-minute timeframe; rebleeding severity within 10 days, as measured by proportions of patients needing additional hemostasis interventions or blood product transfusion; length of hospital stay; and other adverse effects not otherwise specified. Using the Mantel-Haenszel method, authors calculated pooled risk ratios for binary events and mean differences with SDs for continuous outcomes. They assessed heterogeneity with the I^2 statistic. Two authors assessed risk of bias based on the *Cochrane Handbook for Systemic Reviews of Interventions*[1] and used the Grading of Recommendations Assessment, Development and Evaluation criteria to assess evidence quality. Authors conducted subgroup analyses of mode and timing of administration, patient age (adult versus child), setting (outpatient versus inpatient), and site of epistaxis (anterior versus posterior). Authors planned to conduct sensitivity analysis for effect of chosen model and risk of bias of included studies.

Authors included 6 randomized controlled trials comprising 692 patients from an initial 680 references. Trial sample sizes ranged from 168 to 216 patients. Three trials were placebo-controlled, double-blinded, randomized controlled trials; 2 were nonplacebo-controlled, single-blinded, randomized controlled trials; and 1 was a double-blinded, nonplacebo-controlled, randomized controlled trial. Two trials included inpatients and 4 included outpatients. Randomized controlled trials used different administration methods for topical tranexamic acid: oral topical tranexamic acid received 3 times daily for 10 days (both inpatient studies), 15 mL of 10% topical tranexamic acid gel (1 trial), a cotton pledget soaked in 15 mL of injectable topical tranexamic acid (2 trials), or a cotton ball soaked with 1 mL of topical tranexamic acid (500 mg in 5 mL) injectable solution (1 trial). Randomized controlled trials differed in their definition of usual care. Moderate-quality evidence suggested that oral or topical tranexamic acid is effective at reducing risk of rebleeding within 7 to 10 days compared with placebo, and that topical tranexamic acid is associated with greater bleeding control within 10 minutes compared with other hemostatic agents (Table). A single trial with low-quality evidence demonstrated no difference in the proportion of patients with hemostasis at 30 minutes with topical tranexamic acid versus placebo. Five randomized controlled trials reported no differences in regard to adverse events between topical tranexamic acid groups versus control groups. No randomized controlled trial reported the need for further intervention, and a single trial with low-quality evidence found no difference in blood transfusion requirements between patients receiving oral topical tranexamic acid versus placebo. Heterogeneity was elevated in length of hospital stay, necessitating omission of analysis in the final review. The overall risk of bias in the included randomized controlled trials was low, with high risk of bias in 2 trials because of absence of blinding. Subgroup analysis did not display a difference in oral versus topical tranexamic acid.

Commentary

Epistaxis affects 60% of people during the course of their lifetime.[2] Although 70% to 80% of cases are idiopathic, there are a variety of other causes such as trauma and coagulopathies.[3] There are a number of interventions for epistaxis such as topical oxymetazoline, cautery, or packing, and recent literature suggests topical tranexamic acid may be efficacious.[4] Topical tranexamic acid is an antifibrinolytic agent that inhibits plasminogen activation.[5] Tranexamic acid has demonstrated utility in a variety of hemorrhagic conditions, including traumatic hemorrhage, postadenoidectomy, and endoscopic sinus surgery.[5-7]

Since 1995, 3 randomized controlled trials have evaluated topical tranexamic acid for epistaxis, with notable changes in cauterization and packing techniques.[4] A previous systematic review assessed the evidence for the use and safety profile of topical tranexamic acid in epistaxis and suggested benefit for the drug.[4] This current meta-analysis sought to examine the efficacy of topical tranexamic acid in controlling epistaxis, finding that in 7 to 10 days, patients administered oral or topical tranexamic acid had fewer episodes of rebleeding compared with those administered usual care, and patients administered topical tranexamic acid compared with other hemostatic agents had greater chance of bleeding control within 10 minutes. Adverse effects did not differ in patients receiving

topical tranexamic acid compared with usual care.[4]

Limitations of this Cochrane review include differences in usual care and topical tranexamic acid administration among included trials, hindering data comparison and increasing heterogeneity. Control groups in both trials by Zahed et al[2,8] received packing compared with the intervention group, who may or may not have received packing according to provider preference, making it difficult to isolate effect size difference to the use of topical tranexamic acid alone. In randomized controlled trials evaluating oral topical tranexamic acid, one trial used packing for the control group, whereas another used packing or cautery.[9,10] Meta-analysis authors could make only an indirect comparison between oral and topical tranexamic acid, using 2 older randomized controlled trials for oral topical tranexamic acid and 1 underpowered randomized controlled trial, respectively.[9-11] Thus, it is difficult to establish whether oral and topical tranexamic acid have a similar effect on rebleeding in epistaxis. Subgroup analyses were limited because of the available data. Newer trials incorporating modern usual care techniques compared with topical tranexamic acid may render different results.

According to these results, patients with epistaxis who receive tranexamic acid have greater rates of bleeding control (with topical tranexamic acid) and decreased rates of rebleeding (with oral or topical tranexamic acid). Further randomized controlled trial data are required to inform topical tranexamic acid efficacy and quantify potential reduction in recurrence of epistaxis and further complications. Studies directly comparing topical tranexamic acid, oral topical tranexamic acid, and clearly defined standard of care are also needed.

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