Topical tranexamic acid for spontaneous epistaxis

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Abstract

Introduction

Spontaneous epistaxis is one of the most frequent problems in emergency services. New treatment alternatives have emerged, including topical tranexamic acid. However, there is controversy about the actual efficacy of this alternative..

Methods

We searched in Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We extracted data from the systematic reviews, reanalyzed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach.

Results and conclusions

We identified five systematic reviews that analyzed only one primary study, corresponding to a randomized trial. We concluded it is not clear whether topical tranexamic acid has any impact on hemostasis or risk of rebleeding because the certainty of the evidence is very low. On the other hand, its use could increase adverse effects.

Problem

Epistaxis is one of the most frequent problems in emergency services. It can result in significant blood loss, particularly in anticoagulant treatment users or in people with comorbidities[1]. The most common approach is cauterization of the bleeding vessel. When the bleeding site is not visible, nasal plugs are used, but they generate discomfort[2], so new therapeutic alternatives are actively sought.

Among many potential treatments for this condition, is tranexamic acid, an antifibrinolytic agent which has proven effective in reducing bleeding in different surgeries, trauma and non-surgical diseases[1,3]. However, the efficacy and safety of topical tranexamic acid in spontaneous epistaxis is unclear

Key messages

- It is not clear whether the use of topical tranexamic acid impacts hemostasis or rebleeding because the certainty of the evidence is very low.
- The use of tranexamic acid could increase adverse effects, but the certainty of the evidence is low.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found five systematic reviews[1,3,4,5,6], which included only one primary study that answered the question of interest[2], corresponding to a randomized trial. This table and the summary in general are based on this trial[2].
What types of patients were included*	The trial[2] included patients aged 18 years or older, with spontaneous epistaxis, coming from both upper, posterior and/or Kiesselbach area of the nasal septum. Patients with a fracture of the skull or nose and perforation of the nasal septum were excluded, as well as patients with a history of hemostasis alteration.
What types of interventions were included*	The trial[2] compared the use of 10% tranexamic acid gel (15 ml) against a glycine gel. After the application, both groups received a piece of cotton that they had to keep for 30 minutes in the nostril.
What types of outcomes were measured	The trial reported multiple outcomes, which were presented by the different systematic reviews as follows: • Severity of epistaxis • Bleeding frequency • Duration of hospitalization • Safety The follow-up of the trial was 10 days.

* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information, we generated a structured summary denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos) using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies when it is possible, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Summary of Findings

The information on the effects of topical tranexamic acid is based on only one randomized trial that included 68 patients[2].

The trial reported hemostasis at 30 minutes (68 patients), rebleeding at 10 days (47 patients) and adverse effects (68 patients).

The summary of findings is the following:

- It is not clear whether the use of topical tranexamic acid impacts haemostasis because the certainty of the evidence is very low.
- It is not clear whether the use of topical tranexamic acid decreases rebleeding because the certainty of the evidence is very low.
- The use of tranexamic acid might increase adverse effects, but the certainty of the evidence is low.

Tranexamic acid for spontaneous epistaxis

Patients Spontaneous epistaxis
Intervention Tranexamic acid (gel)
Comparison Placebo (glycine in gel)

Outcome	Absolute effect*		Relative effect (95% CI)	Certainty of evidence (GRADE)
	WITHOUT tranexamic acid	WITH tranexamic acid		
	Difference: patients per 1000			
Hemostasis at 30 minutes	763 per 1000	603 per 1000	RR 0.79 (0.56 to 1.11)	⨁◯◯◯[1,2] Very low
	Difference: 160 less (Margin of error: 336 less to 84 more)			
Rebleeding at 10 days**	655 per 1000	446 per 1000	RR 0.68 (0.38 to 1.21)	⨁◯◯◯[1,2] Very low
	Difference: 209 less (Margin of error: 406 less to 138 more)			
Adverse effects***	79 per 1000	100 per 1000	RR 1.27 (0.28 to 5.83)	⨁⨁◯◯[2,3] Low
	Difference: 21 more (Margin of error: 57 less to 381 more)			

Margin of error: 95% confidence interval (CI).
RR: Risk ratio.
GRADE: Evidence grades of the GRADE Working Group (see later).

*The risk WITHOUT tranexamic acid is based on the risk in the control group of the trials. The risk WITH tranexamic acid (and its margin of error) is calculated from relative effect (and its margin of error).

** Frequency of patients who having achieved hemostasis at 30 minutes, had rebleeding in the next 10 days.
*** Mainly bad taste.

[1] The certainty of the evidence was downgraded in one level for risk of bias, since the trial did not clearly report most of the aspects needed to determine the presence of bias (randomization sequence generation and concealment, blinding of assessors, completeness of follow-up, completeness of report).
[2] The certainty of the evidence was downgraded in one level for imprecision because the decisions that would be made at the extremes of the confidence interval vary substantively.
[3] We decided not to downgrade for risk of bias, since its hypothetical absence would reinforce the conclusion of increased adverse effects.

Follow the link to access the interactive version of this table (Interactive Summary of Findings – iSoF)

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕
High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕◯
Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate.

⊕⊕◯◯
Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕◯◯◯
Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

* This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision

Other considerations for decision-making

To whom this evidence does and does not apply

The evidence presented in this summary applies to adults with spontaneous epistaxis, without signs of nasal or skull fracture, perforation of the nasal septum or a history of altered hemostasis. The bleeding could come from upper, posterior or Kiesselbach area of the nasal septum.

About the outcomes included in this summary

The outcomes presented in the summary of findings table are those considered critical for decision-making by the authors of this summary, and in general coincide with those selected by main systematic reviews identified.

Balance between benefits and risks, and certainty of the evidence

It is difficult to make a balance between the risks and benefits of tranexamic acid for epistaxis due to the high level of uncertainty. Although they might increase the adverse effects, these were mild and with questionable clinical relevance.

Resource considerations

The cost of tranexamic acid is relatively high. However, it is difficult to make a balance between costs and benefits due to the uncertainty about the latter.

What would patients and their doctors think about this intervention

Variability in the decision-making regarding this intervention can be expected. Patients and clinicians who place more value on an uncertain benefit could lean in favor of its use. Those who put more value on the certainty of the evidence, the costs or the adverse effects, are likely to lean against it.

However, most clinicians should lean against the use of this intervention, as it is an alternative of uncertain benefit and relatively high cost.

Differences between this summary and other sources

This summary presents information concordant with the five included systematic reviews, because they conclude it cannot be established if this intervention is effective and safe, due to the limitations of the existing evidence.

No relevant international guidelines addressing this question were identified.

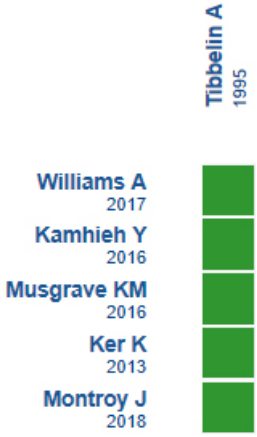
Could this evidence change in the future?

The probability that future evidence changes the conclusions of this summary is high due to the existing uncertainty.

We identified one ongoing systematic review[7] in the International Prospective Register of Systematic Registries (PROSPERO) and one ongoing trial[8] in the International Clinical Trials Registry Platform of the World Health Organization, which could provide additional relevant information regarding the efficacy of topical tranexamic acid for the management of spontaneous epistaxis.

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



An evidence matrix is a table that compares systematic reviews that answer the same question.
Rows represent systematic reviews, and columns show primary studies.
The boxes in green correspond to studies included in the respective revisions.
The system automatically detects new systematic reviews including any of the primary studies in the matrix, which will be added if they actually answer the same question.

Follow the link to access the **interactive version:** Acupuncture for Parkinson's disease

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier.

After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

This article is part of the Epistemonikos Evidence Synthesis project. It is elaborated with a pre-established methodology, following rigorous methodological standards and internal peer review process. Each of these articles corresponds to a summary, denominated FRISBEE (Friendly Summary of Body of Evidence using Epistemonikos), whose main objective is to synthesize the body of evidence for a specific question, with a friendly format to clinical professionals. Its main resources are based on the evidence matrix of Epistemonikos and analysis of results using GRADE methodology. Further details of the methods for developing this FRISBEE are described here (http://dx.doi.org/10.5867/medwave.2014.06.5997)

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database

www.epistemonikos.org.

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