

## Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

Medwave 2015;15(Suppl 3):e6330 doi: 10.5867/medwave.2015.6330

### Is tranexamic acid effective for acute upper gastrointestinal bleeding?

**Authors:** Sebastián Flores[1,3], Carolina Avilés[1,3], Gabriel Rada[2,3,4,5,6]

#### Affiliation:

[1] Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[2] Departamento de Medicina Interna, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[3] Proyecto Epistemonikos, Santiago, Chile

[4] Programa de Salud Basada en Evidencia, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[5] GRADE working group

[6] The Cochrane Collaboration

**Citation:** Flores S, Avilés C, Rada G. Is tranexamic acid effective for acute upper gastrointestinal bleeding?. *Medwave* 2015;15(Suppl 3):e6330 doi: 10.5867/medwave.2015.6330

**Publication date:** 4/12/2015

#### Abstract

Upper gastrointestinal bleeding constitutes a medical-surgical emergency given its important associated morbidity and mortality. The antifibrinolytic tranexamic acid might help stopping bleeding, but controversy remains about its role in this setting. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified five systematic reviews including eight randomized trials. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded tranexamic acid probably decreases rebleeding and mortality, without increasing thromboembolic adverse effects in patients with upper gastrointestinal bleeding.

#### Problem

Acute upper gastrointestinal bleeding is a common condition in emergency departments and critical care units. Most cases are self-limited, but there is a percentage of patients close to 30% in which bleeding persists or recurs, leading to high morbidity and mortality [1].

Tranexamic acid, an antifibrinolytic that reduces fibrin degradation assisting in the formation of blood clot, has been postulated among treatment options. This drug has proven effectiveness in trauma patients, but its role in upper gastrointestinal bleeding is not yet clearly defined.

#### Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary 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, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

#### Key messages

- Tranexamic acid probably decreases bleeding and mortality from upper gastrointestinal bleeding without increasing the risk of thromboembolic side effects.
- Risk/benefit and cost/benefit of use of tranexamic acid are probably favorable.
- An ongoing study of high methodological quality and big sample size will provide valuable information to increase the certainty of the evidence.

## About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found five systematic reviews [2],[3],[4],[5],[6] that consider 11 primary studies reported in 13 references [7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19], including eight randomized controlled trials [7],[8],[9],[10],[11],[13],[14],[19]. This table and the summary in general are based on the latter.
What types of patients were included	In six studies, the average age exceeded 50 years [7],[8],[9],[13],[14],[19]. The remaining two studies did not report the age of the patients [10],[11] Confirmation of gastrointestinal bleeding was performed using medical records in one study [14], through the presence of hematemesis or melena in four studies [8],[9],[10],[11], with upper gastrointestinal endoscopy in two studies [7],[19], and one study did not report this aspect[13]. Regarding severity, two studies included patients with massive gastrointestinal bleeding and unstable hemodynamics [9],[13], one study included severe upper gastrointestinal bleeding [7], and the remaining five studies did not report severity [8],[10],[11],[14],[19].
What types of interventions were included	Three studies administered tranexamic acid orally [9],[11],[14], while the other five studies used it orally or intravenously. One study used tranexamic acid for less than three days[9], two studies between 3 and 4 days [7],[14] and five studies for over 5 days to a maximum of 7 days [8],[10],[11],[13],[19]. All studies compared against placebo or standard treatment.
What types of outcomes were measured	Different systematic reviews reported meta-analysis for the following outcomes: Mortality, rebleeding, need for surgery, required transfusions, adverse events (acute myocardial infarction, pulmonary embolism, stroke, deep vein thrombosis).

## Summary of findings

Information on the effects of tranexamic acid in upper gastrointestinal bleeding is based on eight randomized controlled studies involving 1701 patients [7],[8],[9],[10],[11],[12],[13],[14],[19]. All studies provided information on mortality, and seven studies provided information on risk of rebleeding [7],[8],[10],[11],[13],[14],[19].

- Tranexamic acid probably reduces mortality in upper gastrointestinal bleeding. The certainty of the evidence is moderate.
- Tranexamic acid probably reduces rebleeding in upper gastrointestinal bleeding. The certainty of the evidence is moderate.
- Tranexamic acid probably does not increase the risk of thromboembolic serious adverse effects. The certainty of the evidence is moderate.

Tranexamic acid in upper gastrointestinal bleeding				
Patients	Patients visiting an emergency department with acute upper gastrointestinal bleeding			
Intervention	Tranexamic acid orally or intravenously			
Comparison	Placebo			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITHOUT tranexamic acid	WITH tranexamic acid		
	Difference: patient per 1000			
Mortality	84 per 1000	50 per 1000	RR 0.60 (0.41 to 0.86)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 34 patients less per 1000 (Margin of error: 12 to 49 less)			
Rebleeding	176 per 1000	143 per 1000	RR 0.81 (0.66 to 1.01)	⊕⊕⊕○ <sup>1 2</sup> Moderate
	Difference: 33 patients less per 1000 (Margin of error: 60 less to 2 more)			
Ischemic-thrombotic adverse effects	The occurrence of thromboembolic serious adverse events such as myocardial infarction, stroke, pulmonary embolism or venous thrombosis was very low and was not different between groups.			⊕⊕⊕○ <sup>1</sup> Moderate
Margin of error = confidence interval 95%. RR: Relative Risk. GRADE: grade levels of evidence of the GRADE Working Group (see back page).				
* The risks <b>WITHOUT tranexamic acid</b> are based on the risk in the control group in the study. The risk <b>WITH tranexamic acid</b> (and its margin of error) is calculated from the relative effect (and its margin of error).				
1 The certainty of the evidence was downgraded in one level because of risk of bias, since most studies had losses to follow-up and other sources of attrition bias.				
2 While the confidence interval includes the possibility of a small effect or even no effect, we did not decrease the certainty of the evidence for imprecision because the point estimate is in the same direction than the point estimate for mortality, and these outcomes are causally connected (any effect on mortality should be caused by a lower incidence of bleeding).				

## 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

- This evidence applies to patients presenting to emergency services with upper gastrointestinal bleeding.
- Even though studies included patients older than 50 years in average, it is reasonable to extrapolate this evidence to younger patients, in whom a similar effect could be expected as there are no major morphological or physiological differences. The risk of adverse effects, if they exist, would be less in the latter since they have a lower baseline risk.
- Studies included patients with severe upper gastrointestinal bleeding, but since there were no major differences with less severe bleeding, it is reasonable to extrapolate the results from this group, although the expected benefit would be lower.

### About the outcomes included in this summary

- We selected mortality, rebleeding and thromboembolic adverse events for inclusion in the summary of findings table, as these constitute outcomes critical for decision-making in the opinion of the authors of this summary. This coincides with the outcomes cited in systematic reviews and major guidelines.

### Balance between benefits and risks, and certainty of the evidence

- The risk of serious adverse events was very low in the studies evaluated in this summary, which is consistent with that observed in multiple studies in other areas [20]. Tranexamic acid may produce nausea, vomiting, anorexia, hypertension, dizziness and diarrhea in some patients.
- While the certainty of the evidence is moderate, the benefits of this intervention on the main outcomes make the balance probably favorable to its use.

### Resource considerations

- The cost of tranexamic acid is relatively low. By contrasting it with the observed benefit makes it probably cost-effective.

### Differences between this summary and other sources

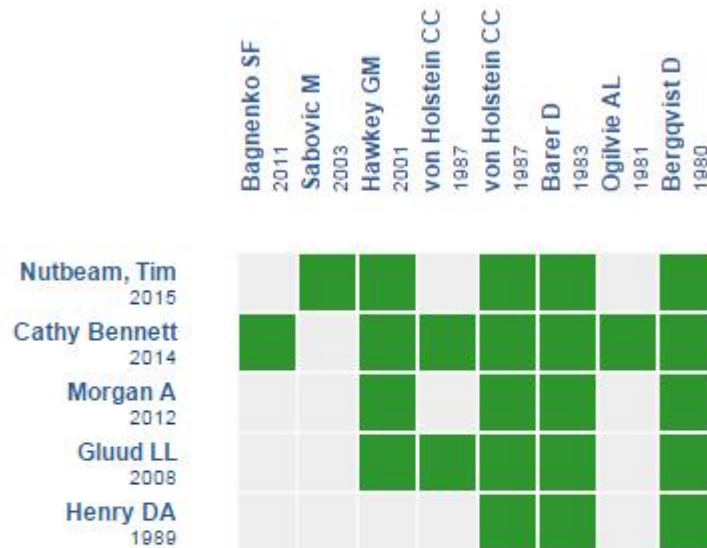
- The findings of our summary are consistent with the conclusion of the systematic reviews identified, although some of them present a more cautious conclusion about the certainty of the evidence.
- Our conclusions differ with the main guidelines; the guideline of the American College of Gastroenterology [21] on peptic ulcer bleeding does not mention the use of tranexamic acid, and the guideline on management of non-variceal bleeding from the European Society of Gastrointestinal Endoscopy does not recommend it, because of the low certainty of the evidence [22].

### Could this evidence change in the future?

- The probability that future evidence change the findings of this summary is low because of the certainty of the evidence.
- The evidence on the benefits of this intervention in similar pathophysiological situations has not changed with the accumulation of new evidence [20].
- The certainty of the evidence will surely increase with data from the HALT-IT study, which is ongoing and expects to incorporate nearly five times more patients than all previous studies combined [23].

## 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.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Tranexamic acid for upper gastrointestinal bleeding](#)

## 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.

The details about the methods used to produce these summaries 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](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

## Conflicts of interest

The authors do not have relevant interests to declare.

## References

1. Hearnshaw SA, Logan RF, Lowe D, Travis SP, Murphy MF, Palmer KR. Acute upper gastrointestinal bleeding in the UK: patient characteristics, diagnoses and outcomes in the 2007 UK audit. *Gut*. 2011 Oct;60(10):1327-35. | [CrossRef](#) | [PubMed](#) |
2. Bennett C, Klingenberg SL, Langholz E, Glud LL. Tranexamic acid for upper gastrointestinal bleeding. *Cochrane Database Syst Rev*. 2014 Nov 21;11:CD006640. | [CrossRef](#) | [PubMed](#) |
3. Glud LL, Klingenberg SL, Langholz SE. Systematic review: tranexamic acid for upper gastrointestinal



- bleeding. *Aliment Pharmacol Ther.* 2008 May;27(9):752-8. | [CrossRef](#) | [PubMed](#) |
4. Henry DA, O'Connell DL. Effects of fibrinolytic inhibitors on mortality from upper gastrointestinal haemorrhage. *BMJ.* 1989 Apr 29;298(6681):1142-6 | [PubMed](#) |
  5. Morgan A, Jeffrey-Smith A. BET 1: should tranexamic acid be given to patients who are having an upper gastrointestinal bleed? *Emerg Med J.* 2012 Sep;29(9):773-7. | [CrossRef](#) | [PubMed](#) |
  6. Nutbeam T. In adult patients presenting as emergencies with upper gastrointestinal bleeding, does tranexamic acid decrease mortality? *African Journal of Emergency Medicine.* 2015 2015;5(2):85-92. | [CrossRef](#) |
  7. Bagnenko SF, Verbitskiĭ VG. [Antifibrinolytic therapy for the treatment of massive ulcerative gastro-intestinal bleedings]. *Khirurgiia (Mosk).* 2011;(4):42-6. | [PubMed](#) |
  8. Barer D, Ogilvie A, Henry D, Dronfield M, Coggon D, French S, et al. Cimetidine and tranexamic acid in the treatment of acute upper-gastrointestinal-tract bleeding. *N Engl J Med.* 1983 Jun 30;308(26):1571-5. | [PubMed](#) |
  9. Bergqvist D, Dahlgren S, Hessman Y. Local inhibition of the fibrinolytic system in patients with massive upper gastrointestinal hemorrhage. *Ups J Med Sci.* 1980;85(2):173-8. | [PubMed](#) |
  10. Biggs JC, Hugh TB, Dodds AJ. Tranexamic acid and upper gastrointestinal haemorrhage--a double-blind trial. *Gut.* 1976 Sep;17(9):729-34. | [PubMed](#) |
  11. Cormack F, Chakrabarti RR, Jouhar AJ, Fearnley GR. Tranexamic acid in upper gastrointestinal haemorrhage. *Lancet.* 1973 Jun 2;1(7814):1207-8. | [PubMed](#) |
  12. Cronstedt J, Ostberg H, Carling L, Lööf L, Wennerholm M, Högberg N, Vogel A. Diagnosis and treatment of acute gastrointestinal haemorrhage in a small district hospital. *Acta Med Scand.* 1976;199(1-2):129-32. | [PubMed](#) |
  13. Engqvist A, Broström O, von Feilitzen F, Halldin M, Nyström B, Ost A, Reichard H, Sandqvist S, Törngren S, Wedlund JE. Tranexamic acid in massive haemorrhage from the upper gastrointestinal tract: a double-blind study. *Scand J Gastroenterol.* 1979;14(7):839-44. | [PubMed](#) |
  14. Hawkey GM, Cole AT, McIntyre AS, Long RG, Hawkey CJ. Drug treatments in upper gastrointestinal bleeding: value of endoscopic findings as surrogate end points. *Gut.* 2001 Sep;49(3):372-9. | [PubMed](#) |
  15. Ogilvie AL, Barer D, Dronfield MW. Trial of cimetidine, tranexamic acid and placebo in the management of acute upper gastrointestinal haemorrhage. *Gut.* 1981;22(10):f20-f.
  16. Ostberg HO, Ulfberg J, Wennerholm M, Zellner K. Acute gastrointestinal haemorrhage. Experience with early panendoscopy and tranexamic acid in a rural hospital. *Acta chirurgica Scandinavica.* 1977.
  17. Sabovic M, Lavre J, Vujkovic B. Tranexamic acid is beneficial as adjunctive therapy in treating major upper gastrointestinal bleeding in dialysis patients. *Nephrol Dial Transplant.* 2003 Jul;18(7):1388-91. | [PubMed](#) |
  18. von Holstein CC, Eriksson SB, Källén R. Tranexamic acid in gastric and duodenal bleeding. *Scand J Gastroenterol Suppl.* 1987;137:71-4. | [PubMed](#) |
  19. von Holstein CC, Eriksson SB, Källén R. Tranexamic acid as an aid to reducing blood transfusion requirements in gastric and duodenal bleeding. *Br Med J (Clin Res Ed).* 1987 Jan 3;294(6563):7-10. | [PubMed](#) |
  20. Ker K, Roberts I. Exploring redundant research into the effect of tranexamic acid on surgical bleeding: further analysis of a systematic review of randomised controlled trials. *BMJ Open.* 2015 Aug 24;5(8):e009460. | [CrossRef](#) | [PubMed](#) |
  21. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol.* 2012 Mar;107(3):345-60; quiz 361. | [CrossRef](#) | [PubMed](#) |
  22. Gralnek IM, Dumonceau JM, Kuipers EJ, Lanas A, Sanders DS, et al. Diagnosis and management of nonvariceal upper gastrointestinal hemorrhage: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy.* 2015 Oct;47(10):a1-a46. | [CrossRef](#) | [PubMed](#) |
  - Roberts I, Coats T, Edwards P, Gilmore I, Jairath V, Ker K, et al. HALT-IT--tranexamic acid for the treatment of gastrointestinal bleeding: study protocol for a randomised controlled trial. *Trials.* 2014 Nov 19;15:450. | [CrossRef](#) | [PubMed](#) |

#### Author address:

[1] Facultad de Medicina  
Pontificia Universidad Católica de Chile  
Lira 63  
Santiago Centro  
Chile



Esta obra de Medwave está bajo una licencia Creative Commons Atribución-No Comercial 3.0 Unported. Esta licencia permite el uso, distribución y reproducción del artículo en cualquier medio, siempre y cuando se otorgue el crédito correspondiente al autor del artículo y al medio en que se publica, en este caso, Medwave.