Tranexamic Acid (TXA) in Upper Gastrointestinal Bleeds – Systematic Review and Meta-analysis

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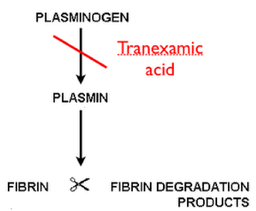
Background

- Tranexamic acid (TXA) is classified as an antifibrinolytic agent used to manage haemorrhage-related trauma.
- TXA has been applied medically in situations where patients face a potential for excessive bleeding. Physicians prescribe it to avert heavy menstrual bleeds during surgery, curb postpartum bleeding, and other situations. Recent studies have begun investigating further applications of TXA.
- The widespread hypothesis is that TXA has utility in upper gastrointestinal (GI) bleeds.



Objective

Does usage of TXA have a significant effect in management of upper GI bleeds?

Methods

A systematic review and meta-analysis. The investigation was conducted according to the Cochrane methodology and reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).

We retrieved 1572 articles from all databases and reference searches. After removing duplicates, 1443 articles were screened against the eligibility criteria.

Eligibility Criteria: RCT/CTs w/ subject involving patient w/ GI bleeds, receiving TXA intervention vs. placebo/control; outcomes involving mortality, rebleeding, adverse events, need for surgery, or need for blood transfusion.

Risk of Bias assessment was carried out by two authors to determine each study's quality and risk of bias. This was performed using the Cochrane Collaboration Risk of Bias tool.

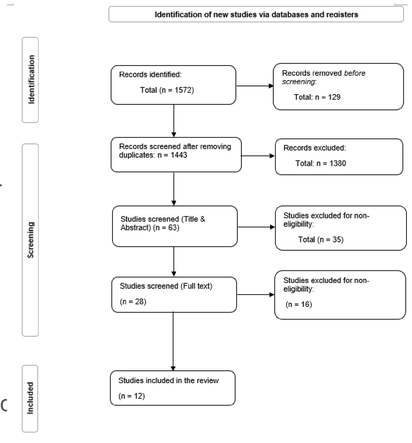
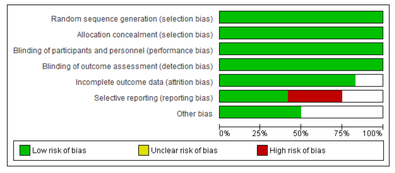


Figure 2: PRISMA flowchart depicting the selection of studies for this systematic review and meta-analysis.

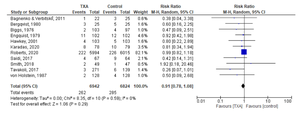
Results

AUTHOR	STUDY TYPE	(n)	CONTROL	INTERVENTION TYPE	ADMINISTRATION & DOSE	OUTCOMES	RESULTS	ADVERSE EVENTS
Biggs (1976)	RCT	103	97	TXA	1g IV stat then 1g PO QDS on day 1, then 1g QDS for 4 days	Mortality, Rebleeding, Need for surgery, Transfusion required	Mortality: 2/103 VS 4/96. Rebleeding: 7/103 VS 21/97. Need for surgery: 7/103 VS 21/97. Transfusion required: 77/103 VS 71/97	–
Bergqvist (1980)	RCT	25	25	TXA	2g PO 4 hourly for two days	Mortality, Need for surgery	Mortality: 3/25 VS 5/25. Need for surgery: 7/25 VS 7/25	–
Hawkey (2001)	RCT	103	103	TXA	2g PO bolus then 1g QDS for 4 days	Mortality, Rebleeding, Need for surgery, Transfusion required	Mortality: 4/103 VS 5/103. Rebleeding: 9/103 VS 10/103. Need for surgery: 5/103 VS 6/103. Transfusion required: 58/103 VS 60/103.	–
Roberts (2020)	RCT	5994	6015	TXA	1g IV stat then 3g infused over 24 hours	Mortality, Rebleeding, Need for surgery, Transfusion required	Mortality: 222/5994 VS 226/6015. Rebleeding: 287/5994 VS 315/6015. Need for surgery: 146/5994 VS 158/6015. Transfusion required: 4078/5994 VS 4129/6015	42/5994 VS 46/6015
Bagnenko & Verbitskii (2011)	RCT	22	25	TXA	10 mg IV/PO TDS for 3 days versus placebo	Mortality, Rebleeding, Need for surgery, Transfusion required	Mortality: 1/22 VS 3/25. Rebleeding: 2/22 VS 5/25. Need for surgery: 1/22 VS 3/25. Transfusion required: 14/22 VS 13/25	–
Tavakoli (2017)	RCT	271	139	TXA	1g administered every 6h (IV) in one group. AND 1g nasogastric tube followed by IV for 24 h	Mortality, Rebleeding, Need for surgery	Mortality: 3/271 VS 6/139. Rebleeding: 20/271 VS 13/139. Need for surgery: 7/271 VS 2/139	55/271 VS 3/139
Smith (2018)	RCT	49	47	TXA	1000mg every 6 hours given orally. Intervention was continued for 4 days	Mortality, Rebleeding	Mortality: 2/49 VS 1/47. Rebleeding: 9/49 VS 12/47	1/49 VS 2/47
Saidi (2017)	RCT	67	64	TXA	1 gram diluted in 250 cc of saline solution via nasogastric tube.	Mortality, Rebleeding	Mortality: 4/67 VS 9/64. Rebleeding: 4/67 VS 12/64	–
Karadas (2020)	RCT	78	79	TXA	2000mg of 5% TXA in 100mL of isotonic saline solution	Mortality, Rebleeding, Need for surgery	Mortality: 8/78 VS 10/79. Rebleeding: 9/78 VS 8/79. Need for surgery: 3/78 VS 3/79.	–
Bashiri (2021)	RCT	35	35	TXA	1g (IV), followed by 3g over 24 h	Rebleeding, Transfusion required	Rebleeding: 8/35 VS 5/35. Transfusion required: 21/35 VS 8/35	–
Von Holstein (1987)	RCT	128	128	TXA	1g every 4 hours for 24 hours then 1.5g PO QDS for 5 days	Mortality, Rebleeding, Need for surgery, Transfusion required	Mortality: 2/128 VS 4/128. Rebleeding: 10/128 VS 19/128. Need for surgery: 3/128 VS 15/128. Transfusion required: 47/128 VS 54/128.	0/128 VS 2/128
Engquist (1979)	RCT	76	73	TXA	1g IV 4 hourly for 1 day then 1.5g PO QDS for 6 days	Mortality, Rebleeding, Need for surgery	Mortality: 11/102 VS 12/102. Rebleeding: 23/102 VS 29/102. Need for surgery: 10/102 VS 18/102	4/102 VS 2/102



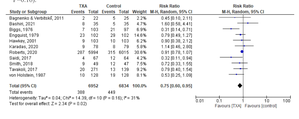
Forest plot of effect of tranexamic acid versus placebo on mortality.

Eleven studies reported on this outcome and their analysis generated a random effects RR 0.91 [0.78, 1.08] at 95% CI (I^2 = 0%, P=0.59).



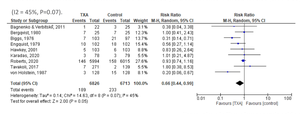
Forest plot of effect of tranexamic acid versus placebo on rebleeding.

Eleven studies reported on this outcome and their analysis generated a random effects RR 0.75 [0.60, 0.95] at 95% CI (I2 = 31%, P=0.16).



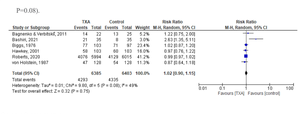
Forest plot of effect of tranexamic acid versus placebo on need for surgery.

Nine studies reported on this outcome and their analysis generated a random effects RR 0.66 [0.44, 0.99] at 95% CI (I2 = 45%, P=0.07).



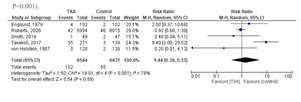
Forest plot of effect of tranexamic acid versus placebo on transfusion required.

Six studies reported on this outcome and their analysis generated a random effects RR 1.02 [0.90, 1.15] at 95% CI (I2 = 49%, P=0.08).



Forest plot of effect of tranexamic acid versus placebo on adverse events.

Five studies reported on this outcome and their analysis generated a random effects RR 1.44 [0.39, 5.33] at 95% CI (I^2 = 78%, P<0.001).



Discussion

- After evaluating P-value of the outcomes (P=0.59 in mortality, P=0.16 in rebleeding, P=0.07 in need for surgery, P=0.08 in transfusion required, and P=0.001 in adverse events), the difference between TXA and placebo in 5/6 of the outcomes was not statistically significant.
- HALT IT Trial by Roberts et al 2020 is the largest study of all, did not find any significant therapeutic effects of TXA in regards to mortality; total causes of mortality 3.77% vs. 4.17%
- 11 studies evaluating rebleed risk combined to give RR 0.75 [0.60, 0.95] at 95% CI (P=0.16), compared to purported rebleeding OR of 9.2 by Hawkey et al 2001; 5.58% vs. 6.57%.
- Similar care was observed in the events of surgery needs [(189/6826 (2.76%) versus 233/6713 (3.47%)] and blood transfusion requirements [4293/6385 (67.23%) versus 4335/6403 (67.70%)].
- Lastly, patients receiving TXA had a higher occurrence of adverse events 102/6544 (1.55%) versus 55/6451 (0.85%), with effects such as nausea, thrombotic events, diarrhoea, dizziness, and hypotension.

Conclusion

The strengths of this investigation were the fact that we strictly used RCTs for the meta-analysis. Additionally, the investigation had low to moderate levels of heterogeneity and low levels of risk of bias. A weakness of the systematic review and meta-analysis is the use of studies with varying means of drug administration. All the same, the reliability of the evidence presented by these studies remains highly significant. In conclusion, we have found that TXA has a degree of therapeutic effects on upper GI bleeds, but it does not significantly affect the outcomes of treatment. Treating upper GI bleeds should be reserved for the currently used standard care procedures. More trials should be conducted on TXA to find a better application niche in upper GI bleeds therapeutic management.

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