ACIDO TRANEXÁMICO EN HEMORRAGIAS DIGESTIVAS

Systematic review: tranexamic acid for upper gastrointestinal bleeding.

Gluud LL, Klingenberg SL, Langholz SE. Aliment Pharmacol Ther. 2008 May;27(9):752-8. Epub 2008 Feb 4.

BACKGROUND: Tranexamic acid may reduce upper gastrointestinal bleeding and stabilize patients before endoscopic treatments. AIM: To review randomized trials on tranexamic acid for upper gastrointestinal bleeding.
METHODS: Manual and electronic searches of The Cochrane Library, MEDLINE, EMBASE and Science Citation Index were combined. Intention-to-treat random effect meta-analyses were performed and results presented as RRs with 95% confidence intervals.
RESULTS: Seven double-blind randomized trials on tranexamic acid vs. placebo were included. Of 1754 patients randomized, 21% were excluded. Only one trial included endoscopic treatments or proton pump inhibitors. Five per cent of patients on tranexamic acid and 8% of controls died (RR: 0.61, 95% CI: 0.42-0.89). No significant differences were found on bleeding, bleeding-related mortality, surgery or transfusion requirements. Adverse events were unclearly reported. Data from three of the included trials suggested that tranexamic acid did not significantly increase the risk of thromboembolic disease.
CONCLUSIONS: The present review suggests that tranexamic acid may reduce all-cause mortality. However, because of limitations in the internal and external validity of included trials, additional evidence is needed before treatment recommendations can be made.

PMID: 18248659 [PubMed - indexed for MEDLINE]

Clinical practice and evidence in endoscopic treatment of bleeding peptic gastroduodenal ulcer.

Adamsen S, Bendix J, Kallehave F, Moesgaard F, Nilsson T, Wille-JÃ¸rgensen P. Scand J Gastroenterol. 2007 Mar;42(3):318-23.

OBJECTIVE: To investigate treatment practice in non-variceal upper gastrointestinal bleeding (NVUGIB) caused by gastroduodenal ulcer and how it adheres to the best evidence as documented in randomized studies and meta-analyses.

MATERIAL AND METHODS: The literature was surveyed to identify appropriate practices, and a structured multiple choice questionnaire developed and mailed to all departments in Denmark treating UGIB.
RESULTS: All 42 departments responded. All had therapeutic gastroscopes and equipment necessary for endoscopic haemostasis; 90% of departments had written guidelines. Adjuvant pharmacologic treatment included tranexamic acid in 38%. Proton-pump inhibitors (PPIs) were used by all departments, with 29% starting prior to endoscopic treatment. Eight departments (19%) used continuous PPI infusion, three of them starting with a bolus dose. In 50% of departments an anaesthesiologist was always present regardless of whether endotracheal intubation (routinely used by 10%) was used or not. Ten percent did not treat Forrest IIa and IIb ulcers, while IIc ulcers were treated by 36%. In 10% of departments clots were never removed, while in 2/3 attempts were made to remove resistant clots by mechanic means. Seven departments (17%) used monotherapy with epinephrine, while 59% always used dual therapy; 19% injected less than 10 ml. In rebleeding, 92% attempted endoscopic treatment before surgery, and used epinephrine in 79% of cases, while the remainder used epinephrine or polidocanol at the discretion of the endoscopist. Two out of three departments used high-dependency or intensive-care units for surveillance. Seventeen percent applied scheduled second-look gastroscopy.
CONCLUSIONS: Practice is variable, even in areas with established evidence based on randomized controlled studies, such as dosage and way of administration and duration of PPI treatment, injection treatment used as monotherapy and the volumen used, including ulcers with clots for treatment, and the use of scheduled second-look endoscopy. Since the rebleeding rate has remained unchanged for decades, and rebleeding implies increased surgery and mortality rates, appropriate practices must be promoted in order to improve results. Development and implementation of national guidelines may facilitate the process.

PMID: 17354110 [PubMed - indexed for MEDLINE]

Tranexamic acid is beneficial as adjunctive therapy in treating major upper gastrointestinal bleeding in dialysis patients.

Sabovic M, Lavre J, Vujkovac B. Nephrol Dial Transplant. 2003 Jul;18(7):1388-91.

BACKGROUND: In a pilot, non-randomized trial we tested the efficacy of tranexamic acid (TXA), a potent fibrinolytic inhibitor, as adjunctive therapy in standard treatment of major upper gastrointestinal bleeding in dialysis patients.
METHODS: Twenty consecutive patients (12 male, eight female; 63+/-8 years) with 36

episodes of major upper gastrointestinal bleeding were included in the study. In 16 episodes of bleeding TXA was used (in a dosage of 20 mg intravenously, followed for the next 4 weeks by 10 mg/kg/48 h orally), whereas in 20 other cases of bleeding, TXA was not used. The decision to use TXA was left to the attending physician's clinical judgement, resulting in all the more severe cases of bleeding being treated with TXA.
RESULTS: Treatment including TXA was shown to be beneficial (relative to cases not treated with TXA) in terms of decreasing the rate of early re-bleeding (in the first week, 0 vs 6, P<0.05), the rate of early and late re-bleeding (in the first month, 1 vs 8, P<0.05), the rate of repeated endoscopic procedures (in the first month, 1 vs 8, P<0.05) and the number of blood transfusions needed (in the first month, 1.4+/-1.3 vs 2.6+/-1.5 units, P<0.05).
CONCLUSIONS: The results of this pilot study suggest that TXA can be beneficial in the treatment of major upper gastrointestinal bleeding in dialysis patients. This remains to be definitely confirmed in a randomized study.

PMID: 12808178 [PubMed - indexed for MEDLINE]

Drug treatments in upper gastrointestinal bleeding: value of endoscopic findings as surrogate end points.

Hawkey GM, Cole AT, McIntyre AS, Long RG, Hawkey CJ. Gut. 2001 Sep;49(3):372-9.

INTRODUCTION: Pharmacotherapy for upper gastrointestinal bleeding has been difficult to evaluate because clinical end points are infrequent and affected by other factors.
AIMS: To evaluate whether blood in the stomach at endoscopy reflected severity of bleeding, predicted clinical outcomes, and could be altered by therapeutic agents.
METHODS: We studied 414 consecutive admissions with suspected upper gastrointestinal bleeding. Patients were randomised to receive lansoprazole 60 mg followed by 30 mg four times daily, tranexamic acid 2 g followed by 1 g four times daily, both drugs, or placebo for four days, until discharge or a clinical end point occurred. Logistic regression analysis was used to determine predictors of endoscopic changes and clinical outcomes, and to investigate the effects of drug treatments on blood in the stomach.
RESULTS: Of 414 patients with suspected upper gastrointestinal bleeding, 379 were endoscoped. Upper gastrointestinal bleeding was confirmed in 316. Sixteen required surgery within 30 days and 16 died on the index admission. Trial treatments were evaluable on a per protocol basis in 228 patients. The amount of blood in the stomach was found to reflect initial risk, with significant associations with high risk categorisation (odds ratio 3.7 (95% confidence interval 1.5-9.4) for more than a trace v none/trace), age (1.5

(1.1-1.9) per decade), and initial pulse (1.02 (1.00-1.04) per beat), and to predict rebleeding (9.2 (4.6-18.7)) and surgery (8.2 (2.9-22.9)). Other stigmata were less significant in these respects. The amount of blood in the stomach at endoscopy was reduced significantly by both lansoprazole (0.22 (0.07-0.63)) and tranexamic acid (0.27 (0.09-0.81)), although there was no evidence of synergy.
CONCLUSIONS: Blood in the stomach reflects clinical features in patients with acute upper gastrointestinal bleeding and is reduced by treatment with lansoprazole and tranexamic acid.

Tranexamic acid for upper gastrointestinal bleeding.

Bennett C, Klingenberg SL, Langholz E, Gluud LL. Cochrane Database Syst Rev. 2014 Nov 21;11:CD006640.

Background Tranexamic acid reduces haemorrhage through its antifibrinolytic effects. In a previous version of the present review, we found that tranexamic acid may reduce mortality. This review includes updated searches and new trials.Objectives To assess the effects of tranexamic acid versus no intervention, placebo or other antiulcer drugs for upper gastrointestinal bleeding.Search methods We updated the review by performing electronic database searches (Cochrane Central Register of Controlled Trials (CENTRAL),MEDLINE, EMBASE, Science Citation Index) and manual searches in July 2014.Selection criteriaRandomised controlled trials, irrespective of language or publication status.Data collection and analysis We used the standard methodological procedures of the The Cochrane Collaboration. All-cause mortality, bleeding and adverse events were the primary outcome measures. We performed fixed-effect and random-effects model meta-analyses and presented results as risk ratios (RRs) with 95% confidence intervals (CIs) and used I^2 as a measure of between-trial heterogeneity. We analysed tranexamic acid versus placebo or no intervention and tranexamic acid versus antiulcer drugs separately. To analyse sources of heterogeneity and robustness of the overall results, we performed subgroup, sensitivity and sequential analyses.Main results We included eight randomised controlled trials on tranexamic acid for upper gastrointestinal bleeding. Additionally, we identified one large ongoing pragmatic randomised controlled trial from which data are not yet available. Control groups were randomly assigned to placebo (seven trials) or no intervention (one trial). Two trials also included a control group randomly assigned to antiulcer drugs(lansoprazole or cimetidine). The included studies were published from 1973 to 2011. The number of participants randomly assigned ranged from 47 to 216 (median 204). All trials reported mortality. In total, 42 of 851 participants randomly assigned to tranexamic acid and 71 of

850 in the control group died (RR 0.60, 95% CI 0.42 to 0.87; P value 0.007; I^2 = 0%). The analysis was not confirmed when all participants in the intervention group with missing outcome data were included as treatment failures, or when the analysis was limited to trials with low risk of attrition bias. Rebleeding was diagnosed for 117 of 826 participants in the tranexamic acid group and for 146 of 825 participants in the control group (RR 0.80, 95% CI 0.64 to 1.00; P value 0.07; I^2 = 49%).We were able to evaluate the risk of serious adverse events on the basis of only four trials. Our analyses showed 'no evidence of a difference between tranexamic acid and control interventions regarding the risk of thromboembolic events.' Tranexamic acid appeared to reduce the risk of surgery ina fixed-effect meta-analysis (RR 0.73, 95% CI 0.56 to 0.95), but this result was no longer statistically significant in a random-effects meta-analysis (RR 0.61, 95% CI 0.35 to 1.04; P value 0.07). No difference was apparent between tranexamic acid and placebo in the assessment of transfusion (RR 1.02, 95% CI 0.94 to 1.11; I^2 = 0%), and meta-analyses that compared tranexamic acid versus antiulcer drugs did not identify beneficial or detrimental effects of tranexamic acid for any of the outcomes assessed.Authors' conclusions This review found that tranexamic acid appears to have a beneficial effect on mortality, but a high dropout rate in some trials means that we cannot be sure of this until the findings of additional research are published. At the time of this update in 2014, one large study(8000 participants) is in progress, so this review will be much more informative in a few years. Further examination of tranexamic acid would require inclusion of high-quality randomised controlled trials. Timing of randomisation is essential to avoid attrition bias and to limit the number of withdrawals. Future trials may use a pragmatic design and should include all participants with suspected bleeding or with endoscopically verified bleeding, as well as a tranexamic placebo arm and co-administration of pump inhibitors and endoscopic therapy. Assessment of outcome measures in such studies should be clearly defined. Endoscopic examination with appropriate control of severe bleeding should be performed, as should endoscopic verification of clinically significant rebleeding. In addition, clinical measures of rebleeding should be included. Other important outcome measures include mortality (30-day or in-hospital), need for emergency surgery or blood transfusion and adverse events (major or minor).

The treatment of haematemesis and upper gastrointestinal bleeding in United Kingdom Armed Forces and other deployed units.

Arr Woodward R, Khan M. J R Nav Med Serv. 2014;100(3):308-15.

INTRODUCTION: Upper Gastro-intestinal (UGI) bleeding is a significant cause of morbidity worldwide. United Kingdom Armed Forces (UKAFs) are not immune to this condition. There is a substantial body of conflicting evidence regarding initial management and risk stratification.

AIM: To provide the background knowledge and treatment pathways required to assess and manage a patient adequately during the first 24 hours of an episode of UGI bleeding.

ASSESSMENT: Clinical grading of hypovolaemic shock is inaccurate, but is a broad indicator of severity; the Rockall Score must not be used to assess requirement for intervention. Where laboratory assets are available, the Blatchford score is adequate to assess requirements for intervention.

MANAGEMENT: The principles of hypotensive resuscitation (target systolic blood pressure 90 mmHg for the first hour) hold true for UGI bleeds. In areas where endoscopy is available within four hours, a restrictive pattern of packed Red Blood Cell (pRBC) transfusion may be beneficial. Despite limited evidence of benefit, Proton Pump Inhibitors (PPIs) should be given routinely in UKAFs. Where available, in cases of variceal and non-variceal UGI Haemorrhage without locally available endoscopy, administration of tranexamic acid and somatostatin or octreotide should be considered.

Treatment of ulcerative colitis by the direct administration of an antifibrinolytic agent as an enema.

Kondo M, Hotta T, Takemura S, Yoshikawa T, Fukumoto K. Hepatogastroenterology. 1981 Oct;28(5):270-3.

Fibrinolytic activity in biopsied colonic mucosa was examined in patients with ulcerative colitis, and most cases were found to have increased tissue fibrinolysis -- due mainly to tissue plasminogen activator -- in the affected mucosa. Five cases, 4 with elevated tissue fibrinolysis and 1 normal, were treated with an antifibrinolytic agent, tranexamic acid (trans-AMCHA) administered as an enema, to inhibit fibrinolysis of the affected mucosa directly. In patients with elevated mucosal fibrinolysis, 2 showed complete remission after tranexamic acid enema alone, and there was one remission in response to combination treatment with oral prednisolone. One case with slightly elevated mucosal fibrinolysis showed clinical improvement, although the radiological findings were unchanged. No response was observed in one case with normal tissue fibrinolysis. It is concluded that tranexamic acid may show a therapeutic effect in ulcerative colitis with elevated mucosal

fibrinolysis when administered via an enema, which allows direct contact of the drug with the affected mucosa.