THE USE OF TRANEXAMIC ACID FOR THE TREATMENT OF ACUTE GI BLEEDING

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Introduction: Tranexamic acid (TXA) is an antifibrinolytic agent that is FDA approved for the treatment of cyclic heavy menstrual bleeding. It has been shown to reduce death due to bleeding in trauma patients and women with postpartum hemorrhage. Presented is a case of a patient with acute transfusion-dependent gastrointestinal bleeding who was successfully treated with TXA.

Case Presentation: An 87-year-old man presented to the emergency room with sudden onset painless hematochezia. He underwent emergent colonoscopy, which demonstrated extensive diverticulosis but no evidence of active bleed. He continued to have intermittent hematochezia over the next three days requiring a total of four units of PRBC's. Additional imaging with tagged red blood cells and CT angiogram failed to identify the source of bleeding. He received a TXA infusion with subsequent resolution of his hematochezia.

Discussion: Acute lower gastrointestinal bleeding is a medical emergency resulting in a mortality rate of approximately 3%. The bleeding site is not always identified on colonoscopy and further treatment may be warranted in patients with ongoing or recurrent bleeding. TXA has been shown to reduce the need for blood transfusion in surgical patients, and has been studied in a variety of conditions including postpartum hemorrhage, intracranial hemorrhage, and trauma. Currently there is an international randomized controlled trial underway investigating the use of TXA in patients with acute gastrointestinal bleeding.

Scholarly Question: What is the role for empiric therapy with TXA for the treatment of acute gastrointestinal bleed?

Conclusion: As illustrated by this case, treatment with TXA could be considered in patients with acute gastrointestinal bleeding, particularly when endoscopy is not readily available. However, currently there is insufficient evidence to support the empiric use of TXA and larger studies are needed to assess its effect on overall morbidity and mortality.

THE USE OF TRANEXAMIC ACID FOR THE TREATMENT OF ACUTE GI BLEEDING

Introduction:

Gastrointestinal bleeding is a common medical emergency with an estimated incidence of approximately 100 episodes per 100,000 persons annually.[1] The mortality rate of GI bleeding can be as high as 10%, and approximately 3% among patients with lower GI bleeds who are admitted to the hospital.[2] A strong predictor of mortality is the risk of re-bleeding.[3] General management of GI bleeds includes resuscitation with appropriate fluid and/or blood products and consultation with gastroenterology for endoscopy early in the hospital course.[4] However, a bleeding site is not always identified with endoscopy, particularly in lower GI bleeds, and the identification of more than one potential bleeding site is not uncommon.[5] When this is the case, further imaging studies can help localize the region of bleeding but do not necessarily allow for direct intervention.

Tranexamic acid (TXA) is an antifibrinolytic agent that binds to plasminogen thereby preventing the degradation of fibrin. It is FDA approved to treat heavy menstrual bleeding and has more recently been shown to reduce acute blood loss in a variety of clinical settings. A 2012 systematic review found that TXA reduced the probability of surgical patients requiring a blood transfusion by about a third.[6] The CRASH-2 trial investigated the effect of early administration of TXA in trauma patients. All-cause mortality and death due to hemorrhage were both significantly reduced in patients receiving TXA within the first eight hours of a traumatic injury without significant increase in vascular occlusive events.[7,8] The MATTERs study showed an overall reduction in mortality when TXA is used in the management of wartime injuries.[9] This

subsequently led to the addition of TXA to the Tactical Combat Casualty Care (TCCC) guidelines in 2011.[10] More recently TXA has been investigated for its use in reducing death due to bleeding in women with postpartum hemorrhage.[11] To date there are only a few smaller trials investigating the use of TXA in gastrointestinal bleeding. One in particular showed a reduced urgency in the timing of endoscopy in patients receiving TXA for gastrointestinal bleed.[12] There is currently a large ongoing randomized controlled trial investigating its use in acute upper and lower GI bleeding.[13] The following is a case of a patient admitted with an acute transfusion-dependent gastrointestinal bleed who was successfully treated with TXA.

Case Presentation:

An 87-year-old man with a history of hypertension and chronic kidney disease stage III presented to the emergency room with sudden onset painless hematochezia. On admission to the intensive care unit, he was hemodynamically stable with a hemoglobin of 9.6 g/dl. He continued to have ongoing bleeding with a subsequent fall in his hemoglobin to 6.5 g/dl, prompting transfusion of one unit of packed red blood cells. He underwent emergent upper and lower endoscopy, which demonstrated extensive left sided diverticulosis affecting the sigmoid and descending colon. Blood clots were present but there was no evidence of active bleeding. Over the next three days of hospitalization, he continued to have intermittent hematochezia with a subsequent fall in his hemoglobin requiring a total of four units of packed red blood cells to maintain his hemoglobin greater than 7 g/dl. Additional nuclear imaging with tagged red blood cells and CT angiogram failed to identify the source of bleeding, despite his ongoing hematochezia. He ultimately received a parenteral infusion of TXA (1g loading dose

followed by a 3g slow infusion over 24 hours), a treatment protocol that was derived from the current HALT-IT trial.[13] He had no side effects or adverse events from receiving the medication. Following the TXA infusion he had complete resolution of his hematochezia. He was monitored for an additional 48 hours in the hospital with stabilization of his hemoglobin and no further bleeding. At his follow up outpatient visit weeks later, he denied recurrent hematochezia and his hemoglobin remained stable.

Discussion:

Early administration of TXA in patients with acute gastrointestinal bleeding could reduce the need for blood transfusion and the risk of re-bleeding. TXA is an antifibrinolytic that prevents breakdown of fibrin blood clots, and therefore could prevent recurrent bleeding which has been associated with higher mortality.[3] It could also reduce the urgency of endoscopy,[12] which would be beneficial in remote locations where this resource might not be readily available.

This case illustrates the successful use of TXA to treat recurrent intermittent gastrointestinal bleeding. Although no definitive source was identified on colonoscopy, CT angiogram or tagged red blood cell imaging, the patient continued to have intermittent hematochezia requiring multiple transfusions with packed red blood cells to maintain his hemoglobin above the transfusion threshold of 7 g/dl.[14] There is a possibility that his bleeding would have resolved with time alone, however he was monitored over several days and continued to require blood transfusions due to persistent bleeding. After receiving a TXA infusion he had complete resolution of his hematochezia and stabilization of his hemoglobin. He had no recurrence of bleeding following the infusion.

There are few clinical trials investigating the use of TXA in the treatment of gastrointestinal bleeds. Most of these trials were underpowered and too small to assess for adverse outcomes.[12,15] Therefore further studies investigating its use are needed. Currently there is a large international randomized double-blind placebo-controlled trial underway investigating the use of TXA in patients with acute upper or lower gastrointestinal bleeding.[13] The HALT-IT trial will help to determine if TXA should be used empirically to treat GI bleeds, based on whether or not it reduces mortality and the need for blood transfusion as it has with trauma patients and hemorrhage from other sources.

The trial will also investigate the potential side effects of TXA when used to treat GI bleeds. In this case, the patient did not develop any adverse reaction to the medication. In the CRASH-2 there was not a statistically significant increase in the risk of thromboembolism.[7] However, both venous and arterial thrombosis have been reported with TXA use in the past and active thromboembolic disease is a contraindication to the use of oral TXA. Seizures have also been a reported side effect particularly with higher doses of TXA and in older patients. [16] In both the MATTERs and WOMAN studies, the majority of participants were under the age of 35, and in CRASH-2 the largest demographic was 35-34.[7,9,11] Given that GI bleeds more commonly affect older patients,[17] it will be interesting to see if this is a significant side effect when TXA is used to treat acute GI bleeds.

Scholarly Question:

What is the role for empiric therapy with tranexamic acid for the treatment of acute gastrointestinal bleed?

Conclusion:

This case report supports the need for further evaluation of TXA in patients with uncontrolled gastrointestinal bleeding. Treatment with TXA could be considered in patients with an acute GI bleed, particularly in areas where endoscopy or advanced imaging modalities are not readily available. Currently there is insufficient evidence to support the empiric use of TXA and larger studies are needed to assess the effect of TXA on overall morbidity and mortality, including the effect on thromboembolic events and other significant adverse effects. However, based on the available evidence, it is important for family medicine physicians, particularly in the military, to be comfortable using TXA to treat a variety of conditions. This includes heavy menstrual bleeding, post-partum hemorrhage, trauma and, pending further evidence, acute gastrointestinal bleeds.

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