**Title:** Tranexamic Acid for Angiotensin Converting Enzyme Inhibitor Induced Angioedema (TrACE)

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**Background:** Angiotensin converting enzyme inhibitors (ACE-Is) prevent the breakdown of bradykinin, which can lead to increased vasodilation, and in some cases, angioedema. Tranexamic acid (TXA) is an antifibrinolytic that inhibits formation of precursors involved in bradykinin synthesis and, in case reports, has been described as a potential treatment for ACE-I angioedema. The purpose of this study is to evaluate its efficacy and safety when added to the standard-of-care for ACE-I angioedema.

**Objective:** To assess the effect of TXA on resolution of angioedema symptoms caused by ACE-I as determined by length of stay (LOS) and other patient centered outcomes.

**Methods:** This was a retrospective study that included patients over the age of 18 who presented to one of 17 emergency departments (EDs) from January 2018 to August 2021 with signs and symptoms of angioedema while taking an ACE-I. Patients were excluded if they presented with urticaria, an active prescription for an angiotensin-receptor blocker, a history of hereditary or NSAID induced angioedema, or a history of C1 esterase deficiency. Patients who received TXA (TXA Group, TXAG) were compared with patients who did not receive TXA (Non-TXA Group, NTXAG). Both groups received standard-of-care medications used to treat ACE-I angioedema at the discretion of the treating physician. Statistical analysis was conducted using the Mann-Whitney U test, Student’s t-test, Fisher's exact, or Chi-square tests as appropriate.

**Preliminary Results:** There were 262 patients included in this study: 73 in the TXAG and 189 in the NTXAG. The most common dose given in the TXAG was 1000mg (87.7% of TXAG cohort). Overall, the median ED LOS was longer in the TXAG than NTXAG (20.9 hours vs 4.8 hours, p<0.001). ICU admission rates were higher in the TXAG compared with NTXAG (45% vs 16%, p<0.001). More patients were intubated in the TXAG compared with NTXAG (12% vs 3%, p=0.018). No difference was seen between TXAG and NTXAG for return within 7 days, complications related to thrombosis, and death in the overall cohort. In patients presenting with severe angioedema symptoms and admitted to the hospital (32 in TXAG and 30 in NTXAG), the median LOS was not statistically different between the two groups (58.7 hours vs 55.7 hours, p=0.61). In this subgroup, there was no difference in any secondary outcomes except for ICU admission rates which were higher in the TXAG (65% vs 31%, p=0.001).

**Conclusion:** Patients who received TXA had longer LOS, higher rates of ICU admission, and greater need for intubation. However, this finding may be related to the severity of presentation in this cohort, and those with severe symptoms and/or requiring hospital admission did not differ in terms of LOS or need for intubation with or without TXA. There were no differences in rates of 7-day return, clotting events, or mortality between the overall groups. Prospective randomized controlled studies should be considered to determine whether TXA is an effective treatment for ACE-I angioedema.