TITLE: Prehospital Pharmacotherapy in Moderate and Severe Traumatic Brain Injury: A Systematic Review

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BACKGROUND
Traumatic brain injury (TBI) affects civilian and military populations with high morbidity and mortality rates and devastating sequelae. As the United States military shifts its operational paradigm to prepare for future large-scale combat operations, the need for prolonged casualty care is expected to intensify. Identifying efficacious prehospital TBI management strategies is therefore vital. Numerous pharmacotherapies are beneficial in the inpatient management of TBI, including beta blockers, calcium channel blockers, statins, and other agents. However, their utility in prehospital management of moderate or severe TBI is not well understood. We performed a systematic review to elucidate agents of potential prehospital benefit in moderate and severe TBI.

METHODS
We searched six databases from January 2000 through December 2021 without limitations in outcome metrics using a variety of search terms designed to encapsulate all studies pertaining to prehospital TBI management. We identified 2142 unique articles, which netted 114 studies for full review. Seven studies met stringent inclusion criteria for our aims.

RESULTS
Studies that met inclusion criteria assessed tranexamic acid (TXA) (n=6) and ethanol (n=1). Of the TXA studies, three were randomized controlled trials, two were retrospective cohort studies,

one was a prospective cohort study, and one was a meta-analysis. Notably absent were papers investigating therapeutics shown to be beneficial in inpatient hospital treatment of TBI. Overall, data suggest that TXA administration is potentially beneficial in moderate or severe TBI with or without intracranial hemorrhage. Severe TBI with or without penetrating trauma was associated with worse overall outcomes, regardless of TXA use.

CONCLUSIONS

Effective interventions for treating moderate or severe TBI are lacking. TXA is the most widely studied pharmacologic intervention and appears to offer some benefit without adverse effects in moderate TBI (with or without intracranial hemorrhage) in the pre-hospital setting despite heterogeneous results. Limitations of these studies include heterogeneity in outcome metrics, patient populations, and circumstances of TXA use. We identified a gap in the literature in translating agents with demonstrated inpatient benefit to the prehospital setting. Further investigation into these and other novel therapeutic options in the prehospital arena is crucial to improving clinical outcomes in TBI.