Tranexamic Acid in Trauma

Introduction

1. Trauma is the leading cause of death in individuals up to 45 years old and the fourth leading cause of death overall for all ages.[1]
2. Uncontrolled hemorrhage is the leading cause of early mortality in major trauma.[2]
3. Trauma-associated hemorrhagic death occurs as an effect of uncontrolled bleeding and trauma-induced coagulopathy.[3]
4. Tranexamic acid is an antifibrinolytic medication that works by forming a reversible complex that displaces plasminogen from fibrin resulting in inhibition of fibrinolysis.[4]
5. Tranexamic acid is readily available, simple to administer, relatively inexpensive, with minimal side effects.

Pharmacology	
	Tranexamic Acid
Dose	• Loading dose: 1 g over 10 minutes started within 3 hours of injury ○ 2 gram via slow IV Push* • Maintenance: 1 g over the next 8 hours as a continuous infusion
Administration	• Loading dose: administer undiluted • Max rate:100 mg/minute • For continuous IV infusions: dilute with compatible solutions and administer at a rate not to exceed 100 mg/minute
PK/PD	Distribution: Vd: IV: 9 to 12 L Protein binding: ~3%, primarily to plasminogen Half-life elimination: ~2 hours Excretion: Urine (>95% as unchanged drug)
Adverse Effects	Hypersensitivity reactions, ocular effects, seizures and myoclonus, thromboembolic effects, abdominal pain, headache, back pain

*Emerging data from prehospital and military data use

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Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
Morrison, 2012	○ Observational (n=896)	○ TXA 1g bolus + repeat prn vs placebo.	○ All-cause mortality overall within 48 hours and in hospital mortality **significantly reduced with TXA**
Roberts, 2013	○ Randomized placebo-controlled (n = 20,2011)	○ TXA 1g bolus + 1g over 8 hours vs placebo	○ **All-cause mortality at 28 days was significantly reduced by TXA** ○ Treatment within 1 hour and 1-3 hours from injury significantly reduced the risk of death due to bleeding
Sprigg, 2018	○ Randomized placebo-controlled (n= 2325)	○ TXA 1 g bolus + 1g over 8 h infusion vs placebo	○ Patients in the tranexamic acid group experienced a reduction in early deaths and serious adverse events, but not long term functional status
Roberts, 2019	○ Randomized, placebo-controlled (n=12737)	○ TXA 1 g bolus + 1g over 8 hours vs placebo	○ Treatment within 3 h of injury reduced head injury-related death.
Rowell, 2020	○ Double-blinded, randomized (n= 966)	● TXA 1 g bolus + 1 g 8-hour infusion vs 2 g bolus bolus + placebo infusion vs placebo bolus + placebo infusion	○ No statistically significant difference in 28-day mortality, favorable neurologic function, 6 month disability rating score, or progression of intracranial hemorrhage
Roberts, 2020	○ Randomized placebo-controlled (n = 12,009)	○ TXA 1 g + 3g infusion vs placebo	○ No significant difference in death due to bleeding within 5 days
Bossers, 2021	● Prospective observational cohort (n = 1827)	○ Pre-hospital TXA vs no TXA patients with TBI	○ No association between TXA and mortality was found at 30 days ○ TXA was associated with increased mortality in patients with isolated TBI
Guyette, 2021	○ Double-blind, placebo-controlled, randomized (n= 927)	○ TXA 1 g bolus only vs TXA 1g + 1 g infusion vs TXA 1g bolus + 1g bolus + 1g infusion vs placebo bolus + placebo infusion	○ Prehospital administration of tranexamic acid compared with placebo did not result in a lower rate of 30-day mortality in this population. ○ No differences were found in 24-hour mortality or in-hospital mortality
Mahmood, 2021	○ Randomized placebo-controlled (n = 1767)	○ TXA 1 g bolus + 1 vs placebo	○ No evidence that TXA prevents IPH expansion
Gruen, 2023	○ Double-blind, randomized, placebo-controlled (n = 1310)	○ TXA 1 g bolus prior + infusion vs matched placebo	○ No difference in survival with a favorable functional outcome at 6 months ○ No difference in 6 months mortality

Conclusions

- Tranexamic acid has been studied in pre-hospital, hospital, and combat setting in patients who have sustained a traumatic injury
- Efficacy of tranexamic acid was demonstrated in some studies above, while other studies failed to show a significant difference in outcomes
- Dosing of tranexamic acid varied significantly in the above studies, however one dosing regimen has been widely adopted

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- Tranexamic acid has minimal adverse effects, is relatively inexpensive, and readily available in many settings

References

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