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Efficacy of tranexamic acid administration in traumatic brain injury patients: A review

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REVIEW

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ABSTRACT

Background
Anti-fibrinolytic medications decrease traumatic intracranial haemorrhage (ICH). Tranexamic acid (TXA) is an anti-fibrinolytic, which recently has shown effectiveness in management of traumatic haemorrhage.

Aims
To summarize the randomized control trials (RCTs) that evaluates the efficacy of tranexamic acid administration in traumatic brain injury (TBI) patients.

Methods
An electronic literature review, including PubMed, Google Scholar, and EBSCO that examining RCTs, observational, and experimental studies which study the efficacy of TXA administration in (TBI) patients.

Results
The current review included 7 randomized studies reported the efficacy of TXA in management of TBI. TXA limit secondary brain injury by preventing the expansion of ICH. Administration of TXA exhibited a tendency to decrease head trauma-related mortality.

Conclusion
TXA significantly lower the risk of ICU expansion m and prevent brain injury related deaths.

Key Words
Tranexamic acid, traumatic brain injury, management of TBI

What this review adds:

1. What is known about this subject?
Tranexamic acid (TXA) has been used to improve outcomes in TBI patient. However, the effectiveness of TXA treatment remains unclear.

2. What new information is offered in this review?
In-patients with TBI, TXA reduce the mortality with reasonable side effect profile.

3. What are the implications for research, policy, or practice?
TXA is a reasonable and cost effective medication that can be utilized in management of TBI.

Background

TBI remains to plague millions of persons worldwide annually. According to the Centres for Disease Control, the total frequency for TBI-related emergency department official visit, hospitalizations, and mortality have amplified in the period 2001–2010.[1] TBI results in high socioeconomic affliction, acquiring high medicinal expenditures and loss of productivity, the prospects of TBI still poor. In the USA, nearly 50,000 persons die and at least 5.3 million live with disabilities associated with TBI per year.[2]

The bleeding caused by TBI is accompanying with a high hazard of coagulopathy, and this might result in rise in haemorrhage size, greater mortality and infirmity. Rise in fibrinolysis, which indicates increased levels of fibrin deprivation products is a mutual form of coagulopathy in TBI. Consequently, antifibrinolytic agents for example TXA could diminish ICH due to trauma.[3]

The exacerbation of intracranial haemorrhage is serious in traumatic brain damage (TBI) patients. Tranexamic acid (TXA) was recognized to enhance the outcomes in TBI cases. Though, the efficiency of TXA management still uncertain.[4]
In recent times, the pathophysiology of coagulopathy has become the emphasis of trauma precaution. Directly after administering the TBI, the level of hyperfibrinolysis peaks in 3h which leads to hematoma extension.[2] Therefore, early (<1h and no later than 3h after injury) management with tranexamic acid (TXA), an anti-fibrinolysis medication, has demonstrated effectiveness in trauma management. Lately, the antifibrinolytic agent tranexamic acid (TXA) confirmed better mortality in comparison to placebo in harshly haemorrhage trauma cases in the CRASH-2 trial, which registered 20,211 cases in 40 nations.[5]

Method

A systematic review was carried out, including PubMed, Google Scholar, and EBSCO using the following terms in different combinations: tranexamic acid, traumatic brain injury, TBI, management of TBI. We included all full texts [randomized controlled trials, observational, and experimental studies] that examined the role of TXA in management of TBI. The authors extracted the data, and then the author's names, year and region of publication, the study type, period of study, and the result were reported (Table 1).

Results

The search of the mentioned databases returned 39 studies that were included for title screening. 37 of them were included for abstract screening, which lead to the exclusion of 22 articles. The remaining 15 publications full-texts were reviewed by two independent authors (K A – L D). The full-text revision lead to the exclusion of eight studies, and seven were enrolled for final data extraction (Table 1).

The CRASH-2 trial deliberated in the Table 1, in which 20,211 trauma cases in 40 countries were enrolled, established the efficacy of TXA treatment for dropping bleeding in trauma cases and decreasing mortality in perinatal haemorrhagic cases.[5]

Also, CRASH-3 confirmed that the hazard of head injury-related mortality was abridged with TXA treatment in cases with mild-to-moderate head injury nonetheless not in cases with severe head injury.[10,11] The administered doses of TXA were as designated in preceding studies (a bolus and a unceasing infusion).[12]

Two preceding studies stated reduced intracranial haemorrhage progress with initial administration of TXA would be watched with carefulness. Hematoma growth has been linked with poor outcome in cases with TBI.[13]

The information that tranexamic acid decreases the hazard of death from traumatic bleeding increases the opportunity that it might also be effective in other circumstances in which bleeding can be life intimidating or incapacitating.[14] Traumatic brain injury is usually escorted by intracranial haemorrhage, which can develop or deteriorate after hospital admission. Traumatic intracranial haemorrhage is accompanying with an augmented risk of death and disability, and regardless of the site, haemorrhage size is powerfully correlated with consequence.[15]

Chakroun-Walha et al. stated higher occurrence of pulmonary embolism in TXA individuals (11.5 *vs.* 2.4%) which may be credited to the open-label randomization, the valuation of this problem was possibly predisposed by the TXA use.[6] Other studies confirmed the correlation between the late administration of TXA and the hazard of thromboembolic problems; and its administration throughout the first 3h next to trauma are assumed to be the harmless.[16]

In the study of Fakharian et al.[17] Cases with TBI were comprised up to 8h after trauma and TXA was not accompanied with an amplified risk of thromboembolic conditions. Long-term administration of TXA in cases with

post-traumatic long-lasting subdural hematoma was likewise studied; it was harmless and was related to the reduction of the bleeding.[18]

Discussion

Numerous systematic reviews and case control studies of TXA management in TBI cases have been available. TXA is an anti-fibrinolytic agent that used to treat or avoid undue blood loss with several medical and surgical indications comprising traumatic brain injury.[2] The pathophysiology of coagulopathy in TBI comprises tissue factor stimulation, thrombocytopenia, platelet dysfunction, protein C stimulation, and hyper-fibrinolysis. The chief mechanism of TBI-related coagulopathy is hyper-fibrinolysis tailed by chief consumptive coagulopathy that is produced by movement of tissue factors from wounded brain tissue to blood.[11]

Conclusion

TXA significantly lower the risk of ICU expansion m and prevent brain injury related deaths.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

Figures and Tables

Table 1: Author, year of publication, study type, and study outcome

Author Study Region Year of publication	Study type	Sample size	Outcome
O. Chakroun-Walha et al.[6] Sfax, Tunisia 2018	A prospective randomized open-label trial	180 patients	TXA is a motivating treatment in hemorrhagic shock. Its competence in head trauma is still controversial. Its influence on the mortality and the desires of transfusion or surgery were not established in this study. Greater occurrence of pulmonary embolism in the treated group.
Fakharian E. et al.[7] Iran 2017	Randomized double blind clinical trial	149 patients	Taking a short dose of TXA does not cause substantial prevention of growth of post-traumatic hemorrhagic lesion or enhancement of medical outcomes.
Ebrahimi P. et al.[8] Iran 2019	Randomized, double-blind, placebo-controlled clinical trial	80 patients	The use of TXA might decrease hemorrhage, though, based on the outcomes of this study, such influence was not statistically substantial in controlling the epidural and subdural hemorrhage, but clinical trials using a higher sample size are recommended for additional investigation in this respect.
A. Jokar et al.[9] Iran 2017	Single-blinded, controlled, randomized trial	80 patients	It has been conventional that TXA, as an current hospital-based management for acute TBI, could reduce ICH progress. In this study TXA significantly reduce the expansion of ICH at 48 hours. High quality
CRASH-2 trial collaborators.[5] UK 2010	Randomized controlled trial	20211 adult	Tranexamic acid carefully compact the risk of death in bleeding trauma cases in this study. On the base of these outcomes, tranexamic acid must be considerably indicated for use in bleeding trauma cases.
The CRASH-3 trial collaborators.[10] UK 2019	Randomized, placebo-controlled trial	967 patients	Tranexamic acid is harmless in cases with TBI and handling within 3 h of trauma reduces head injury-related mortality. cases should be managed as soon as conceivable after injury
Yokobori, Shoji et al.[2] Japan 2020	A systematic review and meta-analysis	---	TXA treatment established a liking to decrease head trauma-related mortality in the TBI individuals, with no substantial occurrence of thromboembolic proceedings. TXA treatment could consequently be recommended in the initial TBI care.