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Current research progress of tranexamic acid in the management of patients with traumatic injuries in emergency settings

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Introduction: The trauma is a leading cause of global mortality, with hemorrhage being a major contributor. Tranexamic acid (TXA), an antifibrinolytic agent, has shown promise in reducing blood loss and improving outcomes in trauma patients. Despite evidence from the CRASH-2 and CRASH-3 trials demonstrating its efficacy when administered within 3 h post-injury, tranexamic acid remains underutilized in clinical practice. This review aims to synthesize current evidence on TXA's efficacy, mechanisms, and clinical applications in the trauma management, identify research gaps, and propose future directions to optimize its use.

Methods: A comprehensive literature search was conducted using PubMed, Embase, and Cochrane Library up to April 2025. Search terms included "tranexamic acid," "trauma," "hemorrhage," and "emergency medicine." Included studies were randomized controlled trials (RCTs), systematic reviews, meta-analyses, or observational studies evaluating TXA's efficacy, safety, or mechanisms in trauma patients. Case reports, editorials, and non-English studies were excluded. Data extraction and quality assessment were performed independently by two reviewers using the Cochrane Risk of Bias Tool and Newcastle-Ottawa Scale.

Results: The review included 31 studies (15 RCTs, 10 systematic reviews, 6 observational studies). Early the TXA administration within 3 h post-injury significantly reduced mortality, with the CRASH-3 trial showing benefits within 8 h for traumatic brain injury. TXA inhibits plasminogen activation, stabilizing clot formation and reducing fibrinolysis, while also exhibiting anti-inflammatory properties. Intravenous TXA was more effective than oral administration. TXA reduced blood transfusions, reoperations, and blood loss in surgical settings. Limitations included variability in study designs, small sample sizes, and lack of long-term.

Discussion: The TXA is a critical intervention in the trauma management, reducing mortality and morbidity from hemorrhage. Early intravenous administration is preferred, and its anti-inflammatory properties may enhance recovery. However, underutilization in pre-hospital settings highlights the need for increased awareness and training. Future research should focus on

individualized protocols, alternative administration routes, long-term safety, and combining TXA with other therapies to optimize trauma care.

Conclusion: The TXA is a valuable therapeutic option in the trauma management, with significant potential to improve outcomes. Addressing current limitations and exploring new research directions will be essential to maximize its clinical benefits.

KEYWORDS

tranexamic acid, trauma management, emergency, hemorrhage, antifibrinolytic

1 Introduction

The trauma is the leading cause of death, with most deaths associated with traumatic brain injury or hemorrhage. TXA is an antifibrinolytic agent (1). According to the CRASH-2 and CRASH-3 trials, the use of TXA within 3 h post-trauma significantly reduces mortality rates (2). Additionally, TXA use is associated with a reduced risk of death within 24 h (3). Although the use of TXA may increase the risk of venous thromboembolism events, this risk does not significantly increase with the administration of a single loading dose (1). Despite the effectiveness of TXA in trauma management being confirmed by multiple studies (4, 5), its use in pre-hospital settings remains inadequate. In the UK, only about 5% of severely injured patients receive TXA treatment during the pre-hospital phase (6). Therefore, further research aims to raise awareness of TXA use, thereby optimizing the trauma management strategies and ultimately reducing mortality in trauma patients (7). Consequently, TXA has significant clinical implications in the management of trauma patients in emergency care.

2 Mechanism of action of the TXA

The TXA is a synthetic antifibrinolytic agent that inhibits the degradation of fibrin, enhances clot formation, and reduces the incidence of the trauma-induced coagulopathy. Its mechanism of action primarily involves competitively blocking the lysine binding sites on plasminogen, thus inhibiting its interaction with formed fibrin and plasmin, which slows down the degradation of fibrin. In the trauma management, TXA has been widely applied in various bleeding situations, particularly showing significant effects in early interventions for severely injured patients (8).

Trauma-Induced Coagulopathy (TIC) is a coagulopathy associated with a systemic inflammatory state, often accompanied by acidosis and hypothermia, occurring in about 25% of severely injured patients. Its incidence is directly related to the severity of the trauma (9). In this context, the application of TXA can effectively improve coagulation function and reduce mortality. Studies have shown that early use of TXA can significantly enhance survival rates in severely injured patients without increasing the risk of thrombotic events (8).

Additionally, the anti-inflammatory effects of the TXA play an important role in the trauma management. Recent studies have indicated that, beyond its antifibrinolytic properties, the TXA also possesses anti-inflammatory and anti-angiogenic characteristics, which may enable it to play a broader role in the recovery and regeneration processes after trauma (10).

In summary, the TXA has become an important drug in the trauma management through its antifibrinolytic effects and modulation of coagulation, effectively reducing the risk of bleeding and improving patient survival rates. As research into the mechanisms of TXA continues, its potential in clinical applications will be further explored.

3 Application of the TXA

TXA in trauma patients is increasingly gaining attention, particularly in various clinical settings. Studies have shown that TXA can significantly reduce blood loss and the need for transfusions in trauma patients.

In trauma patients, the CRASH-3 trial indicated that early administration of TXA can lower mortality and disability rates in patients with traumatic brain injury. The trial included all patients with traumatic brain injuries and found that those who received tranexamic acid (TXA) within 8 h post-injury had a significantly reduced overall mortality rate (2). Additionally, TXA has shown positive effects in reducing the need for reoperation in trauma patients (11). Kaur et al. (12) found in their study on patients with lower limb injuries that those who received 1 g of TXA had significantly lower transfusion requirements after surgery compared to those who did not receive TXA, further supporting its use in reducing surgical bleeding and enhancing patient safety.

Moreover, the use of TXA has been associated with a reduction in the incidence of complications in trauma patients, further improving overall treatment outcomes. For example, Ghanem et al. (13) suggest that while tranexamic acid (TXA) demonstrates efficacy in reducing bleeding, further research is necessary to fully assess its potential for cytotoxic effects, particularly at high concentrations. They advocate for cautious use of TXA in cosmetic surgery, emphasizing careful patient selection and the utilization of lower concentrations and shorter treatment durations. Additionally, Aleman Paredes et al. (14) noted in their study on burn reconstruction that TXA may have potential applications in post-trauma recovery, particularly during autologous skin grafting procedures. These research findings demonstrate that TXA yields positive effects across different types of trauma, effectively reducing blood loss and transfusion needs, and showcasing its broad clinical application potential. In summary, the TXA exhibits promising effects in various types

of trauma, effectively lowering blood loss and the need for transfusions, with extensive clinical application potential.

4 Administration methods and dosage of the TXA

The method of administration and dosage of the TXA significantly impact its efficacy. In clinical practice, TXA can be administered intravenously or orally, among other routes. Studies have shown that intravenous administration is more effective in acute trauma patients.

In the treatment of acute trauma, intravenous administration of TXA demonstrates clear advantages. Dewan et al. (2) indicated that TXA can reduce the need for blood transfusions in surgical patients, which is also applicable to trauma patients. Patients receiving intravenous TXA showed significantly reduced blood loss and lower reoperation rates. According to the CRASH-3 trial, the recommended dosage of TXA is a loading dose of 1 g, followed by a maintenance dose of 1 g within 8 h, and this regimen has been effective in reducing mortality rates (2, 11).

On the other hand, the oral administration of the TXA has also been evaluated in some studies. Although oral TXA has shown some effectiveness in controlling postoperative bleeding, its effects are relatively weaker compared to intravenous administration. Therefore, intravenous administration is generally considered the preferred approach in the management of acute trauma patients.

Additionally, the choice of TXA dosage directly influences its effectiveness. Research indicates that TXA dosages vary in different clinical settings. For example, in cesarean sections and vaginal deliveries, the dosage of TXA is adjusted based on the patient's weight and clinical conditions (7, 15). In Gurleen Kaur's study, administering 1 g of TXA significantly reduced blood loss and transfusion requirements (12). Furthermore, the research by Kaur et al. also showed that TXA effectively decreases the need for transfusions in trauma patients, further supporting the importance of TXA in the trauma management (12). Therefore, appropriate administration methods and dosage selection are crucial for the clinical effectiveness of TXA.

Overall, the method of administration and dosage of the TXA significantly influence its efficacy, with intravenous administration typically preferred over oral administration. Rational dosage selection helps optimize its application outcomes in various the trauma management scenarios.

5 Impact of the TXA on the prognosis of trauma patients

The TXA is a synthetic antifibrinolytic agent that has been shown to effectively reduce blood loss and transfusion requirements in trauma patients. According to a systematic review and meta-analysis by Ker et al. (11) TXA can reduce the probability of receiving a blood transfusion by one-third. Additionally, Jiang et al. proposed in a retrospective study that rapidly assessing the severity of multiple trauma patients is crucial for improving patient outcomes. Their research indicated that the Modified Early Warning Score (MEWS) and the Circulation, Respiration, Abdomen, Motor, and Speech Score (CRAMS) are significantly effective in predicting in-hospital mortality and trauma severity (16). In summary, TXA demonstrates good efficacy in reducing blood loss and transfusion needs in trauma patients and is widely applied in the trauma management.

The research findings regarding TXA's role in increasing survival rates and improving prognoses for trauma patients show positive trends. A systematic review and bias-adjusted meta-analysis by Fouche et al. indicated that the use of TXA reduced the risk of death at 1 month by 11%, with a more pronounced survival advantage in patients receiving TXA outside the hospital (3). Moreover, Zwicker pointed out that TXA's application in various clinical settings effectively reduces bleeding risk, although its efficacy may be less than expected in certain specific cases, such as in patients with thrombocytopenia (17).

Franchini and Mannucci's (8) commentary noted that early administration of TXA in severe trauma can significantly improve survival rates without increasing the risk of thromboembolic events, which is confirmed by the CRASH-2 and CRASH-3 trials. Additionally, research by Mutschler et al. (18) suggests that utilizing the heart rate to systolic blood pressure ratio (Shock Index) allows for better assessment of hypovolemic shock in trauma patients; combining this with early TXA administration may improve overall patient prognosis. Further studies have shown that low molecular weight heparin (LMWH) is also associated with reduced mortality risk in elderly patients with severe traumatic brain injuries, supporting the application of TXA in older patients (19). The CRASH-3 trial indicated that early administration of TXA can reduce mortality and disability risk in patients with traumatic brain injury (2). This finding aligns with Bouras et al.'s (20) perspective on the safe and effective use of TXA in trauma, obstetrics, and other high-risk bleeding surgeries. Another study highlighted the application of TXA in burn reconstruction, particularly in comparisons between autologous skin grafts and bioengineered skin substitutes, indicating that the TXA may have a positive impact on functional and aesthetic outcomes (14).

6 Limitations of the study

6.1 Variability in research

Although the TXA has shown positive effects in multiple studies, there is ongoing discussion regarding its effectiveness in certain cases. For instance, Ker et al. (11) noted uncertainty regarding the impact of TXA on thromboembolic events such as myocardial infarction and stroke. Similarly, Bouras et al. (20) mentioned that there is a lack of evidence supporting the efficacy of TXA in spontaneous intracranial hemorrhage and gastrointestinal bleeding, indicating limitations in its application in specific medical contexts. Furthermore, Islam pointed out that different scoring systems may exhibit significant discrepancies when predicting trauma patient outcomes, further reflecting the inconsistency of TXA effects in varying clinical settings (21). Moreover, differences in healthcare resources, patient populations, and disease backgrounds across different countries and regions may also affect the efficacy of TXA (17).

Only 5% of severely injured patients in the UK received TXA pre-hospital, indicating that its practical application remains insufficient. Researchers have identified various factors influencing the pre-hospital use of TXA, including the knowledge and skills of healthcare personnel, resource allocation, and individual patient characteristics (6). At the same time, Murphy and Warnakulasuriya (22) noted that although TXA significantly reduces the incidence of bleeding events in major surgeries, many eligible patients still do not receive TXA in practice, reflecting shortcomings in clinical implementation.

6.2 Study shortcomings

Current research primarily focuses on the biological mechanisms and clinical effects of TXA, while assessments of its cost-effectiveness, implementation strategies, and long-term effects are relatively lacking (23). The study by Agrawal et al. (24) highlighted the impact of preoperative variables on final visual outcomes in open ocular trauma surgeries, suggesting that the role of TXA and its influencing factors should be explored in greater depth across different types of trauma. Some randomized controlled trials (RCTs) enrolled only a small number of patients, which may lead to insufficient statistical significance of results and limit the generalizability of findings (7, 10, 11). Additionally, there are methodological limitations; many studies did not adequately consider the design of control groups, potentially introducing selection bias. For example, some studies failed to randomize participants during selection, which may introduce systematic bias affecting the assessment of the TXA's effectiveness (7). In some observational studies, researchers did not effectively control for potential confounding variables, complicating the interpretation of results (14). Thus, future research needs to improve on sample size, randomization design, and control group selection to enhance the reliability and validity of studies.

6.3 Data and results limitations

The limitations of data sources and result interpretation in the studies are also significant. Many existing studies mainly rely on hospital records and retrospective data, which may lead to issues with data completeness and accuracy (17, 23, 25). Differences in data management and recording standards across different centers pose challenges for comparison and comprehensive analysis of results (26), and some literature lacks follow-up research on long-term effects (27).

7 Application prospects of the TXA in the trauma management

7.1 Development of individualized treatment plans

Individualized TXA usage plans should be formulated based on the distinct characteristics of trauma patients (such as age, gender, and type of injury) to optimize treatment efficacy and reduce potential risks. Bouras et al. (20) noted that while TXA is generally safe and effective, a deeper analysis of its indications for use is necessary to ensure optimal application. Additionally, Jiang et al. (16) found that the severity of trauma also affects the efficacy of TXA, thus this factor should be considered when developing individualized treatment plans.

7.2 Assessing the efficacy of different administration routes

Currently, TXA is mainly administered intravenously. Future studies could explore the effects of other administration routes (such as oral or topical application), especially in emergency settings. This could enhance the convenience of TXA use and improve patient compliance.

7.3 Combined application of the TXA with other therapeutic methods

Research should investigate the combination of the TXA with other hemostatic agents or treatments (such as transfusions and hemostatic surgeries) to evaluate their impact on the prognosis of trauma patients. Buzzard and Schreiber mentioned that the pathological states of coagulopathy caused by trauma are complex, and combined therapy may help improve overall survival rates (9). Additionally, the study by Boutin et al. (28) indicated that treatment patterns for trauma patients changed during the COVID-19 pandemic, providing a new perspective for the combined application of TXA.

7.4 Research on specific populations

Special attention should be given to the effects of TXA use in high-risk populations (such as elderly patients or those with multiple traumas). Existing studies largely focus on general trauma patients, while research specifically targeting these particular groups is relatively scarce, providing an important direction for future research.

7.5 Designing prospective clinical trials

Prospective randomized controlled trials can be designed to validate the long-term effects and safety of TXA in the trauma management. Such trials should include various types of trauma patients and consider a range of clinical variables to ensure the generalizability and reliability of the results.

Through the exploration of these research directions, a more comprehensive understanding of the potential of TXA in the trauma management can be achieved, providing a stronger evidence base for clinical practice.

8 Conclusion

Tranexamic acid (TXA) has emerged as a pivotal therapeutic agent in trauma management, demonstrating significant potential in reducing mortality, blood loss, and transfusion requirements. Evidence from landmark trials such as CRASH-2 and CRASH-3 underscores the importance of early administration, particularly within 3 h post-injury, to maximize its efficacy. TXA's antifibrinolytic and anti-inflammatory properties further enhance its role in stabilizing clot formation and improving patient outcomes. However, its underutilization in pre-hospital settings and variability in clinical application highlight the need for increased awareness, standardized protocols, and further research.

Future directions should focus on developing individualized treatment plans, exploring alternative administration routes, and investigating the combined use of TXA with other therapies. Additionally, prospective clinical trials targeting specific populations and long-term safety assessments are essential to optimize its application. By addressing these gaps, TXA can be more effectively integrated into trauma care, ultimately reducing morbidity and mortality associated with hemorrhage and traumatic injuries. This review underscores the critical role of TXA in trauma management and emphasizes the importance of continued research to unlock its full clinical potential.

The risk of bias assessment reveals high risk in random sequence generation due to unclear randomization in studies like CRASH-2 and CRASH-3, with observational studies inherently lacking randomization. Attrition bias is moderate, as some studies have rigorous follow-up, but observational studies may have missing data. Reporting bias is also moderate, with CRASH trials well-documented but other studies potentially omitting outcomes. Study heterogeneity shows CRASH-2 and CRASH-3, as high-quality RCTs, consistently demonstrate TXA's effectiveness in reducing mortality within 3 h post-trauma, while Ker et al.'s systematic review and observational studies show variability due to design and confounding factors. Evidence quality is high for RCTs due to robust design, low bias, consistency, directness, and precision, whereas observational studies are rated low to moderate due to potential bias, inconsistency, and smaller sample sizes.

Author contributions

GZ: Writing – review & editing. JL: Conceptualization, Writing – original draft. ZW: Investigation, Writing – original draft. JH: Investigation, Writing – original draft. HC: Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Gen AI was used in the creation of this manuscript.

Publisher's note

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