



Exploring the disenchantment with tranexamic acid in liver surgery: A hopeful outlook for future developments

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INTRODUCTION

The exploration of tranexamic acid (TXA) in surgical contexts has garnered significant attention over the past few years, particularly regarding its effectiveness in minimizing blood loss during various surgical procedures. The literature reveals a growing body of evidence on the application of TXA, highlighting both its benefits and the complexities surrounding its use (1). Emphasizes the critical role of TXA in reducing perioperative bleeding, which is essential for improving surgical outcomes and minimizing complications such as hematoma and the need for blood transfusions. This systematic review illustrates the shift towards TXA as a primary antifibrinolytic agent following the withdrawal of aprotinin, marking its ascendance in surgical practice.

Further, the comparative analysis conducted by (2) between topical and intravenous administration of TXA in bone surgery adds depth to the understanding of its application. Their findings indicate that both methods effectively reduce blood loss, thereby supporting the notion that TXA can be adapted to various surgical modalities. However, the authors also point out the lack of comprehensive guidelines for optimal dosing, highlighting an area of uncertainty that warrants further investigation (3). Provide a broader narrative on the efficacy and safety of TXA across surgical disciplines, noting its inclusion in the World Health Organization's list of essential medicines. They acknowledge the limited side effects associated with TXA but caution about the potential thromboembolic risks that remain inadequately defined. This narrative review underscores the need for continued research to clarify these risks and optimize dosing strategies, as the clinical evidence for TXA's effectiveness in certain contexts remains inconclusive.

In a more recent umbrella review (4), synthesize findings from multiple studies, reinforcing TXA's protective role against vascular adverse events while also acknowledging the associated risks, particularly at high doses. Their work highlights the variability in effect sizes across different meta-analyses, which introduces a layer of complexity in interpreting the overall efficacy of TXA in surgical settings (5). shift the focus to a specific surgical context -middle ear surgery- where intraoperative bleeding poses significant challenges. Their narrative review reveals a resurgence of interest in TXA, particularly in light of its potential to enhance surgical field visibility. However, they also note the limitations in current literature, including the small number of studies and the heterogeneity in TXA administration methods and bleeding assessment scores. This variability complicates the ability to draw definitive conclusions about TXA's impact on surgical outcomes in this specialty.

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Collectively, these articles illustrate the evolving landscape of TXA usage in surgery, revealing both its promise and the challenges that accompany its application. The critical evaluation of these studies highlights the need for further research to address the uncertainties surrounding TXA, particularly in relation to its safety profile and optimal usage protocols across diverse surgical fields.

Literature Review

The article "A Systematic Review of TXA in Plastic Surgery: What's New?" by (1) provides a comprehensive examination of the role of TXA in surgical settings, particularly in the context of plastic surgery. The main thrust of the article revolves around the necessity of minimizing perioperative bleeding to mitigate complications such as hematoma, anemia, and the requirement for allogeneic transfusions. This focus is especially pertinent given the implications of blood loss on patient outcomes, including overall survival rates.

Scarafoni elucidates the pharmacological mechanisms by which TXA operates, highlighting its function as a synthetic derivative of lysine that effectively inhibits fibrinolysis. By blocking the binding sites of plasminogen, TXA prevents the activation of plasmin and the subsequent degradation of fibrin clots, thereby enhancing clot stability. This mechanism is critical in surgical procedures where maintaining hemostasis is essential for patient recovery.

The systematic review synthesizes findings from multiple trials, affirming that TXA is associated with a reduced likelihood of blood transfusions and a decrease in the volume of blood transfused during elective surgeries. Notably, the article emphasizes that the use of TXA does not correlate with an increased risk of thromboembolic events or other significant complications, which supports its safety profile in various surgical contexts. The findings are particularly relevant in light of the withdrawal of aprotinin from the market in 2008, which positioned TXA as a primary agent for managing surgical bleeding.

However, while the article presents a robust case for the efficacy of TXA, it is crucial to consider the broader implications of its use in diverse surgical specialties, including liver surgery. The review does not delve deeply into the specific nuances of TXA application in liver surgery, an area that may require further exploration, especially given the unique hemostatic challenges presented in hepatic procedures. The hopeful outlook for future developments in TXA application could benefit from additional research that addresses its role in this specific surgical context, potentially leading to tailored protocols that optimize patient outcomes.

The article titled "Efficacy of topical vs intravenous TXA in reducing blood loss and promoting wound healing in bone surgery: A systematic review and meta-analysis" by (2) presents a thorough examination of the role of TXA in surgical settings, specifically

focusing on its application in bone surgery. The authors provide a systematic review and meta-analysis, emphasizing the efficacy of both topical and intravenous TXA in minimizing blood loss and enhancing wound healing.

One of the critical insights from the article is the comparative analysis of topical versus intravenous administration of TXA. The findings indicate that both methods effectively reduce blood loss when juxtaposed with placebo outcomes. Notably, the study reveals no significant difference in the effectiveness of topical TXA compared to intravenous TXA in the context of blood loss reduction during bone surgeries. This suggests that topical administration could be a viable alternative to intravenous methods, potentially offering advantages such as lower dosage requirements and reduced medical costs.

Moreover, the article highlights a significant gap in the literature regarding comprehensive guidelines for the safe administration of topical TXA, which remains a contentious issue among surgeons. The authors call attention to the need for standardized protocols to optimize the use of TXA in surgical practices, particularly as its application expands beyond traditional uses. This lack of consensus on dosing and administration methods underscores the importance of further research, especially in varying surgical contexts, including liver surgery.

The article titled "TXA for the prevention and treatment of bleeding in surgery, trauma and bleeding disorders: a narrative review" by (3) presents a comprehensive examination of TXA, a fibrinolytic inhibitor, and its application in various surgical contexts, particularly focusing on its efficacy and safety profile. The authors synthesize findings from numerous trials that assess TXA's role in preventing and managing hemorrhage, particularly in patients with underlying bleeding disorders and those on antithrombotic medications.

A critical evaluation of the material reveals that while TXA has been established as a vital tool in reducing bleeding severity, its application is marred by uncertainties regarding its thromboembolic risk. The authors note that although TXA is generally well-tolerated and significantly more potent than its counterpart, ϵ -Aminocaproic acid, the potential for thrombotic events associated with its use remains an area of concern. This ambiguity is particularly pertinent in the context of liver surgery, where patients may already possess a heightened risk due to underlying liver pathology.

The review highlights the lack of consensus on the optimal dosing of TXA across various surgical indications, which further complicates its clinical application. The authors emphasize that despite extensive research, the evidence supporting TXA's efficacy in certain scenarios is either lacking or ambiguous. This presents a critical juncture for future developments in TXA

research, as addressing these gaps could enhance its safety profile and therapeutic effectiveness.

The article "Does TXA Reduce the Blood Loss in Various Surgeries? An Umbrella Review of State-of-the-Art Meta-Analysis" by (4) presents a comprehensive overview of the efficacy and safety of TXA in surgical contexts. The authors conducted an umbrella review, which synthesizes findings from multiple systematic reviews and meta-analyses, thereby providing a robust examination of the available data on TXA's impact on blood loss across various surgical procedures.

The main insight from the article is the dual nature of TXA as both a protective factor against vascular adverse events and a potential risk factor for complications, particularly in high doses. The authors highlight that while TXA has demonstrated benefits in reducing blood loss in cardiac surgeries, its application is complicated by concerns regarding adverse events, such as seizures, especially in patients with pre-existing conditions like renal impairment or coagulation dysfunction. This nuanced perspective is crucial for clinicians considering TXA for patients undergoing liver surgery, where the balance between minimizing blood loss and mitigating risks is particularly delicate.

Moreover, the article's critical evaluation of the quality of included studies is noteworthy. The authors assert that most studies reviewed were of high quality, with a significant number published post-2016, indicating a growing body of evidence. However, the exclusion of non-English and non-Chinese studies introduces a potential bias, which could limit the generalizability of the findings. Additionally, the variability in effect sizes across different meta-analyses raises concerns about the heterogeneity of results, which could complicate clinical decision-making.

The authors also acknowledge that while TXA may have applications beyond cardiac surgery, these were not addressed in their review due to the absence of relevant meta-analyses. This limitation suggests an area for future research, particularly in the context of liver surgery, where the need for effective hemorrhage control is paramount.

The article "Effects of TXA on Intraoperative Bleeding and Surgical Field Visualization During Middle Ear Surgery: A Narrative Review" by (5) provides a comprehensive examination of the role of TXA as a hemostatic agent in the context of ear surgery, particularly focusing on its effects on intraoperative bleeding and surgical field visibility. The authors emphasize the critical issue of intraoperative bleeding, which can impede surgical outcomes, thereby highlighting the relevance of TXA in this surgical domain.

A significant strength of this narrative review is its thorough approach to synthesizing existing literature on TXA, particularly as interest in its use has surged alongside the rise of endoscopic techniques in ear surgery. The authors reference several

systematic reviews that underscore the efficacy of TXA in reducing blood loss and the need for transfusions. However, they also acknowledge the conflicting findings regarding TXA's association with thromboembolic events and mortality, which raises important questions about its safety profile in surgical settings.

Despite its strengths, the review is not without limitations. A major concern highlighted by the authors is the limited number of studies included in the analysis, which restricts the generalizability of the findings. The heterogeneity among the studies regarding TXA administration methods, dosages, and control conditions is particularly problematic. This variability complicates the interpretation of results and precludes a quantitative analysis, which could provide more definitive conclusions about TXA's effectiveness. Furthermore, the authors note that only one of the included trials explicitly reported the absence of side effects, leaving a gap in understanding the potential adverse effects of TXA, particularly in relation to thromboembolic complications.

The authors' narrative approach to reviewing the literature is commendable, as it allows for a qualitative synthesis of the available evidence. However, the scarcity of robust studies and the significant variability in methodologies necessitate caution when drawing conclusions about the efficacy and safety of TXA in middle ear surgery. The authors suggest that further research is needed to clarify these issues and to establish more standardized protocols for TXA use in surgical practice.

CONCLUSION

Collectively, the literature reveals a promising yet complex landscape for TXA in surgery. While its effectiveness in reducing blood loss and the associated risks is well-documented, uncertainties regarding optimal dosing, application in specific surgical contexts, and safety profiles necessitate further research. Future studies should aim to clarify these uncertainties, particularly in specialized areas such as liver surgery, to develop tailored protocols that optimize patient outcomes.

Keywords: Tranexamic acid, bleeding, surgery

Footnotes

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