

Perspective

Integration of Tranexamic Acid into Massive Transfusion Protocols: Current Evidence and Clinical Considerations

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Hemorrhage remains one of the leading causes of preventable death in trauma, accounting for up to 40% of deaths within the first 24 hours after injury [1]. In this context, modern hemorrhage control strategies have increasingly incorporated the rational use of blood products in association with antifibrinolytic agents, particularly tranexamic acid (TXA). TXA acts by inhibiting fibrin degradation through competitive binding to lysine sites on plasminogen, thereby stabilizing clot formation [2]. The early incorporation of TXA into Massive Transfusion Protocols therefore represents a significant shift in contemporary trauma care practice.

From a pathophysiological perspective, hemorrhagic shock triggers a cascade of events that profoundly compromise vascular integrity. One of the earliest targets of the systemic inflammatory response is the endothelial glycocalyx, a complex layer of proteoglycans and glycoproteins responsible for regulating vascular permeability, cellular signaling, and hemostatic balance [3]. Disruption of this structure, mediated by tissue hypoxia, catecholamine release, and inflammatory mediators, leads to increased capillary permeability, amplified inflammation, and accelerated consumption of coagulation factors, thereby significantly worsening trauma-associated coagulopathy [4,5].

Within this often-silent phase of hemodynamic deterioration, simple assessment tools assume particular importance. The Shock Index, calculated as the ratio between heart rate and systolic blood pressure, has proven to be an effective marker for early detection of occult shock [6]. Values greater than 0.9 are associated with increased mortality, higher requirements for massive transfusion, and a greater likelihood of urgent surgical intervention, even in patients who remain normotensive [7]. Its simplicity allows rapid bedside application in the trauma bay, supporting early therapeutic decisions such as timely TXA administration.

The scientific evidence supporting the use of tranexamic acid in trauma care is robust. The CRASH-2 study, a large multicenter randomized controlled trial, demonstrated a significant reduction in mortality among bleeding trauma patients when TXA was administered within three hours of injury [8]. Subsequently, the CRASH-3 trial, which focused on patients with traumatic brain injury, further reinforced the safety and efficacy

of TXA, showing reduced mortality in mild to moderate TBI without an increased incidence of thromboembolic events [9].

Based on these findings, international guidelines recommend the administration of 1 g of TXA as an intravenous bolus, followed by an additional 1 g infused over eight hours, provided treatment is initiated within three hours of trauma [10]. Administration beyond this time window is not only ineffective but may also be associated with an increased risk of thrombotic complications. Furthermore, TXA should be used with caution or avoided in patients with a recent history of deep vein thrombosis, ischemic stroke, or active seizure disorders [11].

In conclusion, early administration of tranexamic acid, when systematically integrated into massive transfusion protocols, represents one of the most important evidence-based interventions for hemorrhage control in trauma. A comprehensive understanding of shock pathophysiology, particularly the role of the endothelial glycocalyx, combined with judicious use of the Shock Index, enhances early identification of patients at high risk for adverse outcomes. High-impact studies such as CRASH-2 and CRASH-3 provide strong scientific support for this practice, making TXA implementation a cost-effective and potentially life-saving strategy.

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