Letter to the Editor

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Tranexamic acid and pre-hospital trauma setting: Is everything clear by now?

https://doi.org/10.1515/ohe-2023-0005
received August 07, 2023; accepted September 06, 2023

Abstract: An early use of tranexamic acid (TXA) in polytrauma patients has long been emphasized, although several conflicting evidence make its applicability still controversial and claims debate. Several multicenter trials have been conducted and the latter appear to collide with recent evidence published in the literature. In particular, the putative effects of early prognostic and hospitalization are still far from a common recommendation. We believe conflicting evidence derives from an unproper standardization of the pre-hospital setting, where non-diversified demographic factors, such as sociodemographic ones and accessibility to resources, still play a significant and detrimental role in patients' outcomes. Moreover, evaluation and investigation of the real benefits of TXA administration in the trauma patient according to the different settings or scenarios are required, as the availability of resources could represent a non-negligible bias that could lead to evidence too far from universal applicability and accessibility.

Keywords: trauma, tranexamic acid, scenario

To the editor,

Tranexamic acid (TXA) is an antifibrinolytic agent which exerts its competitive mechanism on coagulation by inhibiting plasminogen lysine binding sites and ultimately reducing hemorrhage. Literature has provided increasing support for the early use of TXA already in an out-of-hospital setting for polytrauma patients. However, several conflicting arguments regarding indications, methods and protocols of administration as well as the presence of real putative benefits and universal applicability still claim discussion. van Wessem et al. [1] highlighted several noteworthy evidence. In this prospective study including 234 trauma patients with traumatic brain injury admitted to a Dutch Level 1 Trauma Center ICU, the authors reported the effects of an early prehospital administration of TXA. A total of 51% of enrolled patients received 1 g TXA bolus. Although patients' cohorts were characterized by peculiar demographic and traumatic differences (preoperative intubation, need for emergency laparotomies), interestingly they did not report prognostically significant differences nor benefits in the administration of TXA in trauma cases (TXA vs no TXA: $p = 0.040$). At the cumulative analysis, an early administration of TXA had no therapeutic or prognostic effects in trauma patients, and prognostic factors were the age, the estimation of the injury severity score, the head, abdomen or external acute injury score as well as the hemoglobin titre, the concomitance of an acidotic state, a decrease in excess bases and the volume of infused crystalloids in the first 24 h. Late prognostic factors were the number of days of ventilation and infectious complications.

This prospective study by van Wessem et al. [1] would seem to struggle against some evidence from the literature. However, emerged evidences should be contextualized claiming a critical reflection about the rationale of TXA adoption in trauma patients, as reported in the CRASH-2 trial [2], which reported a significant reduction in the relative risk of mortality (RR 0.68, 95% CI: 0.57–0.82; $p < 0.0001$) and in all-cause mortality from 16 to 14.5% (RR 0.91, 95% CI: 0.85–0.97, $p = 0.0035$) in cohort of TXA patients was reported. On the other hand, evidence emerging from the abovementioned prospective study would appear to concur with conclusions of the recent CRASH 3-trial [3]. But, results appear somewhat dissonant with those reported by a German propensity score-based matched study [4], where it was reported that the prehospital TXA bolus was associated with a reduction in early mortality rates (1.9 vs 9.3%, $p < 0.001$) although the in-hospital

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mortality rates did not significantly differ (14.7 vs 16.3%, $p = 0.72$).

We firmly believe that the scarcity and fragmentation of evidence can be attributed to a general lack of characterization of the pre-hospital setting. However, the cornerstone remains whether prehospital administration adds any benefit outweighting fearfull arms in complex scenarios. The inapplicability of universalistic models leading to standardized procedures as well as the absence of protocols make the question still open and claiming debates. In our opinion, what appears to be a crucial aspect is the role of TXA in those prognostic factors masterfully reported by van Wessem et al. [1]. The evaluation of the TXA effects on trauma-related mortality cannot be taken out of context from a study design contemplating a subanalysis of demographic risk factors. In summary, we still face a fragmentation and paucity of evidence that supports the use of TXA in the prehospital setting still too far from international multicenter studies involving applicability, variability and universalistic models as primary design.

Conflict of interest: The authors state no conflict of interest.

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