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Tranexamic acid in the prehospital setting: Israel Defense Forces' initial experience

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ABSTRACT

Background: The leading cause of preventable death in the military setting is haemorrhage. Accumulating evidence has established the benefit of tranexamic acid (TXA), an antifibrinolytic, for treating traumatic haemorrhage in the hospital setting. The use of TXA in the prehospital setting, however, has not been previously described. The present study details our initial experience with a field protocol that advances TXA administration to (or as close as possible to) the point of injury.
Methods: We present a series of all casualties treated with TXA by Israel Defense Forces' (IDF) prehospital advanced life support providers between December 2011 and February 2013. Data were abstracted from the IDF Trauma Registry at the Research Section of the Trauma and Combat Medicine Branch, Surgeon General's Headquarters.
Results: Forty casualties who received TXA in the prehospital setting were identified. Most casualties were male ($n = 35$; 88%) and young adults (median 28 years). The mechanism of injury was penetrating in 22 cases (55%). TXA was administered earlier than it could have been in the hospital setting without delaying evacuation. There were no reports of adverse outcomes that could be reasonably attributed to TXA. Casualties who received TXA per protocol were sicker than those who received it not per protocol.
Conclusions: We have shown that TXA may be successfully given in the prehospital setting without any apparent delays in evacuation. In light of recent evidence, the ability to give TXA closer to the time of wounding represents an important step towards improving the survival of trauma victims with haemorrhage, even before definitive care is available. While this may be especially relevant in austere combat environments, there is likely benefit in the civilian sector as well. The safety profile of TXA is an important consideration as prehospital personnel tended to overtreat casualties without indications for TXA per protocol. We suggest that TXA be considered a viable option for use by advanced life support providers at or near the point of injury.

Introduction

Haemorrhage is the leading cause of potentially preventable death in the military setting among both regular and special operations forces [1–3]. While tourniquets, direct pressure, and hemostatic dressings are of proven benefit for accessible bleeding sites, fluid resuscitation and prompt evacuation have been the mainstays for addressing non-compressible haemorrhage in the forward setting. An antifibrinolytic, tranexamic acid (TXA), has recently been shown to be an important part of the hospital-based provider's armamentarium for treatment of traumatic haemorrhage. Its use in the prehospital setting, however, has not yet been evaluated.

In a large, international, hospital-based study of civilian trauma patients suspected of having haemorrhagic shock, TXA was shown to reduce mortality ("CRASH-2") [4]. Importantly, no increase in vascular occlusive events was observed. A subsequent analysis using the same data made it clear that early administration was crucial, with late administration (>3 h) possibly reducing survival [5].

TXA has also been evaluated in the military field-hospital setting ("MATTERs") [6]. This retrospective, observational study at a surgical field hospital (role 3) examined the use of TXA in combat

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victims who received at least 1 unit of packed red blood cells (PRBCs); TXA was administered within 24 h of admission. The authors found that TXA improved survival, especially among massively transfused casualties; the number needed to treat to achieve a mortality benefit in this latter group was 7. In contrast to the prospective, randomized civilian study mentioned above, this observational study in a military setting did find an increased rate of venous thromboembolism (VTE) in casualties treated with TXA, though there were no fatalities attributed to these events.

Because earlier administration of TXA was associated with improved survival, TXA should be strongly considered for use in the prehospital setting, where the time interval from injury to administration can be even further reduced [7].

As part of our comprehensive effort to improve casualty care and eliminate preventable death, the Israel Defense Forces (IDF) approved TXA for prehospital use in trauma in 2011, releasing a treatment protocol for use by IDF advanced life support providers (physicians and paramedics). The present study describes our initial experience with advancing TXA administration to (or as close as possible to) the point of injury. Though this case series is relatively small, we felt it appropriate to publish these preliminary findings because of the potential for saving lives.

Methods

IDF TXA protocol for prehospital use in trauma

The IDF protocol for TXA administration was developed at the Trauma & Combat Medicine Branch (TCMB), at the Surgeon General's Headquarters. For scientific input, the TCMB established a task force composed of the country's leading trauma surgeons and haematologists. The protocol was designed to be sensitive at the expense of decreased specificity, to ensure that casualties with possible haemorrhagic shock, especially those who may require massive transfusion, would be included. According to the protocol, TXA should be given in 2 circumstances:

1. Any penetrating injury to the torso, including the neck, axillae, groin, and buttocks.
2. Blunt or penetrating injury accompanied by signs of shock. Shock was defined as the presence of any of the following: systolic blood pressure (SBP) $<$90 mmHg, heart rate (HR) $>$100 beats per minute on repeated measurement, delayed capillary refill ($>$2 s), or altered level of consciousness in a casualty without blunt head trauma. This definition of shock was chosen to be consistent with the IDF fluid resuscitation protocol for trauma [8]. If shock is diagnosed, TXA is given even if haemorrhage has ceased.

Adult casualties are given 1 g intravenously, either by slow push (5–10 min) or mixed with crystalloid for infusion. (Paediatric dosing was not included in the protocol as paediatric trauma cases are rarely encountered by our providers.) If the casualty is in the field for an extended period (i.e., greater than 3 h) due to delayed evacuation, a second 1 gram dose of TXA is given 3 h after the initial dose. In exceptional circumstances (i.e., where obtaining IV access would delay transport or in a mass casualty setting), TXA may be given orally at a dose of 1.5 g. TXA is given at the end of the secondary survey with other treatment adjuncts such as analgesics and antibiotics. Administration of TXA should not interfere with the initial resuscitation that is part of the primary survey, or delay evacuation efforts, though it may be started or continued during evacuation. The casualty's medical record must indicate that TXA was given and when it was given. The protocol was approved in May 2011. Upon completion of procurement in August 2011, we began TXA distribution to medical field units. The first prehospital use of TXA by IDF providers occurred in December 2011.

Data acquisition

The Research Section of the TCMB receives brief reports regarding all trauma victims, whether military or civilian, treated by IDF prehospital medical teams, usually within hours of the incidents. These initial reports have very concise data regarding location, mechanism, treatment, casualty status, and means and destination of the evacuation. For the purposes of monitoring TXA use, these reports also contain an explicit data field indicating whether TXA was given. The reports are all followed, usually within several weeks, by medical investigations performed by the regional medical commanders of the various units. A senior representative from the TCMB attends these after-action debriefings to clarify aspects of casualty care, including whether TXA should (or should not) have been given, and the timing and means of administration. If the casualty was evacuated by the IDF's elite Airborne Search, Rescue, and Evacuation Unit, further details were available from their internal event reports and debriefings. All of the above data, as well as in-hospital data, were entered by trained abstractors into the IDF's trauma registry (ITR), maintained at the TCMB.

IDF medical teams are almost exclusively ground-based and are composed of at least 1 paramedic or physician, in addition to medics. Evacuation is generally by IDF or civilian EMS mobile ICU teams, using both ambulances and helicopters. The IDF airborne medical teams are physician-based and are equipped with PRBCs, with civilian level 1 trauma centres serving as their destinations, except in extenuating circumstances.

Study design

This study is a case series of all subjects known to be treated with TXA by IDF medical providers in the prehospital setting from December 2011 through February 2013. To minimize the possibility that any cases of TXA administration were missed, regional medical commanders were periodically contacted directly.

Prehospital data collected included demographic information; injury mechanism; nature and severity of injury; vital signs including Glasgow coma score (GCS); procedures performed, including life-saving interventions (defined to include intubation, cricothyroidotomy, needle thoracostomy, and chest tube thoracostomy); and time of and indication for giving TXA. In cases where it was not known exactly when TXA was given, the maximum possible elapsed time was used (e.g., if it was known that TXA was given before the evacuating helicopter arrived, then the known time of helicopter arrival was used to compute the elapsed time before TXA was given). Hospital data included severity of injury, vital signs, and select laboratory blood work taken upon hospital arrival; procedures and operations performed; blood products transfused; length of hospital and ICU stay; whether there were complications, specifically deep venous thrombosis or pulmonary emboli; Injury Severity Score (ISS); and status upon discharge.

For determining whether TXA was indicated, two senior medical officers from the TCMB reviewed the event reports submitted by the field providers, including mechanism (penetrating versus blunt or other), location of injury (torso with or without head, or other), and vital signs including GCS. Any residual uncertainty was addressed at the debriefings; if they were not informative, hospital data were used for determining mechanism and location. (Field data were used in preference to hospital data because the protocol addresses the field provider's assessment of