African Journal of Emergency Medicine 9 (2019) S52–S55

Contents lists available at ScienceDirect

African Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/afjem

ORIGINAL ARTICLE

Development of a nurse-led tranexamic acid administration protocol for trauma patients in rural South Africa

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ARTICLE INFO

Keywords:
Nurse-led care in health technology
Triage
Trauma
Emergency medicine

ABSTRACT

Introduction: Administration of tranexamic acid (TXA) has been shown to effectively reduce all-cause mortality in trauma patients when given within three hours of injury. We found that many trauma patients in our hospital were not receiving TXA. This was due to a variety of factors, including late presentation to hospital, lack of staff awareness, short staffing, and unavailable drugs or equipment. Our aim was to develop a protocol for safe, nurse-led administration of TXA in the emergency centre in order to increase the number of eligible patients treated.
Methods: We developed a protocol based on the inclusion criteria of the CRASH-2 study, opting to use physiological observations along with criteria from the South African Triage Scale to allow nursing staff to identify patients with, or at risk of, significant haemorrhage. We tailored the protocol to the equipment and training available in our poorly resourced rural healthcare setting.
Results: In a two-month period, 14 patients were given TXA by nurses before the arrival of a doctor. 13/14 (92.9%) were deemed appropriate, with 1/14 (7.1%) deemed inappropriate due to the time since injury. 12/13 (92.3%) patients received the correct infusion dose, with 1/13 (7.7%) only receiving the infusion once the doctor arrived. No adverse events were reported.
Conclusions: Nursing staff in resource poor rural settings can use a protocol based on the South African Triage Scale and the CRASH-2 study to safely administer TXA to trauma patients. We believe this to be the first published literature on nurse-led administration of TXA. Mortality from trauma may be reduced in rural settings by the timely administration of TXA in the prehospital and rural primary healthcare settings.

African relevance

- Tranexamic acid is an inexpensive and effective drug to reduce all-cause mortality when given early in trauma.
- Many patients who could benefit from tranexamic acid do not receive it.
- A nurse-led protocol may improve patients' access to tranexamic acid.

Introduction

Trauma is a disease that disproportionately affects low- and middle-income countries (LMICs). Over 90% of deaths due to injury worldwide occur in LMICs [1]. Compared to high-income countries, LMICs have double the overall death rate, and triple the disability adjusted life years (DALYs) from trauma [2]. South Africa is a country renowned for its burden of injuries, accounting for 27% of all attendances to emergency centres in our province [3].

Haemorrhage is one of the leading causes of deaths after trauma, accounting for 40% in the UK [4]. In recent years, there has been an increasing recognition of the importance of haemorrhage control; balanced resuscitation; and prevention of hypothermia, coagulopathy and acidosis, known as "the lethal triad" of trauma. Patients who develop acute traumatic coagulopathy have significantly higher mortality [5].

Tranexamic acid (TXA) is an anti-fibrinolytic that has been demonstrated to reduce bleeding and save lives in trauma. The CRASH-2 (Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage 2) trial was a randomised, placebo-controlled trial. It included over 20,000 patients and over 40 countries across the world, including several LMICs. It demonstrated a reduction in all-cause mortality when given early after trauma [6]. The earlier the drug was given, the better the mortality benefit; however, the benefit was lost three hours after injury [7].

This importance of early administration was mirrored in the WOMAN trial which looked at TXA in post-partum haemorrhage [8]. A meta-

Peer review under responsibility of African Federation for Emergency Medicine.
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https://doi.org/10.1016/j.afjem.2018.10.001
Received 18 September 2018; Accepted 3 October 2018
Available online 08 January 2019

analysis of the amalgamated results from both trials found that survival benefit decreased by 10% for every 15 minutes of treatment delay [9]. Patients across the whole of the injury severity spectrum benefit from TXA, not just the most severely injured [10]. The MATTERs study which looked at TXA administration in military personnel who sustained combat injuries that caused haemorrhage and required blood transfusion showed a significant reduction in mortality (17.4 vs 23.9%) despite the TXA group having a higher mean injury severity score [11].

It is estimated that TXA could save over 100,000 lives a year globally. In South Africa alone, 1189 deaths could be averted if TXA was given within three hours of injury, rising to 1359 if given within one hour of injury [12]. An assessment of the economic impact of TXA shows that it is a very inexpensive and effective drug. The estimated incremental cost per life year gained in India, a middle-income country like South Africa, is $66. In Tanzania, a low-income country, it is just $48 [13].

In recognition of these findings, TXA was added to the World Health Organisation list of essential medicines in April 2013 [14]. It was also added to the South African Medical Formulary and the Essential Medicines List in 2015 [15] as well as the 10th edition of the Advanced Trauma Life Support course in 2017 [16]. Recognition of the need for timely administration has led to inclusion in paramedic guidelines in the UK and USA [17–19].

Despite the inclusion in national guidance, we found that TXA was not in use in our hospital for trauma patients. Responsible factors included delays in patient arrival or time to be seen by a doctor, as well as lack of knowledge, equipment or the actual drug. Under-utilisation of TXA has been reported in other South African emergency centres [20].

Methods

Our 363-bed rural district hospital has 16 doctors, and receives walk in patients, referrals from nurse-led primary health clinics and the ambulance service. The majority of patients coming to attend the hospital, both for routine and emergency care, enter via the outpatient department (OPD). All patients are seen by a nurse and triaged using the South African Triage Scale (SATS) [21]. We have a very limited number of doctors to cover multiple clinical areas. This can inevitably lead to delays in even critically injured patients being reviewed by a doctor.

The use of a protocol and an educational package has been shown to increase the number of eligible patients receiving TXA [22]. However, this still relies on a doctor seeing the patient early. We were concerned that requiring a doctor to be present before TXA could be administered would result in survival benefit being lost. Additionally, with the regular turnover of doctors, especially locum doctors working out of hours, it would have been hard to deliver a package of education that would reach all of them.

We hypothesised that a nurse-led protocol could increase the number of patients receiving TXA in a timely fashion by improving consistency in administration. Thus, increasing the number of eligible patients to receive the drug and maximising the survival benefit.

The aims of our protocol were to:

1. Select patients likely to benefit from TXA
2. Be easy to use by nurses after basic training
3. Have clear administration guidelines
4. Not require specialised equipment
5. Not delay further resuscitation
6. Promote good trauma care in line with national and international guidelines

The Acting Medical Manager of Benedictine Hospital provided authorisation to perform this implementation process and outcome audit, and its subsequent presentation and publication.

As the CRASH-2 study is the only randomised control trial looking at TXA in trauma, we chose to use it as the basis of our selection criteria and treatment guidelines. The paper included patients who had "*significant haemorrhage (systolic blood pressure < 90 mm Hg or heart rate > 110 beats per* min*, or both) or who were considered to be at risk of significant haemorrhage*" [6].

Quantitative physiological criteria were taken directly from CRASH-2's inclusion criteria. Qualitative criteria to select those *"at risk of significant haemorrhage"* were more difficult to set, when the target audience were nurses with varying levels of experience and training.

As patients were triaged using SATS, we defined any patient triaged as orange or red as being at risk of significant haemorrhage. If using the SATS strictly, all motor vehicle accident victims were coded orange. In reality, the triage nurses were risk-stratifying patients independently, and did not apply this to all patients. They typically only applied it to the more seriously injured patients, and thus, were inherently deemed to be at risk of significant injury and/or bleeding.

The other selection criterion we included was any patient seriously injured enough for the nurse or prehospital practitioner to put them on a stretcher in OPD. We had a maximum of four stretchers available, so any patient deemed to require one by staff would typically be high risk for significant injury/bleeding. Three hours from injury was the cut off time for administration. We encouraged the nursing staff to use their judgement when deciding the likely period of time elapsed.

Once a patient had been selected to receive TXA, the nurse would give 1 g as a slow intravenous bolus, and then a further 1 g diluted in a 500 ml bag of 0.9% saline. We chose to give the infusion dose of TXA in a 500 ml bag of 0.9% saline instead of via an infusion pump. Typically, the nursing staff would insert an intravenous cannula and give a bag of crystalloid fluid to all seriously injured patients. Given that crystalloids can worsen coagulopathy [23], this had the advantage of slowing fluid administration, decreasing iatrogenic harm as well as not requiring infusion pumps that were in very limited supply.

Once the protocol was completed and ratified by senior nurses, we delivered teaching sessions to the OPD nurses and doctors. The finalised protocol is shown in Fig. 1. The drug vials were kept in an individual box in the resuscitation area, clearly marked with the printed protocol on the lid. A book was kept in the box for nurses to record when they administered TXA.

Results

Fig. 2 shows a breakdown of the patients receiving nurse-led TXA over two months. Fourteen patients were given TXA by nurses before the arrival of a doctor. Overall 13/14 (92.9%) were deemed appropriate, with 1/14 (7.1%) deemed inappropriate as it was more than three hours since injury. It was noted that 12/13 (92.3%) patients also received the correct infusion dose, with 1/13 (7.7%) delayed, receiving the infusion once the doctor had arrived. No adverse events were reported.

One additional patient was identified by a doctor as being eligible for TXA but had not received it in advance from the nursing staff. This young patient was in the early stages of haemorrhagic shock, but had not yet become haemodynamically compromised to the point of having abnormal vital signs. However, the patient was on a stretcher and therefore should have received TXA according to the protocol. This reinforced the concept that physiological parameters alone could not identify 'at risk' patients that would benefit from TXA.

Discussion

As the benefit of TXA is being increasingly recognised, strategies to deliver it to bleeding patients have been developed. The first step was inclusion into hospital major haemorrhage protocols, and as the importance of early administration became more apparent, prehospital usage has followed [17–19]. However, these strategies have all generally trickled down from high-income countries. There has been little focus on LMICs, despite their wide contribution to the CRASH-2 evidence base and high incidence of trauma deaths [24].

It is known that TXA is an inexpensive, safe and effective drug when given correctly, and which has the potential to save many lives in LMICs

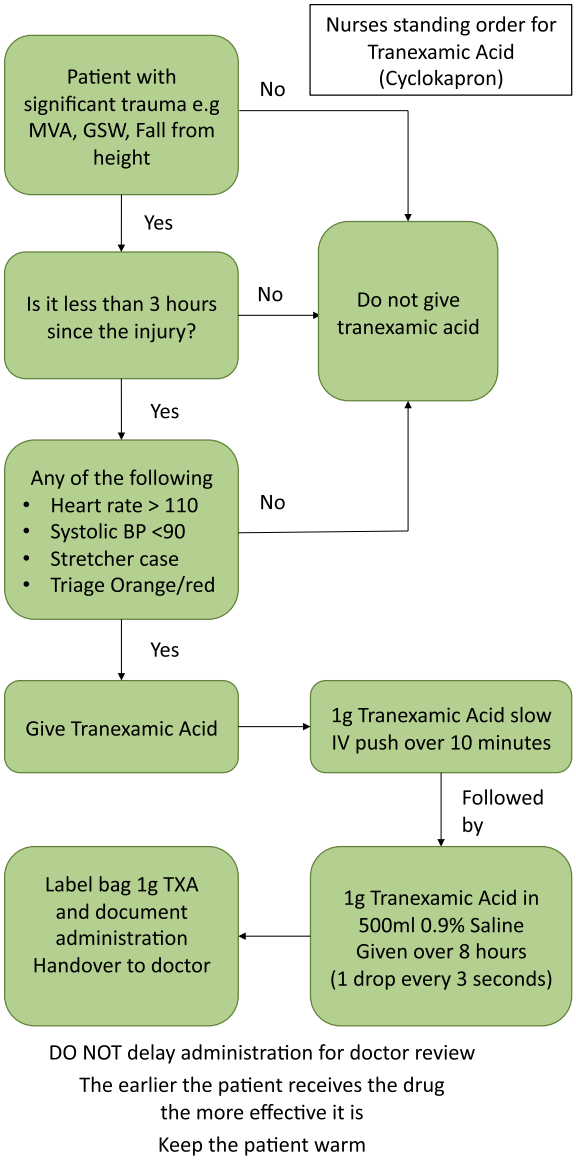

Fig. 1. Nurse-led tranexamic acid protocol in the emergency centre. *Note*. MVA, motor vehicle accident; GSW, gunshot wound; BP, blood pressure; IV, intravenous; TXA, tranexamic acid.

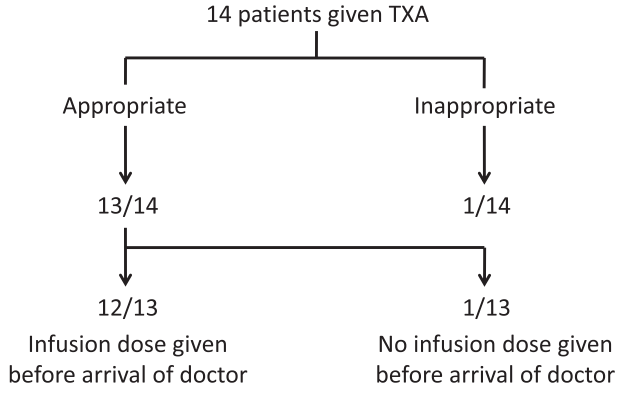

Fig. 2. Results of a nurse-led tranexamic acid (TXA) protocol over a two-month period.

[13]. Of the 26 countries in which TXA is predicted to be able to avert more than 1000 deaths a year, only one is not a LMIC [12]. Little focus has been given to how best to use this drug in settings that have few doctors, meaning that many patients will never reach one in time to receive the drug. In these places, there must be strategies for other healthcare professionals who will have earlier contact in the patient journey to administer TXA independently.

In our small study, we have shown that nurses working in an emergency centre setting can identify suitable patients and safely administer TXA to a similar level described in the prehospital literature [17].

We noted that our protocol rested on the triage system to work effectively. Without patients being seen by nurses and having vital signs taken and recorded efficiently, the protocol could not have run at all.

Patients reaching the physiological criteria included in CRASH-2 were easy to spot. However, getting nurses with more basic training to select those at risk of significant haemorrhage was more difficult. Given the good safety profile of TXA when used early, and the increased survival benefit in doing so [7,10], we felt a less restrictive approach to patient selection was best.

Our study has limitations, particularly in its size and single centre experience. With our patient numbers it would be extremely challenging to demonstrate change in mortality or patient outcome. We felt that a sample of 14 patients was probably a poor reflection of the number of seriously injured patients that were seen during the two-month period.

A key reason for the low number of injured patients given TXA was that many arrived more than three hours after injury. Large geographical distances, a lack of ambulances and a tendency to consult traditional medicines and healers before attending hospital all contributed to this delay in seeking treatment at hospital. The large geographical area covered by a small number of ambulances is compounded by the emergency telephone numbers often not working. The World Health Organisation estimates that only 50–74% of seriously injured patients in South Africa are transported to hospital by ambulance [25]. It was not uncommon for patients to present the following day, especially if intoxication had led to the injury occurring.

It is also possible we may have lost some patients from our analysis. Alternatively, suitable patients may have not been correctly identified or given TXA. We found that some nurses took to the protocol better than others, but that there seemed to be an improving attitude toward it after time and more education.

For many reasons our protocol may not transfer exactly to other settings, particularly those with better resources or availability of suitably trained staff. Our subjective treatment criteria will not be suitable for every setting (for instance using stretcher cases may not be applicable if a centre has no shortage of stretchers); however, we feel the general principle is transferable and should stimulate discussion on a local level. Different settings need to set subjective criteria based on their own individual profiles and to ensure that the protocol is implemented with a sufficient package of education and support.

We have demonstrated that nursing staff in resource-poor rural settings can use a protocol based on the South African Triage Scale and the CRASH-2 study to correctly identify suitable trauma patients and safely administer TXA. We believe this to be the first published literature on nurse-led administration of TXA.

Mortality from trauma may be reduced in rural settings by the timely administration of TXA in the prehospital and rural primary healthcare settings. This is likely to especially benefit healthcare systems in low- and middle-income countries where patient to doctor ratios are greater.

Acknowledgments

The authors would like to thank the nursing staff of the Benedictine Hospital Outpatient Department for their hard work and good humour, without which our work would not have been possible.

Conflicts of interest

The authors declare no conflicts of interest.

Dissemination of results

The results were presented orally at the 6th Emergency Medicine Society of South Africa (EMSSA) International Conference in Johannesburg, 2017.

Authors' contributions

Authors contributed as follows to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: CW contributed 90% and JS contributed 10%. All authors agree to be accountable for all aspects of the work in ensuring that any questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

[1] World Health Organization. Injuries and violence: the facts. http://www.who.int/violence_injury_prevention/key_facts/en/ [accessed 14.09.2018].
[2] Chandran A, Hyder AA, Peek-Asa C. The global burden of unintentional injuries and an agenda for progress. Epidemiol Rev 2010;32(1).
[3] Lutge E, Moodley N, Tefera A, et al. A hospital based surveillance system to assess the burden of trauma in KwaZulu-Natal Province South Africa. Injury 2016;47(1).
[4] Thomas D, Wee M, Clyburn Blood P, et al. transfusion and the anaesthetist: management of massive haemorrhage. Anaesthesia 2010:65(11).
[5] Brohi K, Singh J, Heron M, et al. Acute traumatic coagulopathy. J Trauma 2003;54:6.
[6] CRASH-2 Collaborators. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010:376.
[7] CRASH-2 Collaborators. The importance of early treatment with tranexamic acid in bleeding trauma patients: an exploratory analysis of the CRASH-2 randomised controlled trial. Lancet 2011:377.
[8] WOMAN TRIAL Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet 2017;289(10084).
[9] Gayet-Ageron A, Prieto-Merino D, Ker K, et al. Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40 138 bleeding patients. Lancet 2018;391(10116).
[10] Roberts I, Perel P, Prieto-Merino D, et al. Effect of tranexamic acid on mortality in patients with traumatic bleeding: prespecified analysis of data from randomised controlled trial. BMJ 2012:345.
[11] Morrison JJ, Dubose JJ, Rasmussen TE, et al. Military application of tranexamic acid in trauma emergency resuscitation (MATTERs) study. Arch Surg 2012;147(2).
[12] Ker K, Kiriya J, Perel P, et al. Avoidable mortality from giving tranexamic acid to bleeding trauma patients: an estimation based on WHO mortality data, a systematic literature review and data from the CRASH-2 trial. BMC Emerg Med 2012;12(3).
[13] Guerriero C, Cairns J, Perel P, et al. Cost-effectiveness analysis of administering tranexamic acid to bleeding trauma patients using evidence from the CRASH-2 trial. PLoS One 2011;6(5).
[14] World Health Organization. WHO Model List of Essential Medicines 18th list. http://www.who.int/medicines/publications/essentialmedicines/18th_EML_Final_web_8Jul13.pdf [accessed 14.09.2018].
[15] South African Department of Health. Standard treatment guidelines and essential medicines list for South Africa fourth edition. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwi-17ni07rdAhVOFMAKHeCHBmYQFjAAegQIABAC&url=http%3A%2F%2Fwww.health.gov.za%2Findex.php%2Fstandard-treatment-guidelines-and-essential-medicines-list%2Fcategory%2F286-hospital-level-adults%3Fdownload%3D2409%3Ahospital-level-adult-2015-v5-0&usg=AOvVaw0e0kCYVAiqraqEKfrovoyT [accessed 14.09.2018].
[16] Royal College of Surgeons. Overview of the ATLS 10th edition. https://www.rcseng.ac.uk/education-and-exams/regional-and-international-centres/practical-resources/atls-10/ [accessed 14.09.2018].
[17] Strosberg DS, Nguyen MC, Mostafavifar L, et al. Development of a prehospital tranexamic acid administration protocol. Prehosp Emerg Care 2016;20(4).
[18] Paudyal P, Smith J, Robinson M, et al. Tranexamic acid in major trauma: implementation and evaluation across South West England. Eur J Emerg Med 2017;24(1).
[19] Joint Royal Colleges Ambulance Liaison Committee. UK Ambulance Services Clinical Practice Guidelines: UK; 2016.
[20] Wiese JGG, van Hoving DJ, Hunter L, et al. Poor adherence to Tranexamic acid guidelines for adult, injured patients presenting to a district, public, South African hospital. Afr J Emerg Med 2017;7(2).
[21] South African Triage Group under the auspices of the Emergency Medicine Society of South Africa. The South African Triage Scale (SATS). https://emssa.org.za/sats/ [accessed 14.09.2018].
[22] Geyer BC, Gates J, Lee J, et al. Implementation of a tranexamic acid protocol in the emergency department. Ann Emerg Med 2013;62(4).
[23] Harris T, Thomas GOR, Brohi K. Early fluid resuscitation in severe trauma. BMJ 2012:345.
[24] Alvarado JC, Dewan Y, Elsayed HF, et al. Tranexamic acid in trauma: we need stronger global health policy. BMJ 2013:347.
[25] World Health Organization. South Africa Road Safety Statistics. www.who.int/violence_injury_prevention/road_safety_status/2013/country_profiles/south_africa.pdf [accessed 14.09.2018].