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Case Report

Tranexamic Acid Use in Pediatric Hemorrhagic Shock From Farm-Related Trauma: A Case Report

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A B S T R A C T

This case describes the use of tranexamic acid as an adjunctive treatment in the management of a pediatric patient in hemorrhagic shock. The case also highlights other components of current best practices for hemorrhagic shock in children, including bleeding source control and prompt resuscitation with blood products. A 20-month old male suffered an agricultural accident with significant injury to the right upper extremity. This led to subsequent extremity hemorrhage and clinical evidence of hemorrhagic shock. As a result of interventions performed by emergency medical services as well as the helicopter emergency medical services team, including the application of a tourniquet, prehospital blood product administration, and tranexamic acid administration, the patient had hemodynamically stabilized by arrival at the level 1 pediatric trauma center and was neurologically intact when discharged from the hospital.

The overarching principles of adult trauma resuscitation also apply to pediatric patients. However, tranexamic acid (TXA) is an intervention that has not gained widespread acceptance for use in pediatric patients for a variety of reasons including a relative paucity of pediatric-specific data for traumatically injured patients. Based on emerging evidence, underlying physiologic principles, and our institution's clinical experience, our service has been proactive in expanding the use of TXA to pediatric patients who have evidence of significant hemorrhage. When given, this intervention comes as an adjunct to the other foundational elements of resuscitation, including bleeding source control and hemostatic resuscitation. We report a case in which principles of hemostatic resuscitation, including TXA administration, were applied in the resuscitation of a pediatric patient in hemorrhagic shock with good effect.

Case Report

Rural community emergency medical services (EMS) and police responded to a family farm for report of an injured 20-month old male. Per report, the family had been working around farm equipment when the patient accidentally placed his right arm in a grain auger. The auger was first invented by Archimedes in 205 BC to move water against gravity using a drill-shaped, rotating screw. The grain auger, which still resembles that original design, is an omnipresent device on farms and is related to severe and fatal injuries.[1,2] The father immediately shut the grain auger off as the child was being pulled deeper into the device. He began extricating the patient from the auger to the best of his ability, and local 911 was notified.

Because of the severity of the injury as well as the distance from the closest level 1 pediatric trauma center (70 miles), 911 dispatch requested the services of the closest helicopter emergency medical service (HEMS), UW Health Med Flight, Madison, WI, a physician–registered nurse staffed, multibased service with advanced trauma resuscitation capabilities, including packed red blood cells, liquid plasma, and TXA.

There was a prolonged extrication performed by EMS services before HEMS team arrival, approximately 30 to 45 minutes after the

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initial incident. The HEMS team found the patient in full spinal precautions on an EMS stretcher in the back of their ambulance with bilateral pressure dressings to the upper extremities and a tourniquet to the right upper extremity, which was the primary source of visible bleeding. A brief history was obtained from the family; there was no known past medical history or allergies, his family was Mennonite, and the patient had not been vaccinated. The handover was completed between the EMS and HEMS teams, a rapid trauma evaluation was performed in the back of the ambulance by the HEMS crew, and further trauma resuscitation ensued.

The patient was alert with a Glasgow Coma Scale of 13, localizing to pain, and opening eyes to speech. He was crying and minimally consolable. He was noted to be pale and had mild perioral cyanosis, with clinical evidence of decreased skin temperature throughout. His vital signs were consistent with shock, with a sinus tachycardia of 170 beats/min and noninvasive systolic blood pressures of 40 to 60 mm Hg (lower extremity). He was noted to have peripheral oxygen saturation of 91% on room air and a respiratory rate of 30 breaths/min. Auscultation revealed bilateral breath sounds and equal chest rise and fall; however, the patient did have significant right-sided chest wall tenderness to palpation. There was associated ecchymosis and abrasions but no flail segments or crepitus appreciated. He had an open right humeral fracture with a tourniquet in place, nonpalpable distal pulses, a right hand with a partial thumb amputation, and scattered partial- and full-thickness lacerations with exposed muscle and subcutaneous adipose tissue. The extremity was cool to the touch. The left upper extremity had multiple abrasions and lacerations but no obvious long bone deformity and was neurovascularly intact, albeit with a diminished radial pulse and capillary refill (presumed secondary to hemorrhagic shock). His abdomen was mildly tender but soft and without frank peritonitis or ecchymosis. His pelvis was grossly stable. The patient was moving all extremities spontaneously but had tenderness and swelling to the right thigh with reduced movement secondary to pain but no gross deformity.

After the initial assessment, interventions were begun. The patient was placed on supplemental oxygen via a nasal cannula with concurrent end-tidal capnography. The patient did not have any intravenous access, so intraosseous access was obtained in the left humeral head. The patient was covered in blankets to prevent worsening hypothermia and expeditiously prepared for transport and loaded in the helicopter. In transport, the patient was given a 20-mL/kg bolus of packed red blood cells and then was administered 1 g of TXA diluted in 100 mL normal saline and administered over 10 minutes as per our program guidelines. The patient responded well with significant improvement in mentation and skin color as well as increased systolic blood pressure and decreased heart rate. The patient otherwise tolerated the flight well and was brought to the trauma bay where his care was transferred to the pediatric trauma team. His vital signs on initial evaluation in the trauma bay were pertinent for a blood pressure of 115/74 mm Hg and a heart rate of 150 beats/min.

The child was found to have a right humeral fracture, right first metacarpal fracture/partial amputation, right femur fracture, left ulnar buckle fracture, left third metacarpal fracture, and fractures of right ribs 2 through 7. Although the majority of his blood loss seemed to be from the extremity injuries, these additional injuries (in particular the femur fracture) could have contributed via occult hemorrhage to his shock state. He had operative intervention on his right upper extremity fractures and was discharged after 5 days in the hospital. He has had continued follow-up with orthopedic surgery and physical/occupational therapy and is anticipated to have full use of function of his right upper extremity as well as his right lower extremity with no long-term deficits from this accident.

Discussion

This case highlights what we feel is cutting-edge prehospital management of pediatric hemorrhagic shock. As in many rural areas, the EMS response was tiered. Visible hemorrhage control was appropriately achieved by direct pressure and tourniquet application by basic life support services. Because of critical acuity and the distance from the level 1 pediatric trauma center, the HEMS team was requested. Additional interventions were then provided by the air medical team, including focused assessments, TXA and blood product administration, and rapid transport.

Trauma is responsible for more than 5.8 million deaths worldwide, and in the United States it is the leading cause of death for individuals from the ages of 1 to 44 years.[3] An important subtype of traumatic injuries is those with a significant contribution from significant hemorrhage and coagulopathy.[4] Antifibrinolytic drugs, such as TXA, reduce bleeding by inhibiting the body's natural breakdown of fibrin clots.[5] Antifibrinolytic drugs have been shown to reduce surgical bleeding and the need for intraoperative transfusion by a third.[6] Additional studies, such as CRASH-2 and WOMAN, have shown that the administration of TXA within 3 hours of bleeding onset reduces deaths from bleeding from trauma and postpartum hemorrhage.[7,8]

TXA was first discovered in the 1950s but has been increasingly used as research has evolved over the last 10 to 20 years. It reduces bleeding by inhibiting the enzymatic breakdown of fibrin blood clots (fibrinolysis). TXA use became much more prevalent after the results of the CRASH-2 trial, which showed that for trauma patients with major bleeding (other than intracranial), early administration of TXA within 3 hours of injury reduced bleeding deaths by a third.[7] Other studies such as the WOMAN trial, MATTERS trial, and a resulting meta-analysis also showed that TXA is more effective when given earlier and that it has little to no significant adverse events.[9,10] It is also an inexpensive medication available in generic formulations. It is relatively easy to administer even in the low-resource prehospital environment when appropriate planning is done.

TXA has traditionally been given once the injured patient reaches the hospital. However, as prehospital care and EMS systems have advanced, administration has become possible in the field and, therefore, temporally closer to the onset of injury. Research shows that most deaths from bleeding occur on the day of injury, and many occur within the first few hours. This is true for both trauma as well as other causes of hemorrhagic shock, such as postpartum hemorrhage. TXA improves survival, but it is believed that treatment delay reduces the benefit.[9] The delay seems less important within the first hour, although researchers suggest that perhaps this is because a larger proportion of patients who die within 1 hour have unsurvivable hemorrhage, such as large penetrating thoracic injuries.[9]

There are several potential benefits to the early administration of TXA. Most deaths from hemorrhage occur within hours of bleeding onset. By reducing hemorrhage, TXA may also help prevent the other sequelae of the traumatic triad (coagulopathy, acidosis, and hypothermia).[5] Also, the benefit of TXA appears to decrease with increasing treatment delays; therefore, early treatment may be critical in order to achieve the maximum effect. Finally, there is little evidence to support significant adverse effects associated with TXA treatment, so there is little downside to using this safe, cheap medication (although we cannot discount the potential added cognitive and procedural burden on the medical providers). Outside of extremely rural areas, the majority of trauma patients have their injuries occur within 180 minutes/3 hours of EMS contact with them. Therefore, they are potential candidates for TXA administration if the EMS service has the capability to provide it.

Unfortunately, it is not only adult patients who suffer from traumatic injuries. Hemorrhagic shock is believed to the leading preventable cause of death in pediatric patients after injury.[11] Unfortunately, the majority of the studies examining TXA have attempted to exclude pediatric patients. However, there are some studies that suggest similar safety and efficacy profiles in the pediatric population. In particular, the PED-TRAX study showed an independent association between receiving 1g TXA and decreased mortality if given within 3 hours of injury. Pediatric patients who received TXA also had a significantly better Glasgow Coma Scale score and were less likely to require mechanical ventilation on discharge or transfer.[12] In addition, TXA has been commonly used in various pediatric surgical fields with success, in particular cardiac and craniofacial surgery. The dosages used here are typically much higher than those proposed for traumatically injured patients, but the safety profile remains acceptable.[13,14] Although there are certainly critical physiological and other differences between pediatric and adult patients, it would not be unreasonable to expect that the core principles of acquired traumatic coagulopathy would be similar, and, therefore, similar treatments could be beneficial. In fact, there are some data to suggest that pediatric patients form blood clots that are less resistant to fibrinolysis than adults; therefore, it could be proposed that adjunctive treatments (such as TXA) to stabilize these clots may be even more beneficial (although this has not been specifically studied to our knowledge).[15]

Based on further review and study, we have since revised our recommended TXA dosing for pediatric trauma patients based on consensus guidelines.[14,16,17] We have moved to a weight-based dosing of 15 mg/kg, up to a maximum of 1 g. However, an argument could be made that a larger "loading dose" (such as an empiric 1 g) is not necessarily harmful when provided initially and as a 1-time treatment, but further research is needed.[13]

As with our TXA guideline, other guidelines have continued to evolve since this patient encounter. As a result of further research studies, we now carry liquid never-frozen plasma as well as packed red blood cells, and we recommend plasma as the initial fluid for resuscitation of hemorrhagic shock.[18,19] We also have guidelines for calcium supplementation during large-volume transfusions, both in adult and pediatric patients.[20,21] By continuing to update our guidelines to reflect evolving research, we aim to consistently provide aggressive, evidence-based critical care resuscitation to our patients.

Conclusion

In summary, we present the case of a 20-month old male who suffered a significant traumatic injury with resultant life-threatening hemorrhagic shock. EMS was instrumental in extricating the patient as well as performing initial hemorrhage control measures, including tourniquet application. The HEMS team then intercepted and provided additional advanced prehospital interventions following guidelines of hemostatic resuscitation and aiming to minimize traumatic shock and coagulopathy. This was combined with rapid transport, and the patient arrived at the hospital already both clinically and hemodynamically greatly improved and had a resulting optimal outcome. We believe that the future will show continued broadening of advanced resuscitation interventions from the adult population to the pediatric population as well as from in-hospital care to prehospital care, particularly in the treatment of traumatic injuries.

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