The primary causes of trauma-related death are head injury and hemorrhage. These injuries result in death at the scene of injury in approximately 50% of all trauma cases, while the remaining 50% are transported to the emergency department for treatment. Hemorrhage may be the result of blunt or penetrating injury, or a combination of both. Regardless of the mechanism of injury in regard to the type of trauma, coagulopathy secondary to hemorrhage, acidosis, and the “bloody vicious cycle” of trauma is a major complication of traumatic injuries. Coagulopathy can exacerbate bleeding, increase the risk for development of multiple organ dysfunction syndrome (MODS), and lead to overall increased mortality and morbidity. Recent studies have shown that coagulopathy may be an inherent problem in trauma victims. A study led by Kashuk et al. found that fibrinolysis occurs early after traumatic injury and exists independently of any dilution of clotting factors by crystalloid resuscitation. In a retrospective analysis of traumatic coagulopathy, Brohi’s group found that abnormal coagulation may be attributed to the injury. In a commentary on the Clinical Randomization of an Antifibrinolytic in Significant Hemorrhage-2 (CRASH-2) study, Levy suggested that coagulopathy in trauma may result from fibrinolysis.

The CRASH-2 trial examined the use of the antifibrinolytic tranexamic acid (TXA) to control coagulopathy associated with trauma. TXA is a lysine analogue that binds to the lysine-binding site on plasminogen, preventing the formation of plasmin, leading to decreased fibrinolysis and blunting of the inflammatory response that is thought to contribute to the development of MODS secondary to hemorrhagic shock. TXA has been used successfully in controlling bleeding since the mid 1960s and has been shown to successfully control bleeding with little risk for thrombosis. Not until the CRASH-2 study was TXA studied in the trauma population, where it was found to have a significant reduction in all-cause mortality. Further analysis of the data demonstrated a greater effect if TXA was administered within 1 hour of injury, while treatment beyond 3 hours post injury seemed to increase the risk of death from bleeding. The authors postulate that this may be due to worsening hypothermia and acidosis as a result of delayed treatment rather than to the effects of the drug itself.

TXA has also been examined in the military setting, and the Military Application of Tranexamic Acid in Trauma Emergency Resuscitation study (MATTERs), conducted by a joint U.S.-U.K. military research group in Afghanistan, also demonstrated a significant reduction in death from hemorrhage. The MATTERs study also suggested that a greater benefit of TXA is seen in patients with a greater severity of injury. Both CRASH-2 and MATTERs failed to demonstrate a reduction in the need for transfusion. This phenomenon is discussed by Sniecinski and Levy as being a complex equilibrium among the parts of whole blood, coagulation factors, intrinsic inhibitors of coagulation, and the fibrinolytic system that are disrupted in traumatic injuries. In instances of massive blood loss related to trauma, red blood cells, platelets, and plasma will all need to be replaced, in addition to the antifibrinolytic agents like TXA.

The results of the CRASH-2 trial were examined in relation to World Health Organization data on trauma deaths worldwide to determine the life-saving potential of widespread use of TXA. The study concluded that if all patients received TXA within 1 hour of injury, 128,000 deaths worldwide might be prevented each year; 112,000 if all patients received TXA within 3 hours of injury. These finding are of particular note because the CRASH-2 trial was an international study conducted across high-, middle-, and low-income countries. The Ker analysis found...
TXA administration to be highly cost effective, regardless of the income status of the country.15

Improving trauma survival is a multifaceted, international problem. Correcting coagulopathy is an important aspect of improving trauma survival. TXA has been shown in 2 large trials to be effective at correcting coagulopathy and reducing mortality. It has the potential to not only decrease hemorrhage and decrease the risk of MODS, but to do so without increasing the risk of venous thromboembolism. Other aspects of improved trauma survival will include earlier control of bleeding, early initiation of a massive transfusion protocol, and early operative management of operable traumatic injuries.

REFERENCES

Submissions to this column are encouraged and may be sent to Kathryn Moore, RN, DNP, CCRN, CEN, ACNP-BC, ANP-BC, GNP-BC
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