TXA is an antifibrinolytic agent that reversibly binds plasminogen, blocks plasmin, stabilizes clot formation, and combats hyperfibrinolysis. It is administered intravenously or orally at variable doses. TXA is more potent than aminocaproic acid. It prolongs thrombin time and can be monitored with TEG. TXA is used for patients undergoing surgery to decrease bleeding and blood transfusions and for patients with bleeding disorders.

The CRASH-2 trial [Shakur H et al. *Lancet.* 2010] of TXA included 20 211 trauma patients at risk for significant hemorrhage, and it demonstrated that TXA significantly reduced all-cause mortality (14.5% vs 16%; $P = .0035$) with similar vascular occlusive events (1.7% vs 2%) as compared to placebo. The military study MATTERs [Morrison JJ et al. *Arch Surg.* 2012] included 896 patients with combat injuries, and it found that patients treated with TXA vs no TXA had reduced mortality (17.4% vs 23.9%; $P = .03$). However, in a single-center US study, mortality in high-risk trauma patients treated with TXA was 27%, as compared with 17% without TXA ($P < .05$) [Valle EJ et al. *J Trauma Acute Care Surg.* 2014]. The PATCH study [Mitra B et al. *Emerg Med Australas.* 2014] is evaluating early administration of TXA in severely injured patients to try to resolve some of this uncertainty.

A 1983 *New England Journal of Medicine* study in patients with acute upper gastrointestinal bleeding found that in-hospital mortality was 6.3% with TXA vs 13.5% with placebo ($P = .0092$). A review of TXA treatment in patients with upper gastrointestinal bleeding found significant improvements in death rates but no significant improvement in rebleeding rates, need for transfusion, or surgery [Morgan A, Jeffrey-Smith A. *Emerg Med J.* 2012]. TXA for routine use in gastrointestinal bleeds needs more prospective data before widespread use can be endorsed.

TSOAs include the direct thrombin inhibitor, dabigatran, and the factor Xa inhibitors rivaroxaban and apixaban. Dabigatran does not require monitoring, but increasing numbers of patients receiving dabigatran have developed bleeding complications. In a prospective review of patients admitted to the hospital for dabigatran- or warfarin-induced bleeding, patients receiving dabigatran had more gastrointestinal bleeding (80% vs 48%), less intracranial bleeding (0% vs 32%), and a shorter hospital stay (3.5 vs 6.0 days) [Berger R et al. *Ann Emerg Med.* 2013].

Dr Patel stated that while the TSOAs do not need laboratory monitoring and have lower rates of drug-drug and drug-food interactions, there is no established antidote for patients who are bleeding or need surgery. Routine supportive care, activated charcoal within 2 hours, and hemodialysis have been suggested for patients on direct thrombin inhibitors with bleeding emergencies [Kaatz S et al. *Am J Hematol.* 2012]. Prothrombin complex concentrate has been shown experimentally to reverse the anticoagulant effect of rivaroxaban but not dabigatran in healthy patients [Eerenberg ES et al. *Coagulation.* 2011]; prothrombin complex concentrates can be considered for use in bleeding emergencies related to both drug classes based on limited data.

TEG is a coagulation test that provides rapid assessment of the coagulation cascade. Studies of TEG have found that test abnormalities correlate with increased transfusion rates and mortality [Carroll RC et al. *Transl Res.* 2009] and that TEG results were accurate when compared with a formal assay [Reed MJ et al. *Eur J Emerg Med.* 2013]. TEG may find nice use in bleeding trauma patients to guide coagulation-directed therapy and resuscitation.

Dr Patel concluded that more data are needed for treating hemostasis with TXA outside of trauma populations. More data are also needed to find the optimal reversal strategies for bleeding emergencies on TSOAs. Finally, TEG is an upcoming coagulation assay that shows promise in our bleeding patients.

ACEP Clinical Policy Updated for New and Refractory Seizures

Written by Emma Hitt Nichols, PhD

Up to 5% of individuals in the United States will experience a nonfebrile seizure during their lifetime. Yet, the accurate diagnosis of seizure can be challenging for emergency department (ED) physicians. Jordan Bonomo, MD, University of Cincinnati Medical Center, Cincinnati, Ohio, USA, discussed the American College of Emergency Physicians' (ACEP) 2014 update regarding the evaluation and management of adult patients presenting to the ED with seizures [Huff JS et al. *Ann Emerg Med.* 2014].

In this update of the 2004 clinical policy, seizure definitions were modified. For example, status epilepticus (SE) was defined as clinical or electroencephalographic (EEG) seizure activity for >5 minutes, continuously or recurrently, without full recovery between events. SE is categorized as convulsive, nonconvulsive, or refractory. Dr Bonomo pointed out that most seizures do not meet these criteria because seizure activity lasts <5 minutes.

The 2014 policy provides level B recommendations that all patients presenting with seizure should be evaluated with blood glucose and sodium levels. In addition, all women should be tested for pregnancy, and immunocompromised patients should undergo lumbar puncture. Although the policy does not provide level

Table 1. Recommendations for Initiating AED

Seizure Type	Recommendation	Level of Recommendation
First provoked seizure	Need not initiate AED	Level C
First unprovoked seizure without brain injury or disease	Need not initiate AED	Level C
First unprovoked seizure with remote history or brain disease or injury	May initiate or defer in coordination with other providers	Level C

AED, antiepileptic drug.

Source: Huff JS et al. *Ann Emerg Med. 2014*. Reproduced with permission from Jordan Bonomo, MD.

A recommendations regarding the use of computed tomography (CT) imaging, cranial CT imaging should be performed on all patients who present with their first-ever seizure. In addition, neurologic experts recommend that magnetic resonance imaging (MRI) should be conducted on first seizure presentation, because up to 15% of patients with a normal CT will demonstrate a suspect lesion on MRI.

Because up to 15% of patients with acute ischemic stroke (AIS) will present with seizure at the onset of the AIS, it is important to determine if a witnessed seizure is an AIS mimic. The only protocol that can accurately screen for AIS is MRI with diffusion-weighted imaging (DWI). In one study, DWI-only MRI was rapid, and the odds ratio of positive DWI findings in patients with >1 symptoms was 9.4 (95% CI, 3.8 to 23.5) [Eichel R et al. *J Neurol Sci.* 2013]. There were no false positives related to seizure reported. The purpose of MRI imaging in patients presenting with seizure is to identify the underlying source of the seizure, such as a malignancy, vascular pathology, or structural issues.

When a patient presents with seizure, it is important that pharmacologic control is achieved [Huff JS et al. *Ann Emerg Med.* 2014]. The speed of termination is important because development of SE is associated with poorer prognosis. Patients presenting with seizure are admitted to the hospital depending on their risk of seizure recurrence, and the morbidity and mortality associated with recurrence. Patients should be discharged from the ED only if they have a normal (or baseline) neurologic exam.

Initiation of antiepileptic drug (AED) treatment in the ED does not affect long-term outcomes in patients presenting with their first seizure; therefore, the 2014 ACEP policy does not recommend that patients with first-time seizure receive an AED in the ED (Table 1).

In patients who present with seizure in the context of subtherapeutic AED levels, a loading dose should be administered. To determine the loading dose, the current corrected serum level should be subtracted from the goal serum level and multiplied by the dosing weight in kilograms. A loading dose of phenytoin can be administered either intravenously (IV) or orally; however, IV phenytoin can be loaded faster so that the patient can be discharged from the ED quicker [Swadron SP et al. *Acad Emerg Med.* 2004].

A patient presenting with SE who continues to experience seizures after receiving benzodiazepine, IV phenytoin, fosphenytoin, or valproate may be administered (level B recommendation), or IV levetiracetam, propofol, or barbiturates may be administered (level C recommendation) [Huff JS et al. *Ann Emerg Med.* 2014]. In such cases, systolic blood pressure and mean arterial pressure should be maintained at >90 and >70, respectively. In addition, the Neurocritical Care Society's (NCS) guidelines for the evaluation and management of SE recommend that these patients quickly receive continuous infusion of midazolam or propofol [Brophy GM et al. *Neurocrit Care.* 2012].

In all patients who are suspected to have nonconvulsive SE, as well as any patient who underwent hypothermia therapy after cardiac arrest, continuous EEG (cEEG) should be performed [Huff JS et al. *Ann Emerg Med.* 2014]. In one study, up to 33% of patients who received hypothermic therapy for cardiac arrest experienced seizures, which was associated with a greater rate of mortality [Knight WA et al. *Epilepsy Res.* 2013]. However, it is unknown whether seizure control decreases mortality in these patients. In patients with suspected nonconvulsive SE, the NCS guidelines recommend that cEEG should be initiated within 1 hour of event onset and continued for at least 48 hours [Brophy GM et al. *Neurocrit Care.* 2012].

In conclusion, Dr Bonomo highlighted that all patients presenting with a first-ever seizure should undergo CT, and potentially MRI, imaging, whereas patients with suspected nonconvulsive SE should be monitored by cEEG. In addition, he pointed out that an appropriate loading dose of phenytoin in patients with subtherapeutic levels is dependent on albumin. Treatment of refractory seizures should be quickly escalated, and propofol may be needed.