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by Jaxson Burkins, PharmD; PGY2 Emergency Medicine Pharmacy Resident, Rush University Medical Center; Anthony M Burda, BSPHarm, DABAT; Clinical Toxicologist, Illinois Poison Center; Carol DesLauriers, PharmD, DABAT; Senior Director, Illinois Poison Center

Tricyclic antidepressants (TCAs) are a class of medications commonly involved in overdoses; large ingestions are potentially fatal. Tricyclic antidepressant toxicity can present as anticholinergic symptoms, coma, seizures, hypotension, and dysrhythmias.<sup>1</sup> Intravenous sodium bicarbonate bolus is a mainstay of treatment for the sodium channel-blocking effects on the heart caused by TCA overdose. Continuous sodium bicarbonate infusion is not routinely recommended, as it is of unproven efficacy. Due to manufacturing delays, intravenous sodium bicarbonate was recently included on the current drug shortages list published by American Society of Health-System Pharmacists.

This drug shortage presents a challenge for the medical community as alternate therapeutic options are needed when intravenous sodium bicarbonate is unavailable. At toxic doses, TCAs cause a blockade of the fast voltage-gated sodium channel in the myocardium, which results in a widening of the QRS complex on an electrocardiogram (EKG). Other EKG abnormalities include rightward shift of the QRS axis, rightward shift of the terminal 40 msec of the QRS complex, and an R-wave of 3 mm or greater in aVR. Ultimately, these EKG changes and cardiac disturbances can result in dysrhythmias. Intravenous sodium bicarbonate provides two mechanisms to correct this widened QRS complex. First, sodium bicarbonate provides additional sodium ions to overcome the channel blockade, which in turn shortens the QRS interval, provides cardiac stability, and may increase blood pressure. Sodium bicarbonate also potentially offers serum alkalization via chemical buffering and altering the binding of the toxin to the receptor site. Additionally, the increased pH enhances the protein binding of TCAs, decreasing the amount of free drug available to bind to receptors. In severe overdoses, the general dosing is 1-2 mEq/kg to target an arterial pH of 7.45-7.55 and a QRS duration of < 120 msec. While sodium bicarbonate is a first-line therapy in TCA overdoses, given the current drug shortage, it is important to be aware of possible alternatives, which are summarized below.

**Hypertonic Saline**

Hypertonic saline can provide enough sodium ions to overcome the sodium

**Directors****ICHP Membership  
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Network Meetings**

Chicago Area Pharmacy  
Directors Network Dinner  
3rd Thursday of Odd Months  
5:30pm

**Regularly Scheduled  
Division and  
Committee Calls**

Executive Committee  
Second Tuesday of each month  
at 7:00 p.m.

Educational Affairs  
Third Tuesday of each month at  
11:00 a.m.

Government Affairs  
Third Monday of each month at  
5:00 p.m.

Marketing Affairs  
Third Tuesday of each month at  
8:00 a.m.

Organizational Affairs  
Fourth Thursday of each month  
at 12:00 p.m.

Professional Affairs  
Fourth Thursday of each month  
at 2:00 p.m.

New Practitioner Network  
Second Thursday of each month  
at 5:30 p.m.

Technology Committee  
Second Friday of each month at  
8:00 a.m.

Chicago Area Pharmacy  
Directors Network Dinner  
Bi-monthly in odd numbered  
months with dates to be  
determined. Invitation only.

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channel blockade resulting from the toxin. While only case reports exist for humans, multiple animal studies have demonstrated the reversal of cardiotoxicity from TCAs with 3% sodium chloride. In one case report, a patient with widening QRS from a nortriptyline overdose was successfully treated with 200 mL of 7.5% sodium chloride through rapid intravenous infusion.<sup>1</sup> When utilized, it is necessary to monitor the patient's acid-base status as hypertonic saline can result in a hyperchloremic acidosis further complicating the clinical picture.

**Hyperventilation (if intubated)**

If a patient is already intubated, therapeutic hyperventilation can be used to reduce serum carbon dioxide. It is important to monitor the serum pH, as an aggressive hyperventilation may cause an over-reduction in carbon dioxide that can result in a severe alkalemia. Hyperventilation may provide the most benefit in patients who cannot tolerate large amounts of sodium, such as those who have acute respiratory distress syndrome or congestive heart failure. One case report demonstrated successful reversal of a life-threatening arrhythmia from an amitriptyline overdose utilizing hyperventilation after prior therapies were unsuccessful.<sup>2,3</sup> Patients should not be intubated solely for a wide QRS complex.

**Intravenous Lipid Emulsion**

Intravenous lipid emulsion is an emerging therapy for many toxins, with recent literature suggesting benefit in TCA overdose. The exact mechanism of action is unknown, but the therapeutic effects are most commonly seen with lipophilic medications. A number of animal studies have shown potential benefit for clomipramine overdose, and some case reports of amitriptyline toxicity have noted positive outcomes following administration of intravenous lipid emulsion.<sup>4,5</sup> Although many current guidelines are neutral, this therapy can be considered in severe cases of TCA overdose with refractory hypotension, ventricular dysrhythmias, or cardiac arrest. For additional information on dosing of intravenous lipid emulsion, contact the Illinois Poison Center or visit [lipidrescue.org](http://lipidrescue.org).

**Sodium Acetate**

Similar to hypertonic saline, sodium acetate may be used to provide additional sodium ions to overcome the sodium channel blockade. Additionally, sodium acetate may buffer the serum, resulting in an alkalemia similar to sodium bicarbonate. The recommended dose of sodium acetate is 1 mEq/kg of sodium, to be administered over 15 to 20 minutes. This slow rate of administration typically precludes its successful use in unstable overdose patients.<sup>6</sup>

**Lidocaine**

Lidocaine is a Vaughan Williams Class Ib antiarrhythmic that may increase the rate of phase 0 depolarization, which is dependent on sodium channels. There are limited studies on the use of lidocaine in TCA cardiotoxicity, but it may serve as a therapeutic alternative. Many emergency departments readily stock lidocaine for injection, and the therapy may be most beneficial in patients who are hypernatremic or severely alkalemic, when other therapies are contraindicated. Other antiarrhythmics such as Class Ia and Class Ic are cardiac depressants that slow phase 0 depolarization; this effect may worsen the widened QRS, making these medications contraindicated in TCA overdose.<sup>7</sup>

During drug shortages, pharmacists are often asked for therapeutic alternatives to medications in short supply. While intravenous sodium bicarbonate plays an important role in the treatment of overdoses, there are therapeutic alternatives that may be considered when the drug is unavailable. For more information, please contact the Illinois Poison Center at (800) 222-1222.

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