

## CORRESPONDENCE

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## American Heart Association Recommendations for Treating Tricyclic Antidepressant-induced Hypotension

*To the Editor:*—Recently, in their case report "Treating Intraoperative Hypotension in a Patient on Long-term Tricyclic Antidepressants: A Case of Aborted Aortic Surgery," Sprung *et al.*<sup>1</sup> concluded that potent, direct-acting sympathomimetics may be the only effective management of hypotension in a patient on long-term tricyclic antidepressant (TCA) therapy.

Sprung *et al.* reason that potent direct-acting sympathomimetics may be the only effective management for TCA-induced hypotension because the adrenergic receptors are either desensitized or because catecholamine stores have been depleted in patients who have received TCAs long term.

An important recommendation of the American Heart Association (AHA) has been omitted from this case report. The AHA recommends that serum alkalinization be the mainstay for treating seriously ill patients with signs of TCA toxicity.

Cardiovascular side effects are rare when tricyclic antidepressants are taken in therapeutic dosages.<sup>2</sup> However, Shannon *et al.* and others found a lack of association between TCA level and blood pressure, such that hypotension, even fatal dysrhythmias, may appear with routine doses at therapeutic serum levels.<sup>3,4</sup> Tricyclic antidepressants are the number one cause of death from overdosage in patients who present to the hospital alive.<sup>2</sup>

The electrocardiographic and hemodynamic warning signs of TCA toxicity are almost identical to those signs seen with therapeutic TCA doses.<sup>5</sup> They are sinus tachycardia, prolonged PR, QRS, QT intervals, ST-T changes, bundle branch block, arrhythmias, second and third degree AV block, postural hypotension, decreased myocardial contractility, congestive heart failure, myocardial infarction, and sudden death.

The AHA's recommendation for managing hypotension resulting from TCAs is to first administer 1 l of intravenous saline. If this fails, the next step is to increase the serum pH to 7.5-7.55. Patients with refractory hypotension may then be treated with dopamine or norepinephrine infusion. The protocol of alkalinization of an unstable patient is the following:

1. Increase pH to 7.45-7.55 with 1 mEq/kg of sodium bicarbonate given over 1 to 2 min.
2. Analyze arterial blood gas levels to confirm pH elevation.
3. Place patient on an infusion of two ampules (50-100 mEq) of sodium bicarbonate in normal saline solution (0.9NS).

4. Run the infusion at 150-200 ml/h until the patient stabilizes, until QRS is less than 100 ms, and until arrhythmia ceases and blood pressure normalizes.

5. Maintain the patient's pH at 7.45-7.55 by routine venous or arterial pH measurements.

Alkalinization decreases the non-protein-bound form of the drug. Alkalinization is the AHA's recommended first pharmacologic maneuver for treating seriously ill patients with TCA-induced cardiovascular changes.

Although Dr. Sprung's patient was not "seriously ill" as a result of TCA toxicity, the proposed surgery was aborted because of early blood pressure changes requiring infusion of a potent vasoactive drug. After induction of anesthesia, it became important to correct the hemodynamic changes that had occurred.

The patient took his usual dose of nortriptyline the morning of surgery. Toxicity of TCAs is expected within 2 h and less than 6 h after ingestion. I suggest nortriptyline bioavailability was present. It was present in the holding room when the abnormal electrocardiographic tracing was obtained and was present in the serum after induction of anesthesia. Therefore, it is reasonable to expect some degree of cardiovascular correction with serum alkalinization.

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**In Reply:**—Dr. Rosenthal raises two issues concerning our report—alternative treatments and the possibility that the hypotension resulted from acute effects, and not long-term effects, of tricyclic antidepressants (TCAs).

We focused our discussion on the controversy of whether direct-acting or indirect-acting sympathomimetics should be given to manage TCA-induced hypotension, an issue of major importance to anesthesiologists dealing acutely with this problem intraoperatively, rather than focusing on the various therapies. We agree with Dr. Rosenthal that the American Heart Association (AHA) guidelines are a mainstay of treatment, and we followed the guidelines; our patient's arterial blood gas pH was 7.47 and the PaCO<sub>2</sub> was 30 mmHg, thus the pH was in the target range the AHA recommends. Reporting the blood gas values would have provided readers with this information. Instead of using bicarbonate to alkalinize the patient with TCA cardiotoxicity, we induced respiratory alkalosis by hyperventilating the lungs. This approach has the same end-effect—it decreases the free form of the drug in plasma. However, even this approach does not guarantee the success, as was seen in our case and in the case presented by Sener *et al.*<sup>2</sup> Another treatment for TCA-induced cardiotoxicity is the administration of glucagon (10-mg bolus followed by an infusion of 10 mg over 6 h).<sup>2</sup> The role of glucagon in managing TCA-induced cardiotoxicity is a dose-dependent increase in intracellular cyclic AMP synthesis and reduction of calcium efflux from the cells.<sup>3</sup> Sener *et al.*<sup>2</sup> found that administration of sodium bicarbonate and volume expansion in their patient with TCA-induced cardiovascular collapse had no effect, whereas administering glucagon immediately normalized the low blood pressure.

Although we did not emphasize the possible acute effects of TCAs, we acknowledged that such effects may be important because for the subsequent surgery, our patient had not taken his TCA dose for 24 h and did not experience severe hypotension. However, an acute effect cannot account completely for the cardiotoxicity of the aborted first surgery because, as we stated, the blood pressure and heart rate were still low during the subsequent surgery, never exceeding 110/

65 mmHg or 80 beats/min. We then concluded that discontinuing TCAs, even 24 h before surgery, may be beneficial because the plasma TCA concentration has a dose-dependent inhibitory effect on sympathetic nerve activity.<sup>4</sup> Whether this acute effect is a result of TCA centrally inhibiting sympathomimetic actions<sup>4</sup> or blocking the peripheral  $\alpha_1$  receptors<sup>5</sup> is not certain, but we did not ignore the possibility of an acute effect, as Dr. Rosenthal implies.

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