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Letter to the Editor

Prolonged QT interval with markedly abnormal ventricular repolarization in diphenhydramine overdose

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Abstract

Diphenhydramine is a histamine-1 receptor antagonist of ethanolamine origin with anticholinergic, sedative, antivertigo, antiemetic, antidyskinetic, and local anesthetic properties. It inhibits the fast sodium channels and, at higher concentrations, also the potassium channels, inhibition of which may result in QT interval prolongation on electrocardiogram. The markedly abnormal ventricular repolarization is rare with diphenhydramine overdose. We report a case where a young woman who took moderate overdose of diphenhydramine (625 mg) along with acetaminophen developed prolonged QT interval with strikingly abnormal T waves. These changes reverted to normal with treatment. Patient did not experience torsade de pointes, possibly secondary to the protective effect of the diphenhydramine overdose-related tachycardia. As the tachycardia caused by diphenhydramine overdose seems to protect against torsade de pointes, it may be practical to avoid bradycardia in acute phase of diphenhydramine toxicity. Acetaminophen has not been shown to prolong QT interval or effect cardiac repolarization.

Keywords: Diphenhydramine; Antihistamines; ECG; QT interval; Long QT syndrome; Torsade de pointes; Drug toxicity

A 40-year-old woman presented to a regional referral center after admitting to taking an overdose of Tylenol-PM (McNeil Pharmaceutical, Raritan, NJ, USA), which is an over-the-counter preparation of diphenhydramine and acetaminophen combination, several hours prior to admission. She had ingested 25 tablets as part of her suicide gesture. The total ingested dose of diphenhydramine was 625 mg and that of acetaminophen 12.5 g. Due to increasing lethargy and inability to protect her airway, emergent intubation was performed in the emergency department. Initial chemistry panels were significant only for mildly elevated transaminases with aspartate aminotransferase of 56 IU/l and alanine aminotransferase of 49 IU/l. Serum magnesium and potassium levels were within normal limits. A corrected serum calcium level was 7.8 mg/dl. An acetaminophen level on admission was considered in the toxic range for the time frame following ingestion and *N*-acetylcysteine therapy was initiated.

As part of admission work-up, a 12-lead electrocardiogram was obtained. This revealed sinus tachycardia with a markedly prolonged QT interval with corrected QT of 588 ms. The ventricular repolarization on electrocardiogram was abnormal with broad, biphasic T waves, which were more apparent in mid-precordial leads (Fig. 1). She was not taking QT interval prolonging medication and had no underlying structural heart disease. Serial electrocardiograms demonstrated slow resolution of QT interval prolongation and of T wave abnormality. By day 2, the QT interval had become normal with a corrected QT of 433 ms and abnormalities in the T wave morphology had been completely resolved (Fig. 2). The corrected serum calcium level remained low. The patient was thereafter extubated and recovered uneventfully. No arrhythmias were noted during hospital stay.

Prolongation of the QT interval and polymorphic ventricular tachycardia has been described in second-generation histamine-1 receptor antagonists, even in therapeutic doses. Although the overdose has frequently been reported, less is known about the cardiac effects of diphenhydramine, a first-generation histamine-1 receptor antagonist. Cardiac effects of diphenhydramine toxicity mainly consist of tachycardia, which could be sinus or wide complex. Radovanovic et al. [1] analyzed 282 cases of diphenhydramine overdoses and found that 55% to 64% had tachycardia. At higher concentrations of diphenhydramine, the potassium channels can be

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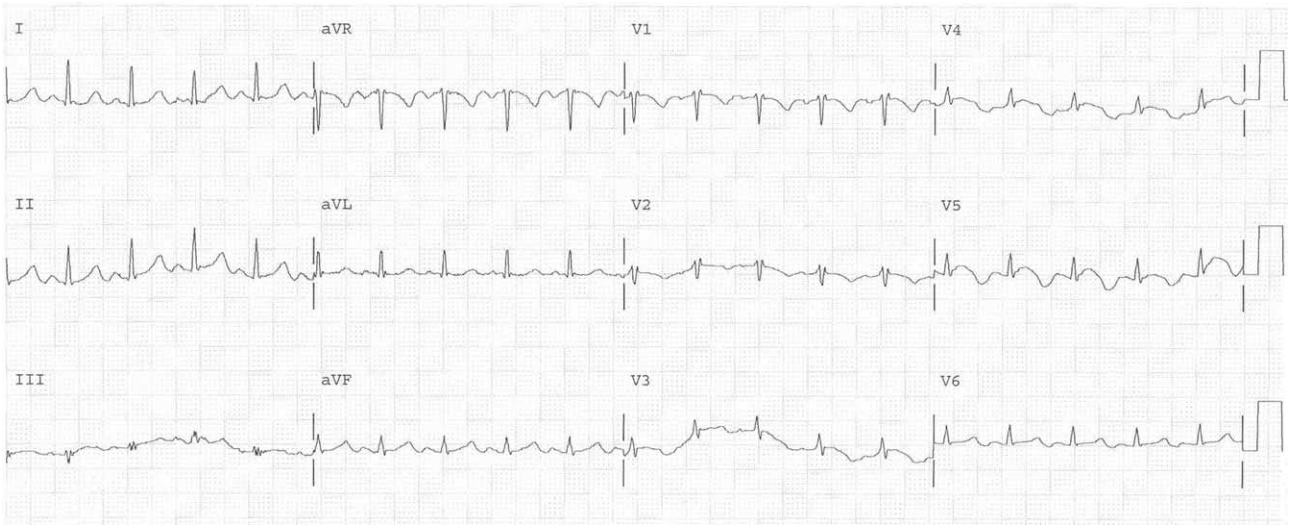

Fig. 1. Admission electrocardiogram showing sinus tachycardia, long QT interval (QTc 588 ms) and abnormal, broad, biphasic T waves, best visible in leads V4 and V5.

inhibited resulting in QT interval prolongation and abnormal ventricular repolarization [2]. A retrospective analysis of 126 patients with diphenhydramine overdose (the majority of cases involving a dose >500 mg) revealed a corrected QT interval (453 ± 43 ms) significantly longer in diphenhydramine overdose patients than that in control subjects (416 ± 35 ms) [3]. Interestingly, none of the patients reported in this study experienced torsade de pointes, which could be secondary to the protective effect of the diphenhydramine overdose-related tachycardia. Although the torsade de pointes is rare with diphenhydramine overdose because of the protective effect of the associated tachycardia, Pratt et al. [4] reported two cases of torsade de pointes associated with diphenhydramine in a retrospective analysis of a computerized prescription records. In addition, bundle branch block, atrio-ventricular block and atrioventricular dissociation have also been reported with diphenhydramine overdose [5,6].

Our patient took a moderate overdose of diphenhydramine but developed strikingly prolonged QT interval with markedly abnormal T waves. Acetaminophen has not been shown to prolong QT interval or effect cardiac repolarization. Although corrected serum calcium was low at admission, the hypocalcaemia might not have been contributory in the reported electrocardiographic changes because, first, it remained low at day 2 when both the QT interval and T

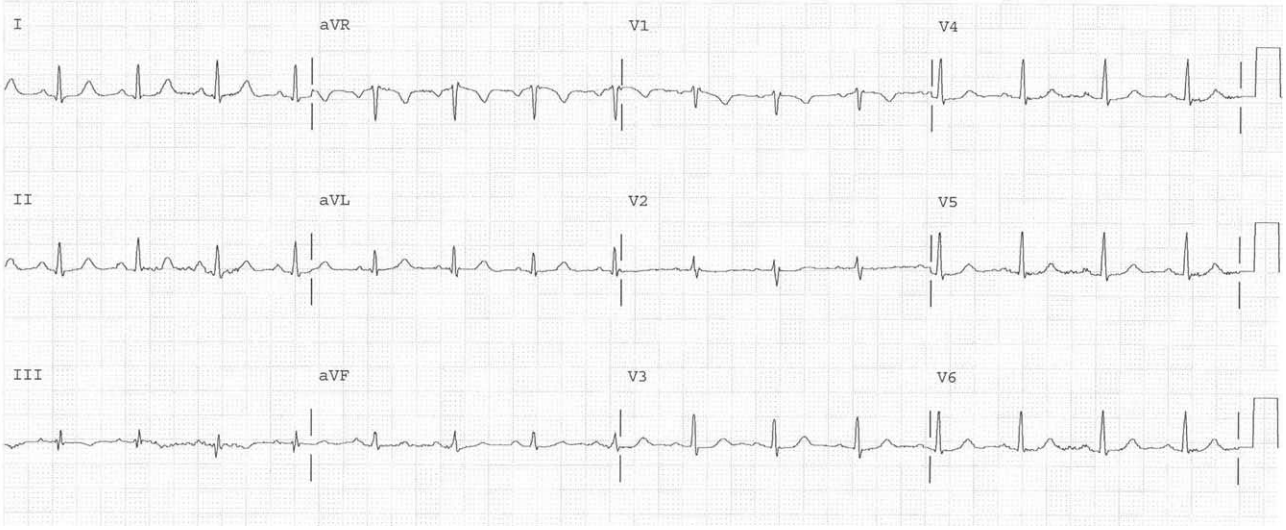

Fig. 2. The electrocardiogram recorded on day 2 shows resolution of sinus tachycardia and of abnormalities in T wave morphology. The QT interval has become normal (QTc 433 ms).

wave had become normal, and, second, in hypocalcaemia, the T wave morphology remains normal and QT interval is prolonged by prolongation of merely the ST segment, which was not the case in our patient. As the tachycardia caused by anticholinergic and hypotensive effects of diphenhydramine seems to protect against torsade de pointes, it may be practical to avoid bradycardia in acute phase of diphenhydramine toxicity.

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