

Diphenhydramine induced QT prolongation and torsade de pointes: An uncommon effect of a common drug

Zehra Husain¹, Khursheed Hussain², Rajiv Nair¹, Russell Steinman¹

¹St. Joseph Mercy Oakland, Internal Medicine/Cardiology, Pontiac, USA

²St. Mary Mercy Livonia, Michigan, USA

Abstract

The histamine I receptor antagonist diphenhydramine is a freely available, over the counter medication for sleep and the most frequently used antihistamine drug. It inhibits the fast sodium channels and, at higher concentrations, the repolarising potassium channels, particularly I_{Kr} , which leads to prolongation of the action potential and the QT interval. The toxicity of diphenhydramine is dose-dependent, with a critical dose limit of 1.0 g. We report a case of a young woman who consumed more than 3 g of diphenhydramine in the setting of alcohol intoxication and developed QTc prolongation with nonsustained polymorphic ventricular tachycardia. These changes reverted to normal with supportive treatment. An overdose of diphenhydramine with concomitant alcohol use can induce torsade de pointes in an otherwise normal heart. (Cardiol J 2010; 17, 5: 509–511)

Key words: diphenhydramine, torsade de pointes, QTc prolongation

Introduction

Antihistamines are among the most frequently prescribed drugs worldwide. Because of their excellent safety record, most can be obtained without prescription. They are common ingredients in non-prescription anti-allergy products and also in sleep aids. Diphenhydramine is an H-1 antihistamine of the ethanolamine type with anticholinergic and local anaesthetic properties [1]. It is a freely available, over the counter medication. Most cases of diphenhydramine overdose present with anticholinergic, neurological and cardiovascular symptoms. Among the cardiovascular manifestations, arrhythmic complications and conduction abnormalities presenting as wide QRS complex, bundle branch block and prolonged QT interval are seen on the electrocardiogram [2, 3]. We present a case with QT interval prolongation and nonsustained poly-

morphic ventricular tachycardia with diphenhydramine overdose.

Case presentation

A 44 year-old female was found unresponsive in her apartment with an almost empty bottle of diphenhydramine. The bottle was supposed to contain 100 tablets of diphenhydramine 50 mg (Night-time Sleep Aid — CVS Pharmacy) but had only 40 tablets remaining. She was immediately brought to the emergency room, where after a few hours, she recovered enough to state that she had ingested 60 tablets of diphenhydramine along with alcohol as a suicidal gesture. She also complained of palpitations and chest pain. The troponins were minimally elevated. The electrocardiogram showed marked QTc interval prolongation at 786 ms (Fig. 1) with nonsustained polymorphic ventricular tachycardia

Address for correspondence: Zehra Husain, MD, St. Joseph Mercy Oakland, Internal Medicine/Cardiology, 44405 Woodward Ave, Pontiac, Michigan 48341, USA, tel: 248 858 3000, e-mail: doczehrah@yahoo.com

Received: 7.09.2009

Accepted: 17.10.2009

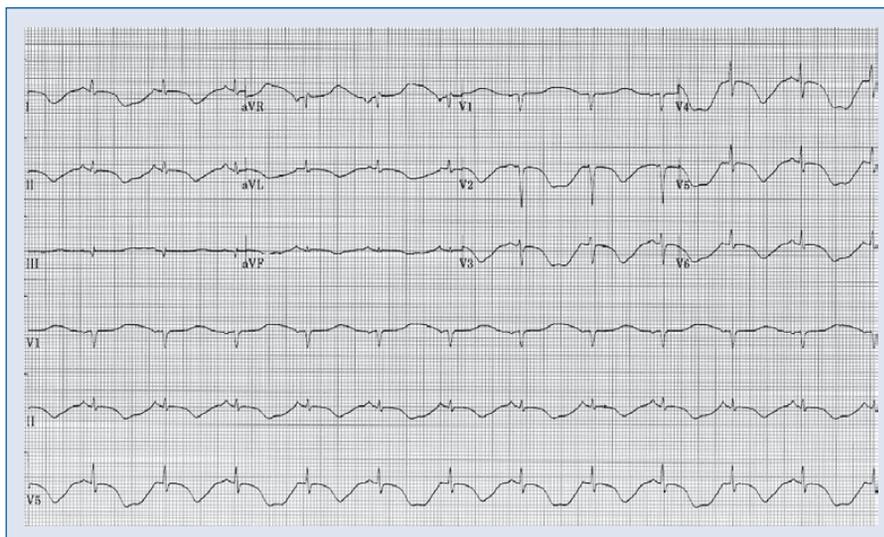


Figure 1. QT prolongation to 786 ms.

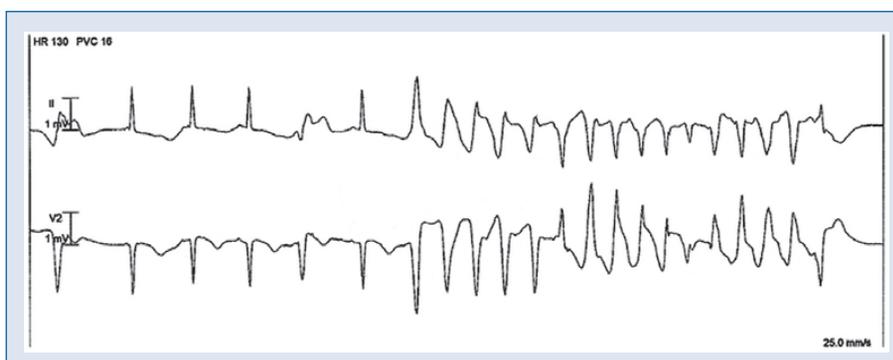


Figure 2. Torsade de pointes.

(Fig. 2). Her potassium and magnesium levels were normal. Her blood alcohol level was 0.21%. She was not on any other QT interval prolonging medications. Echocardiography revealed a structurally normal heart and cardiac catheterization showed normal coronaries. Serial electrocardiograms showed a gradual resolution of the QT interval prolongation and the T wave abnormality. By Day 5, the QT interval had become normal (400 ms) and T wave abnormalities had resolved (Fig. 3). No further arrhythmias were noted and her hospital course remained uneventful. Psychiatry consultation was obtained and the patient was later discharged home with a psychiatry follow-up.

Discussion

The older antihistamines are known for their anticholinergic and sedative effects. Some of them

have the same potential for causing arrhythmias as the newer non-sedative antihistamines. To date, most research in this area has been directed at studying the newer non-sedating antihistamines. Although an overdose of older antihistamines has frequently been reported, less is known about their cardiac effects. The manufacturer's labeling for one of the oldest agents, diphenhydramine, lists "palpitations, tachycardia and extrasystoles" as potential adverse effects [4]. A suggestion that diphenhydramine could cause torsade de pointes (TdP) was found during an analysis of computerized prescription records reported by Pratt et al. [5]. They compared the risk of occurrence of life-threatening ventricular arrhythmias with terfenadine with that for non-prescription antihistamines. The authors described two cases of TdP associated with diphenhydramine and could not detect any difference in the risk of life-threatening arrhythmias between

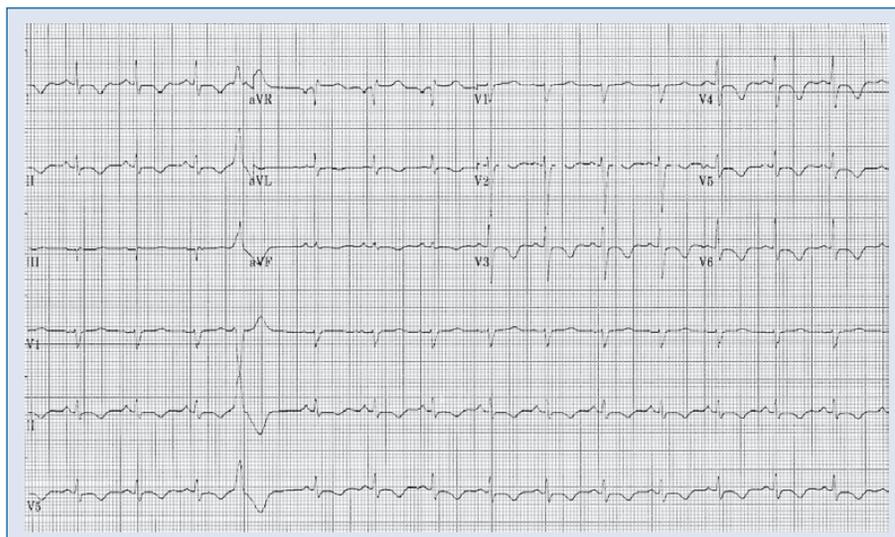


Figure 3. Reversal of QT prolongation with T wave inversion.

terfenadine and non-prescription antihistamines, mainly diphenhydramine. This raises the question of whether diphenhydramine, one of the most commonly used drugs in the world, may also be able to induce TdP.

TdP is a syndrome of polymorphic ventricular tachycardia that occurs in the setting of marked prolongation of the QT interval on the surface electrocardiogram. It occurs due to the slowing of repolarization due to the block of the delayed rectifier potassium current (I_{kr}) that leads to action potential duration prolongation. This slowing of repolarization consistently precedes and is associated with activation of a depolarizing current. The resultant bradycardia tends to predispose to TdP.

Diphenhydramine toxicity is dose-dependent. At higher concentrations, it inhibits the potassium channels, resulting in QT interval prolongation and abnormal ventricular repolarization. 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) [6]. Interestingly, none of the patients reported in this study experienced torsade.

Our patient took 3 g of diphenhydramine, and along with alcohol ingestion, developed torsade de pointes with markedly abnormal T waves. TdP is rare with diphenhydramine overdose, possibly be-

cause of the 'protective' effect of the associated tachycardia caused by the anticholinergic and hypotensive effects of diphenhydramine.

This case of torsade is, to our knowledge, only the third reported case in English literature of diphenhydramine toxicity.

Acknowledgements

The authors do not report any conflict of interest regarding this work.

References

1. Cirillo VJ, Tempero KF. Pharmacology and therapeutic use of antihistamines. *Am J Hosp Pharm*, 1977; 33: 1200–1207.
2. Hestand HE, Teske DW. Diphenhydramine hydrochloride intoxication. *J Pediatr*, 1977; 90: 1017–1018.
3. Mary F, Michael H, John T. Response of life threatening dimenhydrinate intoxication to sodium bicarbonate administration. *Clin Toxicol*, 1991; 29: 527–535.
4. Woosley RL ed. Diphenhydramine. In: *Physician's desk reference*. Med Econ Data, Montvale, NJ 1994: 1719–1720.
5. Pratt CM, Hertz RP, Ellis BE et al. Risk of developing life threatening ventricular arrhythmia associated with terfenadine in comparison with over the counter antihistamines, ibuprofen and elemastine. *Am J Cardiol*, 1994; 73: 346–352.
6. Zareba W, Moss AJ, Rosero SZ et al. Electrocardiographic findings in patients with diphenhydramine overdose. *Am J Cardiol*, 1997; 80: 1168–1173.