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International Journal of Cardiology 98 (2005) 341–343

International Journal of Cardiology

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Letter to the Editor

QT interval prolongation in diphenhydramine toxicity

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Received 19 June 2003; accepted 28 October 2003
Available online 6 May 2004

Abstract

Diphenhydramine overdose in one of the frequent reported causes of acute poisoning. Patients with diphenhydramine overdose can present with central nervous system manifestations, anticholinergic manifestations and cardiovascular symptoms. The cardiovascular symptoms of diphenhydramine overdose include myocardial depression and refractory hypotension. Massive ingestions have been reported to cause myocardial depressant effect with widening of QRS complex and prolonged QT interval on electrocardiogram. We report an adolescent male with moderate diphenhydramine ingestion, who was found unresponsive with seizure like activity. Electrocardiogram on presentation showed wide complex tachycardia with right bundle branch block pattern and QT interval prolongation. These changes reverted to normal with treatment. Diphenhydramine overdose may occasionally result in prolongation of QT interval.

Keywords: Diphenhydramine; Antihistamines; Electrocardiogram; QT interval; Long QT syndrome; Torsade de pointes; Drug toxicity; Right bundle branch block; Wide complex tachycardia

1. Introduction

Diphenhydramine is an H-1 antihistamine of the ethanolamine type with anticholinergic and local anesthetic properties [1]. Overdose has frequently been reported, although fatalities are rare. Most cases of diphenhydramine overdose present with anticholinergic symptoms. Arrhythmic complications and conduction abnormalities of massive diphenhydramine overdoses can manifest as wide complex tachycardia, bundle branch block and QT interval prolongation [2,3]. We present a case with right bundle branch block and QT interval prolongation with moderate diphenhydramine overdose.

2. Case presentation

A 17-year-old male was found unresponsive on a park bench. The emergency personnel found an empty bottle of diphenhydramine bought over the counter. The bottle was supposed to contain 40 tablets of 50 mg diphenhydramine. Patient was unresponsive to verbal commands and was witnessed to have general seizure like activity. He was tachycardiac (heart rate 150/min) and tachypneic (respiratory rate 32/min) on arrival to emergency department at 10:30 p.m. His blood pressure was 160/90 mm Hg and temperature was 100 °F. Electrocardiogram showed heart rate of 150/min with right bundle branch block and QT interval prolongation at 522 ms (Fig. 1). Initial arterial blood gas showed metabolic acidosis with pH of 7.21. The pupils were 8 mm bilaterally dilated and sluggishly reacting to light. In emergency department nasogastric tube was placed and sorbitol with 100 g of charcol was given. Patient later became hypotensive (systolic blood pressure 80 mm Hg) which improved with normal saline infusion. One ampule of sodium bicarbonate was given. Patient was also noted to have tonic-clonic seizure like activity and intravenous benzodiazipines were given. After consulting with poison control center 0.5 ml of physostigmine was administered. Patient started to have verbal communication and admitted to have taken 40 tablets of diphenhydramine with suicidal intention. Blood work showed normal metabolic profile, cardiac enzymes, blood indices and coagulation profile.

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doi:10.1016/j.ijcard.2003.10.051

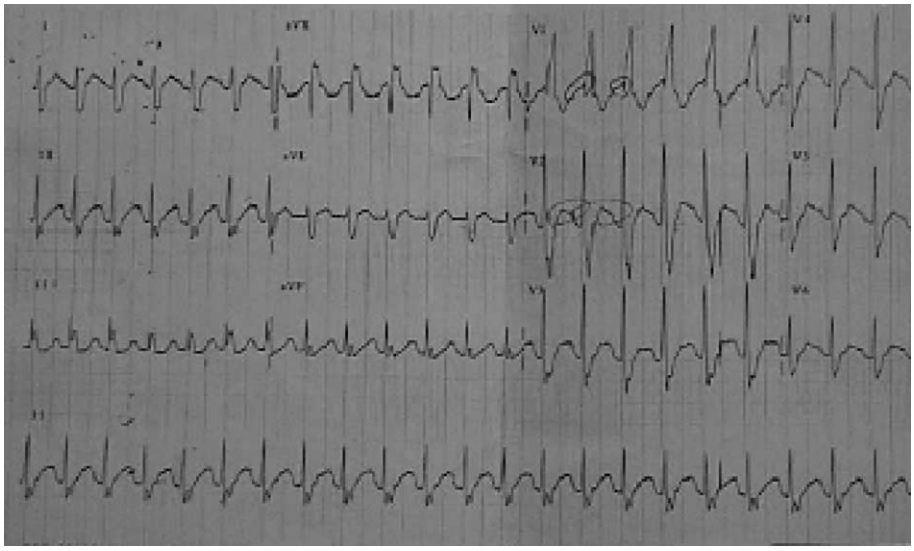

Fig. 1. Wide complex tachycardia with right bundle branch block and prolonged QTc interval (522 ms).

Further course in hospital remained uneventful. Electrocardiogram changed to normal sinus rhythm with normal QT interval over the course of treatment. Psychiatry consultation was obtained and patient was later discharged home with psychiatry follow up.

3. Discussion

Diphenhydramine is a histamine-1 receptor antagonist of ethanolamine origin and has significant anticholinergic, sedative, antivertigo, antiemetic, antidyskinetic and local anesthetic properties [1–5]. Diphenhydramine is a reversible competitive inhibitor of histamine. Most patients with diphenhydramine toxicity presents with nervous system manifestation of impaired consciousness, seizures, hallucinations, acute extrapyramidal movement disorders, toxic psychoses, ataxia, tachycardia, hypertension, hypothermia, convulsions, delirium, syncope and respiratory failure as diphenhydramine can cross blood brain barrier easily. Koppel et al. [6] reviewed 136 patients with diphenhydramine overdose and reported somnolence, lethargy and coma in 55% of patient while catatonic stupor occurred in 15% of patients. Anticholinergic manifestations can include fever, tachyarrhythmias, hallucinations, urinary retention, blurred vision and mydriasis.

Cardiac effects of diphenhydramine toxicity mainly consists of tachycardia accompanied by hypertension or hypotension, which could be due to multiple factors like age of the patient, state of hydration, co-morbid conditions and vascular tone. Wide complex tachycardia can occur, the mechanism of which is through inhibition of fast sodium channels. Characterization of wide complex tachycardia has not been done extensively in cases of diphenhydramine overdoses. At higher concentrations of diphenhydramine, the potassium channels can also be inhibited resulting in QT interval prolongation. Massive ingestions of diphenhydramine have been reported to produce a membrane depressant effect and widening of QRS with myocardial depression and refractory hypotension [7]. Diphenhydramine could cause torsade de pointes as suggested during an analysis of computerized prescriptions record by Pratt et al. [8], where authors reported two cases of torsade de pointes associated with diphenhydramine. In addition, left and right bundle branch block, atrioventricular dissociation, and atrioventricular blocks have been reported with diphenhydramine overdose [3,9]. Radovanovic et al. [10] analyzed 282 cases of diphenhydramine overdoses and found that 55% to 64% had tachycardia and 22% to 27% had electrocardiographic changes. Although clinical features of diphenhydramine toxicity are well described, information about electrocardiographic changes has not been studied extensively even though tachycardia with electrocardiographic changes remains as one of the commonest presentation. The present case reiterates that diphenhydramine overdose may occasionally result in prolongation of QT interval.

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