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Selected Topics: Toxicology

ACUTE PEDIATRIC COLCHICINE TOXICITY IS ASSOCIATED WITH MARKED BRADYDYSRHYTHMIAS

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☐ **Abstract—Background: Colchicine ingestion is rare but highly lethal. Patients usually die of multiorgan failure and cardiogenic shock. Colchicine is not only associated with depressed myocardial function but also with fatal heart rhythm disturbances, such as complete heart block, ventricular tachycardia, and asystole. While histologic changes of myocytes are well known, the mechanism by which colchicine affects cardiac impulse generation and conduction is not fully understood. Case Report: We present a case of colchicine ingestion with sinus bradycardia, marked sinus arrhythmia, and first- and second-degree heart block. A 10-year-old previously healthy boy was brought to the emergency department for the sudden onset of dizziness, abdominal pain, and vomiting after ingesting his grandfather's colchicine and furosemide. His symptoms improved with ondansetron and intravenous normal saline. However, because of the colchicine ingestion, he was admitted to the pediatric intensive care unit for observation. He first developed PR prolongation (∼4–30 h postingestion) followed by marked sinus bradycardia and sinus arrhythmia along with second-degree heart block (∼48–60 hours postingestion). The minimum heart rate was 40 beats/min. Marked sinus arrhythmia was observed, suggesting an increase in parasympathetic activity. His heart rhythm improved initially with less sinus arrhythmia followed by resolution of heart block. He was discharged home without any sequelae. Holter monitoring 1 week after discharge showed normal heart rate variability for age. Why Should an Emergency Physician Be Aware of This?: This case provides novel insights into how colchicine may affect the heart's electrophysiology. Colchicine may increase the parasympathetic tone enough to cause sinus bradycardia and different degrees of heart block.** © 2018 Elsevier Inc. All rights reserved.

☐ **Keywords—colchicine toxicity; heart block; parasympathetic tone**

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INTRODUCTION

Colchicine, an alkaloid extracted from the meadow saffron plant (*Colchicum autumnale*), is an old and well-known drug; its name is derived from Colchis, an ancient region on the coast of the Black Sea. Colchicine's primary mechanism of action is to prevent microtubule assembly, thereby downregulating microtubule-based inflammatory processes, such as inflammatory cell chemotaxis and cytokine formation (1). Colchicine's unique anti-inflammatory properties have been used to treat gout, familial Mediterranean fever, amyloidosis, Behçet disease, and autoimmune disorders. Recently, colchicine has also been used to treat pericarditis, atherosclerosis, and atrial fibrillation after cardiac surgery with some success (1).

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Despite its merits, colchicine is highly toxic because of a narrow therapeutic index. An acute overdose of colchicine, although rare, constitutes a medical emergency with high morbidity and mortality. Colchicine's toxicity is thought to be dose dependent (2). However, death and severe sequelae are well documented at low doses (3–5). Nausea, vomiting, abdominal pain, and diarrhea are the first clinical symptoms of colchicine poisoning. Multiorgan involvement soon follows with bone marrow suppression and respiratory and kidney failure. Death usually results from multiorgan failure caused by ensuing sepsis or cardiogenic shock secondary to direct colchicine cardiac toxicity.

Colchicine causes direct cellular myocardial insult leading to impaired contractility (6). Colchicine has been thought to also disrupt cardiac impulse generation and conduction (7). The mechanism of these abnormal rhythms has not been well understood, likely because of its rare occurrence.

We present a case of pediatric colchicine ingestion in a 10-year-old boy whose cardiac symptoms suggest that colchicine causes bradycardia and heart block by stimulating parasympathetic tone.

Case Report

A 10-year-old previously healthy African American boy was brought to the emergency department with sudden onset of dizziness, abdominal pain, and 6 episodes of nonbloody, nonbilious emesis after ingesting his grandfather's colchicine and furosemide. While the presenting symptoms quickly resolved, he subsequently developed PR prolongation (~4–30 h postingestion) followed by marked sinus bradycardia and sinus arrhythmia along with second-degree heart block (~48–60 h postingestion). His cardiac rhythm was concerning for the potential to progress to hemodynamically significant sinus arrest or higher degrees of heart block.

Clinical Findings

Approximately 4 h before presentation, the patient ingested an estimated 0.2 mg/kg of colchicine (4.8 mg, 8 × 0.6-mg tablets) and 10 mg/kg of furosemide (240 mg, 6 × 40-mg tablets). He developed gastrointestinal symptoms within an hour of ingestion. Upon arrival in the emergency department, he was mildly tachycardic with a heart rate of 99 beats/min, but otherwise he had a normal physical examination. Initial laboratory values were remarkable for a normal total white blood cell count, creatinine kinase 263 IU/L, lactic acid 2.2 mmol/L, and normal troponin. The urine drug screen was negative. Initial and subsequent laboratory values are detailed in Table 1. An electrocardiogram showed a mildly

Table 1. Laboratory Values

	WBC Count (K/μL)	Neutrophils, %	Hgb (g/dL)	Plt (K/μL)	PT (sec)	aPTT (sec)	BUN (mg/dL)	Cr (mg/dL)	AST (IU/L)	ALT (IU/L)	CK (IU/L)	Lactic Acid (mmol/L)	Na (mmol/L)	K (mmol/L)	Ca (mg/dL)	iCa (mmol/L)	Mg (mg/dL)	Troponin I (ng/mL)
Presentation, hours	9.09	77	14.4	324	12.2	25	11	0.58	59	29			139	5.5	9.6		1.7	<0.017
8							8	0.59	85	27	263	2.5	139	4.4	9.3			
16							6	0.55	95	33		0.6	139	3.3	8.5			
24	9.44	84	13.3	291	15.3	27.5	5	0.62	104	37	656	1.2	141	3.6	8.9		1.6	<0.01
32							4	0.55	91	35	733	1.6	140	3.3	8.7		1.7	0.02
40							3	0.52	77	31	664	1	140	3.2	8.5		1.9	<0.01
48	4.77	64	12.3	240	12.7	27.7	3	0.58	79	35	670	1	140	3.4	9		1.7	<0.01
56							3	0.57				1.6	139	3.1	9	1.15	2	
64							4	0.58				1.3	141	3.2	9	1.23	1.9	
72	4.69	50	12.8	265	11.9	26.5	4	0.6	127	95	482	1.8	141	3.5	9.3	1.26	1.8	
84							4	0.6	104	102		2.5	140	3.6	9.5	0.93	2.3	
96	6.92	57	13.5	303	11.2	26.4	9	0.8	62	85	285	1.8	141	4	10	1.1	2.1	

ALT = alanine aminotransferase; aPTT = activated partial thromboplastin time; AST = aspartate aminotransferase; BUN = blood urea nitrogen; Ca = calcium; CK = creatine kinase; Cr = creatinine; Hgb = hemoglobin; iCa = ionized calcium; K = potassium; Mg = magnesium; Na = sodium; Plt = platelet; PT = prothrombin time; WBC = white blood cell.