Case Letter

Acute salbutamol toxicity in the emergency department: A case report

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Dear editor,

Salbutamol is a common medication used in a variety of clinical settings. While there have been many reported cases of orally ingested salbutamol toxicity, there have only been a few reports of inhaled salbutamol overdose. We describe a case of acute inhaled salbutamol toxicity with a combination of clinical findings that have not been previously reported together in a single case. Given the ubiquitous use of salbutamol, many patients may experience symptoms of overdose on a spectrum that ranges from mild side effects to severe toxicity, which may be under-recognized by emergency physicians. We believe that it is important for all emergency clinicians to be aware of and recognize the syndrome of β_2-agonist toxicity.

CASE

A 16-year-old female was brought to the emergency department (ED) for altered level of consciousness. Cardiac monitors and electrocardiogram (ECG) showed supraventricular tachycardia at 160 beats per minute with a prolonged corrected QT interval (QTc 525 ms) (Figure 1A). Her respiratory rate was 35 breaths per minute. The remaining vital signs were normal: oxygen saturation on room air 100%, blood pressure 110/84 mmHg (1 mmHg=0.133 kPa), temperature 36.7 °C, and point-of-care glucose 7.0 mmol/L. Her initial Glasgow Coma Scale (GCS) was 14.

The patient's medical history was significant for asthma and her only medication was a salbutamol (Ventolin HFA, GlaxoSmithKline) inhaler. The patient reported experiencing an "asthma attack" a few hours before presenting to the ED and using her salbutamol inhaler approximately 15 times during that time. She also reported taking two tablets of acetaminophen but denied any other ingestions.

On physical examination, the patient was agitated, with no increased work of breathing or airway compromise. The patient's chest was clear to auscultation, with no wheezes or crackles. Cardiac exam revealed a fast and regular rhythm, with no murmurs. Abdominal and screening neurologic exams were unremarkable.

The patient was given diltiazem (20 mg intravenously) for her supraventricular tachycardia and 1 L normal saline.

An initial venous blood gas (VBG) revealed respiratory alkalosis with metabolic acidosis and lactate 8.1 mmol/L. Other significant findings on bloodwork included potassium 2.9 mmol/L, phosphate 0.43 mmol/L (reference range 0.92–1.55 mmol/L), and acetaminophen level 86 μmol/L. The anion gap was 17 mmol/L and the osmolal gap was normal. Creatine kinase and troponin were normal. Serum salicylate and ethanol levels were undetectable. Serum β-human chorionic gonadotropin was negative. Chest radiograph and non-contrast computed tomography of the head were unremarkable.

On clinical reassessment 1.5 hours after her initial presentation, the patient was oriented and ambulatory, and had no complaints. Repeat ECG showed sinus tachycardia at 115 beats per minute (QTc 473 ms) (Figure 1B). Serial VBGs showed improvement of her lactic acidosis. The four-hour acetaminophen level was undetectable. Six hours after her initial presentation, the patient was discharged home from the ED with instructions about proper use and dosing of her salbutamol inhaler.

DISCUSSION

We describe a case of inhaled salbutamol toxicity presenting with supraventricular tachycardia, QTc

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prolongation, hypokalemia, and marked lactic acidosis. There are only a few reports of inhaled salbutamol toxicity and no previous case has reported the combination of clinical findings that we have described.[1–4]

Mechanisms

Salbutamol stimulates β_2-adrenergic receptors to provide rapid bronchodilation through cyclic adenosine monophosphate (cAMP)-mediated bronchial smooth muscle relaxation.[5] While salbutamol is relatively selective for β_2-adrenergic receptors, it has been shown to have β_1-receptor effects in the myocardium.[5] In addition, β_1- and β_2-adrenergic receptors coexist in the heart.[6] Stimulation of cardiac β_2-receptors increases both chronotropy and inotropy and increases myocardial oxygen demand. In overdose, receptor specificity may be lost and β_2-agonists may cause tachycardia, cardiac ischemia, and arrhythmias such as atrial fibrillation, supraventricular tachycardia, and ventricular tachycardia.[6]

Salbutamol causes hypokalemia primarily through β_2-stimulation of the Na^+/K^+-ATPase pump in skeletal muscle, which shifts potassium intracellularly.[7] Hypokalemia caused by β_2-agonists can be significant enough to produce ECG changes such as QT prolongation and U-waves. During exacerbations of chronic obstructive lung disease, concomitant hypoxemia and alterations in plasma pH may further increase the risk of cardiac arrhythmias.[3]

Acute salbutamol toxicity may also cause lactic acidosis. β_2-adrenergic stimulation is thought to increase cAMP-mediated gluconeogenesis and lipolysis.[4] This causes increased plasma glucose, leading to increased conversion to pyruvate and lactate. This mechanism is in keeping with salbutamol also having been shown to cause transient hyperglycemia.[1]

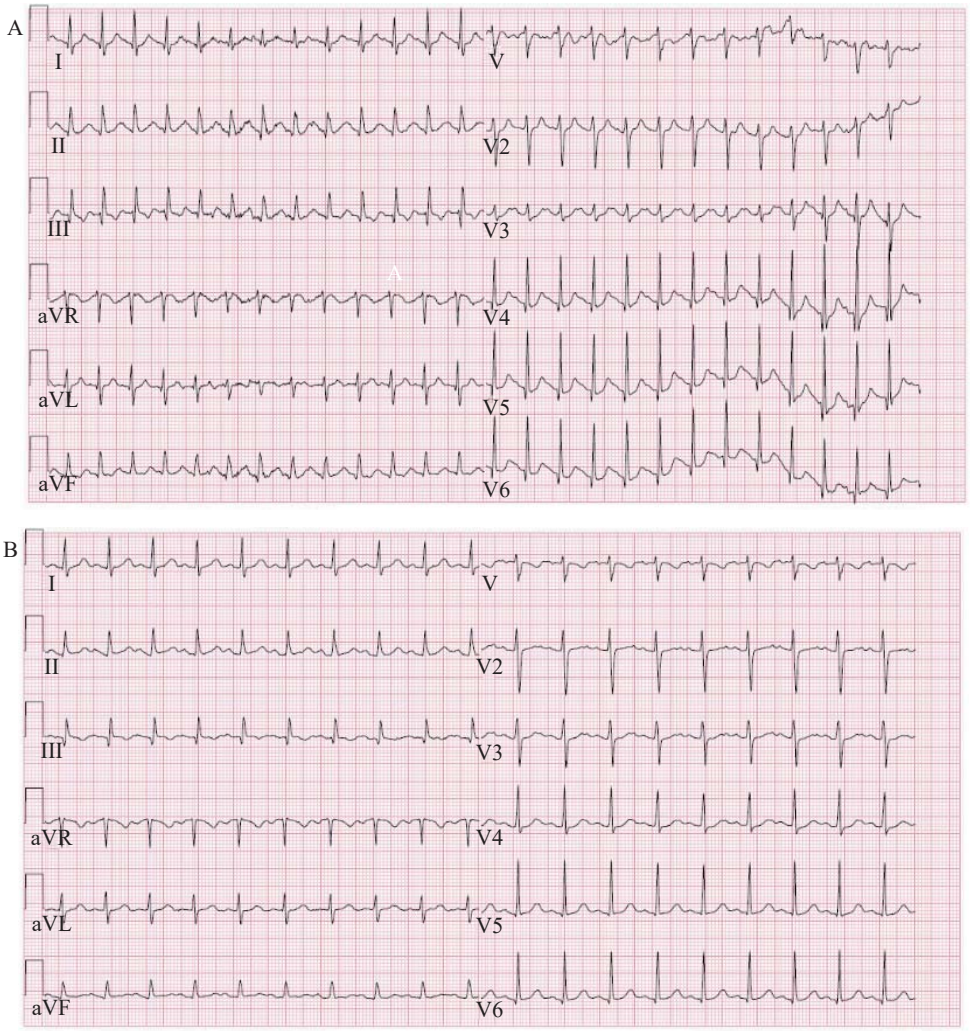

Figure 1. Serial electrocardiograms of a 16-year-old patient with acute salbutamol toxicity. A: initial electrocardiogram at presentation showing supraventricular tachycardia at 160 beats per minute; movement artifact was due to intermittent tremors; B: repeat electrocardiogram 1.5 hours after initial presentation and treatment with diltiazem showing sinus tachycardia at 115 beats per minute.

Diagnosis and management

The diagnosis of salbutamol toxicity can be made based on clinical and laboratory findings as illustrated in our case. At high therapeutic doses, salbutamol can cause tachycardia, tremors, and hypokalemia. In overdose, salbutamol can additionally cause hyperglycemia, lactic acidosis, and cardiac arrhythmias.

Management of salbutamol toxicity is mainly supportive. Ramoska et al[8] reported that β-blockers may be considered for highly symptomatic patients in the absence of contraindications. Cardiac arrhythmias should be managed according to Advanced Cardiac Life Support Guidelines. Salbutamol-induced hypokalemia should be treated judiciously, if at all, since the underlying mechanism is transcellular shift and not a total body deficit.[3] While lactic acidosis is a known side effect of salbutamol overdose, clinicians should also carefully assess for other underlying causes of lactic acidosis.[4] Hyperventilation is a common finding among patients with metabolic acidosis. In the context of salbutamol toxicity, hyperventilation is typically a compensatory mechanism for metabolic acidosis as opposed to a sign of worsening respiratory distress that requires more β_2-agonist therapy.[4]

CONCLUSIONS

Inhaled salbutamol overdose is uncommon, but the syndrome of β_2-agonist toxicity is an important presentation to recognize. The diagnosis can be made based on clinical and laboratory findings. Key features include tremors, hypokalemia, hyperglycemia, lactic acidosis, and cardiac arrhythmias. The management is mainly supportive, including discontinuation of the offending agent and β-blockers for symptomatic treatment. Given the ubiquitous use of salbutamol and other β_2-agonists, emergency physicians should be familiar with the diagnosis and management of β_2-agonist toxicity.

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