

Fatal Dysrhythmia Following Potassium Replacement for Hypokalemic Periodic Paralysis

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We present a case of fatal rebound hyperkalemia in a patient with thyrotoxic periodic paralysis (TPP) treated with potassium supplementation. Although TPP is a rare hyperthyroidism-related endocrine disorder seen predominantly in men of Asian origin, the diagnosis should be considered in patients of non-Asian origins presenting with hypokalemia, muscle weakness or acute paralysis. The condition may present as a life threatening emergency and unfamiliarity with the disease could result in a fatal outcome. Immediate therapy with potassium chloride supplementation may foster a rapid recovery of muscle strength and prevent cardiac arrhythmias secondary to hypokalemia, but with a risk of rebound hyperkalemia. [West J Emerg Med. 2010; 11(1):57-59.]

INTRODUCTION

Hypokalemic paralysis is a rare cause of muscle weakness and cardiac arrhythmias that primarily affects male patients of Asian descent. Because it is rare in non-Asians¹ it can be misdiagnosed. Thyrotoxic periodic paralysis (TPP) is caused by a sudden shift of potassium into cells, leading to hypokalemia and muscle weakness and can lead to near-fatal or fatal arrhythmias. Immediate therapy with potassium chloride supplementation may foster a rapid recovery from weakness and prevent arrhythmias but risks rebound hyperkalemia.^{1,2} We present a case of fatal rebound hyperkalemia in a patient with TPP treated with potassium.

CASE REPORT

A 40-year-old Hispanic woman called 911 for worsening chest tightness, generalized weakness and vomiting of two days. On arrival, paramedics performed an EKG that revealed sustained monomorphic ventricular tachycardia at 160-180 beats/minute. Blood pressure and oxygen saturation were normal. She was treated with 40 mg intravenous lidocaine after which she converted to normal sinus rhythm. In the emergency department (ED), she was alert and complained of weakness of all four extremities. She denied shortness of breath. She had a history of hyperthyroidism and hypertension but took no medicines. Vital signs were blood pressure of 126/70 mm of Hg, pulse of 90 beats/minute and

respiratory rate of 18 breaths/minute. She was afebrile, and oxygen saturation was 96% in room air. Cardiac and lung examinations were normal. There was no thyromegaly. Neurological examination showed 2/6 strength and hypoactive reflexes in all four extremities. Cranial nerves and sensations were normal. Initial laboratory tests showed potassium of 2.3 mEq/L (normal: 3.5-5.5mEq/L) with normal anion gap. Magnesium, chloride, calcium and creatinine were normal. Urinary toxicology screen was negative. A 12-lead electrocardiogram showed normal sinus rhythm. In the ED the patient received 40 mEq of oral potassium chloride, and intravenous (IV) potassium was started at 20 mEq/hour. Repeat laboratory testing after three hours showed potassium of 1.9 mEq/L. Thyroid-stimulating hormone was low (0.01 μ unit/ml; normal: 0.5-5.0 μ unit/ml) with high free thyroxine (7.77 ng/dL; normal: 0.75 to 1.8 ng/dL). The patient complained of worsening weakness in her legs. She was given additional 40 mEq of oral potassium. Potassium was increased to 30 mEq/hour IV, and the patient was admitted to medical intensive care unit.

A diagnosis of TPP was made based on clinical presentation and laboratory results. Blood drawn after eight hours showed potassium of 6.6 mEq/L. Intravenous potassium was stopped, and intravenous dose of 1 gm calcium, 50% solution of 50 ml dextrose, and 10 units of insulin were given urgently to correct hyperkalemia. Despite these, the patient

developed episodes of ventricular fibrillation and despite several attempts at electrical cardioversion, she died. Her potassium level was 10.1 mEq/L at the time of her death.

DISCUSSION

In the United States, the incidence of TPP in the non-Asian population is 0.1-0.2%.³ It occurs mostly during summer and winter and with increased consumption of sweet drinks, outdoor activities and exercise. TPP primarily occurs in persons aged 20-40, and the most common symptoms are leg muscle weakness, aching cramps and stiffness. Although most patients with thyrotoxicosis are female, men with TPP outnumber women approximately 20:1.¹ While TPP is associated with hyperthyroidism, personal or family history of hyperthyroidism may be absent. As in the case of our patient, nearly half of patients with TPP have no obvious symptoms related to hyperthyroidism during an attack.¹⁻⁵

Differential diagnosis of TPP includes familial periodic paralysis (FMPP), barium intoxication, hypochloremic metabolic alkalosis and hyperchloremic metabolic acidosis.^{1,2} In contrast to TPP, FMPP occurs most often in Caucasians and early in life (rarely after age 25).⁶ And also in contrast to FMPP, TPP does not occur during exercise but in a period of rest after exercise.¹ Barium intoxication should be considered and could result from the ingestion of contaminated food causing hypokalemia by blocking the potassium channels in the cell membrane that normally allow cellular potassium to diffuse into the extracellular fluid.⁷

In the ED, a diagnosis of TPP should be considered in men of Asian or Hispanic descent who present with hypokalemia, muscle weakness or paralysis and cardiac arrhythmias. Leg weakness, which usually begins proximally, is most commonly symmetrical and can progress to flaccid quadriplegia.¹ Deep tendon reflexes are decreased or absent, but ocular, bulbar, and respiratory muscles are usually spared, as are sensation and level of consciousness, although ventilator impairment has been reported.⁶ The EKG findings are those of hypokalemia with increased P wave amplitude, prolonged PR interval, widened QRS complexes, and prolonged QT and U waves. These EKG findings were absent in our patient. Life-threatening intraventricular conduction abnormalities and ventricular fibrillation also have been reported.⁸ Urgent blood investigations in the ED should include a thyroid function test, and patient should have continuous EKG monitoring.

Although the pathogenesis of TPP remains unclear, it is believed to be related to increase in sodium-potassium-adenosine triphosphate (Na/K-ATPase) pump activity. Thyroid hormone coupled with enhanced beta adrenergic response in thyrotoxicosis state increases Na/K-ATPase activity, leading to influx of potassium into the intracellular space causing hypokalemia.⁹ High carbohydrate diet in the setting of a hyperadrenergic state in TPP stimulates insulin

release from pancreatic beta cells, which in turn stimulates N/K-ATPase activity.¹ The chemical structure of thyroxine is similar to catecholamines and exerts its cellular effect via catecholamine receptors. This may explain the usefulness of nonselective beta blockers in the treatment of TPP-associated hypokalemia.^{1,10,11}

A patient with a serum potassium concentration of 2 mEq/L may have a 400 to 800 mEq potassium deficit.¹² The serum potassium concentration can rise acutely by as much as 1 to 1.5 mEq/L after an oral dose of 40 to 60 mEq, and by 2.5 to 3.5 mEq/L after 135 to 160 mEq.¹³ Our patient had received approximately 240 mEq of potassium (oral and IV) in eight hours. We expected our patient would have a potassium level of 3.5-4.5 mEq/L after receiving 200 mEq of potassium after eight hours. But due to rebound hyperkalemia, potassium levels increased to 10.1 mEq/L. This discrepancy between the expected calculated potassium and the real potassium is in part caused by the fact that during the recovery phase of TPP, potassium release from muscle occurs at the rate of up to 15 mEq/hr.¹⁴

Body potassium stores are normal in patients with TPP.¹² A few studies have looked at potassium replacement in TPP. In a case-controlled study by Lu et al.,¹⁵ average recovery time was cut in half in patients with intravenous potassium chloride supplementation at the rate of 10 mEq/h vs controls (6.3±3.8 vs 13.5±7.5 hr). Rebound hyperkalemia occurred in 70% of patients 2-3 hours after recovery from TPP treated with IV potassium chloride while rebound hyperkalemia was rarely seen with potassium supplementation of 50 mEq or less as a total dose. In a retrospective study, Manoukian et al.¹⁶ reported that rebound hyperkalemia occurred in approximately 40% of patients with TPP, especially if more than 90 mEq of potassium chloride was given within 24 hours.¹⁶

An alternative approach focusing on treating the adrenergic drive has been reported using beta blockade. Both oral and IV propranolol appear to be effective in reversing TPP without risk of rebound hyperkalemia.^{10,11,17} Controlled studies are needed to document the effectiveness of combined nonselective beta-blockers and low-dose potassium.

CONCLUSION

TPP appears to present a problem in potassium distribution rather than potassium deficiency; hence, we believe that in most patients potassium supplementation is not indicated, unless the patient is having life-threatening arrhythmias due to hypokalemia or is experiencing respiratory insufficiency. The risk of life-threatening arrhythmias caused by the potential of rebound hyperkalemia outweighs the morbidity of the temporary paralysis. If potassium supplementation must be used, as in the case of unstable arrhythmias due to hypokalemia, very low doses should be given (less than 10 mEq/hr) with close monitoring of potassium level to reduce the risk of rebound hyperkalemia.¹⁵

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