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Case Report
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Development of Acute Metabolic Acidosis in a Pediatric Patient with Idiopathic Intracranial Hypertension Treated with Acetazolamide: A Case Report

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Abstract

Background: Idiopathic intracranial hypertension (IIH) treatment consists of both lifestyle modification and medical/surgical therapy. Acetazolamide, a carbonic anhydrase inhibitor, is the primary medical treatment with adverse effects including neurologic symptoms and the development of metabolic acidosis.

Case Presentation: We present a case report of a pediatric patient (with pre-diabetes treated with metformin) who acutely developed metabolic acidosis and paresthesias following treatment with acetazolamide for IIH diagnosis.

Conclusion: Special awareness by the clinician must be undertaken when acetazolamide is initiated in the presence of current treatment with additional medications that could contribute to the furthering of metabolic acidosis.

Keywords: Metabolic acidosis; Acetazolamide; Idiopathic intracranial hypertension; Metformin

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Introduction

Idiopathic intracranial hypertension (IIH; formerly pseudo tumor cerebri) is a disorder involving the elevation of intracranial pressure. IIH is a disease seen more commonly amongst women, particularly obese women, of childbearing age [1]. The treatment of IIH involves modification of lifestyle factors (such as lowering sodium intake or reducing body weight), eliminating potential causal factors (such as discontinuing tetracyclines or vitamin A therapies), followed by medical/surgical therapy. Acetazolamide has been used effectively to lower intracranial pressures by reducing production of cerebrospinal fluid (CSF). This is done via inhibition of carbonic anhydrase in the choroid plexus [2]. While this treatment has become one of the mainstays of medical therapy for IIH, it is not without risk. Recent randomized, controlled clinical trials have demonstrated that the odds of developing paresthesias, nausea/vomiting, fatigue, and dysgeusia were higher with acetazolamide compared with placebo [3]. Additionally, the development of metabolic acidosis in patients treated with acetazolamide has been evidenced and diagrammed previously in patients with renal insufficiency [4]. We report a case of a pediatric patient, on treatment for prediabetes with metformin, displaying normal renal function who developed paresthesias and metabolic acidosis following treatment of IIH with acetazolamide.

Case Report

A 14-year-old obese female with a past medical history significant for prediabetes treated with metformin presented to the emergency department (ED) secondary to a chief complaint of intermittent bifrontal and occipital headaches that lasted for hours at a time. The patient had presented previously to the emergency department for similar symptoms where imaging and laboratory studies were performed and reported to have been normal. Given ongoing symptoms, the patient and family decided to seek additional evaluation. At the time of this evaluation in the ED, the patient denied any neurologic complaints including numbness, weakness, and paresthesias. The patient was given analgesic medication for treatment of headache. Given patient's age, gender, and weight there was concern for IIH. A lumbar puncture was performed and opening pressure was found to be 30cm of H2O. Following drainage of CSF, acetazolamide therapy was initiated at a dose of 500 mg orally twice daily. The patient was discharged from the ED to follow up with a pediatric

Table 1: Pertinent laboratory results from day of admission.

	Day 0	Day 1	Day 2
Complete Metabolic Panel			
Glucose (mg/dL)	93	108	105
Creatinine (mg/dL)	0.67	0.74	0.76
Sodium (mmol/L)	139	139	143
Potassium (mmol/L)	3.9	3.7	3.8
Chloride (mmol/L)	110	109	112
CO_2 (mmol/L)	12	14	17
Venous Blood Gas			
pH	7.3	7.32	
pCO_2 (mmHg)	30	28	
pO^2 (mmHg)	160	67	
O_2 saturation (%)	100	93	
Base Deficit (mmol/L)	10.6	10.6	
Bicarbonate (mmol/L)	15	15	
Lactate	1		

neurologic specialist.

Two days following the patient's above evaluation in the ED, the patient re-presented with complaint of a two-day history of paresthesias localizing to the bilateral lower extremities as well as facial swelling. The patient and family noted that symptoms began following a total of three prescribed doses of acetazolamide. Laboratory evaluation (Table 1) in the ED demonstrated decreased plasma bicarbonate concentration 12 mmol/L (normal range 21 mmol/L to 29 mmol/L). Given diminished plasma bicarbonate concentration, a venous blood gas (VBG) was drawn. VBG demonstrated pH of 7.30, base deficit of 10.6 and bicarbonate of 15. Anion gap was found to be elevated at 17. Given the patient's concomitant treatment with metformin, a serum lactate concentration was drawn to assess for signs of lactic acidosis. Lactate was found to be normal at 1.0 mmol/L. The patient was admitted to the hospital with signs concerning for an anion gap metabolic acidosis with appropriate respiratory compensation and superimposed non-gap metabolic acidosis. The patient was admitted to a general pediatrics service, monitored and given intravenous fluids. Metformin and acetazolamide were discontinued. Repeat laboratory studies following admission demonstrated normalization of anion gap and improvement in plasma bicarbonate concentration. Presenting symptoms also improved following admission and discontinuation of pharmacotherapies. The patient was discharged on hospital day 2.

Discussion

There is minimal information in the literature describing drug-drug interactions between acetazolamide and metformin resulting in acidosis. Acetazolamide is a carbonic anhydrase enzyme inhibitor most commonly used for treatment of altitude sickness, glaucoma and other indications where decreasing the formation of CSF would be advantageous [5]. Its mechanism of action is likely multifactorial and most commonly attributed to the inhibition of the carbonic anhydrase enzyme leads to decreases in CSF and aqueous humor of the eye resulting in decreases in ICP and intraocular pressure. Acetazolamide is known to alter the taste of foods, decreasing caloric consumption, thus resulting in weight loss [2]. A diuretic action occurs when acetazolamide increases the excretion of bicarbonate in the renal tubule leading to sodium, potassium, and water losses. This action is believed to be the cause of hyperchloremic metabolic acidosis [5,6]. Acidosis has been more commonly reported in patients with underlying renal insufficiency, elderly populations or in those with diabetes who are concomitantly treated with acetazolamide [5].

Metformin is an oral antidiabetic medication commonly used in the treatment of noninsulin-dependent diabetes. Metformin decreases glucose absorption from the gastrointestinal tract, hepatic production of glucose, increases peripheral glucose utilization and is exclusively eliminated by the kidneys [7]. The manner in which metformin precipitates lactic acidosis is controversial and multiple different mechanisms have been proposed. The first is related to increased drug plasma levels due to renal injury or dehydration and second involves alterations in mitochondrial respiration [8,9].

The patient in this case report did not have a lactic acidosis as is typical of metformin accumulation due to dehydration. The diuretic action of the acetazolamide likely resulted in dehydration thus transiently increasing metformin plasma levels adding to the hyperchloremic acidosis that was potentially occurring from the acetazolamide.

To evaluate the likelihood of this patient presentation being the result of a medication adverse event application of the Naranjo Adverse Drug Reaction Scale Probability Scale was applied. Based on the application of this scale the patient case described above is categorized as possible as it appeared after the acetazolamide was initiated, improved upon discontinuation and other potential causes of the disease state and patient specific factors were not identified [10].

Conclusion

The treatment of IIH with the carbonic anhydrase inhibitor acetazolamide is well documented in medical literature, although uncommonly seen by most in clinical practice. The case presented catalogues the development of acute metabolic acidosis in a pediatric patient concomitantly treated with metformin, which has been known to result in the development of acidosis. The medical provider must be aware that adverse events can develop in the pediatric patient treated with acetazolamide. Providers must also consider the impact that concomitant therapies like metformin could have on developing more serious adverse events such as metabolic acidosis.

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