

D-Lactic Acidosis In a Diabetic Patient with a Short Bowel

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Since the initial report by De Wind and Payne¹ in 1976 on intestinal bypass surgery for the treatment of obesity, several cases of D-lactic acidosis have been described.²⁻⁶ This syndrome is characterized by episodic increases in levels of plasma D-lactate (an isomer of L-lactate) produced from bacterial carbohydrate metabolism. D-Lactate is the anion responsible for the associated metabolic acidosis as described by Oh and colleagues.² Surgical procedures that cause anatomic or functional short bowel facilitate the overgrowth of D-lactate-producing gram-positive organisms (such as *Lactobacillus* species, *Streptococcus bovis*, *Bifidobacterium* species, and *Eubacterium* species) at the expense of the gram-negative flora.³

Treatment of D-lactic acidosis has been successful with carbohydrate restriction and oral antibiotics, such as vancomycin, metronidazole, clindamycin, tetracycline, neomycin, and kanamycin.²⁻⁶

In patients who are taking metformin to control their diabetes, the development of metabolic acidosis is an alarming sign, because mortality is high⁷ if the acidosis is metformin induced. It is thus important to differentiate between the two conditions, give appropriate treatment, and prevent further recurrences of either condition.

Case Report

A 53-year-old woman with a history of type 2 diabetes mellitus diagnosed in 1998, hypertension, and hyperlipidemia was initially seen at our outpatient clinic in July 1999. Her diabetes and hypertension were well controlled at that time. Oral medications included metformin 1000 mg twice a day, two 20-mg glipizide tablets each day, and

sustained-release verapamil 180 mg each day. Her surgical history was pertinent for a colectomy and colostomy in 1995 secondary to ulcerative colitis and a cholecystectomy in 1995.

On 22 March 2000 benazepril (Lotensin) 5 mg a day was added to her medication regimen.

On 6 April 2000 she complained of nausea, fatigue, dizziness, and generalized pain. Her plasma glucose values were normal. She was hypotensive (blood pressure of 100/60 mm Hg). The low blood pressure was thought to be due to the addition of benazepril, which was discontinued.

On 12 April 2000 her symptoms worsened, and she was hospitalized for hypotension and acute renal failure. Her serum creatinine was 11.0 mg/dL. In the hospital she received aggressive volume replacement. She had a severe anion-gap acidosis, but no further evaluation was pursued to determine the cause of this acidosis.

On 15 April 2000 she was released from the hospital with markedly improved renal function. Her serum creatinine at her release was 2.0 mg/dL. Mild acidosis persisted. All her medications were continued, including metformin.

On 26 April 2000 she complained of nausea, vomiting, and fatigue. In addition to the above symptoms, she also reported diarrhea from her colostomy stoma. She was readmitted to the hospital, where she was again determined to be hypotensive and acidotic. At admission, her blood pressure was 80/47 mm Hg, her pulse rate was 115 beats per minute, and her mucus membranes were dry. The stoma site was unremarkable. Notable laboratory results at admission included the following values: sodium 141 mEq/L, potassium 4.3 mEq/L, chloride 64 mEq/L, total carbon dioxide 16 mEq/L, an anion gap of 38, blood urea nitrogen 108 mg/dL, creatinine 11.6 mg/dL, glucose 68 mg/dL, serum ketones were negative, pyruvate 0.7 mmol/L (normal 0.5–1.5 mmol/L), and lactate 2.3 mmol/L (normal <2.4 mmol/L). The arterial blood gases had a pH of 7.28. Stool was negative for fecal leukocytes and

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Clostridium difficile. Her condition was diagnosed as anion gap acidosis and acute renal failure secondary to volume depletion. The diagnosis of D-lactic acidosis was made. Metformin-induced lactic acidosis was ruled out because serum L-lactate levels were normal.

This patient was again given aggressive volume replacement. She was also given oral neomycin to treat the presumptive production of D-lactate by overgrowth of intestinal bacteria. Because serum D-lactate values were not available, it was presumed the anion gap acidosis was due to the D-lactate production. She recovered completely after receiving adequate volume replacement. The diarrhea resolved. She was released from the hospital on 1 May 2000 with markedly improved renal function. Her serum creatinine level on discharge was 1.8 mg/dL, and it returned to normal at 1.2 mg/dL during the next 2 months. She has remained asymptomatic since that time.

Discussion

In humans L-lactate is formed directly from pyruvic acid as a product of anaerobic carbohydrate metabolism. Some intestinal bacteria metabolize carbohydrate into D-lactate by the action of isomer-specific D-lactate dehydrogenase. Even though mammals can generate small amounts using the methylglyoxal pathway,⁸ plasma D-lactate is derived mostly from intestinal absorption produced by these bacteria.

In patients with short small bowel, D-lactic acidemia and lactic aciduria are caused by intestinal lactobacilli.⁹ It was found that more than 60% of the fecal flora of patients with short small bowel, who are not receiving antibiotics, consists of lactic-acid-producing lactobacilli. In blood, D-lactic acid was the prominent metabolite.¹⁰ Further, it was observed that acidosis in these patients was related to increased serum D-lactate, increased anion gap, and decreased serum bicarbonate and pH levels. D-Lactic acidosis after gastrointestinal surgery, particularly jejunioileal bypass, usually occurs 5 to 10 years later, but it can occur as long as 23 years later.¹⁰

D-Lactic acidosis should be recognized and treated appropriately to resolve the underlying problem. It should also be differentiated from

metformin-related L-lactic acidosis, in which L-lactate levels are high. Anion gap acidosis can occur as a result of acute renal failure, but the level of anion gap does not increase beyond 22 even when the creatinine level is 12.0 mg/dL (the anion gap was 38 in the above case).

Routine measurement of serum lactate only determines L-lactate levels. In the above case, for instance, the L-lactate levels were normal. It was thus presumed that the D-lactate level was high and was the cause of lactic acidosis. D-Lactate measurements are not routinely available in our laboratory, and an attempt was made to get these levels from an outside laboratory.

Conclusion

The diagnosis of D-lactic acidosis should be considered in a patient with metabolic acidosis and high serum anion gap, normal lactate levels, short-bowel syndrome, or other forms of malabsorption.¹¹

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