Title
Case 23-2013: A 54-Year-Old Woman with Metformin Toxicity

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not mention thiamine deficiency as an important cause of lactic acidosis.

In 2004, Klein et al. described thiamine deficiency as a cause of fatal metabolic acidosis.[1] Their patients were Thai workers who lived in Israel and ate polished rice. Since then, we have also treated several patients with thiamine deficiency that has caused life-threatening lactic acidosis. These patients were either workers from the Far East or malnourished persons with alcoholism.

Thiamine deficiency can be responsible for a number of serious medical problems, none more so than lactic acidosis. Thiamine is a cofactor in the normal functioning of pyruvate dehydrogenase, and with its deficiency, lactate accumulates, causing lactic acidosis.[2] Fortunately, early therapy with intravenous thiamine is lifesaving.[3]

Thiamine deficiency should also be considered in infants who are receiving parenteral nutrition without adequate thiamine supplements.[4]

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TO THE EDITOR: Kalantar-Zadeh et al. describe a 54-year-old woman with metformin accumulation, acute renal failure, pancreatitis, and lactic acidosis. The authors use an approach that is based on the following formula for the expected respiratory response in metabolic acidosis: 1.1 Δ (serum bicarbonate level) = Δ partial pressure of carbon dioxide (pCO_2).[1] This formula is misleading and not advocated in major textbooks. In this patient, the pH was 6.62, the pCO_2 was 18 mm Hg, and the serum bicarbonate level was below 2 mmol per liter. Despite a life-threatening low pH, the authors conclude that the patient had a "remarkable and effective compensatory hyperventilation." With the use of Winters' formula,[2] the expected pCO_2 would be 11 mm Hg (1.5 × the serum bicarbonate level + 8 mm Hg), and because the pCO_2 was 18 mm Hg, the extremely low pH was due to additional respiratory acidosis, perhaps because of the decreased sensorium or exhaustion.

The exceptionally high anion gap (the sodium level minus the chloride level minus the serum bicarbonate level) of 61 mmol per liter was multifactorial. Dehydration increased the sodium concentration. Renal failure and lactic acidosis decreased the bicarbonate level. The decreased chloride level maintained electroneutrality after the disproportionate increase in the phosphorous level to 19.3 mg per deciliter (6.2 mmol per liter) because of lactic acidosis.[3,4]

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TO THE EDITOR: We would like to emphasize three peculiarities of metformin-induced lactic acidosis. First, hypoglycemia is not the rule, possibly because metformin primarily inhibits the endogenous overproduction of glucose, with a minor effect on peripheral consumption.[1] Second, venous hyperoxia is common, since mitochondrial respiration is globally inhibited.[2-4] As a consequence, oxygen extraction decreases and venous oxygen content increases. Third, the outcome is usually favorable.[2,4]

We have reviewed the data sheets of 17 patients (13 women and 4 men; mean [±SD] age, 68±8 years) with metformin intoxication (mean serum drug level, 52±26 μg per milliliter) and lactic acidosis (mean arterial pH, 7.03±0.18, and mean lactate level, 18±9 mmol per liter) in whom central or mixed venous blood oxygen-saturation levels were monitored.[2,4] The initial mean blood glucose level was 117±84 mg per deciliter (6.5±4.7 mmol per liter) (only 6 patients had a