Letter to the Editor

Cardiopulmonary arrest from metformin-induced lactic acidosis

To the Editor:

Metformin is one of the most widely used agents to treat type 2 diabetes mellitus. The most serious adverse effect is anion gap metabolic acidosis from lactic acid induced by elevated metformin levels. We report on a case of a 67-year-old female who underwent cardiopulmonary arrest secondary to extreme acidosis from metformin-induced lactic acidosis.

The patient presented to the emergency department with persistent hypoglycemia and falls. Initial labs revealed metabolic acidosis with HCO$_3$ 11 mEq/L, anion gap 25 mmol/L, potassium of 5.6 mmol/L, and creatinine 9.43 mg/dL. While waiting for the initiation of hemodialysis, the patient went into asystolic cardiopulmonary arrest. Cardiopulmonary resuscitation (CPR) was initiated, including chest compressions, calcium gluconate, epinephrine, sodium bicarbonate, and intubation with mechanical ventilation. Return of spontaneous circulation was achieved after 17 minutes of resuscitation. Repeat labs post-CPR showed HCO$_3$ 11 mEq/L, anion gap 39 mmol/L, glucose 416 mg/dL, lactic acid 32.0 mmol/L, and arterial pH 6.62, with pCO$_2$ of 28 mmHg.

Metformin toxicity was suspected early, given the new worsening kidney function, severely elevated lactic acid, and extreme metabolic acidosis. Emergent hemodialysis was started with an improvement of the patient’s acidosis. The severe acidemia improved with repeat labs showing arterial pH 7.35, HCO$_3$ 14, and lactic acid 26.3. The patient was then transitioned to continuous renal replacement therapy with no significant worsening of the patient’s acidosis and resolution of the lactic acid elevation over the next 48 hours. On hospital day 3, the continuous renal replacement therapy was transitioned to scheduled hemodialysis treatments.

An oral biguanide, metformin is used to treat hyperglycemia by increasing insulin receptor responsiveness at the cell membrane, decreasing glucose absorption at the gastrointestinal tract and decreasing gluconeogenesis by hepatocytes. Metformin induces metabolic acidosis through inhibition of Complex I in the chain of oxidative phosphorylation, inducing rapid turnover of adenosine triphosphate (ATP) and limited ability to recycle excess hydrogen ions created from hydrolysis of ATP within the mitochondria. The estimated incidence of metformin-induced lactic acidosis ranges from 1 to 47 per 100,000 patient-years, with mortality reaching 25–50%. The risk of lactic acidosis was also associated with renal function less than 60 mL/min/1.73 m$^2$. Hyperlactatemia can be induced either by an overdose of metformin or decreased elimination in the setting of poor renal function. Risk factors for unintentional elevated metformin levels may include dehydration, excessive emesis, and diarrhea, leading to decreased renal perfusion and acute renal injury secondary to a volume contracted state. Other clinical causes include congestive heart failure, acute liver injury, underlying infection contributing to relative hypoperfusion.

Metformin-induced lactic acidosis is a rare but deadly adverse effect that can rapidly progress to multiple organ dysfunction, including cardiovascular collapse. Extended hemodialysis and continuous renal replacement therapy can be effective in normalizing the acidosis and elevated lactic acid levels.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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