Metformin-Associated Lactic Acidosis Requiring CRRT

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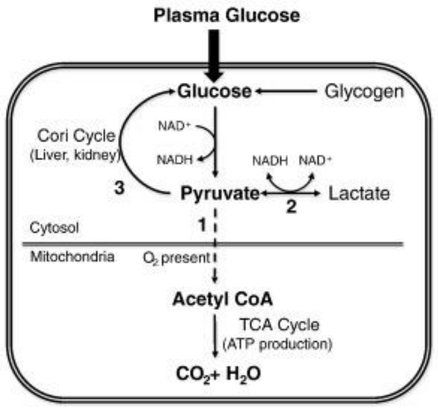
INTRODUCTION

Metformin is frequently the first line drug for patients with diabetes mellitus. Metformin associated lactic acidosis (MALA) occurs in approximately 3-10 per 100,000 patients per year and can be fatal; this is a serious sequela of medication of patients with diabetes mellitus and chronic kidney disease not to be forgotten. It is rare that lactic acidosis caused by metformin in the setting of acute renal failure necessitates the use of hemodialysis.



PATHOGENESIS

Type A Lactic Acidosis:

Evidence of Systemic Hypoperfusion and Hypoxia

- Acute Hypoxia
- Anemia
- Carbon Monoxide Poisoning
- Cardiogenic Shock
- Hemorrhagic Shock
- Septic Shock

Type B Lactic Acidosis:

Absence of Hypoxia

Toxin-Induced Impairment

- Systemic Disease
  - Liver failure or malignancy
- Dugs/toxins
  - Metformin, cyanide, methanol, propofol, anti-viral therapy
- Type D - short bowel syndrome, DKA

CASE REPORT

73-year-old female with past medical history significant for atrial fibrillation, CAD, anxiety, HTN, CKD 3, and type 2 diabetes mellitus, presented to the emergency room with her husband due to altered mental status for several days.

Found to be in acute anuric renal failure, septic shock due to UTI, and to have a severe elevated anion gap metabolic acidosis from lactic acidosis, she was admitted to the ICU and required vasopressor support.

The patient's diabetes medications, including her metformin, were discontinued at time of admission; despite cessation of this medication and intervention with conservative measures, such as rehydration with intravenous fluids and administration of bicarbonate, the patient's kidney function continued to decline.

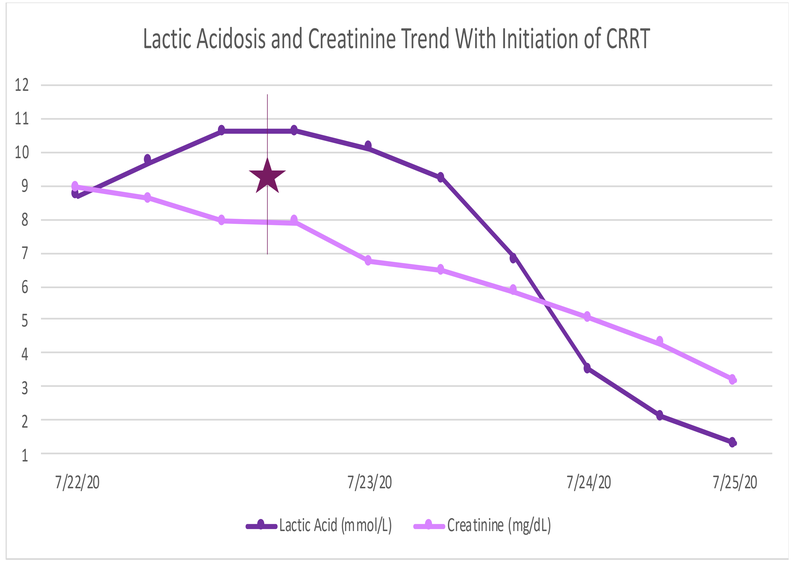


Figure 1. Lactic Acidosis and Creatinine Trend With Initiation of CRRT. A form of hemodialysis, continuous renal replacement therapy (CRRT) was deemed necessary to start due to hyperkalemia, anuric, and volume overload the day of admission. The **star** marks the timing as to when this therapy was initiated in relation to the patient's critical lab values for creatinine and lactic acid. Both showed drastic improvements following this therapy, which was completed for a total of 4 days with no need for permanent dialysis therapy.

CRITICAL FINDINGS

LAB VALUES

- Creatinine: 8.93 mg/dl at admission
- ABG: pH 6.84, pCO2 <16
- Lactic Acidosis: 10.6mmol/L
- Urinalysis: yellow, cloudy sample, specific gravity 1.015, pH 6.0, total protein 3+, 2+ leukocyte esterase, 12-25 WBC
- Urine Culture: >100,000 colonies of *Klebsiella pneumoniae*

DISCUSSION

The primary mechanism in which metformin is known to cause lactic acidosis is by inhibiting gluconeogenesis by blocking pyruvate carboxylase leading to increased serum lactate levels. Metformin is excreted by the kidney unchanged, causing to an accumulation of the medication in the blood stream, thus amplifying the effect on gluconeogenesis.

In our patient, discontinuing the medication alone was not adequate. She required neutralization with IV sodium bicarbonate for her lactic acidosis but ultimately needed hemodialysis therapy. Metformin is moderately dialyzable, allowing for this intervention to be therapeutic.

The patient was discharged with insulin therapy instead of her home metformin 1,000mg twice a day. She followed with nephrology and one month after admission, the creatinine level returned to baseline (1.72mg/dL).

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