5-2020

Metformin Induced Lactic Acidosis

Saad Chaudhry

Michael Ramalia

Alan Mundakkal

Omokayode Osobamiro

Metformin Induced Lactic Acidosis

Saad Chaudhry MD, Michael Ramalia, OMS4, Alan Mundakkal OMS4, Tony Singh, OMS4, Omokayode Osobamiro MD

Henry Ford Health System, Detroit, Michigan

Background

Metformin induced lactic acidosis is an uncommon but potential severe toxicity resulting from excess metformin accumulation in the setting of renal failure or hepatic impairment. The lactic acidosis caused by metformin is believed to be due in large part from inhibition of gluconeogenesis within the liver resulting in lactic acid accumulation. Typically, lactic acid accumulation is mitigated through the activities of the kidneys and liver through clearance and metabolism, respectively. However, impairment of these systems can result in metformin accumulation and profound acidosis. This patient's presentation with altered mental status, hypotension, and lactic acidosis represents a lengthy differential necessitating extensive investigation. Ultimately in the setting of metformin use, significant renal impairment, and a severely elevated metformin level on analysis a diagnosis of metformin induced lactic acidosis was reached. Although metformin is a very well tolerated medication in the management of type 2 diabetes, metformin induced lactic acidosis is a potentially major complication especially with progressive or acutely arising disease.

Case

A 61 year old male with a history of type 2 diabetes mellitus on metformin, prior CVA with residual left sided weakness, CKD, and HTN on losartan was admitted for lethargy with symptoms that appear to have began three days prior to presentation per discussion with family. On presentation he was afebrile, hypotensive and experiencing an altered mental status. He was immediately intubated for airway protection and a significant metabolic acidosis was present on blood gases. Urine drug screen was negative and imaging of the head, chest, abdomen and pelvis were unremarkable except for evidence of prior cerebral infarct. The patient was subsequently started on IV ceftriaxone, vancomycin, and ampicillin for suspected meningitis and was started on hemodialysis due to oliguria. Blood cultures were positive for enterococcus and antibiotics were later de-escalated to IV ampicillin while lactic acid levels continued to rise. Patient was evaluated with EEG without findings of seizure activity. Over the course of hospitalization, patient's mental status improved and could minimally cooperate with elements of exam. However, towards the end of his hospital course, family had elected to withdraw care due to progressive clinical decline.

Metformin

- Diabetes affects approximately 9.4% of individuals in the United States
- Metformin being the first line pharmaceutical treatment of type II diabetes has meant its near ubiquitous presence
- Metformin's has an excellent safety profile with reasonable efficacy
- Prevalence of Metformin induced lactic acidosis has been found to be less then 10 cases per 100,000 patients
- Contraindications to metformin include eGFR less then 30 mL/ 1.73 m squared

Inciting Events

1. Chronic Kidney Disease
2. Infection
3. Losartan Use
4. Progression to Septic Shock
5. Hypoxemia and Hypotension
6. Heart failure
7. Acute Kidney Injury superimposed over CKD

Clinical Features/Treatment

- Nausea
- Vomiting
- Diarrhea
- Altered Mental Status
- Dyspnea
- Hypotension
- Tachycardia
- Tachypnea

- Characterized by high lactate levels in the setting of metformin usage
- Anion gap metabolic acidosis
- Acidosis is often severe with a pH <7

- Prompt discontinuation of metformin
- Hemodialysis is generally regarded as the most efficacious approach to correcting a severe metformin induced lactic acidosis
- Managing contributing condition

Photos

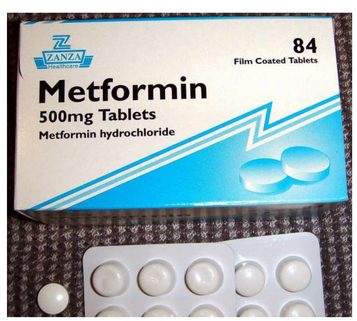

Figure 1

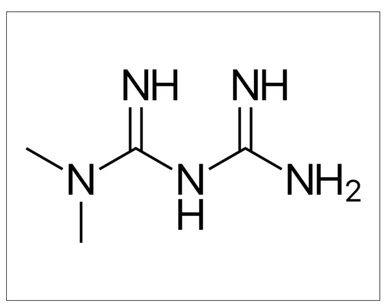

Figure 2

Laboratory Values

Sodium: 136 mmol/L
Potassium: 6.8 mmol/L
Carbon dioxide: <5 mmol/L
Anion Gap: 20
BUN/Cr: 59 mg/dL/ 3.22 mg/dL
eGFR: 20 mL/1.73 m^2
Lactic Acid: 12.2 mmol/L
WBC: 37.5 K/uL
pH: 6.89
pCO2: 24.1 mmHg
Metformin level: 30 mcg/mL (reference limit 0.10 mcg/mL)
Blood Culture: Enterococcus Faecalis

Conclusion

Altered mental status with significant metabolic acidosis in the setting of acute kidney injury creates a significant differential diagnosis that was further confounded by various overlapping features. The patient's case is presumed to have arise as a result of bacterial infection with concurrent usage of losartan causing an acute kidney injury superimposed on chronic kidney disease allowing for toxic levels of metformin accumulation. Lactic acid can be generally thought as type A due to tissue hypoperfusion such as from sepsis or type B without hypo perfusion with causes including metformin, malignancy, and alcohol. This patient's case is thought to have favored both type A and type B.

Bibliography

1. [1] "New CDC Report: More than 100 Million Americans Have Diabetes or Prediabetes." Centers for Disease Control and Prevention, Centers for Disease Control and Prevention, 18 July 2017, www.cdc.gov/media/releases/2017/p0718-diabetes-report.html.
2. [2] Metformin-associated lactic acidosis: Current perspectives on causes and risk
3. DeFronzo, Ralph et al.
4. Metabolism - Clinical and Experimental, Volume 65, Issue 2, 20 - 29
5. [3] Al-Abri, Suad A. "Metformin ." Poisoning & Drug Overdose, edited by Kent R. Olson , 7th ed., McGraw-Hill Education, 2018.