Nucleoside analog reverse transcriptase inhibitor induced lactic acidosis treated with continuous renal replacement in the medical intensive care unit

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Abstract

Lactic acidosis due to nucleoside analog reverse transcriptase inhibitors is a known complication of highly active antiretroviral therapy. This possible complication is not widely known to intensivist, and as such there are no definite treatment modalities. The current standard of care is a bicarbonate drip and discontinuing the offending medications. Herein is presented a case of a 40-year-old African American female who developed lactic acidosis due to her HIV medications and was successfully treated with continuous renal replacement therapy (CRRT) as well as the standard of care. In conclusion, CRRT may be a viable treatment option in a patient with nucleoside analog reverse transcriptase inhibitor lactic acidosis.

Key words: Lactic acidosis, nucleoside analog reverse transcriptase inhibitor, critical care, continuous renal replacement.

Introduction

Systemic lactic acidosis is due to several different causes. One of the lesser causes of lactic acidosis in the intensive care setting is due to antiretroviral medications for the treatment of Human Immunodeficiency Virus (HIV). The optimal treatment of this condition is not known. The current treatment of this condition involves the infusion of sodium bicarbonate. We present a case of systemic lactic acidosis successfully treated with continuous renal replacement therapy (CRRT) in the intensive care unit.

Clinical case

A 40-year-old African American female was transferred to our facility for management of acute kidney injury thought to be secondary to refractory intravascular volume depletion.

She complained of several bouts of non-bloody vomitus and non-bloody diarrhea in the preceding days. The patient's sister had been sick with "a cold". No other known sick contacts and no recent travel outside the country. The patient denied tobacco, alcohol, or illegal/recreational drug usage. She went to a nearby emergency room and was diagnosed with acute bronchitis. The patient then returned as the symptoms had not improved. The patient was started on ceftriaxone, vancomycin and then transferred to our facility. The patient's medical history was remarkable for hypertension, and diabetes mellitus for which her daily medications consisted of metoprolol, hydrochlorothiazide, omeprazole, insulin detemir, and pioglitazone . Her medical history was also remarkable for HIV infection, and she had recently been started on raltegravir, lamivudine, and zidovudine.

On arrival at our institution, she had a blood pressure of 94/50 mmHg, heart rate 130/minute, respiratory rate 16/minute and temperature 97.6 degrees Fahrenheit. Her physical examination was unremarkable. Biochemical profile was remarkable for bicarbonate of 14 mmol/L,

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BUN 20, creatinine 5.6, lactic acid 9.6, serum ketones were negative, creatinine kinase 1056, white blood cell count 6000, hemoglobin 9.9, platelet count 127, neutrophils 42%, bands 2%, lymphocytes 36%, monocytes 18%. CD4 count was 190. Arterial blood gas (ABG) analysis showed a pH of 7.29, pO2 94, pCO2 24, bicarbonate 11.

She had adequate intravascular volume replenishment, but her mental and respiratory status quickly declined necessitating intubation/mechanical ventilation. Arterial blood gas revealed a pH of 6.89, pCO2 23, pO2 114, bicarbonate 5. Repeat lactate was 17. She was hypotensive and received aggressive volume resuscitation. She was placed on norepinephrine as well as empiric antibiotics. Extensive evaluation failed to reveal evidence of infection or bowel infarction to explain the evolving lactic acidosis. In light of the acute kidney injury, anuria, hypotension and progressive lactic acidosis, continuous renal replacement therapy was started with continuous veno-venous hemofiltration (CVVH). The patient was also started on a bicarbonate drip. By day 5 of CVVH the patient's lactate decreased to 3.3 with an ABG with pH 7.34, pCO2 43, pO2 65. The patient was then changed to continuous veno-venous hemodialysis (CVVHD). By day 6, the patient no longer required vasopressors and the lactate normalized. She was successfully extubated and transferred to a rehabilitation facility.

Discussion

Lactic acidosis has many different causes but when it is due to hemodynamic mismatch, it is associated with high mortality (1) and is predictive of outcome. (2) Lactic acidosis is usually classified as type A (impaired mitochondrial oxidative capacity in the setting of tissue hypoxia), type B1 (dysregulation of cell metabolism related to underlying disease), type B2 (related to drugs or toxins) and type B3 (associated with inborn errors of metabolism). (3-5) One of the less commonly seen form of lactic acidosis encountered in the medical intensive care unit is reverse transcriptase inhibitor induced lactic acidosis. Reverse transcriptase inhibitors can cause mitochondrial toxicity leading to impaired pyruvate oxidation and increased lactate accumulation. (6) Certain resources suggest that many of the HIV medications interfere with polymerase gamma, and thus the body has fewer mitochondria that function normally. As the functional mitochondria decrease the body increasingly shifts to an anaerobic metabolism thus producing the increased lactate. This is a potential side effect of the HIV medications but it does not appear to happen routinely in patients that take HIV medications.

A review of the current literature revealed that previous cases of HIV medication lactic acidosis were treated with cessation of the offending medication and administration of a sodium bicarbonate infusion. (7) When continuous renal replacement therapy (CRRT) was started along with sodium bicarbonate, the lactic acidosis usually resolved within the first week. (8) When sodium bicarbonate was used only, the patient appeared to remain acidotic for a longer period of time.

Renal replacement therapy can be used to correct systemic acidemia, however with high-efficiency intermittent hemodialysis the rapid flux of bicarbonate from dialysate to patient can generate excess CO2 requiring hyperventilation to maintain the acid-base balance. (9) This concern may not apply to CRRT because the rate of buffer delivery is much slower than that with intermittent hemodialysis. (10)

Conclusion

Renal replacement therapy is a viable option for the treatment of nucleoside analog reverse transcriptase inhibitor induced lactic acidosis. Whether CRRT can be used as primary therapy or should only remain as adjunctive therapy still remains to be seen. More research is needed to help define the role of CRRT in treating this condition.

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