Two L's: Linezolid Induced Lactic Acidosis

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INTRODUCTION

- The use of powerful antibiotics in severe drug resistant infections becomes limited in certain cases due to the adverse effects associated with treatment options.
- Linezolid is an oxazolidinone that inhibits bacterial protein synthesis, used mainly for gram positive infections including vancomycin-resistant enterococcus.
- Common side effects include myelosuppression, headache, nausea, diarrhea but can also lead to more severe complications such as serotonin syndrome, Clostridium difficile infection, and lactic acidosis.
- We present a case of lactic acidosis after a course of linezolid.

CASE PRESENTATION

- Patient is a 70-year-old female with a past medical history of epilepsy, liver cirrhosis, diabetes mellitus, prior hepatic encephalopathy, morbid obesity, and uterine cancer who presented with confusion and shaking from home after her concerned husband called emergency medical services.
- Workup at the time of admission revealed septic shock secondary to Escherichia coli urinary tract infection (UTI) and bacteremia.
- Patient was started on ceftriaxone for the UTI and moved to the neurological intensive care unit for multifactorial encephalopathy and further work-up including video EEG for potential seizures.
- After a prolonged hospital course, the patient was found to have toxic metabolic encephalopathy and also found to be bacteremic with vancomycin-resistant enterococcus faecium (VRE) and Candida. Patient was started on fluconazole and linezolid.
- After six days of linezolid, the patient was found to have elevated lactic acid of 7.8 mmol/L from a previous lactic acid of 2 mmol/L and an anion gap of 18.
- Linezolid was stopped and there was a significant improvement of the lactic acid to 6.3 mmol/L and anion gap to 15.
- Lactic acid continued to downtrend after discontinuation of linezolid and without any other significant intervention. Patient was not hypoxemic, anemic or in a low cardiac output state during this time.

DISCUSSION

- The first line agent for VRE infections and bacteremia in the majority of cases is linezolid although it is a bacteriostatic drug.
- Lactic acidosis from linezolid use results from interactions between linezolid and mitochondrial ribosomes causing a decrease in aerobic energy production and increasing anaerobic glycolysis and generation of lactate, despite no hypoxia. (Figure 1)
- In a review of case reports, it was found that the incidence was ~6.8%, mortality associated with linezolid lactic acidosis was 25.5% and found that male gender may be related to increased mortality.

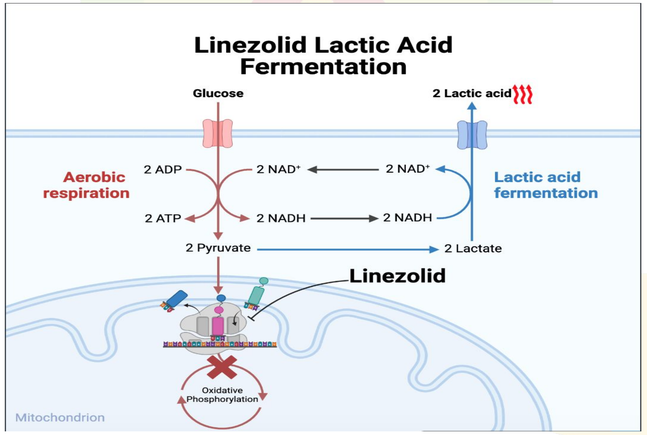

Figure 1. Linezolid Lactic Acid Fermentation. Linezolid inhibits mitochondrial ribosomes which in turn increases lactic acid production.

CONCLUSION

- Due to the highly lethal nature of this adverse reaction, close monitoring and prompt discontinuation of linezolid is paramount in lactic acidosis.
- Further studies on risk factors and interactions that may exacerbate lactic acidosis in patients on linezolid may potentially lead to better patient outcomes.

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