



## Metformin and Meloxicam: Una Mezcla Muy MALA

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### BACKGROUND INFORMATION

Metformin remains one of the top ten most-prescribed medicines in the United States, according to the IMS Institute for Medical Informatics. While generally viewed as having fewer side effects than the sulfonamides, metformin has rarely been associated with the development of potentially fatal lactic acidosis (metformin-associated lactic acidosis or "MALA"). Its etiology remains unclear; however, numerous cases have developed in the setting of renal insufficiency and combination use with non-steroidal anti-inflammatory drugs (NSAIDs). We report a case of severe lactic acidosis, accompanied by altered mental status, acute-on-chronic renal insufficiency and shock in an elderly woman. This case of MALA resolved with supportive therapy, hemodialysis, and cessation of metformin and meloxicam therapy.

### CASE PRESENTATION

A 72 y/o female presented to the emergency department with acute disorientation, memory loss, and personality change, as reported by her husband. She had complained of headache, chest and abdominal pain the preceding day. Past medical history included type 2 diabetes, arthritis, hypertension, and peripheral neuropathy. Medications included metformin, glipizide, amlodipine, gabapentin, and meloxicam at standard doses. Physical examination revealed a temperature of 34.2°C, a heart rate of 93/min, respiratory rate of 22/min, blood pressure 215/115 mmHg and oxygen saturation of 98% on room air. She was pale with dry mucous membranes, lethargic, oriented only to person and able to follow some commands. The exam was otherwise normal. Laboratory studies revealed a white blood count of 21,700/ $\mu$ L, hemoglobin of 10.1 g/dL, hematocrit of 34% and platelet count of 316k/ $\mu$ L. The serum electrolytes (mmol/L) were sodium 140, potassium 6.4, chloride 95, carbon dioxide 5 and anion gap 40. The serum glucose was 100, BUN 58 and creatinine 9.09 (all in mg/dL). Serum lactate was 22 mmol/L. Arterial blood gases on 10L O<sub>2</sub> via simple face mask revealed a pH of 6.7, pCO<sub>2</sub> of 10.4 mm Hg, and pO<sub>2</sub> of 152 mm Hg. A urine drug screen was positive for opiates. Serum potassium, BUN and creatinine had been only mildly elevated one month earlier. EKG revealed peaked T waves without ST elevation. Serum tropo-

nin was 0.26 ng/mL. Unfortunately, serum metformin concentration was not obtained. Chest radiograph was unremarkable; non-contrast cranial computed tomography revealed no acute abnormalities. The patient was intubated for airway control and unresponsiveness. One-half hour later, the blood pressure dropped to 60 mm Hg and the cardiac monitor showed sinus bradycardia. A central line and Quinton catheter were placed and a norepinephrine infusion started which improved the patient's heart rate and blood pressure. The patient was transferred to the medical intensive care unit where she underwent hemodialysis and packed cell transfusion for worsening anemia. She was extubated on hospital day 4 and transferred to the floor on hospital day 6. She was discharged home on hospital day 8 with mental status and lab results similar to her baseline.

### DISCUSSION

Metformin has been associated with development of lactic acidosis (MALA), often occurring with renal insufficiency, although multiple studies have failed to establish either a definite causal relationship or the mechanism of action. The combination of non-

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steroidal anti-inflammatory drugs (NSAIDs) and metformin has previously been implicated in the development of metabolic acidosis and acute renal failure, both of which were present in our case.<sup>1-7</sup> Two published cases of MALA in association with NSAID use were also associated with acute pancreatitis.<sup>1,4</sup> Therapy involves fluid repletion and correction of acidosis and renal insufficiency. Both continuous veno-venous hemofiltration<sup>6,7</sup> and hemodialysis<sup>1,4</sup> have been successfully employed in its treatment. Awareness of this potentially deadly problem is important in El Paso due to the large numbers of diabetic patients in the region, the widespread use of metformin for diabetes, and the ease with which patients obtain and use NSAIDs for simple ailments, such as headaches and arthritis pain. We encourage primary care physicians to discuss the use of over-the-counter NSAIDs with their patients prescribed metformin and to carefully consider other diabetes medications for those patients requiring NSAID therapy. We also encourage manufacturers of NSAIDs and metformin to include a reference to MALA on warning labels.

### REFERENCES

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