

The EM Educator Series

Mini-Case: MALA exists and is bad for you!

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A 39-year-old woman with a past medical history of depression, DM, and HTN presents to the ED 2 hours after a suicide attempt by drug ingestion. She reports feeling upset with her home situation, and she ingested a “handful” of Metformin 500 mg tablets in addition to drinking three 40 oz beers. Initial vitals are HR 109, BP 165/96, Temp 36.4 and SpO2 on RA of 98%. Review of pill count from the Metformin bottle provided by EMS is significant for 30 missing pills (15 g of Metformin). Her lactate returns at 5.4 mg/dL.

Questions for Learners:

- 1) How does metformin-associated lactic acidosis present / when to consider it?
- 2) Gastroenteritis mimics
- 3) Contraindications to metformin
- 4) DDX of shortness of breath with clear lungs
- 5) Systematic approach to anion gap metabolic acidosis – what else to consider and not miss?
- 6) Approach to lactic acidemia
- 7) ED-relevant management of MALA

Suggested Resources:

✓ Articles:

- <https://lifeinthefastlane.com/ccp/metformin-related-lactic-acidosis/>
- <https://coreem.net/podcast/episode-124-0/>
- <http://www.emdocs.net/metformin-associated-lactic-acidosis-mala-ed-focused-management/>
- <http://www.thepoisonreview.com/2014/02/13/6-pearls-about-metformin-and-lactic-acidosis/>
- <https://lifeinthefastlane.com/ccp/lactic-acidosis/>
- <http://www.emdocs.net/gastroenteritis-mimics-emergency-physician-consider/>
- <https://emergencymedicinecases.com/metabolic-acidosis/>

Answers for Learners:

1) How does metformin-associated lactic acidosis present / when to consider it?

- Common initial symptoms are non-specific and include nausea, vomiting, diarrhea, abdominal pain, malaise, and decreased oral intake. In severe cases, altered mental status, tachypnea, hypothermia or cardiovascular collapse may occur.
 - “Suspect MALA in any patient on metformin who presents with abdominal pain, nausea and vomiting and/or AMS.”
- “Patients with MALA will have a low pH, a high-anion gap metabolic acidosis and high lactate levels.”
- “Add metformin toxicity to the differential diagnosis in appropriate patients suspected of having sepsis, mesenteric ischemia, or respiratory failure.”

2) Gastroenteritis mimics

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| <ul style="list-style-type: none"> ▪ Appendicitis ▪ Bowel Perforation ▪ Mesenteric Ischemia ▪ Ischemic Colitis ▪ <i>C. diff</i> Colitis ▪ AAA ▪ Volvulus ▪ Bowel Obstruction | <ul style="list-style-type: none"> ▪ Diverticulitis ▪ Biliary Colic / Cholecystitis ▪ ACS ▪ Myocarditis ▪ PID/TOA ▪ Neutropenic enterocolitis ▪ Inflammatory Bowel Disease ▪ Liver Abscess |
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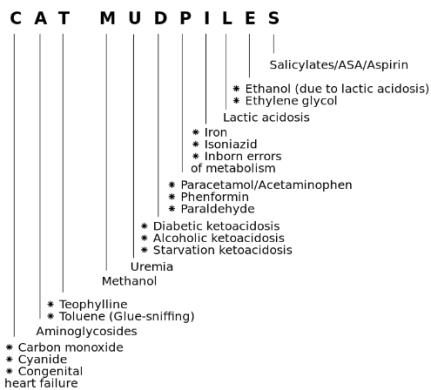
3) Contraindications to metformin

- Metformin is excreted unchanged by the kidneys. In most cases where intentional ingestion is not the culprit, MALA occurs secondary to decreased Metformin excretion (due to kidney dysfunction). The elimination half-life is approximately 17 hours and 90% of the drug is excreted by the kidneys within 24 hours. One can see how someone who is on Metformin chronically can develop MALA in the setting of renal insufficiency.

4) DDX of shortness of breath with clear lungs

- Pulmonary embolism
- Underlying metabolic acidosis – A CAT MUDPILES – Find the etiology!

Causes of high anion-gap metabolic acidosis

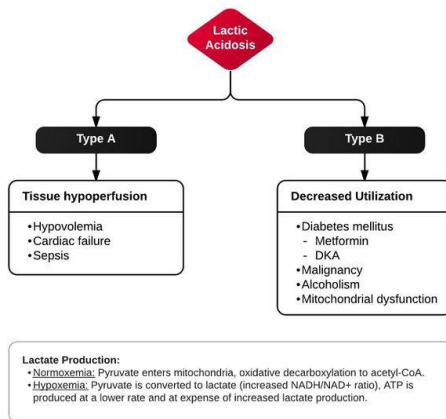


5) Systematic approach to anion gap metabolic acidosis – what else to consider and not miss?

- [emCrit Acid-Base Sheet](#)
 - a. Diagnose and correct the underlying condition
 - b. Restore adequate tissue oxygen delivery
 - c. Ensure appropriate compensatory hyperventilation where possible

6) Approach to lactic acidemia

- Type A vs Type B vs Type D
- False Positives
 - Beta-agonists or beta stimulation
 - Extreme exercise
 - Seizures, immediate ictal period
 - Hepatic failure
 - Lactate ringer's solution unlikely to cause false positive except in hepatic failure



Original chart by Tom Fadial (<http://ddxof.com/>). Used with permission.

7) ED-relevant management of MALA

- The initial step in treating any patient with a poisoning should be to call the poison control center at 1-800-222-1222. A toxicologist should be involved early in these cases.
- The mainstay of treatment is supportive care. Patients will need frequent blood gases and lactate measurements. Certainly, Metformin should be discontinued during any critical illness or in any patient with elevated lactate levels. Sodium bicarbonate infusions may be used to correct acidosis.
 - While low arterial pH and high lactate have been reported as prognostic factors, a recent review of pharmaco-vigilance data demonstrated a lack of prognostic value of these measures, with survival of patients even with pH as low as 6.5.
- The extracorporeal removal of Metformin has also been considered and utilized in a number of cases. Metformin has low molecular weight and limited protein binding, but a large volume of distribution. Continuous renal replacement therapy may need to be continued for longer periods of time if the goal is drug removal, due to this large Vd, especially after large overdoses. While there are currently no clear indications for dialysis methods for MALA, it can be considered for the associated renal failure, in the setting of very large overdoses or to correct severe acidemia.