Chronic acetaminophen use: a rare but emerging cause of 5-oxoproline-induced increased anion gap metabolic acidosis

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Acute metabolic acidosis is a common metabolic disorder in hospitalized patients. Rapid and correct identification of its etiology is important because delay in diagnosis and treatment is associated with increased morbidity and mortality.

♀, 74-year old

High-dose glucocorticoids for suspected diagnosis polyarteritis nodosa + antibiotic combination therapy with **flucloxacillin** for infection. Pain treatment: **paracetamol** 4*1g/day.

Clinical: volume overloaded, altered mental state, hyperventilating

Biochemical: *HCO3- 9.4 mmol/L, anion gap 33.34 mmol/L, eGFR 27, pH 7.13, pO2 81.3, pCO2 22.3, lactate level 1.2 mmol/L, ketones --*

Urine: 5-oxo, 3-OH-butyrate, acetoacetate ↑

Diagnosis: 5-OXO induced HAGMA (high anion gap metabolic acidosis) + AKI (acute kidney injury)

Therapy: ICU, ~~acetaminophen (APA)~~, N-acetylcysteine (NAC) → rapid improvement

G	Glycols
O	5-Oxoproline (5-OXO)
L	Lactate
D	D-lactic acid
M	Methanol, other toxines (ethanol, Aldehyde)
A	Aspirin, salicylates
R	Renal failure
K	Ketoacidosis

Risk factors: chronic use of APA, female gender, diabetes mellitus, chronic kidney disease, simultaneous intake of flucloxacillin, malnourishment, sepsis and liver disease (especially alcohol).

Cause: accumulation of 5-OXO due to longstanding depletion of glutathione and cysteine stores.

Treatment: immediate discontinuation of the drug and supportive care. Treatment with NAC leads to repletion of glutathione and cysteine stores.

In absence of other possible etiologies, acetaminophen-induced metabolic acidosis should be suspected in patients with HAGMA & recent APA use in combination with other risk factors.