

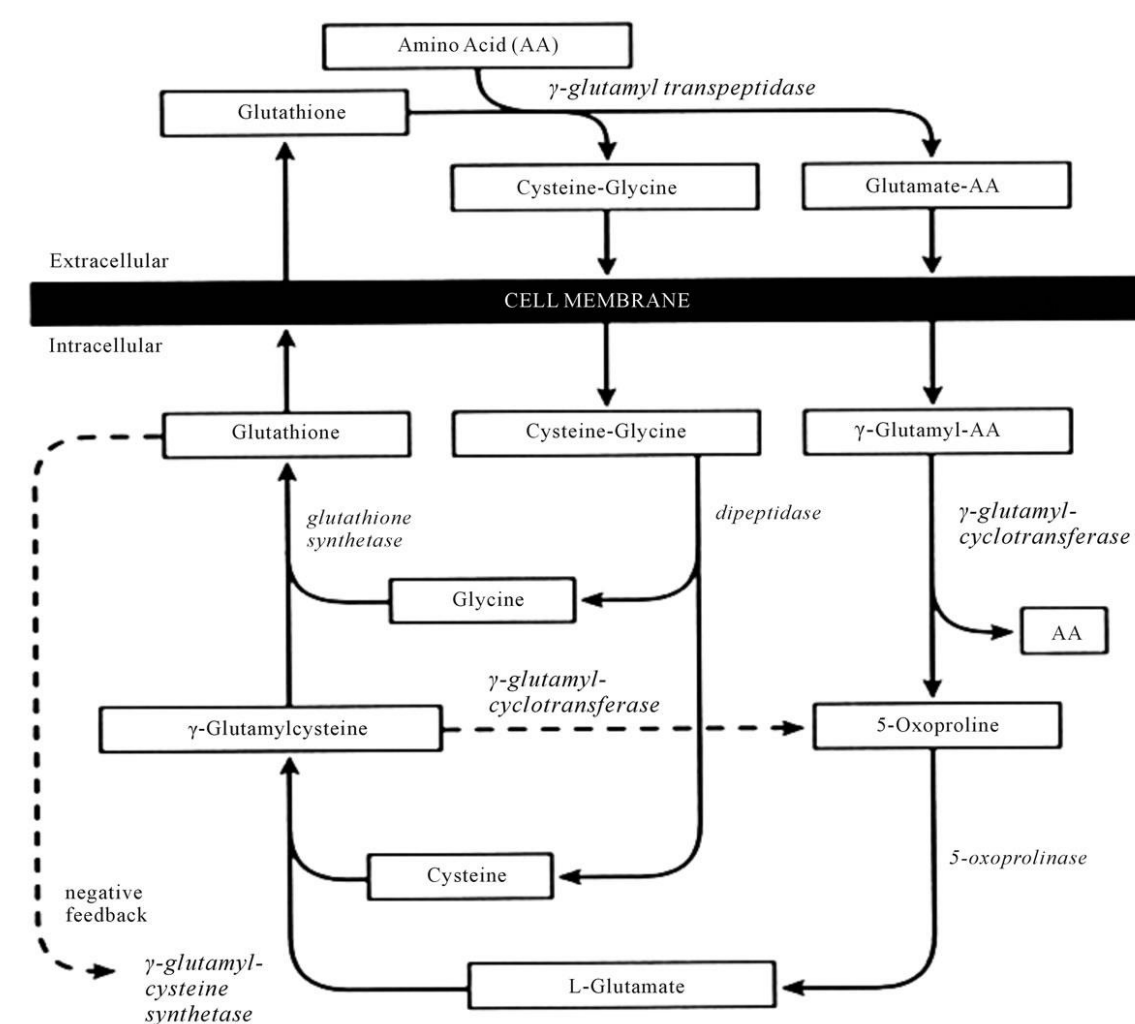
Introduction

- Pyroglutamic acidosis: 5-oxoprolinemia is an under recognized cause of high anion gap metabolic acidosis (HAGMA).
- Acetaminophen disrupts the gamma glutamyl cycle causing depletion of glutathione stores leading to 5-oxoproline accumulation.
- We report a case of a malnourished woman who received low doses of acetaminophen resulting in severe anion gap metabolic acidosis and was treated successfully with oral N-acetyl cysteine (NAC)

- A 57 year old woman with schizoaffective disorder, seizures, status post tracheostomy following Chronic obstructive pulmonary disease exacerbation, presented with severe anemia and acute kidney injury with BUN of 70 mg/dl and serum creatinine (Cr) of 1.26 mg/dl, HCO₃ 15 mmol/L and anion gap (AG) 18 mmol/L.
- She received 2 units of PRBCs and volume resuscitation with IV bicarbonate solution.

- On day 5 of admission, her BUN/Cr improved to 20mg/dl and 0.9 mg/dl, HCO₃ 22 mmol/L and AG 15.
- By day 9, she developed worsening HAGMA with HCO₃ of 13 mmol/L and AG 25.
- She received 325 to 650 mg a day of acetaminophen, from day 6 to day 11, with a total dose of 1625 mg of acetaminophen over 5 days.
- She received a total of 2100 mmol of IV sodium bicarbonate from day 7 to 21 but acidosis persisted.
- On day 12, this prompted to check 5-oxoproline level in urine which was reported as > 10,000 mmol/mol creatinine with a negative serum acetaminophen level.
- On day 21, she was started on oral NAC 1200 mg PO twice daily for 4 days with complete resolution of metabolic acidosis requiring no further bicarbonate infusion.
- Urine anion gap was measured and calculated to be positive, suggesting unmeasured urinary anions, which most were pyroglutamic acid.
- Urine anion gap is classically used in NAGMA, but in our case it was used as a utility in high anion gap acidosis.

The g-gutamyl cycle



Follow Up

- Acetaminophen added in her allergy list.
- 6 months later for follow up: HAGMA resolved with Anion Gap 10 mmol/L with normal serum bicarbonate.

Discussion

The mnemonic GOLDMARRK for HAGMA: stands for Glycols, 5-Oxoproline, L-lactate, D-lactate, Methanol, Aspirin, Renal failure, Rhabdomyolysis and Ketoacidosis

Discussion

- Pyroglutamic acidosis: 5-Oxoproline can occur in acetaminophen use, poor nutrition, renal failure, female gender, infections, use of fluoxacillin, chronic alcohol use.
- Glutathione plays an important role in amino acid transport and detoxification of endogenous waste products.
- This cycle becomes futile in acquired deficiency of cellular glutathione, which results in accumulation of 5-oxoproline.
- This case is interesting that the patient received low therapeutic doses of acetaminophen and still developed pyroglutamic acidosis in the absence of acetaminophen level.
- Her persistent HAGMA was likely related to poor nutrition status resulting in acquired glutathione deficiency
- Pyroglutamic acid: 5-oxoproline levels should be checked in an unexplained HAGMA in hospitalized patients as acquired glutathione deficiency can be corrected effectively by oral NAC and good nutrition.