Proton Pump Inhibition in the Management of Hypokalemia in Anorexia Nervosa with Self-Induced Vomiting

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DOI: 10.22374/cjgim.v13i3.255

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Submitted: October 26, 2017. Accepted: January 2, 2018. Published August 27, 2018.

Abstract

Eating disorders with purging behaviours can lead to hypokalemia through increased renal potassium loss. Severe hypokalemia ($K^+ < 2.5$ mmol/L) can cause rhabdomyolysis, cardiac arrhythmias, and death. Hypokalemia in patients with eating disorders with persistent self-induced vomiting can be refractory and difficult to treat due to decreased intake and ongoing potassium wasting. We report a case of severe hypokalemia due to anorexia nervosa (binge-purge subtype) successfully treated with a proton pump inhibitor as an adjunct to standard therapy, which suggests that this class of medications may have a role in the management of refractory hypokalemia in patients with eating disorders.

RESUME

Les troubles de l'alimentation avec des comportements de purge peuvent entraîner une hypokaliémie par une augmentation de la perte de potassium rénal. Une hypokaliémie sévère ($K^+ < 2,5$ mmol/L) peut provoquer une rhabdomyolyse, des arythmies cardiaques et la mort. L'hypokaliémie chez les patients présentant des troubles de l'alimentation avec des vomissements persistants auto-induits peut être réfractaire et difficile à traiter en raison d'une diminution de l'apport et de l'atrophie continue du potassium. Nous rapportons un cas d'hypokaliémie sévère due à l'anorexie mentale (sous-type binge-purge) traité avec un inhibiteur de la pompe à protons en complément du traitement standard, suggérant que cette classe de médicaments pourrait jouer un rôle dans la prise en charge de l'hypokaliémie réfractaire avec des troubles de l'alimentation.

Background

Hypokalemia is a dangerous complication in severe cases of eating disorders with self-induced vomiting and can result in rhabdomyolysis, cardiac arrhythmias, and death. Self-induced vomiting leads to hypokalemia through two pathways. First, loss of gastric acid causes hypochloremic metabolic alkalosis, which increases filtered bicarbonate load in the nephron (exceeding the

tubular resorptive threshold), and subsequently increases distal sodium bicarbonate delivery. Secondly, hypovolaemia causes activation of the renin-angiotensin-aldosterone axis. Increased distal sodium delivery and mineralocorticoid activity together cause urinary potassium wasting. Standard management of severe hypokalemia in patients with anorexia or bulimia nervosa and persistent self-induced vomiting includes intravenous replacement

of potassium and correction of hypovolaemia. However, hypokalemia is often refractory in eating disorder outpatients who have ongoing self-induced vomiting after discharge. We present a case of hypokalemia due to anorexia nervosa, binge-purge subtype with self-induced vomiting successfully treated with a proton pump inhibitor (PPI) in addition to standard therapy.

Case

A 23-year-old woman presented to an internal medicine post-discharge rapid assessment clinic for reassessment of refractory hypokalemia and chronic metabolic alkalosis secondary to self-induced vomiting. She had a long-standing history of anorexia nervosa, binge-purge subtype since the age of 17, with persistent and frequent self-induced vomiting. She was severely underweight with a body mass index of 14, and her past medical history was significant for past suicidal ideation, chronic low mood and anxiety, and a remote admission for drug overdose. She had been admitted to hospital four times for severe hypokalemia, most recently five months and one month before the current episode. These two recent admissions followed a similar pattern, with presentation to the emergency department with severe hypokalemia (K^+ 2.2 mmol/L at the first visit and 1.8 mmol/L at the second), T-wave inversions on electrocardiography, metabolic alkalosis, hypovolaemia, and acute kidney injury (serum creatinine 100–120 μ mol/L, from a baseline of 78 μ mol/L). Her fluid and electrolyte abnormalities improved and her electrocardiogram normalized during both admissions following the administration of intravenous potassium chloride (KCl) and saline. She was discharged home each time on oral potassium supplements (40 mmol/d KCl tablets and 80 mmol/d KCl elixir) and quetiapine 100 mg daily. Following the second admission, her potassium

had fallen from 4.0 on discharge to 3.0 and then 2.7 over two clinic visits. The third clinic visit revealed a potassium level of 2.1, prompting readmission to hospital (Table 1).

During this current episode, we treated her on day 1 with intravenous saline and KCl infusion and added amiloride 10 mg once daily to decrease renal potassium excretion. However, given her history of repeat admissions for hypokalemia and her continued self-induced vomiting, we were concerned about the likelihood of recurrence of hypokalemia after discharge. We sought advice for additional management strategies through crowdsourcing on Twitter (using hashtag #askrenal), and a nephrologist suggested that adding a PPI might reduce renal excretion of potassium through reduction of gastric acid losses.¹ Given a favourable benefit-harm ratio and evidence from one previous case report in the literature, the patient was started on pantoprazole 40 mg po daily on day 2. Her potassium increased from 2.7 mmol/L to 5.2 mmol/L by Day 3, marking the most rapid increase in her admission history. The patient declined an inpatient bed on the psychiatry ward and was therefore discharged after restoration of normokalemia and improvement in her alkalemia. In addition to 40 mg pantoprazole once daily, her discharge medications were KCl tablets 16 mmol, amiloride 10 mg, quetiapine 200 mg, nabilone 1 mg, and magnesium oxide 100 mg (all once daily).

One week after discharge, the patient had continued to take the PPI in addition to oral potassium supplements and amiloride; her potassium remained within normal limits at 3.8 mmol/L, and her alkalemia was stable. The patient continued on this medication regimen but moved overseas shortly after and was lost to follow-up.

Table 1. Initial Laboratory Results for a Patient Presenting with Refractory Hypokalemia Secondary to Anorexia Nervosa, Binge-Purge Subtype with Self-Induced Vomiting

	Measured Value at Presentation (Day 1)	Measured Value at Day 2	Measured Value at Discharge (Day 3)	Measured Value One Week Later	Normal Range	Units
Sodium	135				135–145	mmol/L
Potassium	2.1	2.7	5.2	3.8	3.5–5.0	mmol/L
Chloride	70				98–106	mmol/L
Creatinine	120	84			50–90	μ mol/L
Bicarbonate	49		44	44	24–30	mmol/L

Discussion

This case highlights a potential role for PPIs (and potassium-sparing diuretics) in the management of severe refractory hypokalemia in a patient with anorexia nervosa with self-induced vomiting. As well, this case demonstrates the power of medical social media to identify treatment options that are neither widely known nor well reported in the medical literature.²

Recurrent hypokalemia is a dangerous complication in eating disorders with purge-type behaviour, and is a contributor to hospital admissions, cardiac complications, and mortality.^{3,4} Our patient had a pattern of recurrent admissions for symptomatic hypokalemia despite ongoing home use of oral potassium supplements. Based on her history and persistent vomiting, a recurrence of hypokalemia following hospital discharge was likely. However, after the addition of pantoprazole to the regimen of intravenous potassium, fluids, and amiloride, her serum potassium normalized rapidly and remained within normal limits at one week of follow-up, despite continued self-induced vomiting. This finding suggests that PPIs may have an under-recognized role in the treatment of refractory hypokalemia secondary to eating disorders with self-induced vomiting.

PPIs are frequently prescribed for various conditions including gastritis, gastroesophageal reflux disease, peptic ulcer disease, and dyspepsia.⁵ PPIs increase pH within the stomach through the irreversible inhibition of gastric acid secretion by parietal cells and have a relatively good safety profile, although adverse events associated with long-term use include increased risks of *C. difficile* infection, community-acquired pneumonia, and metabolic bone disease.⁴ We performed a literature search of OVID Medline, 1946-present (Box 1) and found only a single report of the use of a PPI in the management of refractory

hypokalemia in a patient with an eating disorder. In 2002 Eiro, Katoh, and Watanabe described using a PPI to treat persistent hypokalemia and metabolic alkalosis in a female patient with anorexia nervosa and a history of self-induced vomiting.⁶ Potassium levels improved after treatment with lansoprazole at a dose of 15 mg per day, and remained normal for one year of follow-up despite persistence of self-induced vomiting.⁶ No other case reports or higher-quality studies were found on the use of PPIs in the treatment of hypokalemia in eating disorder patients.

The mechanism through which pantoprazole corrected hypokalemia in this case can be inferred from the pathophysiology of hypokalemia in persistent vomiting. Although some potassium is lost directly from the stomach, the concentration of potassium in gastric secretions is relatively low, and renal excretion of potassium is the primary driver of hypokalemia.⁷ Gastric acid (HCl) loss during emesis results in a hypochloremic metabolic alkalosis and an increase in serum bicarbonate. At the level of the nephron, the increased filtered bicarbonate levels exceed the resorptive ability of the proximal tubule, resulting in increased sodium bicarbonate delivery to the distal nephron.^{6,7,8} Increased distal sodium delivery results in a greater potential for potassium loss as sodium is reabsorbed via epithelial sodium channels. Bicarbonate functions as a non-reabsorbable anion in the distal tubule, and alters renal potassium handling by increasing potassium-hydrogen exchange at the apical membrane and increasing the excretion of potassium as an accompanying cation.^{7,8} This mechanism is potentiated by reduced potassium-chloride co-transport due to hypochloreaemia and secondary hyperaldosteronism due to hypovolaemia, resulting in a net increase in potassium excretion in the urine.⁸ PPIs inhibit secretion of HCl into the gastric lumen, and therefore decrease gastric losses of hydrogen and chloride ions in vomitus. The reduction in proton loss during emesis will improve the hypochloremic metabolic alkalosis and reduce the excess filtered bicarbonate levels that help drive potassium loss in the distal nephron.⁷ Therefore, PPIs may reduce renal excretion of potassium during persistent vomiting, and can act as an adjunct to fluid and potassium replacement therapies in treatment for hypokalemia secondary to frequent purging episodes.

There are two key limitations to our interpretation of the effect of PPIs. Amiloride also decreases potassium excretion and was started one day prior to the addition of pantoprazole. The patient was also lost to follow-up shortly after beginning pantoprazole therapy, preventing the collection of data on long-term effect on potassium levels. However, the rapid increase in serum potassium after PPI administration and maintenance of normokalemia for one week after discharge with pantoprazole is a promising signal regarding the effect of PPIs on potassium excretion.

Box 1. Literature Search

1. exp hypokalemia/
2. hypokalemia.mp.
3. hypokalaemia.mp.
4. exp "Feeding and Eating Disorders"/
5. anorexia.mp.
6. bulimia.mp.
7. purging.mp.
8. exp Proton Pump Inhibitors/
9. (esomeprazole or omeprazole or lansoprazole or rabeprazole or pantoprazole).mp.
10. proton pump.mp.
11. 1 or 2 or 3
12. 4 or 5 or 6 or 7
13. 8 or 9 or 10
14. 11 and 12 and 13

While treatment of the underlying psychiatric disorder is of the utmost importance in patients with eating disorders, effective management of associated electrolyte disorders could in theory reduce morbidity and mortality. We suggest that PPIs could be considered as a potential adjunctive therapy to potassium supplementation in purging-type patients with severe refractory hypokalemia and persistent vomiting. This therapy could also be considered in other situations in which persistent loss of gastric acid may be expected to result in hypokalemia.

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