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Correspondence

Gitelman syndrome triggered by proton-pump inhibitor use

Dear Editor,

A 33-years-old male was admitted in July 2017 to our care following a 2-month history of heartburn and dry cough. He underwent upper GI endoscopy, which detected only the presence of hiatal hernia. A daily therapy with 30 mg lansoprazole and sodium alginate was therefore started, with quick resolution of symptoms. Around 20 days later, the patient suffered from diarrhea (10 bowel movements/day), deep asthenia, nocturia, and rapid weight loss of 6 kg.

He was admitted to the Emergency Department, and diagnosed with severe hypokalemia (1.6 mEq/l, n.v. 3.7–4.8 mEq/l) and hypomagnesaemia (1.0 mg/dl, n.v. 1.9–2.5 mg/dl), and treated with intravenous supplement of potassium and magnesium. In the following two months he showed persistent hypokalemia and hypomagnesaemia, and was therefore admitted to the Nephrology Department. During his hospital stay, no significant instrumental or laboratory alteration was found except for persistent hypokalemia and hypomagnesaemia. On suspicion of salt-losing tubulopathy, research of SLC12A3 gene was performed, and biallelic inactivating mutations in this gene were found. Diagnosis of Gitelman syndrome (GS) was therefore posed, and the patient was discharged with oral supplement of potassium and magnesium, and recommendation to avoid proton-pump inhibitors (PPI).

At the last examination (November 2018), the patient was doing well under treatment with oral supplementation of potassium and magnesium and with mucosal esophageal cytoprotector (EsoxxOne^{TM}).

GS is a salt-losing tubulopathy characterized by hypokalemic metabolic alkalosis with hypomagnesaemia and hypocalciuria [1]. GS is believed to be the most frequent inherited tubulopathy with a prevalence of 1–10 per 40,000 people [2]. The disease is caused by biallelic inactivating mutations in the SLC12A3 gene encoding the thiazide-sensitive sodiumchloride cotransporter expressed in the apical membrane of cells lining the distal convoluted tubule [3]. To date, >350 mutations scattered throughout SLC12A3 have been identified in GS patients [4]. The majority of patients are compound heterozygous for SLC12A3 mutations, but a significant number of GS patients are found to carry only a single SLC12A3 mutation.

This is the first reported case of GS triggered by PPI, and why this occured is unknown. We can hypothesize that PPI could inhibit not only gastric ion pump H/K-ATPase but also renal ion pump Na/K-ATPase, which are similar. This pathogenetic mechanism, that could also explain some cases of acute kidney injury under treatment with PPI [5] in some genetically predisposed subjects, could trigger GS. This case teaches us therefore that PPI use could be a trigger factor for kidney diseases in genetically predisposed subjects.

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Looking for women in hepatology: Sex authorship differences in clinical practice guidelines and position statements

First female authorship is slowly increasing in scientific publications, but it is still inconsistent and seems to vary across different medical disciplines and specialties [1–4]. When looking at the authorship in gastroenterology and/or hepatology original papers, it was estimated that the proportion of first female authors increased from 9% in 1992 to 29% in 2012, whereas for last authors, the proportion of female authors increased from 5% in 1992 to 14% in 2012 [5]. However, clinical practice guidelines or position statements may potentially adopt different authorship rules when compared to original articles [3,4]. To date, information regarding the representation of first, second and last female authors in hepatological clinical practice guidelines and position statements published in the last five years is scarce. We searched *PubMed* for clinical practice guidelines or position statements on liver disease management/diagnosis/liver imaging, published in English from 1st January 2014 to 31st December 2018. Based on this selection, we found 165 clinical practice guidelines and/or position statements. Subsequently, we excluded from the analysis those in which the authorship list was not clearly reported or those with only panel members (n = 32, 19.4%). As shown in Table 1, of the 133 included documents, 44 were published in 2018, 30 in 2017, 23 in