



## PPI INDUCED HYPOMAGNESEMIC HYPOKALEMIC ILEUS – A UNIQUE COMPLICATION SEEN AFTER FUNDOPLICATION FOR GERD.

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### ABSTRACT

Proton Pump Inhibitors (PPIs) are first line therapy for Gastro Esophageal Reflux Disease (GERD). Although its efficacy remains time trusted, it can present with dyselectrolytemias especially with long term usage. Hypomagnesaemia is a well documented and known such abnormality which can cause symptoms of upper abdominal /chest discomfort and also ileus as in our case presentation. We present a case of GERD which developed such complications after surgery – laparoscopic fundoplication and caused diagnostic difficulties. Our case presentation highlights the importance of knowing the history of long term PPI use prior to surgery to be aware of the possibility of such electrolyte abnormalities and ensure smooth post operative recovery and decrease patient distress. We also exert importance of such evaluation prior to initiating long term PPI therapy for all patients with GERD.

**KEYWORDS :** GASTROESOPHAGEAL REFLUX DISEASE (GERD) LAPAROSCOPIC FUNDOPLICATION HYPOMAGNESEMIAS HYPOKALEMIA ILEUS

### INTRODUCTION

Laparoscopic Fundoplication is the surgery of choice for (GERD) Gastro Esophageal Reflux Disease patients. This surgery is offered when the patient has poor response to medical management especially Proton Pump Inhibitors (PPIs).<sup>1,2,3</sup> PPIs have a tendency to cause dyselectrolytemias especially hypomagnesaemia and concomitant hypokalemia / hypocalcaemia which can cause postoperative complaints of upper abdominal / chest discomfort, increased gas bloat syndrome, and as in the presented case report, ileus.<sup>4</sup> It is important to have an awareness of such predilections to ease postoperative recovery and symptomatic distress of the patient already tormented with intractable GERD.

### CASE REPORT

A 30 year old man was diagnosed with GERD grade 3 and Hiatus Hernia with poor response to conservative management mainly Proton Pump Inhibitors (PPIs). [FIG (1)] In distress the patient had become accustomed to PPI self medications without physician consultation. The patient was offered surgical treatment – Laparoscopic Nissen Fundoplication as treatment after more than 2 years of conservative management. He consented for surgery and after anesthesia fitness Laparoscopic Nissen Fundoplication was performed. His post operative recovery was uneventful and he tolerated liquids orally on first post operative day.

The subsequent follow up visits were uneventful. Diet was gradually introduced by the second week and he was tolerating well. His review barium swallow study and endoscopy revealed an adequate correction with no evidence of dysphagia or reflux. [FIG (2), (3)] No medications were prescribed to the patient in the post operative phase.

After approximately a month and a half of the procedure the patient complained of gas bloating, upper abdominal/lower chest wall discomfort especially on left side along with left arm/left jaw pain and palpitations. His (electrocardiogram) E.C.G. and cardiac enzymes were normal along with biochemical and hematological parameters. Ultrasonography of the abdomen was insignificant and x-ray of the abdomen was also unremarkable with mild small bowel gaseous loops. His complaints continued and despite reassurances and evaluations no abnormality was identified. The patient resorted to PPI self therapy for relief.

After 1-2 weeks an emergency admission was done on account of small bowel distension and abdominal distress. An X-ray of the abdomen revealed dilated small bowel loops throughout the abdomen.[FIG (4)] A diagnostic laparoscopy done to rule out adhesive small bowel obstruction and to inspect the operative site was insignificant. He was reassured and given supportive

management mainly with prokinetics and PPIs. He pointed at this conjuncture that he had been suffering with constipation also although it was not a major complaint.

Further evaluation was considered in form of thyroid function tests, electrolyte and calcium levels, along with complete cardiac evaluation. His entire re evaluation was insignificant apart from erratic E.C.G. changes revealing occasional skipped beats, borderline hypokalemia and borderline hypomagnesaemia. He underwent an endoscopy, a barium swallow and a CT scan of the whole abdomen which only revealed post fundoplication changes and no other abnormalities. With these findings hypomagnesaemia correction was advised and oral correction was initiated. He responded to the correction and had significant improvement in all his symptoms. He was reassured and asked to avoid PPIs without prescription. He was asymptomatic on review for the same.

### DISCUSSION

Proton Pump Inhibitors (PPIs) are the mainstay of treatment for GERD.<sup>1, 2, 5, 6</sup> A prolonged regimen is suggested to the patient in view of the severity of symptoms and surgery options are usually kept for patients with poor response or with PPI – dependency. An inadequate knowledge usually exists among general practitioners who prescribe such medications and amongst the patients who take the medications regarding the adverse effects of long term usage of PPIs.

Fundoplication is usually superior to medical management for the treatment of such intractable GERD and present surgical techniques usually allow faster recovery, and complete recovery from symptoms.<sup>1, 2</sup> Usual complications of the procedure are related to under correction or overcorrection of the lower esophageal sphincter and the present techniques are fail proof in experienced hands. The general satisfaction index of post-fundoplication patients is high and recurrences of GERD rare.<sup>1</sup>

The patient in discussion although initially presented with symptoms suggestive of surgical overcorrection, his evaluations concerning the same were not evident in any of the investigations performed. Coexisting complaints of palpitations, tremors, agitation and most importantly ileus-related constipation prompted complete electrolyte evaluation along with cardiac and gastrointestinal checkups.<sup>4, 7</sup> It was only hypomagnesaemia which could explain all the symptoms and the treatment of which resulted in relief for the patients symptoms on the whole.

Hypomagnesaemia even though borderline may present with symptoms which are severe and distressing. Co existent hypokalemia and even hypocalcaemia can also worsen the

presentation as in our case.<sup>8</sup> Though usually seen in an intensive care unit setting (hospitalized patients), it may be seen along with renal disorders, gastrointestinal absorptive causes, genetic disorders, and mainly drugs. In the present setting PPIs were evidently involved and mainly because of long term abuse.<sup>9</sup>

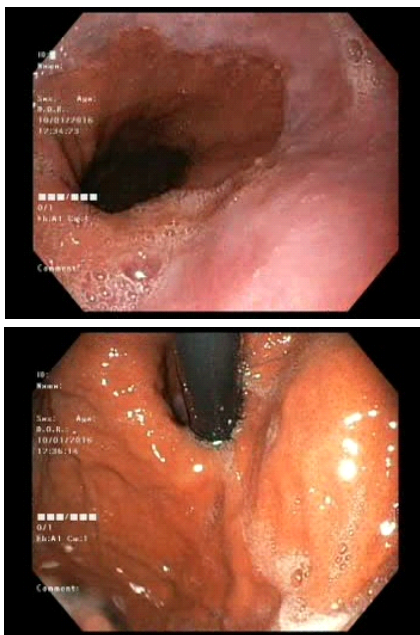
PPIs though should be suggested for all patients as first line therapy of GERD, its long term usage warrants caution.<sup>10</sup> Electrolyte assessments and patient counseling should be performed in such situations and if need be H2-blockers like ranitidine can be substituted for the same.<sup>11</sup> When surgical therapy is contemplated for such patients it is of prime importance to know the history of duration of PPI usage prior and if need be check and correct the electrolyte abnormalities if any, especially hypomagnesaemia.<sup>3</sup> Such practices can prevent the abuse of important first line drugs like PPIs and also ease surgical post operative recovery avoiding diagnostic confusion and patient distress.<sup>12</sup>

## CONCLUSION

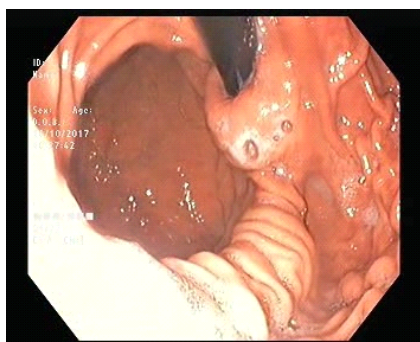
Although PPIs form the mainstay of GERD treatment their long term usage needs to be with caution.<sup>13</sup> The possibility of electrolyte abnormalities like hypomagnesaemia and co-existent hypokalemia, hypocalcaemia can be seen in settings of hospitalized patients, renal diseases and also in the community.<sup>9</sup> An evaluation prior to long term use and also prior to surgery if contemplated saves the patient unwanted distress of the symptoms all dyselectrolytemias especially hypomagnesaemia.<sup>3, 12</sup>

## FIGURES

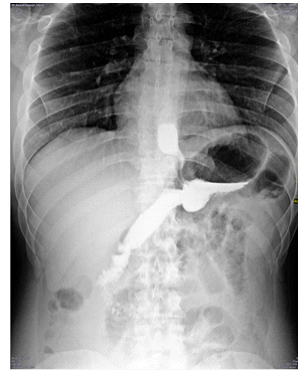
**FIG. (1) PREOPERATIVE ENDOSCOPY IMAGES SUGGESTING GERD GRADE 3 AND HIATUS HERNIA.**



**FIG (2) POSTOPERATIVE ENDOSCOPY IMAGES REVEALING CORRECTION OF PREOPERATIVE FINDINGS.**



**FIG (3) BARIUM SWALLOW POST OPERATIVELY TO SUGGEST ADEQUATE CORRECTION BY SURGERY.**



**FIG (4) ILEUS SUGGESTED BY DIFFUSE SMALL BOWEL DILATATION THROUGHOUT THE ABDOMEN**



## REFERENCES

- 1) Frazzoni M1, Piccoli M1, Conigliaro R1, Frazzoni L1, Melotti G1. Laparoscopic fundoplication for gastroesophageal reflux disease. *World J Gastroenterol.* 2014 Oct 21;20(39):14272-9. doi: 10.3748/wjg.v20.i39.14272.
- 2) Mermelstein J1, Chait Mermelstein A2, Chait MM3. Proton pump inhibitor-refractory gastroesophageal reflux disease: challenges and solutions. *Clin Exp Gastroenterol.* 2018 Mar 21;11:119-134. doi: 10.2147/CEG.S121056. eCollection 2018.
- 3) dos Santos LM1, Guerra RA2, Lazaretti-Castro M3, Vieira JG1, Portes Ede S2, Dias-da-Silva MR4. An approach to the diagnosis and management of a case presenting with recurrent hypomagnesaemia secondary to the chronic use of a proton pump inhibitor. *Magn Res.* 2015 Dec;28(4):136-45. doi: 10.1684/mrh.2015.0395.
- 4) Ayuk J1, Gittoes NJ. Contemporary view of the clinical relevance of magnesium homeostasis. *Ann Clin Biochem.* 2014 Mar;51(Pt 2):179-88. doi: 10.1177/0004563213517628. Epub 2014 Jan 8.
- 5) Alzubaidi M1, Gabbard S2. GERD: Diagnosing and treating the burn. *Cleve Clin J Med.* 2015 Oct;82(10):685-92. doi: 10.3949/ccjm.82a.14138.
- 6) Nehra AK1, Alexander JA2, Loftus CG2, Nehra V3. Proton Pump Inhibitors: Review of Emerging Concerns. *Mayo Clin Proc.* 2018 Feb;93(2):240-246. doi: 10.1016/j.mayocp.2017.10.022.
- 7) Cheungpasitporn W1, Thongprayoon C1, Kittanamongkolchai W1, Srivali N2, Edmonds PJ3, Ungprasert P4, O'Corragain OA5, Korpaisarn S6, Erickson SB1. Proton pump inhibitors linked to hypomagnesaemia: a systematic review and meta-analysis of observational studies. *Ren Fail.* 2015 Aug;37(7):1237-41. doi: 10.3109/0886022X.2015.1057800. Epub 2015 Jun 25.
- 8) Luk CP1, Parsons R, Lee YP, Hughes JD. Proton pump inhibitor-associated hypomagnesaemia: what do FDA data tell us? *Ann Pharmacother.* 2013 Jun;47(6):773-80. doi: 10.1345/aph.1R556. Epub 2013 Apr 30.
- 9) Ayuk J1, Gittoes NJ2. Treatment of hypomagnesaemia. *Am J Kidney Dis.* 2014 Apr;63(4):691-5. doi: 10.1053/j.ajkd.2013.07.025. Epub 2013 Oct 4.
- 10) Markovits N1, Loebstein R, Halkin H, Bialik M, Landes-Westerman J, Lomnicki J, Kurnik D. The association of proton pump inhibitors and hypomagnesaemia in the community setting. *J Clin Pharmacol.* 2014 Aug;54(8):889-95. doi: 10.1002/jcph.316. Epub 2014 May 6.
- 11) Famularo G1, Gasbarrone L, Minisola G. Hypomagnesaemia and proton-pump inhibitors. *Expert Opin Drug Saf.* 2013 Sep;12(5):709-16. doi: 10.1517/14740338.2013.809062. Epub 2013 Jun 29.
- 12) Semb S1, Helgstrand F2, Hjørne F2, Bytzer P3. Persistent severe hypomagnesaemia caused by proton pump inhibitor resolved after laparoscopic fundoplication. *World J Gastroenterol.* 2017 Oct 7;23(37):6907-6910. doi: 10.3748/wjg.v23.i37.6907.
- 13) Corsonello A1, Lattanzio F2, Bustacchini S2, Garasto S1, Cozza A1, Schepisi R1, Lenci F3, Luciani F4, Maggio MG5, Ticinesi A5, Butto V5, Tagliaferri S5, Corica F6. Adverse events of proton pump inhibitors: potential mechanisms. *Curr Drug Metab.* 2017 Dec 7. doi: 10.2174/1389200219666171207125351. [Epub ahead of print]
- 14) Park CH1, Kim EH1, Roh YH2, Kim HY2, Lee SK1. The association between the use of proton pump inhibitors and the risk of hypomagnesaemia: a systematic review and meta-analysis. *PLoS One.* 2014 Nov 13;9(11):e112558. doi: 10.1371/journal.pone.0112558. eCollection 2014.