

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33680

Title: Persistent severe hypomagnesemia caused by proton pump inhibitor resolved after laparoscopic fundoplication

Reviewer's code: 02885958

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2017-02-27

Date reviewed: 2017-03-08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Dear authors This is a case report regarding PPI-induced hypomagnesemia (PPIH). Reports on PPIH is recently getting increased in the developed countries, and we are requested to pay attention to this adverse effect. Thus, I believe this report is timely and informative. In this report, medical information is well demonstrated, and the discussion is carefully written by focusing on PPIH. So, I consider this report is adequate for the publication by the present form. I would like to indicate just one issue that the author may consider the intestinal inhibition of Mg uptake as an only cause of PPIH. It is well known that just 1% of Mg is existed in ECF, and majority of Mg is stored in ICF. Intracellular Mg freely moves-in and out to ECF for the regulation of Mg concentration, and it is hard to imagine that the intestinal Mg absorption directly contribute to the regulation of Mg concentration during the short term. Averaged daily Mg intake is 12 mmol, and 4 mmol of them is absorbed in the intestine and released to ECF. On the other hand, in the kidney, approximately 84 mmol of Mg is daily filtered through glomerulus

and 80 mmol of them is reabsorbed in the tubules. Thus, principal organ to regulate the Mg metabolism might be the kidney. Involvement of TRPM6 in the Mg reabsorption in the kidney is approximately 5% of filtered Mg, however, TRPM6-regulated Mg reabsorption in DCT segment of tubules is a final regulatory part of urine Mg excretion, and therefore, Mg reabsorption through TRPM6 is involved in the multiple drug-induced hypomagnesemia such as thiazide, anti-EGFR anti-cancer medications and cyclosporin A which also affects on the Mg reabsorption in TAL segment. Hypothesis of pH-related changes in the intestinal TRPM affinity to Mg ion is very interesting and attractive, however, it is tough to explain the rapid restoring Mg concentration immediately after discontinuation of PPI and its rapid falling in PPI challenge test only by the changes in intestinal Mg absorption. Thus, it is interested how the urine Mg excretion rate, not its urine concentration itself, is changed before and after discontinuation of PPI or PPI challenge test. If an increase in the urine Mg excretion rate would not be apparent under the condition of continuous administration of PPI and Mg supplementation, the hypothesis might be more persuasive. If some additional data regarding Mg-handling in the kidney is available, they would be a great help to support the author's conclusion. If not, it would be better to refer to the possible involvement of renal Mg loss in the PPI-induced hypomagnesemia. Again, I believe this article is excellent and revision is not indispensable for the agreement of acceptance of this article.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33680

Title: Persistent severe hypomagnesemia caused by proton pump inhibitor resolved after laparoscopic fundoplication

Reviewer's code: 03034546

Reviewer's country: India

Science editor: Ze-Mao Gong

Date sent for review: 2017-03-15

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript is well written. However patients undergoing fundoplication may also need PPIs at a later date. This may be mentioned in the manuscript. Further, how oral supplementation of magnesium helps in presence of continued usage of PPIs may be discussed since the PPIs act by altering the intestinal absorption of magnesium.