



PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 46301

Title: Proton pump inhibitors and adverse effects in kidney transplant recipients: A meta-analysis

Reviewer’s code: 03742333

Reviewer’s country: United Kingdom

Science editor: Ying Dou

Reviewer accepted review: 2019-02-12 09:17

Reviewer performed review: 2019-02-16 13:46

Review time: 4 Days and 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have read with great interest the manuscript entitled “Proton Pump Inhibitors and Adverse Effects in Kidney Transplant Recipients: A Meta-Analysis”. I would like to congratulate initially the authors on the well written and scientifically sound manuscript.



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In this meta-analysis the authors investigate the risk of several adverse effects in kidney transplant recipients on PPI compared with those without the exposure. They conclude that PPI use was associated with a high risk of hypomagnesemia. The manuscript's methodology is appropriate, in accordance with the PRISMA guidelines and the subject of clinical interest. Please see major comments below for your attention and clarification:

Major comments: 1- The introduction discusses extensively the possible issues associated with the interaction between MMF and PPI. I wonder if this is the only class of immunosuppressor that interacts with PPI? In addition, is there any possible mechanistic explanation for all the adverse effects associated with PPI? While those questions do not need extensive discussion in the introduction, they may be touched minimally. 2- For the hypomagnesemia, the forest plot presented in Figure 4 shows that only three studies were analysed to generate the pooled OR of 1.56. From Table 1, two of them were cross-sectional and one a retrospective study. The number of patients in each experimental group (PPI vs. Non-PPI) and the immunosuppressive regimen do not seem to be available for all the three studies (Table 1). From Table 4, the variation in plasma magnesium levels is apparently minor and not likely to lead to any clinical complication. Those patients may be potentially receiving oral magnesium supplementation, or not, as we cannot say accordingly to the information available in the meta-analysis. Therefore, in face on all these limitations, most of them acknowledged by the authors in the discussion, they should be careful to draw definitive conclusions from the present study. The conclusion of the study should be revised accordingly, the phrase "In the long-term, PPI use may also be associated with kidney dysfunction and increased overall mortality" is not supported from data analyses available in the manuscript and it seems more a personal impression from authors. 3- The last two phrases of the penultimate paragraph ("Interestingly, Uludag et al... is associated with worse outcomes") are repetitive, and not part of the limitations of the study, which is the topic of the paragraph. This should



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INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Transplantation

Manuscript NO: 46301

Title: Proton pump inhibitors and adverse effects in kidney transplant recipients: A meta-analysis

Reviewer’s code: 03291363

Reviewer’s country: Australia

Science editor: Ying Dou

Reviewer accepted review: 2019-02-15 22:16

Reviewer performed review: 2019-02-21 05:09

Review time: 5 Days and 6 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

A lot of work has gone into this study and it is an interesting study design and result.

My comments: 1. I have a problem with the adequacy and completeness of the data in the 8 studies used. Some data for the outcomes are absent we are told; inconsistency in



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the definitions of rejection etc. The authors should explain the extent to which data is complete with respect to each outcome measures. 2. The study needs to have a statistician review the methodology. Given the multiple outcomes measures is it powered adequately?

INITIAL REVIEW OF THE MANUSCRIPT

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