Author’s response to reviews

Title: Volume, distribution and acidity of gastric secretion on and off proton pump inhibitor treatment: A randomized double-blind controlled study in patients with gastro-esophageal reflux disease (GERD) and healthy subjects

Authors:

Andreas Steingoetter (steingoetter@biomed.ee.ethz.ch)
Matthias Sauter (matthias.sauter@usz.ch)
Jelena Curcic (curcic@biomed.ee.ethz.ch)
Dian Liu (liu@biomed.ee.ethz.ch)
Dieter Menne (dieter.menne@menne-biomed.de)
Michael Fried (michael.fried@usz.ch)
Mark Fox (dr.mark.fox@gmail.com)
Werner Schwizer (gasschwi@usz.uzh.ch)

Version: 2 Date: 20 August 2015

Author’s response to reviews: see over
Dear Editorial team

We herewith submit our detailed responses to the reviewer comments and the revised manuscript with number 1544284290174018 and title ‘Volume, distribution and acidity of gastric secretion on and off proton pump inhibitor treatment: A randomized double-blind controlled study in patients with gastro-esophageal reflux disease (GERD) and healthy subjects’ for potential publication in BMC Gastroenterology.

Response to the editors:

(1) Please change the title of the Disclosure section to Competing Interests
Done

(2) Please move the Funding information to the Acknowledgements section.
Done

Response to Reviewer comments:

We thank the reviewers for their overall positive and critical feedback on our work.

Reviewer: Michele Cicala

GERD Patients were either affected by erosive esophagitis or uncomplicated, although confirmed by pH test, disease. How many of them belonged to the erosive population? This is not certain because of prior use of PPI. In order to avoid somewhat misleading (and meaningless) information, we didn’t including this number in the manuscript. The severity of disease was assessed by physiological studies – the reference standard investigation for diagnosis of GERD.

Similarly, findings of the symptom scores are not reported following placebo. We reported the effect size (13±4, p=0.003) in the improvement of symptoms after PPI compared to placebo. 8 of 12 patients had a clinically relevant improvement under PPI.

Besides the position - right decubitus - in which patients were investigated, another limitation of this study is the test meal (pure liquid), both are unphysiologic conditions.

We added the following statement in the discussion:

“Another issue is that liquid nutrients do not represent a "normal meal"; however, this is necessary to allow estimates of secretion volume and distribution of secretion within the stomach. Note that a previous study demonstrated no difference in acid reflux events between liquid and solid meals with identical nutritional composition (Fox, M., et al. (2007). "The effects of dietary fat and calorie density on esophageal acid exposure and reflux symptoms." Clin Gastroenterol Hepatol 5(4): 439-444).”

Finally, the different distribution of gastric secretions within the proximal stomach in GERD patients vs healthy subjects may be due, apart from different morphology, to different motility of the proximal stomach in the two groups.

We added the following statement in the discussion:

“The effect of gastric accommodation or motility on the proximal distribution of gastric secretion was not assessed, however, recent papers provide little evidence that accommodation of the stomach (or intra-gastric pressure) is different in health and GERD (Pauwels A et al. Neurogastroenterol Motil. 2014 Apr;26(4):581-8; Curcic J et al. Am J Gastroenterol. 2014 May;109(5):658-667).”
Reviewer: Giovanni Sarnelli
I understand that the simultaneous assessment of pH-metry and MRI is technically difficult, but this represent a point of weakness. The authors should further comment this point in the discussion and tone down their results.
We now mention under limitations in the discussion section that: "current catheter and sensor technology for the measurement of intragastric pH are not MRI compatible and, thus, required a sequential rather than a combined measurement protocol for MRI and pH-metry.

Given the great progress of the MRI technique do the authors have any data magnetic resonance spectroscopy? If not this should reported as a potential future application.
1H or 13C Magnetic Resonance Spectroscopy (MRS) may be potentially attractive for the in vivo assessment of lipids or specific metabolites, respectively. So far, the use of 1H MRS has only been demonstrated for the measurement of the global fat fraction of ingested oil emulsions. However, the same may be achieved using MR Imaging methodology offering the advantage of additional 3D spatial information of the intragastric fat fraction.

Given the key limitations of MRS include very long scan times, poor spatial resolution and high sensitivity to motion, at present, MR Imaging is the more powerful tool for the in vivo imaging of the human GI motility and function. Therefore we refrain from commenting on the use of MRS in the manuscript.

Reviewer: Nicola de Bortoli
This is a very interesting paper and really innovative in this field.
It is rare to find article well designed and written as it is.
I"ve no comment for the author.
The authors thank the reviewer for his confident support of the work!

Sincerely yours,

Andreas Steingötter and Matthias Sauter (on behalf of the authors)