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*Observational Study*

**Efficacy and tolerability of a hydrogen carbonate-rich water for heartburn**

Beer, A-M, Uebelhack, R, Pohl, U.

### **Point by point response to reviewer's comments**

**Reviewed by 02546914**

**Dear Authors, I had the pleasure to read and revised your paper entitled "Efficacy and tolerability of a hydrogen carbonate-rich water for heartburn". This is a well designed and written paper that aimed to explore the efficacy of a hydrogen carbonate-rich water in patients with heartburn showing a very nice reduction in heartburn perception and the duration of heartburn per week. The statistical analysis has been well conducted.**

Thank you very much.

**I had some questions regarding your paper: It has been described that hydrogen carbonate-rich water was efficacy in patients with dyspepsia. How many patients in your population recorded early satiety or post-prandial fullness? I'm quite sure that some patients reported some other symptoms other than heartburn.**

For eligibility, the patients had to report having had heartburn at least twice a week for at least 3 months prior to study; the frequency of heartburn was also checked per diary before intake of the investigational product. During the study, additional symptoms have been queried per validated Reflux Disease Questionnaire (RDQ), such as regurgitation and dyspepsia.

**Have you explored the efficacy of the water in patients with regurgitation?**

Yes - thank you. The patients were selected according to appearance of heartburn symptoms, yet during the study also regurgitation was assessed directly per RDQ.

**The hypothesized mechanism for hydrogen rich-carbonate water is due to high concentration of HCO<sub>3</sub> anions that could have a direct buffer effect on the protons of the gastric acid. This is quite interesting.**

Yes, this is interesting.

**Have you found any patients who recorded symptom recurrence after water drinking due to a gastrin rebound effect?**

This effect has not been directly assessed in the study, however given the fact that heartburn and other symptoms have continuously diminished along the course of the study, one could hypothesise that the affect of elevated gastrin levels that may occur during chronic inhibition of gastric acid secretion would not be expected with the reported water treatment

**Recently I read a nice paper published on NMO by de Bortoli and co-worker (Neurogastroenterology and Motility 2014;26(1):28-35) in which they described a good outcome after PPI treatment in patients with pathophysiological characteristic of functional heartburn. The authors speculated that it could be due to a placebo effect too. Can you shortly discuss regarding this hypothesis?**

We cited this paper in the discussion section, and remarked on a possible placebo effect.

The possibility of a placebo effect for the examined mineral water is further mentioned within the section „limitations“ within the discussion.