Author's response to reviews

Title: Erythromycin Lacks Colon Prokinetic Effect in Children with Functional Gastrointestinal Disorders, A Retrospective Study

Authors:

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Response to Reviewer’s comments:

Reviewer: Hiroyuki Kuwano

1. The authors added the sentence in the discussion that “it is possible that the colon motilin receptors may have reduced affinity for erythromycin compared to the antral nerves or the expression of motilin receptor may be reduced in the colon”. Then, the authors concluded that Erythromycin lacks colon prokinetic effect in children with chronic constipation evaluated by colon manometry. I agree with authors’ discussions and conclusion. However, the authors described that the AUC following erythromycin was significantly less compared to the fasting phase of the study. Therefore, the mechanism of this interesting phenomenon would better to be discussed, too.

Characteristically small bowel MMC are seen during sleep and the colon is quiescent at night. This may be one of the reason why stimulating the small bowel with erythromycin and inducing MMC may cause reduced colon contractions. We are not aware of any studies which have looked into this. We would prefer not to speculate regarding the cause of reduced colon contractions after erythromycin. If the reviewer would like us we can include this explanation in the discussion.

2. The AUC unit was described in “mmHg”. The AUC revealed the area under the curve. Is there another AUC unit except “mmHg”?

This was a typing error and it should read as mmHg/sec. We have made appropriate changes in the manuscript.

Reviewer: Philippe Ducrotte

Was the end of the manometric probe located in the caecum in every child?

The tip of the colon motility catheter was positioned in the cecum/ascending colon in all subjects and the position was confirmed by fluoroscopy.

Were the children anaesthetized for the colonoscopy. If the answer if yes, how long was the interval of time between colonoscopy and manometric recording? Indeed, the AUC seems very low.

All children were anesthetized without a muscle relaxant. We waited for the child to recover completely from the effects of the drug before starting the motility tests (i.e. at least 3 hours after the anesthesia). Most pediatric GI motility centers follow a similar protocol for clinical colon motility studies. In our study, the AUC is in mmHg/sec while some previous studies have reported this in mmHg/min.
Is the definition of the gastrocolonic response an "home-made" definition?

Increase in motility index following a meal is considered a gastrocolonic response. Previous studies have shown that the increase is at least 30 percent. We have removed 30 percent in view of the reviewers concern as this does not affect the results or the conclusion of our study.

What is a meal appropriate for the age?

In children unlike adults, standardized meals cannot be given as the fat and calorie intake varies with age. The meal provided >30% of daily calorie requirement. This is standard protocol followed by most pediatric GI motility center. (Reference: Manometry studies in children: minimum standards for procedures. C. Di Lorenzo et al. Neurogastroenterol. Mot (2002) 14. 411-420)

The tracings were only analyzed quantitatively. Did erythromycin induce specific motor patterns (clusters of contractions...)

We did not observe any specific motor patterns after erythromycin administration.

The last paragraph of the discussion is useless

We have removed the last paragraph as suggested by the reviewer.