Iron sensing by the intestine: A new model for iron-induced changes to GI motility

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Background: Iron is an essential micronutrient predominately absorbed in the duodenum and jejunum. Iron deficiency is currently the leading nutritional disorder in the world, and is most commonly treated with supplementation. However, iron supplementation is known to cause gastrointestinal (GI) side effects including vomiting, nausea and diarrhoea which may be due to high doses of inorganic iron causing damage to the intestinal mucosa. Levels of many dietary nutrients affect the motility and/or secretion of the GI tract which may help to enhance their absorption. We hypothesized that lower concentrations of iron found in the diet may, like fatty or amino acids, act on the GI tract to alter motility. Thus, our aim was to investigate the effects of physiological concentrations of intraluminal ferrous sulphate ($FeSO_4$) on jejunal motility.

Methods: Segments of guinea pig jejunum were cannulated and the intraluminal pressure recorded with a pressure transducer while movements of the jejunum were recorded with a video camera. The pressure was increased at the oral end until 4 peristaltic contractions occurred; with this pressure being the peristaltic threshold. The nutrients decanoic acid (1mM; short chain fatty acid) and L-phenylalanine (50mM; amino acid) and the mineral $FeSO_4$ (1mM) were infused intraluminally. We also tested the effect of $FeSO_4$ and the nutrients on electrochemically detected serotonin (5-HT) release from *in vitro* tissues, both at rest and when the mucosa was mechanically stimulated.

Results: Luminal $FeSO_4$ solution reduced jejunal peristaltic threshold in the majority of tissues; the control threshold was on average 30 ± 2 mmH_2O, while in the presence of $FeSO_4$ (1 mM) peristaltic threshold was significantly lower at 23 ± 3 mmH_2O (n=8, $P<0.05$, paired t-test). Decanoic acid (1 mM) significantly lowered the mean peristaltic threshold from 27 ± 2 mmH_2O (control, n=7) to 14 ± 2 mmH_2O (n=7, $P<0.05$, paired t-test). Similarly, L-phenylalanine (50 mM) caused a significant reduction in the mean peristaltic threshold from a control value of 30 ± 3 mmH_2O to 14 ± 3 mmH_2O (n=6, $P<0.05$, paired t-test). Of the three, only decanoic acid induced segmentation while $FeSO_4$ inhibited decanoic acid induced segmentation. Resting 5-HT release was increased by $FeSO_4$ (128% of control), but mechanically evoked 5-HT release was reduced (70% of control). In contrast, neither decanoic acid nor L-phenylalanine affected resting or mechanically evoked 5-HT release.

Conclusions: These data suggest that the luminal effects of relatively low concentrations of inorganic iron on jejunal motility are probably mediated through a pathway involving release of 5-HT. A better understanding of the interaction between luminal iron and 5-HT containing enterochromaffin cells could improve iron supplementation strategies and thus reduce side effects and increase patient compliance.