Examining a role for gastric acid in iron absorption

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Introduction: Iron deficiency is the most common micronutrient deficiency worldwide. The prevalence of persistent, severe iron-deficiency anemia following gastrectomy or gastric bypass surgery has begotten the dogma that gastric acid is necessary for iron absorption since a significant amount of patients after these surgeries developed iron deficiency anemia; however, little has been done to test this directly. The notion is that gastric acid promotes the solubility of iron salts and complexes, aiding in iron absorption.

Aims: To test the hypothesis that gastric acid is required for iron absorption in the mouse, by examining iron homeostasis and iron absorption in two mouse models of achlorhydria.

Methods: (1) We measured blood-iron variables, tissue iron stores, and the expression of iron-related genes in C57BL6 mice lacking the gastric H^+/K^+ ATPase ("proton pump") α-subunit, i.e. *ATP4a*$^{-/-}$. (2) We measured iron-59 absorption in female wild type 129S6 mice treated with the proton pump inhibitor omeprazole (60 mg/kg I.P.) or vehicle alone. 2 h after injection, mice were administered 0.1 µCi Fe-59 per kg via oral–intragastric dose. We measured the appearance of Fe-59 in the blood over 4 h, then euthanized the mice and measured Fe-59 content in liver, spleen, and enterocytes.

Results: Only *ATP4a*$^{-/-}$ female mice fed on low iron diet exhibited lower iron stores as measured by liver nonheme iron content, yet they maintained similar iron levels in the blood compared to control mice; female *ATP4a*$^{-/-}$ mice on normal diet were able to maintain both liver and blood iron values similar to control. Female wild type 129S6 mice did not exhibit a difference in Fe-59 content in the blood when treated with omeprazole compared to treatment with vehicle. Control mice had a significantly higher Fe-59 content in the liver as compared to omeprazole treated mice, yet had similar Fe-59 content in the spleen and enterocytes.

Conclusions: Our study reveals iron absorption does not rely on the presence of gastric acid. Therefore, treatment after gastric bypass or gastrectomy may be more geared towards replenishing gastric components other than acid that are thought to promote the solubility of iron, such as citrate, which can aid in absorption and prevent iron deficiency.

Acknowledgments: This study was funded primarily by NIH grant R01 DK080047 (to B.M.). M.O. and R.R.B. were supported by NIH grant T35DK060444.