Investigations into the ileal hormone Fibroblast Growth Factor 19 (FGF19) in Crohn’s disease and diarrhea

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Symptoms of diarrhea feature prominently in patients’ concerns and in clinical disease activity scores for Crohn’s disease (CD). Fecal bile acid (BA) loss is important in producing the secretory diarrhea in CD, as reabsorption of BA normally occurs in the terminal ileum. The peptide hormone FGF19 is secreted from the ileum in response to absorbed BA and regulates hepatic BA synthesis. In human cell lines, FGF19 transcription has also been shown to be suppressed by pro-inflammatory cytokines. We hypothesized that in CD patients, serum FGF19 levels would be inversely correlated (1) to length of resected ileum, and (2) to disease activity in those without resection.

Median serum FGF19 levels were found to be significantly lower overall in 55 patients with CD, both active and inactive disease, compared to healthy controls, or to disease controls (idiopathic chronic diarrhea). FGF19 was inversely correlated to the length of previously resected ileum (p = 0.006). In 33 patients without resection, FGF19 was significantly lower in patients with diarrhea compared to those without diarrhea (p = 0.02), and in those with active ileal disease compared to those with inactive disease (p=0.04). Significant inverse correlations between FGF19 and disease activity, stool frequency, stool consistency and CRP were also found. In longitudinal studies in patients with ileal disease, FGF19 was significantly increased during medically-induced remission compared with periods of disease activity.

We have also shown that expression of FGF19 transcripts in ileal mucosa obtained at ileocolonoscopy was greatly induced (>300-fold) by exposure to natural and semi-synthetic BA in explant cultures. We have preliminary data comparing FGF19 induction in tissue obtained from patients with CD, including microscopic and macroscopic ileitis and those with neo-terminal ileum.

In conclusion, FGF19 is reduced by ileal resection and active inflammation in patients with CD. This will lead to excessive BA synthesis and increase the diarrhea symptoms. We propose that induction of FGF19 will benefit Crohn’s patients.

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