Rifaximin Effective in FD, Suggesting Intestinal Microbiota Involvement

Written by Lynne Lederman, PhD

Functional dyspepsia (FD) is a common gastrointestinal disorder for which effective treatments are not available. FD and the related irritable bowel syndrome (IBS) often coexist and share symptoms of bloating, abdominal discomfort, and pain. Dysbiosis of the intestinal microbiota may be involved in the pathogenesis of functional gastrointestinal disorders, including FD. The nonabsorbable antibiotic rifaximin has shown efficacy in relieving IBS symptoms [Pimentel M et al. *N Engl J Med*. 2011].

Victoria P. Tan, MBBS, University of Hong Kong, Hong Kong, China, discussed a double-blinded placebo-controlled pilot study [NCT01643083] to test the ability of rifaximin in patients with FD to improve global dyspepsia symptoms, belching, and bloating. This trial enrolled adults with FD per Rome III criteria, with normal gastroscopy results within the last 2 years, and with active symptoms in the prior month. Patients who had IBS and other chronic conditions or who had taken proton pump inhibitors or antibiotics within the last 8 weeks were excluded.

During screening, a 3-hour hydrogen breath test (HBT) was performed. Baseline characteristics were similar between the 2 arms; however, Prof Tan noted a slight excess of patients with belching in the placebo group (73.9%) as compared with the rifaximin group (55%), which could affect how results are interpreted.

Patients were randomly assigned 1:1 to rifaximin (n = 40) 400 mg TID or placebo (n = 46) TID for 2 weeks. Follow-up assessments were performed at weeks 2, 4, and 8. Patients who took ≥ 75% of their treatment medication included 33 in the rifaximin group and 39 in the placebo group.

Global dyspeptic symptoms, the primary outcome, improved with rifaximin at week 2; at week 8, 23.5% in the rifaximin group vs 47.4% in the placebo group had moderate to severe global dyspeptic symptoms.

Secondary outcomes included belching and bloating. At week 4, moderate to severe belching occurred in 14.3% of patients in the rifaximin group vs 35.7% of the placebo group ($P = .03$); however, by week 8 of follow-up, there was no significance between groups.

Moderate to severe bloating decreased in both groups: at week 4, it occurred in 20% of the rifaximin group and 42.9% of the placebo group ($P = .03$); at week 8, it increased in the rifaximin group and decreased in the placebo group, until the difference was no longer significant.

A subgroup analysis of female patients with FD showed a decrease in moderate to severe global dyspeptic symptoms in both treatment groups during the study: at week 4, symptoms were reported in 20.8% of the rifaximin group vs 59.4% in the placebo group ($P = .006$); at week 8, the differences were still significant (20% for rifaximin vs 48.4% for placebo; $P = .048$).

Table 1. Secondary Outcome: Hydrogen Breath Test Results

	Rifaximin	Placebo	*P* Value
H_2 peak above baseline	2.94 (11.1)	0.11 (12.22)	.29
H_2 AUC, ppm	+43.64 (1033.07)	−49.71 (1360.78)	.76
OCTT, min	+24.23 (38.50)	+16.50 (49.72)	.68

Values presented in mean (SD).

AUC, area under the curve; OCTT, oral-cecal transit time; ppm, parts per million.

HBT results at week 8 vs baseline are presented in Table 1.

There were no significant differences between treatment groups for major or minor adverse events at week 2, 4, or 8.

One limitation of this study is that it was a 2-institution pilot study with a small sample size. In addition, the durability of the rifaximin effect was unclear, and response was associated with changes in HBT.

To conclude, the efficacy of rifaximin in FD—particularly for global dyspeptic symptoms, belching, and bloating—suggests a role for the gut microbiota in the pathogenesis of FD. These results should be confirmed in a large multicenter study.

Ramosetron Is Effective in Women With IBS-D

Written by Lynne Lederman, PhD

Controlling symptoms in irritable bowel syndrome with diarrhea (IBS-D) can be challenging. Studies have suggested a role for serotonin 5-hydroxytryptamine ($5\text{-}HT_3$) receptors and antagonists in the gastrointestinal tract in the pathogenesis of IBS-D. In one study, ramosetron, a $5\text{-}HT_3$ antagonist, significantly improved stool consistency when compared with placebo in Japanese men ($P < .001$) [Fukudo S et al. *Clin Gastroenterol Hepatol.* 2014]. Of note, ramosetron is not FDA approved.

Shin Fukudo, MD, PhD, Tohoku University Graduate School of Medicine, Sendai, Japan, presented the results of a double-blind placebo-controlled phase 3 trial designed to determine the effects of ramosetron vs placebo in women with IBS-D and to assess adverse events (AEs) [NCT01736423]. Women with IBS-D were randomly assigned to oral ramosetron 2.5 μg (n = 292)