Gut Flora Presents a Novel IBS Treatment Target

Modifying bacteria levels via antibiotics and probiotics may ease symptoms, but concerns persist.

BY BRUCE JANCIN
Denver Bureau

HONOLULU — Modification of the gut flora is emerging as a promising new treatment approach for the common and vexing problem of irritable bowel syndrome.

Two therapeutic strategies are being pursued. One entails adding bacteria to the gut in the form of oral probiotics. The other involves selectively subtracting bacteria from the gut flora with a non–systemically absorbable antibiotic. Evidence that both approaches alter irritable bowel syndrome (IBS) pathology and modulate symptoms was presented at the annual meeting of the American College of Gastroenterology.

The gut flora has been called "the forgotten organ." But that's changing, said Dr. Eamonn M.M. Quigley, professor of medicine at of the National University of Ireland, Cork. He presented a full IBS spectrum from diarrhea to the constipation-predominant subtype.

The probiotic resulted in a double-blind trial involving 165 women with IBS randomized to 4 weeks of daily capsules containing the novel probiotic bacterium *Bifidobacteria infantis* 35624 or placebo. Baseline bowel movement (BM) frequency ranged across the significant improvement in BM frequency, concentrated among patients at either end of the frequency distribution. Women with constipation—those in the bottom 15th percentile in terms of baseline BM frequency—experienced a significant increase in frequency that brought them within the 1-2 movements per day range defined by investigators as normal. In contrast, patients with diarrhea as defined by a BM frequency in the 81st percentile or above experienced a significant decrease in frequency to within normal range.

The probiotic resulted in a net 23% improvement over placebo in terms of IBS symptom scores across the entire study population. Patients in the middle range of baseline BM frequency experienced no significant change with the probiotic compared with placebo.

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DR. TALLEY

A composite score based on abdominal pain, bloating, and bowel habit satisfaction was significantly improved with probiotic therapy over placebo in patients with diarrhea-predominant IBS, showed a strong but not statistically significant favorable trend in the smaller group of women with constipation-predominant IBS, and no change in alternator-type patients. There were no probiotic-related side effects. The improved stool function and other benefits of *B. infantis* 35624 lasted 1-3 weeks after treatment discontinuation, the gastroenterologist added.

Dr. Quigley stressed that not all probiotics are alike. They're not classified as drugs, so they're prone to the same quality-control issues that arise with other health food–type products. The most clinically effective of them—as he and others have shown true for *B. infantis* 35624 in animal studies—have the ability to not only modify the gut flora, but more importantly to modulate immune activity between the flora and gut mucosa.

Dr. Mark Pimentel presented a double-blind trial in which 87 patients with all types of IBS were randomized to the nonabsorbable antibiotic rifaximin (Xifaxan) at 400 mg t.i.d. or placebo for 10 days. Of patients in the rifaximin group, 38% were deemed clinical responders based upon a greater than 50% improvement in global symptom scores, compared with 16% of those on placebo. The improvement was durable, lasting for roughly 2 months following just 10 days of treatment.

The clinical response rate was greater in patients with diarrhea-predominant IBS: 49%, compared with 23% with placebo. Bloating was also significantly improved. Constipation was not, although the number of affected patients was too small to draw definitive conclusions, according to Dr. Pimentel, director of the gastrointestinal motility program at Cedars-Sinai Medical Center, Los Angeles.

Prior studies suggest that many IBS patients have small bowel overgrowth of hydrogen or methane-producing bacteria. In the current study, the presence and extent of methane production on a lactulose breath test correlated strongly with constipation severity. This suggests that knocking out methane-producing bacteria in the small bowel may be a good therapeutic strategy in patients with constipation-predominant IBS, he added.

Session cochair Dr. Nicholas J. Talley said he doesn't think probiotics or antibiotics are ready for prime-time use in IBS; it's still unclear how common small bowel bacterial overgrowth is in IBS. Also, the gut flora is very well adjusted. "It's there with you for life. It doesn't want to go. If you change it, you have to keep changing it. So this is going to be maintenance therapy, not on-off antibiotic therapy. And I'm never going to be able to recommend antibiotics every 2 weeks to my patients for the rest of their lives. That's just not safe or practical, no matter what you use," said Dr. Talley, professor of medicine at the Mayo Medical School, Rochester, Minn. In contrast, there is now general agreement that probiotic therapy is safe for the patient and community. It is being successfully used in clinical practice for two conditions—infectious diarrhea and pouchitis secondary to ulcerative colitis surgery—backed by solid clinical trials data. But key questions remain regarding its use in IBS.

Dr. Quigley is a consultant to and stock shareholder in Alimentary Health, which is developing *B. infantis* 35624 for commercial applications. Dr. Pimentel is a consultant to Salix Pharmaceuticals Inc., which markets rifaximin for the indication of traveler's diarrhea. ■

Tegaserod Boosts IBS Patients' Work Productivity, Attendance

BY BRUCE JANCIN
Denver Bureau

HONOLULU — The use of tegaserod in women with constipation-predominant irritable bowel syndrome resulted in improved work attendance and productivity in a large, open-label, naturalistic study designed to reflect actual clinical practice, Dr. Nigel Flook reported at the annual meeting of the American College of Gastroenterology.

These findings, from the observational Zelnorm Advancing Quality of life (ZAQ) study, have important implications in terms of both quality of life and health economics. An earlier study showed that individuals with irritable bowel syndrome (IBS) miss three times as many work days as colleagues without IBS, according to Dr. Flook of the University of Alberta, Edmonton.

He reported on 2,381 women with symptoms of abdominal pain and discomfort, bloating, and constipation who participated in the Novartis-sponsored ZAQ study. Three-quarters were at least 40 years old; one-quarter were over age 60 years. Overall, 78% reported at least a 2-year history of IBS symptoms, and 30% said they had lived with IBS for longer than 10 years.

The major caveat regarding the ZAQ study data concerns the possibility of selection bias. Only 20% of participants completed the study by returning their week-12 questionnaires, Dr. Flook noted; data were collected at baseline and 12 weeks.

Baseline use of prescription and over-the-counter medications to treat gastrointestinal symptoms was extremely common: 28% of participants were taking more than one prescription drug, and 40% were on more than one OTC drug for their IBS symptoms.

All participants were placed on 6 mg b.i.d. of tegaserod, a selective serotonin receptor agonist that acts as a promotility agent and is the first drug approved for irritable bowel syndrome.

Analysis of self-reported questionnaire data obtained after 12 weeks of treatment with tegaserod showed that 27% of patients missed fewer days at work or school, although 7% missed more days, compared with baseline. Also, 50% indicated they experienced improvement in what they accomplished at work, school, or home, and 40% reported fewer canceled or rescheduled activities. ■

Poor Physician Communication Faulted for Colon Screening Rates

Aversion to colonoscopy and lack of physician communication are major reasons Americans avoid colon cancer screening, according to a survey of 1,200 people aged 50 to 70 years.

The survey, conducted in February by Harris Interactive, suggests that three out of four eligible Americans are not being screened regularly for this second leading cause of cancer death, a screening rate far lower than rates reported for breast, cervical, and prostate cancers. Only one-third of respondents said they had been screened at least once for colon cancer.

The primary reasons for not being screened included, "don't want to have a colonoscopy" (28%), "doctor did not discuss screening with them" (26%), "did not have any symptoms" (24%), "did not feel they were at risk" (17%), "did not follow through on MD [doctor] recommendations" (9%), "did not know they should be screened" (8%), "did not have time" (5%), and "embarrassed to discuss screening with MD" (4%). Respondents were able to select from more than one category.

Screening rates were highest among those who claimed to be the most knowledgeable about colon cancer. Only 35% of those that considered themselves lacking knowledge about colon cancer had ever been screened. On the other hand, 79% of respondents who felt they were "knowledgeable" or "very knowledgeable" had been screened.

A personal or family history of the disease was reported by one in five people. However, only half of respondents considered themselves knowledgeable about the disease, and far fewer understood the need for, and benefits of, screening. More than a third of adults said they were in "excellent" or "very good" health, and three-quarters felt they were doing a good job of managing their own health.

The survey also asked respondents why they would not undergo a colonoscopy—which is still considered the most accurate screening test—in the future. Topping that list was "invasiveness" (20%), followed by "laxatives/enemas," "preparation," "general inconvenience," "embarrassment or lack of privacy," "time off from work required," "safety," and "dietary and medication restrictions."

—Bruce K. Dixon