

Prebiotics Show Promise in Crohn's and Colitis

BY HEIDI SPLETE
Senior Writer

ROCKVILLE, MD. — Prophylactic use of dietary prebiotics could benefit patients with ulcerative colitis and Crohn's disease, based on data from preliminary but promising studies, said Dr. Leo Dieleman of the division of gastroenterology at the University of Alberta, Edmonton.

In contrast to probiotics, which are live microorganisms that benefit their hosts, prebiotics are nondigestible fermentable dietary oligosaccharides that affect the growth and activity of certain types of protective bacteria found in the gastrointestinal tract.

Previous studies of probiotics have shown that adding probiotic bacteria to the diets of patients with inflammatory bowel disease (IBD) improved their symptoms, Dr. Dieleman said. Certain types of probiotics such as *Lactobacilli* and *Bifidobacteria* species, when added to the diet, can be protective against IBD, he added.

But for probiotics to be effective, patients must consume large

amounts of them, which can be difficult and inconvenient, Dr. Dieleman said at a meeting sponsored by the National Institutes of Health. Prebiotics might be a viable alternative because they are inexpensive, easy to administer in the diet—in powder form, for example—and they have been shown to be safe, he said.

Based on the promising results of probiotic research, investigators have begun to study prebiotics for treating IBD patients.

"Everyone has a unique intestinal microbiotic profile," Dr.

Dieleman said. But inflammation tends to reduce the diversity of microflora in the gut, and studies have shown that a subset of Crohn's disease and ulcerative colitis patients have distinctly abnormal microflora, compared with non-IBD controls.

Patients with IBD tend to have a microbiotic profile that is deficient in firmicutes and bacteroidetes, organisms that are thought to be associated with a

healthy gastrointestinal tract. Sometimes ingesting probiotics can help these patients. "But not all probiotics are effective for each patient," Dr. Dieleman said.

Because prebiotics stimulate the growth of several different intestinal protective bacteria, there may be a place for prebiotics in IBD treatment.

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Dr. Dieleman identified three criteria that make prebiotics potentially useful for treating gastrointestinal disorders.

First, prebiotics are nondigestible ingredients. As such, they transfer unchanged into the large intestine. Second, prebiotics are fermented by colonic bacteria that already exist in the large intestine. Third, prebiotics induce selective stimulation of bacterial growth and activity. Studies have

shown that prebiotics change the profile of intestinal microflora by increasing the growth of specific protective intestinal bacteria. After ingestion of prebiotics, there will be more protective bacteria in the gut.

The prebiotics that have been used most often in clinical trials completed to date are the compounds inulin and oligofructose. Studies of other compounds are ongoing, he said.

Data from a randomized pilot study of 20 adults with ulcerative colitis showed that those who took Synergyl, an oral combination of oligofructose and inulin, at a dose of 12 g/day for 2 weeks showed significant improvement in disease activity scores and significant reductions in levels of fecal calprotectin (a calcium-binding inflammatory protein found in feces), compared with those who took a placebo (*Aliment. Pharmacol. Ther.* 2007;25:1061-7).

Prebiotics also have shown positive effects on adults with

Crohn's disease, Dr. Dieleman said. The results from a recent open-label study of 10 patients with mild to moderate Crohn's disease showed that treatment for 3 weeks with 15 g/day of a 30% inulin/70% oligofructose combination supplement was associated with improved disease activity and increased expression of the anti-inflammatory interleukin-10, which is expressed in dendritic cells (*Gut* 2006;55:348-55).

Dr. Dieleman also described an ongoing open-label study at his institution, the University of Alberta, in which 25 patients with active ulcerative colitis are being treated with oligofructose-enriched inulin when they experience flaring on a stable dose of 5-aminosalicylate. The patient evaluations will include assessment of disease activity, including endoscopy results, and analyses of microflora and mucosal cytokines.

"Animal models have taught us a lot about the pathogenesis of IBD," Dr. Dieleman said. But larger studies in humans are needed to better characterize the role of prebiotics, he added. ■

CBT Promising for Treatment Of Irritable Bowel Syndrome

BY BRUCE JANCIN
Denver Bureau

VIENNA — Irritable bowel syndrome can be conceptualized as an anxiety disorder—and, as such, responsive to cognitive-behavioral therapy, according to Dr. Sergej Andreewitch.

"Core symptomatology of IBS is clearly physiological, but the cause of suffering and severe loss of function affecting many patients is better accounted for by the catastrophizing appraisal of symptoms and the related avoidance behavior," Dr. Andreewitch said at the annual congress of the European College of Neuropsychopharmacology.

A program of cognitive-behavioral therapy (CBT) targeting the negative evaluation of GI symptoms and resultant dysfunctional avoidance behaviors associated with IBS brought substantial improvement to participants in his pilot study. Next, Dr. Andreewitch, who is affiliated with the Karolinska Institute, Stockholm, plans to develop the treatment program into an Internet-based intervention.

He reported on 13 consecutive women with a mean age of 32 years and an 11.5-year history of IBS who had been referred for CBT from Stockholm-area GI clinics. The treatment program involved a 2-hour session weekly for 10 weeks, with four or five patients per group. The therapeutic strategy was modeled on well-established CBT programs for a variety of anxiety disorders.

As is typical in IBS, psychiatric comorbidity was common in this cohort. Nine of the 13 patients met diagnostic criteria for a specific phobia, panic disorder, generalized anxiety disorder, or dysthymia.

The psychotherapeutic intervention showed substantial efficacy. Scores on the daily patient-rated GI Symptoms Checklist of abdominal pain, tenderness, bloating, diarrhea, and constipation dropped from a baseline mean of 31.4 to 17.2 at conclusion of the CBT program and remained there at reassessment 4 weeks later.

Similarly, mean scores on the Sheehan Disability Scale plummeted from 13.2 to 3.8, while Montgomery-Asberg Depression Rating Scale scores dropped from a baseline of 12.7 to 6.8, and Anxiety Sensitivity Index ratings went from 25.1 to 11.7. Meanwhile, mean scores on the IBS Quality of Life Index improved from a baseline of 53.1 to 83.0.

These outcomes compare quite favorably with conventional treatments, which typically are only moderately effective. These treatments include stool-modifying agents, analgesics, antidepressants, and dietary restriction, Dr. Andreewitch said.

The etiology of IBS is poorly understood. One current concept is that noxious stimuli in the gut activate the brain-gut axis, resulting in stimulation of fear and arousal centers in the central nervous system. It is second only to the common cold as a cause of work absences. Affected patients often have inordinately high rates of medical services utilization, he noted. ■

Mesalamine, Folic Acid May Cut Colorectal Ca in IBD Patients

BY MITCHEL L. ZOLER
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PHILADELPHIA — Treatment with either folic acid or mesalamine was linked to about a 90% reduction in the incidence of colorectal cancer in a case-control study including 48 patients with inflammatory bowel disease.

Both agents "appear to be very promising cancer chemopreventive agents," but the findings need to be confirmed in additional inflammatory bowel disease (IBD) patients, especially because the study involved such a modest number of patients, Dr. Jeffrey Tang said at the annual meeting of the American College of Gastroenterology.

The analysis showed that patients who took a cumulative dose of at least 4,500 g of mesalamine had a statistically significant, 91% drop in their incidence of colorectal cancer (CRC), said Dr. Tang, a gastroenterologist at Henry Ford Hospital in Detroit. The usual mesalamine dose used by IBD patients at Henry Ford was 1.6 g/day.

Patients who took at least 1 mg of folic acid daily also had about a 90% cut in their CRC incidence during follow-up, compared with the controls. Two additional analyses showed that the effects of mesalamine and folic acid on CRC prevention were completely independent of each other.

"The strength of the associations [in this study] is big and very important,"

commented Dr. Carol A. Burke, director of the Center for Colon Polyp and Cancer Prevention at the Cleveland Clinic.

The apparent efficacy of folic acid in patients with IBD in Dr. Tang's study contrasts with a report published in June which found no protective effect from folic acid when it was given to men and women who did not have IBD (*JAMA* 2007;297:2351-9), she said in an interview.

Both drugs are safe, and the new findings hold promise for using these agents to reduce the risk of CRC in patients with IBD, Dr. Burke said.

Dr. Tang and his associates reviewed the records of 1,784 patients with IBD who were seen at Henry Ford Hospital from 1970 to 2005. During an average follow-up of 8 years, 30 of the patients developed CRC; 25 had ulcerative colitis, and 5 had Crohn's disease.

The researchers then attempted to match each of the incident cases with up to two control patients with IBD who did not develop CRC during an average follow-up of 12 years. A total of 30 control patients were identified to match with 18 of the incident cases. No matches were found for the remaining 12 IBD patients who developed cancer during follow-up, and they were dropped from the analysis.

The cases and controls were similar on several parameters, including gender, race, smoking status, family history, and age when IBD first appeared. The cases included 15 patients with ulcerative colitis and 3 patients with Crohn's disease. ■