Consumer Probiotics May Make Too Many Health Claims

BY ROBERT FINN
San Francisco Bureau

BEVERLY HILLS, CALIF. — The Food and Drug Administration provides little regulation of probiotic products, and those products available to the consumer vary greatly in quality and the level of evidence supporting their label claims, Lynne V. McFarland, Ph.D., said at the International Probiotic Association World Congress.

Even consumers who make concerted efforts to research probiotic products may come up short, said Dr. McFarland of the Veterans Affairs Puget Sound Healthcare System, Seattle. "When the consumers go in and they want to buy their own probiotic … it's chaos. There are so many different probiotic products out on the market, and the diversity of quality can be all the way from fine pharmaceutical manufacturers to [someone who makes it] in his bathtub."

For probiotics, 'the diversity of quality can be all the way from fine pharmaceutical manufacturers to [someone who makes it] in his bathtub.'

Dr. McFarland recently attempted to track down the contents and evidence base behind three probiotic products brought to her by patients. Using information from the manufacturers' Web sites—and a few persistent phone calls—she sought details on VitAdvance Flat Stomach capsules, Activia yogurt, and Culturelle capsules.

► VitAdvance Flat Stomach, manufactured by Avon Products Inc., has promotional literature that reads, in part, "Battling belly bulge means staying away from the bar and picking up a barbell. But a new pill is promising to beat bloat and tighten the tummy."

On the manufacturer's Web site, Dr. McFarland found no information on the probiotic species in the capsules, the dose, or the evidence for the manufacturer's claims. After several phone calls to the manufacturer, she finally found a technician who was able to tell her that the product contains *Lactobacillus acidophilus*, although he was unable to determine the dosage.

The flat-stomach claim appears to be based on a single randomized, controlled trial involving 18 women with irritable bowel syndrome. In that trial, the *L. acidophilus* had no effect on global IBS symptoms, no effect on cramping, and no effect on flatulence, but did appear to reduce bloating.

"They have one little piece of the significant evidence, and they built their whole product around this, and called it Flat Stomach," Dr. McFarland said. "We should not allow this kind of stuff to happen."

► Activia yogurt, made by Dannon Co., claims to "help with the slow intestinal transit and contains a unique culture—*Bifidus Regularis*." There is no recognized organism correctly classified as *Bifidus regularis*.

The product's Web site reveals that this is a trade name for Bifidobacterium animalis strain DN-173 010, but it includes no information on dose.

However, the Web site does have information on three randomized clinical trials involving a total of 113 normal volunteers showing a 9-hour reduction in transit time. Dr. McFarland pointed out that these normal volunteers are not likely to be representative of patients with constipation, and the company mentioned no trials in constipated patients.

Furthermore, the company recommends that consumers eat Activia yogurt daily, although there is no mention of long-term studies demonstrating the value of daily intake.

► Culturelle, made by Amerifit Brands Inc., has the best evidence base of the three products in support of its claims. The label includes the species (*Lactobacillus rhamnosus GG*), dose (10^{10} live organisms per capsule), and expiration date.

The product's Web site lists information on 42 randomized clinical trials, 25 of which had a positive effect directly related to the label's health claim. "This is a really nice example of what every Web site for a probiotic product should look like," Dr. McFarland said.

Dr. McFarland acknowledged serving on the speakers bureau of Klaire Laboratories and Biocodex Inc. ■

Probiotics May Be Linked With Adverse Reactions

BY ROBERT FINN
San Francisco Bureau

BEVERLY HILLS, CALIF. — The jury may still be out on whether probiotics are beneficial, but at least they do no harm and can be safely recommended to patients, right? Not so, said Dr. David R. Mack at the International Probiotics Association World Congress.

Several recent studies have uncovered some risks associated with probiotic use. "We [physicians] are always looking for new things, but we're a conservative, skeptical lot, and safety is a primary concern," Dr. Mack said.

One of the most concerning studies is also one of the newest, noted Dr. Mack of the University of Ottawa (Ont.). Investigators randomized 298 patients with predicted acute pancreatitis to receive probiotic prophylaxis or placebo. The probiotic preparation consisted of six live bacterial species: *Lactobacillus acidophilus, L. casei, L. salivarius, Lactococcus lactis, Bifidobacterium bifidum*, and *B. lactis*.

Not only did the probiotic preparation fail to reduce the risk of infectious complications, but the mortality rate was 2.5 times higher among the patients receiving probiotics than among those receiving placebo. Twenty-four (16%) of the patients in the probiotics group died, compared with nine (6%) in the placebo group.

Nine of the patients in the probiotics group developed bowel ischemia (eight with fatal outcomes), compared with none in the placebo group. The other deaths involved multiorgan failure (Lancet 2008;371:651-9).

According to some studies, probiotics are associated with increased asthma and wheezing in children. In one study, for example, children exposed to *L. rhamnosus GG* at birth had 3.4 times the risk of having asthma at age 7 years as a control group had (J. Allergy Clin. Immunol. 2007;119:1019-21). In another study involving the use of *L. rhamnosus GG* to prevent atopic dermatitis, 26% of the children in the probiotic group vs. 9% in the control group developed wheezing bronchitis (Pediatrics 2008;121: e850-6 [Epub doi:10.1542/peds.2007-1492]).

And there is further evidence of possible allergic complications following probiotic use. One study in France showed that two out of three common probiotic preparations contained cow's milk proteins (J. Allergy Clin. Immunol. 2007;119:746-7), and a separate case report described a child who developed anaphylaxis after taking a probiotic containing cow's milk proteins. Dr. Mack noted that one in five babies is allergic to cow's milk (Allergy 2006;61:507-8).

Beyond these known adverse reactions, there are other reasons to be concerned about the possible long-term effects of probiotics in young children. When adults take probiotics, it's rare to see extended colonization by the probiotic bacterial species, but outcomes appear to be different in young children: Some probiotic species have been detected in stool samples years later. The consequences of this extended exposure to probiotic organisms are unknown, he said.

Speaking of these studies as a group, he added, "These are a little warning shot across the bow," and safety trials are needed. ■

Ulcerative Colitis: Patients and Physicians Don't Always Agree

BY KATE JOHNSON
Montreal Bureau

MONTREAL — When rating the impact of ulcerative colitis, patients and physicians are not always on the same page, according to a study presented in two posters at the Canadian Digestive Diseases Week.

Adult patients with ulcerative colitis (UC) report a heavier psychological burden than do adult patients with rheumatoid arthritis (RA), migraine, or asthma, but gastroenterologists often underestimate the impact of this disease, reported Dr. David T. Rubin of the University of Chicago Medical Center, and his colleagues.

The UC: New Observations on Remission Management and Lifestyle (NORMAL) study, sponsored by Shire Pharmaceuticals, included 451 adult UC patients and 300 gastroenterologists. The participants completed an online survey in February and March 2007. The survey also included 309 RA patients, 305 migraine patients, and 305 asthma patients, all of whom were adults.

The UC patients were not necessarily being treated by the physicians in the study, as both groups were recruited separately.

Based on discussions with their physicians, 20% of the UC patients reported mild disease, 63% reported moderate disease, and 13% reported severe disease. Gastroenterologists tended to underestimate the frequency of disease flares in these patient groups, with 58% estimating only one flare per year in the mild UC group (patients self-reported a mean of five).

For the moderate UC group, 70% of the physicians estimated two or three flares, whereas patients self-reported a mean of eight. For the severe UC group, 22% of the physicians estimated 6 or more flares, whereas patients self-reported a mean of 11.

Furthermore, gastroenterologists underestimated how many patients thought that feeling unwell was a part of normal life, predicting this would be true for 37% of patients, when actually 73% of patients reported this, the authors wrote.

Compared with patients who had other illnesses, a significantly higher proportion (53%) of UC patients felt that their disease was controlling their lives, compared with RA patients (44%), migraine patients (37%), or asthma patients (19%). Stress, depression, and embarrassment were reported by 82%, 62%, and 70% of UC patients, respectively, compared with significantly lower proportions among all the other patients.

Physicians and patients had more similar views regarding the challenges of treatment with 5-aminosalicylic acid (5-ASA) medications. Whereas 41% of physicians believed patients were not adherent, 46% of patients reported that they had missed taking some of their medication in the previous week. Almost all (90%) of the gastroenterologists and 42% of the patients reported that it was difficult to take the medication at the prescribed intervals. Most patients (89%) reported that they would be interested in trying a once-daily 5-ASA medication.

"Patients with UC may benefit from improved disease management strategies (including simplified therapeutic regimens), disease education, and enhanced communication with gastroenterologists," the authors concluded.

The meeting was sponsored by the Canadian Association of Gastroenterology. ■