Ablation Beats Surveillance in Barrett's Esophagus

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SAN DIEGO — Interim results from a randomized, controlled trial suggest that radiofrequency ablation is more effective than frequent surveillance for Barrett's esophagus.

The study compared 84 patients who underwent ablation with 43 who underwent a sham operation. All of the patients received high-dose acid suppression (40 mg esomeprazole twice daily). The ablation patients with high-grade dysplasia underwent endoscopic biopsies at 3, 6, 9, and 12 months, whereas those with low-grade dysplasia underwent endoscopic biopsies at 6 and 12 months, Dr. Nicholas Shaheen said at the annual Digestive Disease Week.

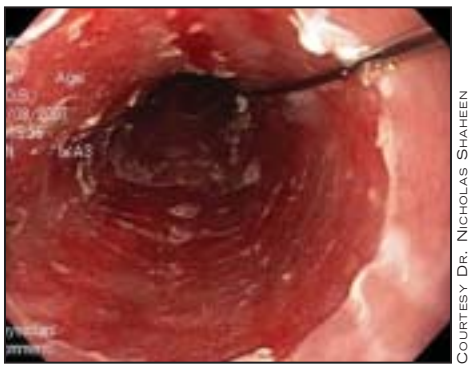
At the end of that time, 80% of the ablation patients with high-grade dysplasia and 90% of those with low-grade dysplasia experienced a complete response, defined as having all biopsies free of any histologic evidence of dysplasia, said Dr. Shaheen of the University of North Carolina, Chapel Hill.

In contrast, 26% of the control patients experienced a complete response. The difference between the ablation and control patients was statistically significant in the intent-to-treat analysis.

Of the patients who underwent ablation, 77% experienced a complete response for intestinal metaplasia, compared with none of the control patients. This difference also was statistically significant.

There was also a significant difference in the rate of histologic progression from low-grade dysplasia to high-grade dysplasia, and from high-grade dysplasia to cancer. Of those receiving a sham operation, 19% experienced progression of the disease, compared with 5% of the ablated patients.

Adverse events were relatively minor. Of the ablated patients, 6% experienced strictures, but all resolved after a mean of two dilations. There were three serious adverse events in the ablated patients and none in those who received a sham operation. One patient experienced an upper GI bleed, and two others experienced chest pain and were admitted overnight for observation.



COURTESY DR. NICHOLAS SHAHEEN

Endoscopic view of a Barrett's esophagus patient after radiofrequency ablation.

"Patients often do have chest pain after the procedure," Dr. Shaheen said in an interview. "This pain is usually mild to moderate, and was managed successfully in 295 of the 297 procedures performed in the trial with oral pain medications or no medications. Two patients had to be admitted for chest pain."

The study, which is ongoing, is being conducted at 19 medical centers in the United States. It was funded by BÂRRX Medical Inc., which manufactures the radiofrequency ablation system used in the study. Dr. Shaheen said she received "other financial benefits" from that company, as well as consulting fees, speaking fees, research support, and/or other financial benefits from AstraZeneca Pharmaceuticals LP, TAP Pharmaceutical Products Inc., Procter & Gamble Co., Eisai Co., Merck & Co., and Ethicon Endo-Surgery Inc. ■

Probiotic Products May Pack More Promise Than Punch

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. "There are so many different probiotic products, and the diversity of quality can be all the way from fine pharmaceutical manufacturers to [someone who makes it] in his bathtub."

Dr. McFarland recently tried 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 maker's claims. After several phone calls, she spoke to a technician who told her 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 with 18 women with irritable bowel syndrome (IBS). In that trial, the *L. acidophilus* had no effect on global IBS symptoms, cramping, or flatulence, but seemed 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. "This [should not be allowed] 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 health professional's portion of 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.

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

► Culturelle, manufactured by Amerifit Brands Inc., has the best evidence base of the three products in support of its claims. The label says that the product "maintains a healthy intestinal tract," and it also includes the species (Lactobacillus rhamnosus GG), the dose (10^{10} live organisms per capsule), and an expiration date.

The 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 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 Prevent Necrotizing Enterocolitis in Premature Infants

BEVERLY HILLS, CALIF. — Two meta-analyses have concluded that probiotics are effective in preventing necrotizing enterocolitis in premature infants, but there is no agreement on which probiotic preparations are best.

With an overall mortality of 15%-50%—approaching 100% in stage III disease—necrotizing enterocolitis (NEC) is one of the most worrisome consequences of prematurity. Even infants who survive the disorder face several adverse outcomes including short bowel syndrome, bowel strictures, liver failure, and possibly neurocognitive deficits, Dr. Maria Oliva-Hemker said at the International Probiotics Association World Congress.

According to a meta-analysis incorporating seven randomized controlled trials and 1,393 infants, probiotics were associated with a 64% decrease in the risk of developing stage II NEC (Lancet 2007;369:1614-20). Another meta-analysis incorporating five randomized controlled trials and 1,207 infants concluded that probiotics were associated with a 57% decrease in the risk of developing stage II or stage III NEC (Cochrane Database Syst. Rev. 2008;23:CD005496). Both results were statistically significant.

The Lancet meta-analysis further concluded that probiotics were associated with a statistically significant 53% reduction in all-cause neonatal mortality as well as a significant decrease in the time needed to reach full feeds.

The Cochrane meta-analysis found no statistically significant effect of probiotics on the number of days the infants received total parenteral nutrition, on the hospital length of stay, or on weight gain.

Although the meta-analyses support the use of probiotics, they provide little guidance on which probiotic preparations to use. No two of the seven studies in the Lancet meta-analysis used the same probiotic preparation. The organisms were *Bifidobacterium breve; B. lactis; Lactobacillus GG; L. casei; Saccharomyces boulardii*; a combination of *L. acidophilus* and *B. infantis*; and a combination of *B. infantis, S. thermophilus*, and *B. bifidus*. The preparations were generally given in a dose of 10^9 colony-forming units once or twice a day.

When the pathophysiology of NEC is considered, it makes sense probiotics might have an effect on the disorder, said Dr. Oliva-Hemker of the department of pediatrics, Johns Hopkins University, Baltimore.

"The majority of [premature] children are born by C-section. They have less chance of being breast-fed. They are exposed not to their mothers' flora in the vagina or the breast but [potential infection] in the NICU. And they are more often than not exposed to multiple antibiotics," she said. "This leads to a delayed establishment [and aberrant composition] of the microbiota. All this, together with inadequate development of the immune system, a bad barrier, and inadequate humoral and cell-mediated immune responses, [show] how everything can come together in a perfect storm, developing NEC in a particular infant."

It's not known what probiotics do to counter this process. They may modulate early bacterial colonization, enhance intestinal barrier function, inhibit adherence and colonization of pathogens, or they may modulate inflammatory pathways.

Dr. Oliva-Hemker said 25 infants need to be treated with probiotics to prevent one case of NEC. This may seem a large number, but given the consequences of NEC, it may be possible to justify the cost-benefit ratio. But "even though we might have a short-term benefit of preventing NEC, we don't know what the long-term consequences to those children will be."

Dr. Oliva-Hemker disclosed that she receives grant support from and serves on the speakers bureau of Nestlé Nutrition, conducts research for Centocor Inc., and serves as a consultant for Abbott Immunology. ■