Fish Oil May Lower Rectal Polyp Burden in FAP

BY DAVID MONAGAN

LONDON — A small, randomized trial suggests that fish oil given in tablet form as eicosapentaenoic acid may have chemopreventive effects, reducing the number and size of precancerous rectal polyps in patients with familial adenomatous polyposis.

The theory that this approach may have benefits in retarding cell proliferation has been tested in a number of other settings, including prevention of pancreatic, kidney, and esophageal cancers. But data on free fatty acid supplementation in the setting of familial adenomatous polyposis (FAP) have generally been confined to animal studies and anecdotal patient reports.

The new study was reported by Dr. N.J. West of St. Mark's Hospital, Harrow, England, at the 13th World Congress of Gastroenterology. The goal was to examine whether eicosapentaenoic acid (EPA) supplementation reduced polyp burden in the setting of FAP, as assessed by blinded outside endoscopists.

The researchers randomized a total of 55 patients into two groups: EPA (28 patients who took a 500-mg capsule twice daily) or placebo (27 patients). All participants first underwent sigmoidoscopy, in which a focal area of rectum was tattooed for identification of baseline polyp number and size by endoscopists blinded to each subject's intended therapy. The patients also underwent rectal biopsies to determine the fatty acid content in their rectal tissue.

After 6 months, patients underwent a second blinded endoscopy, and the results "were highly statistically significant" in favor of EPA supplementation. EPA patients had a 12.6% reduction of their polyp burden in the targeted area. In contrast, placebo patients showed a 22.4% increase in their polyp count.

The difference between the groups amounted to an overall 24% relative retardation in polyp growth with EPA supplementation. Moreover, the blinded endoscopists found a 30% smaller mean polyp size in patients receiving the fish oil. In addition, EPA levels in the rectal mucosa increased by 159% in the EPA group, compared with the placebo group.

"Compared to placebo, EPA decreased the polyp burden in treated patients and decreased the polyp size at 6 months. The treatment was safe and well tolerated, and may deserve serious consideration as an alternative therapy for FAP," Dr. West concluded.

Dr. Douglas K. Rex commented in an interview that "sulindac remains the cornerstone of chemoprevention in FAP. Celecoxib is an alternative when there is low cardiac risk and high risk of GI toxicity from NSAIDs. Fish oil is attractive because of its low risk profile, and it could be offered to FAP patients for this reason pending the results of additional studies of efficacy."

"Endoscopists should remember that no chemopreventive treatment replaces endoscopic monitoring in FAP, and no chemopreventive therapy clearly prevents cancer in FAP," cautioned Dr. Rex, who is distinguished professor of medicine at Indiana University, Indianapolis, and director of endoscopy at Indiana University Hospital.

Dr. West acknowledged that this trial was limited by its size and duration, and thus could not show whether changes in polyp burden following EPA could actually reduce the likelihood of future colorectal cancer. Nor could it answer the question of how long such therapy might need to be delivered to prevent colorectal cancer.

But he noted that EPA supplementation involves fewer side effects (and less expense) than was seen in trials of the COX-2 inhibitor celecoxib, which has been associated with adverse inflammatory and cardiovascular effects. "Free fatty acid has the potential to serve as an important therapeutic option if these results can be borne out by larger trials," he observed. ■

Disclosures: *The study is an offshoot of a British polyp registry that was developed, with support from the National Cancer Institute, Pfizer, and Ilex Oncology, to conduct clinical trials of agents of interest.*

Health Impact of Lactose Intolerance Tough to Assess

BY JEFF EVANS

BETHESDA, MD. — The health effects of lactose intolerance in people who avoid dairy foods have not been adequately studied to determine if there are nutritional deficiencies or long-term effects on bone and cardiovascular health, according to findings from a panel of experts assembled by the National Institutes of Health.

In a draft "state of the science" statement, the 14-member panel was not able to estimate the prevalence of lactose intolerance from a systematic review of 54 studies but concluded that a substantial proportion of people who have little or no lactase activity do not have lactose intolerance and may be missing out on the health benefits of nutrients in dairy foods, primarily calcium and vitamin D.

A substantial proportion of people who have little or no lactase activity do not have lactose intolerance and may be missing out on the benefits of nutrients in dairy foods.

"Particularly in children and adolescents, it's very difficult for them to receive the required amounts of calcium and vitamin D if they avoid dairy products completely," panel chairperson Dr. Frederick J. Suchy said in a press briefing. "Sometimes parents perceive themselves as being lactose intolerant when they're not and then impose that condition on their child without any testing," said Dr. Suchy, professor of pediatrics at Kravis Children's Hospital at Mount Sinai Hospital, New York.

The panel defined lactose intolerance as onset of gastrointestinal symptoms in an individual with lactose malabsorption, after a blinded, single-dose challenge of ingested lactose but not after ingestion of an indistinguishable placebo. None of the studies in the panel's review used this definition or evaluated a representative sample of the U.S. population.

Many studies reviewed by the panel did not verify if gastrointestinal symptoms resulted from lactose malabsorption (which may or may not be symptomatic) in people who have lost most or all lactase expression in their small intestine. These so-called lactase nonpersisters form the majority of all people worldwide.

Evidence suggests that adults and adolescents who have been diagnosed with lactose malabsorption could ingest at least 12 g of lactose (equivalent to the lactose content of 1 cup of milk) with no or minor symptoms, the panel found.

The panel advised creating individualized strategies for patients with real or perceived lactose intolerance, such as eating small amounts of dairy foods with other meals and spreading dairy intake throughout the day. Calcium-fortified soy or rice drinks, fruit juices, soy products, dried beans, and leafy greens are good nondairy sources of calcium, the panel noted. ■

Disclosures: *None of the panelists reported relevant conflicts of interest.*

A copy of the draft statement is at http://consensus.nih.gov/2010/lactose.htm.

Intestinal Metaplasia Tied to High Risk of Gastric Cancer

BY SHERRY BOSCHERT

SAN DIEGO — The risk for gastric cancer was more than 200 times higher in patients with gastric intestinal metaplasia on initial or repeat upper endoscopy, compared with the control population, in a retrospective study of 11,600 male veterans.

Of the cohort of 354 veterans, 3% were diagnosed with gastric intestinal metaplasia (GIM) over a 19-year period; the researchers compared their records with those of 355 randomly selected patients seen at the GI clinic of the Brooklyn campus of the Veterans Affairs New York Harbor Healthcare System.

Among veterans with GIM, 6% (21 patients) were diagnosed with gastric cancer, a rate 200-fold higher than the rate in the control group, Dr. Naveen Anand and his associates reported at the annual meeting of the American College of Gastroenterology.

Half of the cancer diagnoses were made on the initial endoscopy, and half were made on follow-up endoscopy, said Dr. Anand, a chief resident at the State University of New York Downstate Medical Center, Brooklyn. Repeat endoscopies were performed on 53% of the cohort (including 11% who underwent four or more endoscopies).

Patients with GIM—especially patients in these higher-risk subgroups—should undergo regular endoscopic surveillance with careful histologic diagnosis of GIM based on biopsies at multiple gastric locations, Dr. Anand suggested. He acknowledged the cost of increased surveillance, but noted that the gastric cancer rate in patients with GIM is similar to that in patients with severe dysplasia. "If patients have severe dysplasia on biopsy, we will bring these patients back for follow-up. So, if we're seeing similar rates of progression to cancer from GIM, these patients probably should be followed up."

He and his associates were surprised to find that having a history of *Helicobacter pylori* infection did not significantly influence pathology results. He attributed that to early intervention (that is, treatment that was initiated whenever *H. pylori* was diagnosed by histology).

Patients with GIM were more likely to be 70-90 years old, whereas those without GIM were more likely to be aged 50-70 years. About half of patients in the GIM and control groups were black and half were white, and there were few veterans of other races or ethnicities. The mean age in blacks was significantly older than in whites (75 vs. 71 years), and blacks accounted for 67% of patients who developed gastric cancer, Dr. Anand said.

"We believe there is a long lead time between the premalignant lesion and intestinal metaplasia and intestinal-type gastric carcinoma, similar to what we see in colon cancer and cervical cancer, which gives us an opportunity for possible surveillance and even possible intervention," he said. ■

Disclosures: *The investigators reported no conflicts of interest.*