Early Use of Biologics May Benefit IBD Patients

BY SALLY KOCH KUBETIN

EXPERT ANALYISIS FROM A RHEUMATOLOGY SEMINAR

SANTA MONICA, CALIF. – Gastroenterologists seem to be taking a page from the rheumatologists' playbook and are starting patients with inflammatory bowel disease on a biologic agent much sooner after diagnosis than has been standard practice.

By doing so, they hope to improve the natural history of the disease, just as rheumatologists have done in rheumatoid arthritis patients, according to Dr. Russell D. Cohen, who spoke at the meeting sponsored by Skin Disease Education Foundation and the University of Louisville.

Arthritis and inflammatory bowel disease (IBD) have more in common than the drugs used to treat them. Arthritis is the most common extraintestinal manifestation of IBD. Onset of joint symptoms may precede the onset of IBD, develop in parallel to it, or be unrelated, he said.

Arthritis is most likely to occur in IBD patients who have other extraintestinal manifestations such as dermatologic, ocular, or renal symptoms. The most commonly involved central joints are in the spine, where the arthritis takes the form of ankylosing spondylitis or sacroiliitis. Peripheral joints can develop arthropathies in IBD as well. About 5%-20% of IBD patients get arthritis. The cartilage and bone usually are spared from destruction. Arthritis in IBD usually involves five or more joints and lasts about 3 years.

The incidence of IBD in rheumatoid arthritis is not well defined. One of the few studies to address this question involved a review of the data sets from two large insurance companies involving 17 million people. The researchers found that the prevalence of IBD was about 0.62%-0.65% and the prevalence of RA was about 0.98%-1.08% in patients aged 47-56 years old living in the Midwest or the South. The odds ratio of having both IBD and RA was 2.1-2.7, and of having IBD and ankylosing spondylitis, about 5.8-7.8 (Inflamm. Bowel Dis. 2008;14:738-43).

The advent of biologics has changed the natural history of ulcerative colitis (UC). But before these agents became available, data from a Danish study showed that during the first year after diagnosis, 10% of UC patients lost their colon, about 23% had lost their colon after 10 years, and 31% had lost their colon 18 years out (Gut 1985;26:158-63).

In the prebiologic era, the natural history of Crohn's disease also was grim. The disease followed an inflammatory path for the first 5 years, then became penetrating with fistula formation between years 5 and 10 in a subset of patients; stricturing could develop after year 10 (Inflamm. Bowel Dis. 2002;8:244-50).

In the past, "virtually all Crohn's disease patients relapsed and most required one or more surgeries," said Dr. Cohen, who is codirector of the inflammatory bowel disease center at the University of Chicago (Gastroenterology 1985;88:1826-33).

An estimated 10% of Crohn's patients had their colons removed surgically within 1 year of their diagnosis with IBD. The disease tended to recur at the site of anastomosis of the previous surgery and to involve as much bowel as had been removed in the previous surgery. About half of the patients needed a second surgery.

Even today, most ulcerative colitis patients are treated with steroids, and many of these patients become steroid dependent. Findings from a study of 63 UC patients placed on steroids showed that at the end of 1 month, 34 achieved complete remission, 19 had a partial remission, and 10 had no response. Follow-up data at 1 year showed that 31 had a prolonged response, 14 were steroid dependent, and 18 needed surgery (Gastroenterology 2001;121:255-60).

These days, there is a move away from making steroids the first drug in the treatment regimen and instead starting with a biologic and adding a steroid only if necessary.

There is some overlap between the biologics used to treat rheumatologic diseases and those used to treat IBD. Recent data show that infliximab in combination with azathioprine induced a steroid-free clinical remission in 44 of 64 patients. In the same study, infliximab plus placebo induced remission in 37 of 65 patients, and azathioprine plus placebo induced remission in 21 of 75 patients. All of the patients had active IBD with a C-reactive protein level of 0.8 mg/dL or higher and lesions that were visible on endoscopy (N. Engl. J. Med. 2010;362:1383-95).

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Aspirin Dose, Not Duration, May Raise GI Bleeding Risk

BY HEIDI SPLETE

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY

SAN ANTONIO – Men who took more than 14 aspirin per week were more than twice as likely to report upper gastrointestinal bleeding as were men who reported no aspirin use, but

Both short- and long-term aspirin users can minimize the risk by using the lowest effective dose.

DR. HUANG

increased duration of use did not appear to raise the risk of GI bleeding, said Dr. Edward Huang.

Evidence regarding the impact of aspirin use on GI bleeding is conflicting because of the limitations of previous studies, said Dr. Huang of Massachusetts General Hospital in Boston.

To examine the long-term effects of aspirin dose and duration on GI bleeding, Dr. Huang and his colleagues conducted a prospective study of 32,989 participants in the Health Professionals Follow-up Study, a longitudinal study of male health professionals in the United States. In 2006 and 2008, participants were asked to report any past episodes of GI bleeding severe enough to require hospitalization or blood transfusion.

During a mean 14-year follow-up period, 707 men had an episode of major GI bleeding. After adjustment for risk factors including use of NSAIDs, age, smoking status, exercise, and body mass index, the risk ratios for upper GI bleeding were 1.05 for men who took 0.5-1.5 standard aspirin tablets (325 mg) per week, 1.31 for those who took 2-5 tablets per week, 1.63 for those who took 6-14 tablets per week, and 2.40 for those who took more than 14 tablets per week, compared with men who reported no aspirin use.

Short-term use was defined as less than 5 years; long-term use was defined as 5 years or longer. "The dose-response relationship is significant regardless of duration of use," Dr. Huang noted.

Longer duration of use was not significantly associated with an increased risk of upper GI bleeding, but individuals who use aspirin the longest tend to use the highest dose, he added.

The average age of the men when they enrolled in the study was 60 years, and those with a history of peptic ulcer disease were excluded.

The results suggest that both short-term and long-term aspirin users can minimize the risk of upper GI bleeding by using the lowest effective dose, Dr. Huang said.

Dr. Huang had no financial conflicts to disclose. ■

Early Colonoscopy Advised in IBD and Sclerosing Cholangitis

BY HEIDI SPLETE

FROM THE ANNUAL MEETING OF THE AMERICAN COLLEGE OF GASTROENTEROLOGY

SAN ANTONIO – Patients with primary sclerosing cholangitis and inflammatory bowel disease were as likely to develop colon cancer within 2 years of diagnosis as they were within 8-10 years of diagnosis, based on data from 54 patients.

Yearly colonoscopies are often recommended for patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease (IBD), but the evidence to support early screening has been limited, said Dr. Erin Thackeray of the Mayo Clinic in Rochester, Minn.

In this study, Dr. Thackeray and her colleagues reviewed medical charts from 54 adults with PSC and IBD who were seen at the Mayo Clinic between 1995 and 2005 and were later diagnosed with colonic neoplasms. Average age at the time of colon cancer diagnosis was 51 years, and 70% of the patients were male.

The occurrence of colonic neoplasms per 100 patient-years of follow-up was 21.5 within 2 years, 20.5 at 2-4 years, 19.3 at 4-6 years, 16.8 at 6-8 years, and 20.4 at 8-10 years.

Fourteen patients had colon cancer: two in the cecum, five in the ascending colon, four in the transverse colon, and three in the rectosigmoid colon. The cancers included two at stage 1, four at stage IIA, four at stage IIIB, two at stage IIIC, and two at stage IV.

VITALS

Major Finding: In patients with primary sclerosing cholangitis and inflammatory bowel disease, the occurrence of colonic neoplasms per 100 patient-years of follow-up was 21.5 within 2 years, 20.5 at 2-4 years, 19.3 at 4-6 years, 16.8 at 6-8 years, and 20.4 at 8-10 years.

Data Source: A review of data from 54 patients seen at the Mayo Clinic, Rochester, Minn., for primary sclerosing cholangitis and inflammatory bowel disease and later diagnosed with colonic neoplasms.

Disclosures: Dr. Thackeray said that she had no financial conflicts to disclose.

Another 7 had high-grade dysplasia, 3 had dysplasia-associated lesions or a mass, and 30 had low-grade dysplasia.

The study population included 37 patients with ulcerative colitis, 6 who had Crohn's disease with colonic involvement, and 11 with indeterminate colitis. A total of 38 patients had IBD diagnosed prior to PSC by a median of 10.8 years, while 9 patients had PSC diagnosed before IBD b y a median of 4 years, and 7 patients were diagnosed simultaneously with both conditions.

The study was limited by its small size, but the results "support early and aggressive screening for colon cancer" in this patient population, Dr. Thackeray said. ■