Success in Arthritis Inspires Early Biologic Use in IBD

BY SALLY KOCH KUBETIN

EXPERT ANALYSIS 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 (SDEF) 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 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 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. Crohn's 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). "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. An estimated 10% of Crohn's patients had their colons removed surgically within 1 year of their diagnosis with IBD.

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). 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 (N. Engl. J. Med. 2010;362:1383-95).

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Vitamin D Status Unaffected by Anti-Inflammatory Treatment

BY DENISE NAPOLI

FROM ANNALS OF THE RHEUMATIC DISEASES

Four months of treatment with the anti–tumor necrosis factor drug adalimumab did not affect serum vitamin D levels in rheumatoid arthritis patients, though it did ease symptoms.

The finding refutes the theory that systemic inflammation may negatively affect circulating serum 25-hydroxyvitamin D (25[OH]D) levels, wrote Dr. Paul Welsh and his colleagues.

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Major Finding: Treatment with adalimumab lowered the disease activity score among a group of rheumatoid arthritis patients, but did not affect serum vitamin D levels.

Data Source: A prospective study of 170 consecutive patients with rheumatoid arthritis seen at an outpatient facility in Amsterdam.

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Moreover, the data confirm a high prevalence of vitamin D insufficiency and frank deficiency among RA patients, they added.

According to Dr. Welsh of the British Heart Foundation Glasgow Cardiovascular Research Center at the University of Glasgow and his associates, there are several reasons why treatment with a potent anti-inflammatory medication, such as the tumor necrosis factor–alpha blocker adalimumab, might be hypothesized to increase vitamin D levels.

Data from a 2006 study showed an inverse relationship between serum vitamin D and DAS-28 scores (Clin. Exp. Rheumatol. 2006;24:702-4). "Furthermore, data for an apparent beneficial effect of statins on circulating 25[OH]D concentrations have been speculated to be attributable to statin 'pleiotropic' anti-inflammatory effects," the researchers said. They also noted that serum vitamin D levels are known to drop in the acute phase following surgery, when inflammation is likely to be elevated.

To test the hypothesis that lowering inflammation would result in an increase of vitamin D, the researchers looked at 170 consecutive patients with RA seen at an outpatient clinic in Amsterdam (Ann. Rheum. Dis. 2010 [doi:10.1136/ard.2010.137265]).

Patients were treated either with adalimumab alone, at a dose of 40 mg administered every 2 weeks, or with adalimumab plus other disease-modifying antirheumatic drugs (DMARDs).

At baseline, 66 patients (39%) were vitamin D deficient, with a serum concentration of less than 15 ng/mL. Sixty-three patients (39%) had vitamin D insufficiency, with levels between 15 and 25 ng/mL. The remaining patients had adequate vitamin D levels.

After 16 weeks of treatment with adalimumab, patients' mean disease activity score-28 (DAS-28) had dropped significantly, from 5.1 to 3.2 (P less than .001). However, median circulating levels of vitamin D were not significantly altered, moving from 18.5 ng/mL at baseline to 19.0 ng/mL at the study's completion (P = .67). Nor did the prevalence of patients with vitamin D deficiency and insufficiency change after treatment, wrote the authors.

"Whether longer-term biological therapy has any beneficial effect on circulating 25[OH]D concentrations requires further study, although any such effect may be attributable to increased sunlight exposure rather than decreasing inflammation," concluded the authors.

"Our observations also weaken the possibility that TNF-alpha blockers, which improve bone mineral density and potentially lower cardiovascular risk, do so via changes in 25[OH]D levels."

They added: "Further research is needed to address determinants of poor 25[OH]D status in RA." ■

Psoriatic Arthritis Patients Have High Depression Risk

BY BRUCE JANCIN

FROM THE INTERNATIONAL CONGRESS OF THE ROYAL COLLEGE OF PSYCHIATRISTS

EDINBURGH – Depression is common, underdiagnosed, and undertreated in patients with psoriatic arthritis.

Psychiatric evaluation of 50 consecutive patients at the University of Glasgow psoriatic arthritis clinic indicated that 15 patients (30%) were depressed. Three were rated as severely depressed based on their scores on the Hospital Anxiety and Depression Scale (HADS); 12 others had moderate depression, Dr. Rajeev Krishnadas reported.

This high prevalence of depression in psoriatic arthritis patients is consistent with reports in the dermatologic literature (Br. J. Dermatol. 2008;159:704-10).

Of note, none of the depressed Scottish patients was on a therapeutic dose of an antidepressant, added Dr. Krishnadas of the Sackler Institute of Psychobiological Research, Southern General Hospital, Glasgow.

This study is part of a larger ongoing investigation into the relationship between systemic inflammation and depression in patients with rheumatoid arthritis or psoriatic arthritis. In this portion of the study, a positive association was noted between HADS scores and C-reactive protein levels in the psoriatic arthritis cohort, although it must be noted that CRP scores accounted for only 7% of the overall variance in HADS scores. Higher HADS scores were associated with worse quality of life as assessed by the Dermatology Quality of Life Questionnaire as well as with higher scores on a self-rated pain scale.

A negative correlation was found between HADS scores and emotional intelligence as measured by the Trait Emotional Intelligence Questionnaire – Short Form. High trait emotional intelligence reflects greater awareness of one's own feelings as well as the feelings of others. Individuals with high emotional intelligence are better able to regulate their emotions than are those with lower trait emotional intelligence.

Patients who scored high in trait emotional intelligence had higher quality of life scores, lower CRP levels, and lower scores on the pain scale.

These findings are consistent with the hypothesis that a poor ability to be aware of and regulate one's emotions predisposes to depression in the presence of a chronic medical condition or other major stressor, said to Dr. Krishnadas, who declared having no conflicts of interest. ■