Guidelines Survey Psoriatic Arthritis Treatments

BY NANCY WALSH
New York Bureau

FORT LAUDERDALE, FLA. — An international group of dermatologists and rheumatologists has published new recommendations for the treatment of the heterogeneous manifestations of psoriatic arthritis, but they caution that randomized data remain sparse and the recommendations may change as new data emerge.

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), which has 250 members from North America, Europe, and elsewhere, performed a formal literature review for the symptoms of peripheral arthritis, skin and nail disease, axial disease, dactylitis, and enthesitis, and formulated treatment guidelines based on this systematic review and consensus opinion.

Significant challenges exist in the management of psoriatic arthritis (PsA), according to lead author Dr. Christopher T. Ritchlin. There have been few double-blind, randomized trials that have examined the efficacy of traditional agents such as sulfasalazine and cyclosporine in PsA, so there is an inadequate evidence base for the use of these drugs. There is also no evidence that the traditional agents slow radiographic progression or are effective for axial disease, dactylitis, or enthesopathy, explained Dr. Ritchlin, who is professor of medicine and director of clinical immunology, University of Rochester (N.Y.) Medical Center.

"But it's not that we know these drugs don't work—the studies simply haven't been done," he said at a meeting sponsored by RHEUMATOLOGY NEWS and Skin Disease Education Foundation.

Particularly problematic is the paucity of data for methotrexate, with only one older double-blind randomized trial having been done, which failed to show efficacy (Arthritis Rheum. 1984;27:376-81). "But that study was underdosed and underpowered," Dr. Ritchlin said.

Improvements in trial design in the intervening years, incorporating more useful and measurable outcomes in PsA, favor the newer biologic agents over the older disease-modifying antirheumatic drugs (DMARDs). While there have been three double-blind trials of tumor necrosis factor (TNF) inhibitors—with these drugs clearly being effective in many patients—there have been no head-to-head trials of methotrexate versus a TNF inhibitor.

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DR. RITCHLIN

GRAPPA, therefore, has attempted to fill these knowledge gaps, to provide physicians with available evidence-based information, and to help physicians in their diagnostic and therapeutic decision making (Ann. Rheum. Dis. 2008 Oct. 24 [Epub doi:10.1136/ard.2008.094946]). The recommendations note that symptoms may be stratified as mild, moderate, or severe for each clinical manifestation, and that treatment decisions may be determined by the most severe clinical presentation. The synergistic, potentially profound impact of multiple manifestations of inflammation also should be taken into account and evaluated with tools such as the patient global assessment and health-related quality-of-life questionnaire.

The GRAPPA investigators noted that their efforts were hampered by a lack of validated tools. For example, they wrote that the assessment and treatment of axial manifestations of PsA are particularly challenging and that by consensus they agreed to follow guidelines of the Assessments in Ankylosing Spondylitis Working Group and adopt the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for determination of severity and response until validated measures for axial disease in PsA can be developed.

In general, the recommendations include the following:

▶ For mild peripheral arthritis, initial treatment can include nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular glucocorticoid injections, and for moderate or severe arthritis, DMARDs or TNF inhibitors may be given.

While TNF inhibitors are recommended for use in patients who have failed at least one DMARD, the recommendations also note that the patient whose prognosis is poor can be considered for a TNF agent without prior DMARD failure. Prognosis is worse in patients with polyarticular disease, an elevated erythrocyte sedimentation rate, previous medication failure, or the presence of joint damage, loss of joint function, or diminished quality of life.

Systemic corticosteroids are typically not used in PsA because of the possibility of psoriasis flare upon withdrawal.

▶ For skin disease, first-line therapies include phototherapy, methotrexate, fumaric acid esters, TNF inhibitors, efalizumab, and cyclosporine; second-line therapies include acitretin and alefacept; and third-line therapies include sulfasalazine and hydroxyurea. Nail disease can be managed with retinoids, oral psoralen plus ultraviolet A, cyclosporine, or TNF inhibitors.

▶ For mild to moderate axial disease, treatment options include NSAIDs, physiotherapy, analgesia, and injection of the sacroiliac joint. Moderate to severe involvement of the spine can be treated with TNF inhibitors.

▶ Mild dactylitis typically can be managed with NSAIDs and injected corticosteroids, but DMARDs or infliximab can be tried if symptoms are resistant.

▶ For mild enthesitis, typically of the Achilles tendon area, NSAIDs, physical therapy, and corticosteroids can be used, while moderate disease can be treated with DMARDs. Severe enthesitis may respond to a TNF inhibitor.

The guidelines also emphasized that many new treatments are in the pipeline, "which will offer new and possibly less expensive therapeutic options."

Dr. Ritchlin also discussed larger management issues in PsA at the meeting. "The evidence is abundantly clear that psoriatic arthritis is an independent risk factor for coronary vascular disease. A lot of these patients are young, and they don't go to their primary care physicians. They come to the rheumatologists and the dermatologists," he said.

"No one is following their cholesterol profiles or advising them about smoking and weight loss, so it's really incumbent on us to make sure these issues are addressed in this patient population. This is a really significant intervention we can make, maybe even more important in some cases than treating their joint and skin disease," Dr. Ritchlin said.

Dr. Ritchlin disclosed that he has received grant research support from Centocor Inc. and is a consultant to Abbott Laboratories, Amgen Inc., and Wyeth. SDEF and this newspaper are owned by Elsevier. ■

After Years of Decline, RA on the Rise Among Women

BY BETSY BATES
Los Angeles Bureau

SAN FRANCISCO — An unexpected, significant uptick in rheumatoid arthritis incidence among women may point to increased exposure to hormonal and environmental risk factors, although investigators remain unsure of a clear explanation.

"What we had seen over the last 50 years was a continuous decline [in RA incidence] from the 1950s to the [mid] 1990s," Dr. Hilal Maradit Kremers said during a press briefing at the annual meeting of the American College of Rheumatology. "We were expecting that decline to continue."

Surprisingly, the trend instead reversed quite dramatically between 1995 and 2004, according to what began as a rather routine update of incidence trends in Olmsted County, Minn., by Dr. Maradit Kremers and her associates at the Mayo Clinic, Rochester, Minn.

The age-adjusted incidence in women was 54 per 100,000 in the post-1995 analysis, compared with 36.4 per 100,000 between 1985 and 2004.

The average age of onset for women was 56.5 years, roughly the same as in previous years.

Among men, the incidence of RA remained steady between 1995 and 2004, at 28.6 per 100,000, compared with previous decades.

Although the Midwestern population included in long-term Mayo Clinic epidemiologic studies underrepresents nonwhite populations, it has the advantage of stability, allowing disease trends to be detected quite accurately. So Dr. Maradit Kremers could say with considerable confidence that "the incidence of this disease is rising again."

What remains a mystery is why the incidence rate would change, and so rapidly. "This was purely an observational study," she said. "At this point we can only speculate that some [unknown] risk factors may be operating to increase the occurrence of this disease."

Smoking, the most well-established risk factor for the development of RA, actually declined among women in the United States between 1990 and 2003, from 23% of women to 19%, according to statistics from the Centers for Disease Control and Prevention.

Obesity, which did escalate during the years of the study, is not generally associated with development of RA, said Dr. Maradit Kremers, a clinical epidemiologist.

Genetics, hormones, diet, and viral exposure have all been proposed as potential risk factors for RA (Scand. J. Rheumatol. 2006;35:169-74).

Since cases in women appear to be driving the recent surge in incidence, hormonal and reproductive factors will undoubtedly be the focus of new scrutiny, she said.

Some 20 studies have explored such risk factors over the years, generally pointing to pregnancy and oral contraceptive use as protective.

The respective roles of childbearing age, total number of children, breast-feeding, and use of hormone therapy are as yet unclear, she said.

Dr. Maradit Kremers said the study has "important implications" for policy makers, especially with regard to resource allocation for a disease suddenly on the rise after years of decline.

"This worrisome increase in occurrence of RA not only offers us clues into the causes of RA, but also highlights the need for more research into the causes and treatment of this devastating disease," Dr. Sherine Gabriel, a Mayo Clinic rheumatologist and lead author of the study, said in a statement.

Dr. Maradit Kremers disclosed that she has received research grants and/or consultant fees from Pfizer Inc. and Amgen Inc., makers of drugs prescribed for rheumatoid arthritis. Neither Dr. Gabriel nor any of the other coinvestigators reported any financial disclosures. ■

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