Intensive Methotrexate Slowed Early RA Better Than Conventional Dosing

BY JEFF EVANS
Senior Writer

WASHINGTON — Treatment of early rheumatoid arthritis with an intensive methotrexate dosing strategy may provide a better overall clinical outcome than would a conventional approach with the drug, Dr. Johannes W.J. Bijlsma reported at the annual meeting of the American College of Rheumatology.

Management of early rheumatoid arthritis with intensive methotrexate treatment not only produced a higher remission rate than did conventional methotrexate treatment, but was relatively easy to administer in clinical practice, said Dr. Bijlsma of University Medical Center Utrecht (the Netherlands).

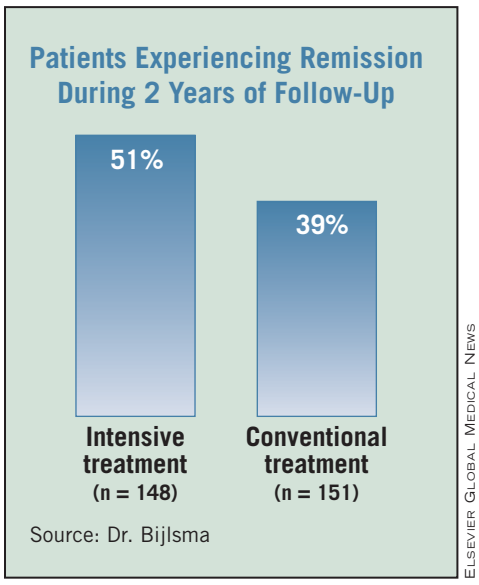
Dosing in the intensive drug regimen was tailored by a computer program.

DR. BIJLSMA

In a multicenter, randomized trial, a significantly greater percentage of 148 intensively treated patients went into clinical remission during 2 years of follow-up than did 151 conventionally-treated patients (51% vs. 39%, respectively).

Clinical remission was defined as having no swollen joints, plus meeting two of the three following criteria for at least 6 months: three or fewer tender joints; an erythrocyte sedimentation rate of 20 mm or less in the first hour; and a visual analog scale score of general well-being of 20 mm or less.

The average time to remission in the intensive treatment group was 11 months, compared with 14 months in the conventional treatment group, while the duration of remission for the two groups was 11 months and 9 months, respectively. Both findings were statistically significant; radiographic joint damage was similarly low in both groups, reported Dr. Bijlsma.



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Adverse events also occurred at similar rates between the groups.

Conventional treatment consisted of one outpatient visit every 3 months in which the dose of methotrexate was increased by 5 mg/week if the number of swollen joints rose. The investigators could reduce the dose of methotrexate by 2.5 mg/week when patients went into remission.

Patients who received intensive treatment had one outpatient visit every 4 weeks. Their dosing regimen was individually tailored by a computer program that used a predefined set of criteria, noted Dr. Bijlsma.

The investigators increased the methotrexate dose if there was 20% or less improvement in the number of swollen joints, and if there was 20% or less improvement in two of the three previously mentioned criteria.

The dose decreased when the patients had no swollen joints for 3 or more months and had greater than 20% improvement in at least two of the three variables. If a patient in either group reached 30 mg/week methotrexate without a response based on the criteria, the patients then received methotrexate subcutaneously. Those who continued to show no response also received cyclosporine, reported Dr. Bijlsma. ■

British Limit Use of Anti–TNF-α Drugs For Arthritis Patients

The tumor necrosis factor–α–inhibitor drugs adalimumab, etanercept, and infliximab should be used to treat rheumatoid arthritis patients only after 6-month trials of methotrexate and one other disease-modifying antirheumatic drug, the clinical effectiveness agency for England and Wales had ruled.

The TNF-α inhibitors should be prescribed only to those patients who have active rheumatoid arthritis as measured by a disease activity score greater than 5.1—or patients with about 8-10 swollen and tender joints—confirmed at least twice, measured 1 month apart, according to the National Institute for Health and Clinical Effectiveness' final appraisal document.

TNF-α–inhibitor therapy should be done in combination with methotrexate, unless contraindicated, according to NICE. In those instances, patients should receive either adalimumab or etanercept as monotherapy.

Physicians should stop treatment with TNF-α inhibitors after 6 months if the patient does not show an adequate response, defined as an improvement in disease activity score of at least 1.2 points.

Infliximab costs between $14,612 and $17,047 a year, while etanercept and adalimumab both cost $17,982 a year, according to the NICE committee examining the effectiveness of the three drugs.

The committee considered TNF-α–inhibitor medications as first-line or second-line therapy after failure of one disease-modifying antirheumatic drug (DMARD). However, the committee concluded, based on cost and efficacy data, that neither was an appropriate use of National Health Service resources.

For first-line therapy, clinical specialists told the appraisal committee that a large number of patients initially respond well to DMARDs, and both the British Society of Rheumatology and European League Against Rheumatism recommend a trial of at least one DMARD.

As a second-line treatment, the appraisal committee did not believe TNF-α inhibitors had demonstrated cost-effectiveness.

—Jonathan Gardner

Personality Trait Worsens Rheumatoid Arthritis Symptoms

BY JANE SALODOF MACNEIL
Southwest Bureau

TUCSON, ARIZ. — A psychological trait associated with heightened awareness of bodily distress may help to explain why some rheumatoid arthritis patients suffer more from achiness, malaise, and fatigue than do others with similar disease severity, Dr. Ilana M. Braun reported at the annual meeting of the Academy of Psychosomatic Medicine.

The trait, somatic absorption, was closely associated with generalized symptoms of rheumatoid arthritis in 87 patients studied by Dr. Braun, a psychiatrist at Harvard Medical School and Massachusetts General Hospital in Boston. It had no relationship to specific symptoms, such as joint pain, swelling, stiffness, and deformity, or to disease severity.

The magnitude of effect was modest, accounting for just 4% of variability in nonspecific symptoms, but Dr. Braun noted that it was significant statistically—and possibly clinically.

People who score high on measures of absorption have a capacity for deep involvement in sensory events, she said. They have a heightened sense of reality that makes them more sensitive not only to bodily distress, but also to hypnosis and to biofeedback.

"There might be a role for psychiatry in the treatment of rheumatoid arthritis," she said, questioning whether some patients might respond to these kinds of interventions for nonspecific symptoms.

"It is a personality style that you can target," Dr. Braun added in an interview. "This is not a disorder. These are perfectly healthy people [mentally]. They just have a certain way of responding to the world."

While she called for more research into the clinical utility of her finding, Dr. Braun suggested that ultimately it may present rheumatologists with an alternative to increasing medication when patients complain they feel poorly in the absence of specific symptoms. "What I am saying is, for the malaise and the fatigue don't double the dose," she said. "Send them to the hypnotist."

The study was supported by a Webb Fellowship from the academy. Dr. Braun enrolled patients from a larger, longitudinal study of rheumatoid arthritis. The largely female population had a median age of 55.5 years. A majority, 85%, had been to college, more than half were employed, and about half were married.

Patients completed the 14-item Rheumatoid Arthritis Symptoms Questionnaire. Dr. Braun and her coinvestigators also used erythrocyte sedimentation rate and a standard 28-joint physical examination by a rheumatologist to measure disease severity. They calculated the total number of medications prescribed for pain and other "disease-modifying agents."

Assessment of somatic absorption was based on the 29-item Somatic Absorption Scale, a measure derived from the Tellegen Absorption Scale. Dr. Braun said the Somatic Absorption Scale focuses on "absorption as it pertains to somatic or visceral experience." For example, a subject might be asked whether she could imagine her arm being so heavy she could not move it, or if she notices how her clothes feel against her skin. The Rand Mental Health Inventory was used as well to identify common symptoms that are neither physical nor psychosomatic of prevalent mental disorders.

Dr. Braun reported somatic absorption was significantly more pronounced in younger subjects, people with more severe psychiatric symptoms, African Americans, and Hispanics. Rheumatoid arthritis symptoms with statistically significant ties to somatic absorption were pain in limbs, pain in back, fatigue, generalized aching, and "feeling sick all over."

In a discussion of the findings, Dr. Stephen J. Ferrando said he found himself looking up the literature on absorption, a personality construct developed in the 1970s to assess which patients might respond to hypnosis and biofeedback.

Dr. Ferrando, a professor of clinical psychiatry and clinical public health at Cornell University in New York, called the findings very interesting and said he looks forward to an analysis of how the subjects fare in the longitudinal study from which the population was drawn. ■