Acupuncture Found to Ease Osteoarthritis Pain

BY ELIZABETH MECHCATIE
Senior Writer

Adding acupuncture to routine care in patients with chronic pain from osteoarthritis of the hip or knee was safe and resulted in "a clinically relevant and persistent benefit" in a large study of such patients, Dr. Claudia Witt and her associates have reported.

Almost 35% of the patients in the acupuncture group were responders, compared with 6.5% in the control group.

The investigators evaluated the impact of physician-administered acupuncture on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores in their study of patients who had osteoarthritis for a mean of 5 years, a baseline WOMAC score of 47, and a mean age of 62 years.

Of the total patients, 322 were randomized to acupuncture and 310 to the control group; 2,921 who refused randomization were treated with acupuncture.

About 57% of the patients had osteoarthritis (OA) of the knee, nearly 15% had OA of the hip, and approximately 30% had both, reported Dr. Witt of Charité University Medical Center, Berlin, and her colleagues.

The patients receiving acupuncture had up to 15 sessions of the therapy over 3 months and no acupuncture during the fourth, fifth, and sixth months; patients in all three groups also received conventional treatment.

At 3 months, scores on the WOMAC had improved by a mean of 17.6 points from baseline among those in the randomized acupuncture group, compared with a mean of 0.9 in the control group, a significant difference.

Almost 35% of those in the acupuncture group were responders (defined as at least a 50% reduction in WOMAC scores), compared with 6.5% of those in the control group.

Improvements in the physical component of the quality-of-life score were also significantly greater at 3 months among those receiving acupuncture.

Responses to treatment among the nonrandomized acupuncture recipients were similar to the responses among those randomized to acupuncture versus osteoarthritis patients in the control group.

In addition, the benefits of acupuncture appeared to persist through 6 months, although patients received no acupuncture after 3 months (Arthritis Rheum. 2006;54:3485-93). ■

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strate a significant reduction of GI events with a cyclooxygenase-2 (COX-2) inhibitor, compared with traditional NSAIDs. Rates of upper GI clinical events were lower with etoricoxib than with diclofenac (0.67 and 0.97/100 patient years, respectively). But there was no difference between groups in complicated upper GI events, such as perforated ulcers.

The nonsignificant difference in complicated upper GI events "is probably the most bothersome thing about the study," since etoricoxib is supposed to be GI-protective and has even more COX-2 selectivity than some other COX-2 selective NSAIDs, such as rofecoxib, Dr. Altman said.

The MEDAL program is a prespecified pooled analysis of three studies. The largest was MEDAL, performed in 23,504 patients during June 2002-May 2006 at 1,380 sites in 46 countries. This study randomized rheumatoid arthritis (RA) patients to treatment with 90 mg etoricoxib once a day or 75 mg diclofenac twice a day. Osteoarthritis (OA) patients were randomized to receive either 75 mg diclofenac twice daily or one of two dosages of etoricoxib, 90 mg or 60 mg.

The other studies in the analysis were the Etoricoxib vs. Diclofenac Sodium Gastrointestinal Tolerability and Effectiveness (EDGE) trial, in which 7,111 patients received 90 mg etoricoxib once daily or 50 mg diclofenac three times daily, and EDGE II, in which 4,086 patients were treated with 90 mg etoricoxib once daily or 75 mg diclofenac twice daily.

In the pooled analysis of the three studies, the primary end point was the first occurrence of any fatal or nonfatal venous or arterial thrombotic event, including MI, unstable angina, intracardiac thrombus, thrombotic stroke, and transient ischemic attack. The rates were 1.24 events/100 patient-years in the etoricoxib group and 1.30 events/100 person-years in the diclofenac group, a nonsignificant difference, reported Dr. Cannon, a cardiologist at Brigham and Women's Hospital, Boston.

Dr. Altman noted that "The hypothesis that diclofenac is partially COX-2 selective I think is not supported" because only one article has ever said that diclofenac has some COX-2 selectivity (N. Engl. J. Med. 2001;345:433-42).

But naproxen "clearly is the one that would have been more helpful to compare" with etoricoxib, he said, because naproxen was compared against rofecoxib in Merck's VIGOR (Vioxx Gastrointestinal Outcomes Research) trial and naproxen is more widely used (over-the-counter and prescription) in the United States than diclofenac.

Dr. Cannon receives research grant support from Merck, which sponsored and monitored the study, and did the statistical analysis. The results were published simultaneously with the presentation in the Lancet 2006; (DOI:10.1016/S0140-6736(06)69666-9).

Etoricoxib is approved for use in more than 60 countries but not yet in the United States.

Several days before the presentation, Merck resubmitted its new drug application to the FDA for the approval of etoricoxib for the symptomatic treatment of only osteoarthritis, instead of indications also in rheumatoid arthritis and other conditions.

In the MEDAL program, RA and OA patients had similar risk for cardiovascular thrombotic events with both drugs, but only 28% of the patients had RA. RA patients also usually require higher doses of NSAIDs, which would emphasize any cardiovascular thrombotic risk. These considerations may have had led Merck to not seek RA as an indication for etoricoxib, Dr. Altman suggested.

Dr. Altman reported that he has been a consultant to Pfizer. ■

Senior writer Jeff Evans contributed to this report.

FDA Recognizes Adalimumab's Joint Protective Effects in Psoriatic Arthritis

BY ELIZABETH MECHCATIE
Senior Writer

The tumor necrosis factor (TNF) blocker adalimumab has been approved by the Food and Drug Administration for inhibiting structural joint damage and improving physical function in patients with psoriatic arthritis, based on study results.

The psoriatic arthritis indication in the product label now says that it is indicated for reducing the signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis. Adalimumab, marketed as Humira by Abbott Laboratories, was approved for treating psoriatic arthritis in October 2005.

The latest approval is based on an extension of a trial of patients with moderate to severe psoriatic arthritis, who had inadequate responses to NSAID treatment, comparing 40 mg of adalimumab every other week with placebo in 313 patients, according to a statement issued by Abbott. After 24 weeks, 285 patients continued in an open-label extension of the trial.

At 24 weeks, those on adalimumab had significantly less joint damage than did those on placebo, as determined by the modified total Sharp score, based on x-rays at baseline, 24 weeks, and 48 weeks. Inhibition of radiographic progression on x-rays was significantly greater among those on adalimumab at 24 weeks, and was maintained at 48 weeks.

The physical function indication is based on the significant improvements in physical function documented in the Health Assessment Questionnaire Disability Index (HAQ-DI), and physical component of the Short Form-36 Health Status Survey (SF-36). Those on adalimumab had significantly greater improvements in the HAQ-DI score, with mean decreases of 47% at 12 weeks and 49% at 24 weeks, compared with mean decreases of 1% and 3%, respectively, among those on placebo. Improvements in physical function, as seen on the HAQ-DI, were maintained for up to 84 weeks, according to the revised label. Those on adalimumab also had significantly greater improvements in the physical component of the SF-36 score, compared with those on placebo at weeks 12 and 24. ■

Seropositive RA Patients Show Greater Response to Rituximab

WASHINGTON — Baseline seropositivity for rheumatoid factor and anticyclic citrullinated peptide among patients with rheumatoid arthritis is associated with a more favorable response to treatment with rituximab, Dr. Paul P. Tak reported at the annual meeting of the American College of Rheumatology.

A post hoc analysis was undertaken to explore the relationship between baseline autoantibody status and rituximab therapy in patients who participated in the 24-week Randomized Evaluation of Long Term Efficacy of Rituximab (REFLEX) study, according to Dr. Tak of the University of Amsterdam.

In REFLEX, patients with long-standing RA who had inadequate responses to one or more anti–tumor necrosis factor (TNF)-α drugs were randomized to receive a course of intravenous rituximab, which consisted of two infusions of 1,000 mg each, separated by 2 weeks, or placebo. All patients also were on background methotrexate in doses of 10-25 mg/week.

Among 309 patients analyzed at week 24, there was a high degree of efficacy for those who were seropositive for either or both of the autoantibodies (see box). Baseline RF greater than 20 IU/mL and anti-CCP greater than 5 IU/mL were considered seropositive.

With regard to the lower level ACR 20 responses, seronegative patients on rituximab also achieved this level to a greater degree than did seronegative patients on placebo.

Seronegative patients receiving rituximab did not achieve greater ACR 50 or 70 responses, however. "This suggests that other mechanisms such as antigen presentation, T-cell co-stimulation, and cytokine release may account for low levels of response, with higher responses to rituximab therapy being mediated primarily by suppression of pathogenic autoantibodies," Dr. Tak wrote in a poster session.

Dr. Tak disclosed that he received research grants and consulting fees from Roche Laborotories Inc.

—Nancy Walsh