Topical May Be Oral Agent OA Alternative

BY NANCY WALSH
New York Bureau

SAN DIEGO — A topical pain-relieving cream found to be safe and effective for knee osteoarthritis in a double-blind controlled study may offer a new approach to treatment that avoids the cardiovascular and gastrointestinal hazards of many oral agents, according to Dr. Thomas J. Schnitzer.

Topical civamide cream 0.075% (Winston Laboratories, Vernon Hills, Ill.) was tested in a multicenter study that included 695 patients with radiographically confirmed osteoarthritis who ranged in age from 40 to 75 years.

At baseline, all study participants had a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score greater than 9 (out of a total 20), despite treatment with NSAIDs or cyclooxgenase-2 (COX-2) inhibitors.

They were randomized to a regimen of civamide cream 0.075% to be applied three times daily, or a control cream containing low-dose (0.01%) civamide.

Blinding was therefore maintained, as both creams cause an initial burning sensation, Dr. Schnitzer reported in a late-breaking abstract session at the annual meeting of the American College of Rheumatology.

The three primary efficacy variables were WOMAC pain, WOMAC physical function, and subject global evaluation, and the primary efficacy analysis was the time-weighted average of change from baseline to day 84.

Statistically significant differences were seen in all variables and on the time-weighted average between the two groups at the conclusion of the study, wrote Dr. Schnitzer, professor of medicine at Northwestern University, Chicago.

The time-weighted average of change from a baseline mean score of 11.97 for WOMAC pain was 3.64 in the active treatment group, compared with a change of 3.3 from a baseline of 11.75 in the control group.

For WOMAC function, the time-weighted average change was 9.99 from a baseline of 38.88 in the active treatment group, while in the control group there was a change of 8.21 from a baseline of 38.2. Significant differences also were seen at the majority of interim time points, which were days 21, 42, and 63.

Dr. Schnitzer disclosed that he has received research grants and consulting fees from Winston Laboratories. ■

Shoe Insoles Fail to Ease Osteoarthritis Knee Pain

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN DIEGO — Wedged shoe insoles may do little for medial knee osteoarthritic pain, according to a small, 18-week trial presented at the annual meeting of the American College of Rheumatology.

"A 5-degree lateral wedged insole was not efficacious in people with medial knee osteoarthritis in this particular trial," said Kristin Baker, Ph.D., of the clinical epidemiology research and training unit at Boston University.

The randomized, double-blind, crossover trial, which enrolled 46 individuals with radiographically confirmed medial knee osteoarthritis, was designed to detect a 10% treatment effect on the pain subscale of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). The wedged insole did not have this effect.

Given the patients' baseline WOMAC pain scores (a mean of 266 on the 0- to 500-point scale), a positive treatment effect would have been a decrease of 26-27 points. The study found that the wedge produced a mean 13-point benefit.

Use of a wedged insole did not result in the participants' being able to take less pain medication.

In a subgroup analysis, individuals with a body mass index (kg/m^2) lower than 30 had a mean 29-point improvement. That finding approached but did not achieve statistical significance, given the smaller number of patients that the analysis involved. A study of more people who weigh less might show a positive effect, Dr. Baker said.

The study began with a 2-week washout period, during which participants kept a pain diary. During the subsequent 6 weeks, subjects wore either a 5-degree lateral-wedge insole or a neutral insole. Then, for 4 more weeks, they did not wear any insole. For the final 6 weeks, participants crossed over and wore the other type of insole.

Patients were expected to wear the insoles for at least 8 hours per day, and their compliance rate was high, Dr. Baker said. ■

ALTERNATIVE MEDICINE

AN EVIDENCE-BASED APPROACH

Rose Hip Powder for Osteoarthritis

Rationale for Use

Studies of the mechanisms of action of a standardized formulation of rose hip powder showed that it lowered in vivo levels of C-reactive protein, from a mean of 8.25 mg/L to 6.67 mg/L. In addition, it reduced the in vitro migration rate of inflammatory polymorphonuclear lymphocytes (Inflammopharmacology 1999;7:63-8).

A proprietary formulation, Hyben Vital (Hyben Vital International, Langeland, Denmark), has been available in Scandinavia for a decade. It is imported to the United States by EuroPharma, Green Bay, Wisc., and marketed as LitoZin. The plants are a specific subspecies, *Rosa canina,* and are grown in Denmark and Sweden according to good agricultural practice. Computerized techniques ensure that temperatures during the drying process do not exceed 40° C, and the dry powder is controlled according to vitamin and mineral content.

► Rose hip powder has shown anti-inflammatory effects in vitro and in vivo.
► Scandinavian clinical trials have found significant benefits and few adverse effects among patients with osteoarthritis treated with a standardized proprietary formulation of rose hip powder.

Early OA: The Danish Study

Hyben Vital was evaluated in a double-blind, placebo-controlled, crossover trial that included 94 outpatients with osteoarthritis (OA) who were recruited from the department of rheumatology at Copenhagen County Hospital Glostrup and from the Institute for Clinical Research, Kolding, Denmark.

The 54 women and 40 men were randomized to 5 g of rose hip powder per day or matching placebo. Those who were using NSAIDs were advised to continue with the same dose throughout the trial, but they were encouraged to reduce their intake of analgesics such as acetaminophen (paracetamol) and opioids after the first 3 weeks of each study period.

The primary outcome measures were scores on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and consumption of analgesics during the treatment periods.

After 3 weeks of active treatment, WOMAC scores for joint pain declined from 33.7 to 29.4, which was a statistically significant reduction. After 3 weeks of placebo, scores increased from 33.7 to 35.3 (Scand. J. Rheumatol. 2005;34:302-8).

Similar, although nonsignificant, results were seen at 3 months.

The percentage of patients who experienced a reduction in their WOMAC joint pain scores after 3 weeks of the active treatment was significantly higher, at 82%, than after placebo, at 49%. This 82% response rate was higher than has been reported in most studies evaluating herbal therapies, according to lead investigator Dr. Kaj Winther, of the department of clinical biochemistry, Copenhagen County Hospital Gentofte.

The use of acetaminophen rescue medication declined by 40% among patients who reported using the drug. There also was a decrease in the use of opioid medications such as tramadol. The authors suggested that this decrease in use of analgesic medications may explain the finding that joint pain scores no longer showed statistical improvements at 3 months.

Advanced OA: The Norwegian Study

In another study, 100 patients with long-standing (2-12 years) OA who were on a waiting list for hip or knee replacement were randomized to 5 g of rose hip powder daily or placebo for 4 months. The primary outcome was hip or knee mobility; secondary outcomes included difficulties in performing activities of daily living, patients' overall assessment of effectiveness, and pain level. Four patients withdrew from the study.

Patients in the active treatment group showed significant improvements at 4 months in passive hip flexion, external rotation, and internal rotation, while those in the placebo group showed significant improvements in passive hip internal rotation but not in flexion or external rotation. Changes in passive flexion of the knee did not differ significantly between the two groups.

Patients in the active treatment group had significant improvements in several activities of daily living such as walking and getting in and out of a car, and had significantly greater pain relief, compared with the placebo group. At month 4, 64.6% (31/48) patients receiving rose hip powder had some pain relief, with some reporting almost total relief. In the placebo group, 56.3% (27/48) reported no pain relief, while 43.8% (21/48) had some degree of pain improvement (Curr. Ther. Res. 2003;64:21-31).

In the rose hip group, seven patients reduced their consumption of NSAIDs and none increased their intake. In the placebo group, four were able to reduce their use of NSAIDs and four increased their use.

Safety and Outlook

In the Danish study, seven patients in each group dropped out of the study. Side effects of rose hip treatment such as diarrhea and constipation were few and comparable with those seen with placebo. The investigators noted that tests on healthy volunteers and patients taking warfarin had shown no involvement or effects on platelet aggregation or on the arachidonic acid pathway, and suggested that this might explain the lack of adverse effects seen with drugs commonly used for OA.

In the Norwegian study, mild gastrointestinal distress in two patients in each group was the only adverse effect reported.

Long-term data are needed to ensure safety, however. Dr. Winther hopes to undertake longer studies and also to investigate rose hip powder as prophylaxis for OA in a large population over a period of 5-10 years.

In an interview, Dr. Winther said he had initially been skeptical about the treatment. Rose hips have long been a popular fruit in Scandinavia for their vitamin C content, he said.

"In my home, we would go out in the autumn and pick rose hips and use them in marmalade for their vitamin C. If you had told me it would help prevent a cold or the flu, I would have believed you, but if you said it would help pain from OA, I wouldn't have believed you. I heard about this for 5 years before I finally decided to do a trial," he said.

—Nancy Walsh