May Fill COX 2 Void

Diclofenac *from page 1*

sual analog scale, and after a 7-day washout period, the pain rating had to increase by 15 mm.

The study took place in 65 U.S. centers. The active gel or the vehicle was to be applied to the base of the thumb and to each digit, and rescue acetaminophen was permitted in doses up to 4 g/day for aches at sites other than the hand.

Three-quarters of the patients were women, mean age was 64 years, and mean body mass index was 28.

The primary efficacy outcome measures, assessed at weeks 4 and 6, were pain intensity during the previous 24 hours, total score on the Australian/Canadian (AUSCAN) Osteoarthritis Hand Index, which is a validated, self-administered questionnaire that assesses pain, disability, and joint stiffness in OA, and global rating of disease activity.

Statistically significant benefits were seen in the diclofenac gel group at weeks 4 and 6 on OA pain intensity and the AUSCAN index, and on global rating at week 6, compared with vehicle. (See chart.)

The treatment effect also was clinically meaningful, with differences in the total AUSCAN index of 6.3 mm and 7.1 mm at weeks 4 and 6, Dr. Altman wrote in a poster session.

Patients in the active treatment group took 0.9 500-mg acetaminophen tablets per day and patients in the vehicle group took 1.1 tablets per day.

The overall incidence of adverse events was slightly higher in the active treatment group, at 52%, compared with the vehicle group, at 44%, according to Dr. Altman of the University of California, Los Angeles. Most side effects were mild to moderate in intensity, he said.

Few adverse events led to discontinuation, with 6% and 2% of patients in the active treatment and vehicle groups, respectively, withdrawing for this reason. The most common adverse event leading to discontinuation was application-site dermatitis, which was seen in 0.5% of both groups.

Other common treatment-emergent adverse events were headache, back pain, and arthralgias. Gastrointestinal adverse events, most commonly diarrhea, were observed in 8% and 4% of the active treatment and vehicle groups, respectively.

Laboratory, physical examination, and vital sign observations were unremarkable.

The proportion of patients in the active treatment group who rated treatment as very good or excellent was 48%, which was significantly higher than the 37% of patients in the vehicle group who accorded the treatment this rating.

How topical diclofenac works in OA is not completely clear, Dr. Altman said in an interview. Studies have shown that the topical drug penetrates the skin and is seen at high levels in the subcutaneous tissues and synovium, with the concentration and persistence in the synovium being similar to orally administered diclofenac.

This local concentration is seen despite the very low systemic levels achieved with the topical diclofenac, even after a week at steady state, and so little of the drug reaches the circulation that systemic effects are unlikely, Dr. Altman said.

"Indeed, in a previous knee OA study where the drug was used on the signal knee only, the contralateral knee worsened, supporting a local effect that is proposed to be anti-inflammatory and antinociceptor," he said.

Nonetheless, like all nonsteroidal anti-inflammatory drugs, diclofenac sodium (Voltaren) gel carries a boxed warning on cardiovascular and gastrointestinal risks.

Topical diclofenac was recently approved by the Food and Drug Administration, and is expected to be available by prescription during the first quarter of 2008, he said.

"This will help fill the void left by the [cyclooxygenase-2 inhibitors], and will also be useful for the elderly, many of whom cannot take nonsteroidal anti-inflammatory drugs [NSAIDS]. Topical diclofenac does not affect the kidney, liver, heart, or stomach, as far as we know," he said.

The study was supported by funding from Novartis Consumer Health. Dr. Altman disclosed he has received research grants and consulting fees from Novartis. ■

Diclofenac Sodium Gel Offers Greatest Osteoarthritis Relief

	Mean decrease from baseline (100-mm visual analog scale)	
	Diclofenac	Placebo
Week 4		
Pain intensity	31	24
Total AUSCAN*	24	17
Global rating of disease	21	15
Week 6		
Pain intensity	34	27
Total AUSCAN*	26	19
Global rating of disease	23	16

*Australian/Canadian Osteoarthritis Hand Index.
Note: Based on a randomized study of 385 patients.
Source: Dr. Altman

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Pain Resolves Quickly

Needling *from page 1*

was injected to withdraw the calcium residue from the broken lesions. The next step is the injection of steroid in the subacromial/subdeltoid bursa. Recovery time was about 1 hour.

The researchers reported 1-year follow-up data for 2,018 patients.

A single treatment was enough to aspirate the calcification fully in 72% of patients. A second procedure was required in 24% of patients because they had more than one calcification. Overall, patients reported both immediate and long-term improvements in pain and mobility, compared with pain levels and mobility limitations prior to the procedure. The improvements were statistically significant, based on a visual analog scale to measure pain, and on a combination of objective and subjective tests of mobility, Dr. Sconfienza said.

In 4% of patients, either the calcification dissolved spontaneously prior to the procedure or the deposits had moved into the subacromial/subdeltoid bursa. The remaining 0.9% of patients had no resolution of symptoms because they had coexisting tendon tears. When calcifications are completely dissolved and the residue is removed, the calcifications do not recur and the residue can't migrate to the bursa, where it might cause bursitis, the researchers noted.

"This is a procedure that is easy to learn, and it is worth learning," Dr. Sconfienza said. "We wanted to reduce the costs of health care," he explained, and patients recover easily and inexpensively. Of course, not every patient's symptoms will be resolved with ultrasound-guided needling, and some patients may still require surgery, he said.

No complications were reported in any of the patients, except for an adverse reaction to steroids in one patient who was unaware that he had diabetes.

The procedure was clearly successful in this study, but it's difficult to say where it would fit into the armamentarium of treatments, which also includes extracorporeal shock wave therapy and ultrasound, said Dr. Russell D. White, professor of medicine in the Department of Community and Family Medicine at the University of Missouri–Kansas City School of Medicine, where he is director of the sports medicine fellowship program.

Dr. White added that in his experience, patients who present with this diagnosis have already had it for several months. By the time they have tried and failed anti-inflammatory medications and physical therapy they frequently start to feel better, he said in an interview. In most cases, the pain resolves on its own within 1-2 years from its onset regardless of the course of management.

None of the researchers had financial conflicts to disclose. ■

Botox Shot Relieved Osteoarthritic Shoulder Pain, Improved Function

BY DIANA MAHONEY
New England Bureau

BOSTON — A single botulinum toxin type A injection can decrease joint pain and improve function in patients with refractory shoulder osteoarthritis, Dr. Jasvinder Singh reported at the annual meeting of the American College of Rheumatology.

In a double-blind, randomized controlled trial involving 43 patients with moderate to severe shoulder arthritis pain, 21 patients were randomized to receive a single, intraarticular injection of botulinum toxin type A (Botox) and 22 patients were injected with a placebo.

Compared with baseline, the 28-day posttherapy pain levels in the treatment group were significantly lower than those reported in the placebo group, said Dr. Singh, staff physician at the Minneapolis VA Medical Center.

In particular, 38% of the patients who received the botulinum injection achieved a minimum 30% improvement in pain scores, compared with a 9% improvement among patients in the placebo group.

Preliminary animal and clincial studies have shown that neurotoxin injection for sustained analgesia is a promising approach to persistent joint pain, said Dr. Singh, noting that the agent may decrease pain by inhibiting vesicle release of neuropeptides—including substance P and calcitonin gene-related peptide—and by disrupting nociceptor function.

The current study assessed the efficacy of the neurotoxin in patients with chronic arthritis-associated shoulder pain who had failed to respond to corticosteroids or other pain medication and who were not candidates for shoulder arthroplasty.

All of the patients had a 6-month history of moderate to severe shoulder pain, which is categorized as greater than 4.5 (on a scale ranging from 0 to 10).

Patients randomized to the treatment intervention received a single injection of 100 units of botulinum toxin type A plus lidocaine, and patients in the placebo group received a single injection of saline plus lidocaine.

Patients were assessed using the Visual Analog Scale (VAS), a numeric rating scale (NRS) for day pain, and the Shoulder Pain and Disability Index (SPADI) pain subscale, said Dr. Singh.

Secondary outcomes included SPADI scores and the proportion of patients achieving clinically meaningful pain relief, defined as a minimum 30% improvement. At baseline, pain outcome variables between the intervention and placebo groups were comparable.

At day 28, the mean VAS pain score in the treatment group was 4.12, significantly lower than the mean 6.54 in the placebo group. Day pain, according to NRS and SPADI pain scores, was significantly improved in the treatment group.

The SPADI score was better at day 28 in the treatment group compared with that in the placebo group, with a trend toward significance, Dr. Singh said.

The investigators are analyzing the duration of the analgesic effect and the associated adverse effects.

The findings thus far provide "the initial proof of concept of effectiveness of botulinum toxin injection for relief of shoulder pain," Dr. Singh said, adding they need to be replicated in a larger, multicenter, randomized trial before the treatment can be recommended.

Dr. Singh reported having received travel funds for previous research projects from Allergan Pharmaceuticals, maker of Botox. The current study was funded by the Arthritis Foundation, the Mayo Clinic, and the Minneapolis VA Medical Center. ■