

Osteoarthritis Drugs Offer Little Real Pain Relief

BY BRUCE JANCIN
Denver Bureau

AMSTERDAM — None of the commonly used pharmacotherapies for pain relief in knee osteoarthritis offer clinically meaningful benefit, said Dr. R. Andrew Moore at a satellite symposium held in conjunction with the annual European Congress of Rheumatology.

"The reality is that the evidence shows the therapies we have at the moment are working statistically but not necessarily being as effective as we'd want. ... There's a whole series of interventions in osteoarthritis where there isn't much evidence of useful efficacy," commented Dr. Moore, professor of health sciences at the University of Wales Swansea.

A new metaanalysis conducted by investigators at the University of Bergen, Norway, included more than 14,000 patients with knee osteoarthritis in 63 randomized, placebo-controlled clinical trials evaluating oral and topical NSAIDs, acetaminophen, intraarticular corticosteroid injections, opioids, glucosamine sulfate, and chondroitin sulfate.

These therapies have received the highest level of recommendation in current European League Against Rheumatism guidelines for the management of knee osteoarthritis, noted Dr. Moore. Yet the metaanalysis showed that pain-relief benefits, compared with those of placebo, were limited to the first 2-3 weeks of treatment and were so small as to be below the minimal patient-defined threshold for clinically perceptible improvement.

"In view of the widespread use of pharmacological agents in [knee osteoarthritis] management, a discussion is needed to

clarify if the limited benefits and considerable costs can justify current recommendations," according to the Norwegian investigators (*Eur. J. Pain* 2006 May 6; DOI:10.1016/j.ejpain.2006.02.013).

The investigators found, for example, that the maximum efficacy of oral NSAIDs or opioids in patients with moderate to severe pain corresponded to a 10-mm greater reduction than with placebo on a 100-mm visual analog scale. Yet prior studies by other investigators have shown that knee osteoarthritis patients define a mean 19.9-mm reduction as the minimal clinically important improvement, and that a shift from "unchanged" to "slight improvement" in pain requires a mean 12.3-mm decrease.

The best performances among the studied treatments came from topical NSAIDs and steroid injections; however, neither offered meaningful pain relief after the first month.

Dr. Moore noted that the "dis-

appointing" findings of the new metaanalysis were entirely in keeping with the results of a study he and his colleagues presented at the EULAR congress. It involved 19,163 participants in 15 randomized osteoarthritis trials in the Pfizer Clinical Trials Registry evaluating various traditional NSAIDs and cyclooxygenase-2 inhibitors.

"The best we could do was get 60% of patients to have a 10-mm improvement on the pain visual analog scale, which isn't by any means a high threshold. That means 40% did not even achieve that low end point," Dr. Moore said at the satellite symposium sponsored by CombinatoRx Inc.

Chronic pain management, he stressed, is an exceedingly challenging matter.

"The one great success we've had in pain has been in cancer pain, where the WHO [World Health Organization] pain ladder has really made an enormous difference over the past 25 years," Dr. Moore asserted. "It's an over-



Shown are marked narrowing of the knee's medial compartment (left) and narrowing of the lateral compartment (right).

all package of care. Nobody yet has tried doing all this in a systematic way in other chronic painful conditions."

The results of the two large metaanalyses fit well with the clinical experience of discerning physicians, according to Dr. Tore

K. Kvien. "I don't mean that NSAIDs don't work in osteoarthritis. The data just show they're not as effective as we usually believe," noted the professor of rheumatology at the University of Oslo, Norway, and immediate past president of EULAR. ■

Survey Says: 40% of Patients Find Pain Management Doesn't Work

It's not just the randomized trials that are saying current drug therapies for osteoarthritis don't bring clinically meaningful pain relief—patients and their physicians have been registering the same complaint as well.

A recent major survey of chronic pain including more than 46,000 adult respondents in 15 European countries concluded 1 in 5 people experience pain of moderate to severe intensity that's present every day or nearly every day for at least 6 months, according to Dr. Moore.

Osteoarthritis is a leading cause of this chronic pain, he added.

Two thirds of survey respondents with chronic pain were taking prescription

medications for it. Overall, 40% characterized their pain management as inadequate and 60% had visited their physician about their pain 2-9 times in the past 6 months. Also, 19% had lost their job, and another 13% had changed work because of their pain (*Eur. J. Pain* 2006;10:287-333).

Investigators at Frenchay Hospital in Bristol, England, conducted a face-to-face survey with 504 British primary care physicians. Of those, 81% indicated that fewer than half of their affected patients experienced optimal control of chronic non-cancer-related pain symptoms, Dr. Moore said at the satellite symposium sponsored by CombinatoRx Inc.

Of the British primary care physicians,

60% expressed reservations regarding the efficacy of available therapies. The other major barriers cited to good control of chronic pain were treatment side effects and patient compliance (*Curr. Med. Res. Opin.* 2003;19:703-6).

Although CombinatoRx is engaged in developing new agents for the treatment of osteoarthritis and other chronic inflammatory diseases, Dr. Moore said he thinks the systematic use of additive combinations of current osteoarthritis pain medications has been a neglected and potentially rewarding area.

"We need pragmatic research of well-designed care pathways," the pain specialist argued.

Microfracture Puts 44% of High-Impact Athletes Back in Game

BY MIRIAM E. TUCKER
Senior Writer

Microfracture is an effective first-line treatment for knee articular cartilage lesions in athletes who participate in high-impact sports, Dr. Kai Mithoefer and associates reported.

Microfracture is a relatively simple technique in which penetration of the subchondral bone induces clot formation containing marrow-derived mesenchymal stem cells, which produce a mixed fibrocartilage repair tissue containing varying amounts of type II collagen. It has become a popular treatment option for knee articular cartilage lesions in athletes, due to its low associated morbidity and rapid postoperative rehabilitation time.

Data are limited, however, regarding its

outcome in athletes who perform high-impact sports with marked mechanical demands, said Dr. Mithoefer of Harvard Vanguard Orthopedics and Sports Medicine and Brigham and Women's Hospital, Boston, and associates (*Am. J. Sports Med.* 2006;34:1413-8).

The study population comprised 32 patients, mean age 38, with single cartilage lesions of the femur. Their mean symptom duration was 28 months. All had regularly participated in high-impact, pivoting sports, including basketball (14), tennis (13), football (9), downhill skiing (7), and soccer (5). All underwent microfracture arthroplasty performed by a fellowship-trained orthopedic surgeon. Seven patients with meniscus tears also received partial meniscectomy.

At a mean follow-up of 41 months (min-

imum 2 years), 21 (66%) of the athletes reported good or excellent results on the Brittenberg rating of knee function; significant improvements were seen on the activity-based Marx activity rating scale and Tegner scores. Improvements occurred in the activities of daily living scale in 71% of patients, on the Marx scale in 58%, and in Tegner scores in 72%. After an initial increase, however, declines in activity scores were observed in 15 athletes, Dr. Mithoefer and associates reported.

A total of 14 athletes (44%) were able to return to regular participation in their high-impact pivoting sports after microfracture. Functional outcome score increases were lower among those who did not return to the sport. Two-thirds of the patients who had been symptomatic for 12 months or less before microfracture were

able to return to their high-impact sport, compared with just 14% who had been symptomatic for more than a year before the procedure.

Athletes who received microfracture as first-line treatment were far more likely to return to their sports than were those who had had previous procedures, but concomitant meniscectomy did not have a significant impact on the ability to return to the sport.

Patients with lesions of 200 mm² or less were more likely to return than were those with larger lesions, but location of the lesion (medial femoral condyle, lateral femoral condyle, or trochlea) did not affect outcome.

No effect was seen for gender or lesion type on the athletes' ability to return to their high-impact sport. ■