Acupuncture's Benefits in Knee OA Are Sham

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

The placebo effect appears to account for most of the improvements associated with acupuncture for osteoarthritis of the knee, according to an analysis of nine trials.

But Eric Manheimer of the Center for Integrative Medicine at University of Maryland, Baltimore, and his associates also appeared to identify at least a small biologic effect of the procedure, since patients who received genuine acupuncture in sham-controlled trials experienced some short-term improvements in both pain and function.

Still, Mr. Manheimer, field administrator in the complementary medicine program concluded, "It is too soon to recommend acupuncture as a routine part of care for patients with osteoarthritis."

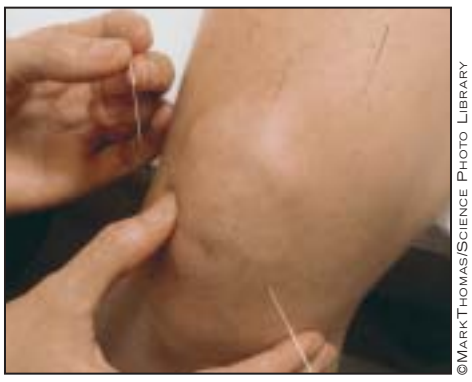
The analysis included 11 randomized controlled trials conducted from 1999 to 2003 and comprised more than 1,000 patients with knee osteoarthritis. Four studies compared acupuncture with wait list. The other seven studies included a sham treatment. Nine of the 11 studies included enough outcomes data to be included in the pooled analysis (Ann. Intern. Med. 2007;146:868-77).

Acupuncture, as compared with the sham control, provided some improvements in pain and function, both in the short term and at 6 months, but these were deemed clinically irrelevant.

Compared with wait-listed patients, those who received acupuncture reported clinically relevant improvements in pain and function, which were sustained at 6 months.

The sham-controlled trials all used different sham procedures, including a combination of penetrating and nonpenetrating needles; needles inserted away from acupuncture points; and patch electrodes delivering current.

This made it difficult to decipher the treatment response, since it was impossible to tell how many patients receiving the various sham treatments truly believed they could be getting real acupuncture. Additionally, two sham protocols involving the use of penetrating needles placed away from acupuncture points were judged possibly to have exerted some biologically active effect.



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In Western medicine, it is believed that the needles stimulate endorphins.

The observation of any improvement, however clinically irrelevant, suggested that acupuncture might be a biologically active procedure, according to the authors. They cautioned, however, that the placebo response probably plays a large role. "The fact that both the acupuncture and sham groups reported greater improvements than [did] those of the usual care control groups suggests that acupuncture may elicit a greater placebo effect … than usual care therapies."

The study may have been limited by the possibility that wait-listed patients were given inaccurate assessments of their actual response to care.

"Patient expectations that acupuncture will work may also affect those on a waiting list. By having to wait for a treatment that they believe is effective, patients waiting for acupuncture may have been disappointed by the delay, which may influence their ratings of subjective outcomes while waiting."

Several large controlled trials are still ongoing, and at least one additional trial has been completed but remains unpublished. The results of these studies may further elucidate what role, if any, acupuncture may have in the treatment of knee osteoarthritis, the researchers noted. ■

Cartilage Damage in Knee OA Is Not a Given

Smoking appears to contribute to the development of knee cartilage loss and defects in individuals with a family history of knee osteoarthritis (OA), according to the results reported by Dr. Changhai Ding and associates of the University of Tasmania in Australia.

In this study the knee cartilage of 345 relatively young individuals (the average age was 45 years) were measured at baseline and again 2.3 years later, and their risk factors were assessed.

Of the 162 persons with at least one parent with severe primary knee OA, 40 current smokers had greater loss in medial and lateral tibial cartilage volumes (beta = –2.20% and –1.45%. respectively) than did 47 former smokers and 75 never-smokers, after adjusting for confounding factors in a logistic regression analysis. Pack-years of smoking were also significantly associated with changes in cartilage volume (Arthritis Rheum. 2007;56:1521-8).

Dr. Ding and associates did not find a similar relationship between smoking status and knee OA measures in 163 individuals with no family history of knee OA.

The only factor significantly associated with smoking status in control individuals was change in lateral tibiofemoral cartilage volume.

"This provides evidence for a gene-environment interaction in the etiology of knee OA," the investigators wrote.

Among those with a family history of knee OA, being a current smoker increased the risk of developing medial tibiofemoral cartilage defects by nearly fivefold during the study period. Similarly, a positive family history increased the risk of lateral tibiofemoral cartilage defects threefold.

The risk increases among heavy smokers (at least 20 pack-years) versus never-smokers were 10-fold and 13-fold, respectively.

The interaction among smoking status, family history of knee OA, and cartilage effects remained significant in regards to change in medial tibial cartilage volume and increases in cartilage defects, both medial and lateral, even after adjusting for potentially confounding factors.

In the overall group, the prevalence of knee pain was higher among current smokers (41%) than it was among former smokers or never-smokers (33%), regardless of family history.

There was no overall association between smoking status and baseline tibial cartilage volume or prevalent tibiofemoral cartilage defects.

—Melinda Tanzola

New NSAID Delivery Technique Goes Deep to Effectively Ease Knee OA Pain

BY FRAN LOWRY
Orlando Bureau

A new technique for delivering an old nonsteroidal anti-inflammatory drug is just as effective as oral celecoxib for relieving the pain of knee osteoarthritis, German researchers report.

The NSAID ketoprofen, approved in both the United States and Europe, when combined in a gel that is capable of penetrating the skin directly to arthritic joints, was significantly better than placebo and comparable with celecoxib in relieving pain associated with an acute flare of knee osteoarthritis. Moreover, it did so without entering the systemic circulation, said Dr. Matthias Rother, head of research and development of IDEA AG, Munich, Germany, and colleagues.

The toxicities of systemic NSAID treatment are well known, and the newer COX-2 inhibitors are associated with elevated cardiovascular risks. Hence, the need for safer therapies, the investigators wrote.

The new technology, called Transfersome, is a special gel made up of nanoparticles too large to be absorbed into the microcirculatory barrier of the skin, Dr. Rother said in a telephone interview.

Numerous gel and cream NSAID preparations are available in Europe. All work by diffusion, with the drugs absorbed systemically when they are applied to the skin. But when an NSAID, in this case ketoprofen, is mixed with the nanoparticle gel, it is able to penetrate into deep muscle and joints and be released. The mixture of ketoprofen and Transfersomes is called IDEA-033, Dr. Rother said.

"Transfersomes are ultradeformable carriers loaded with an active substance and applied epicutaneously in an aqueous suspension. Once they are on the skin, the water in the suspension begins to evaporate, and this draws the carriers containing ketoprofen through the skin barrier to the specific target areas," he explained.

To compare this form of ketoprofen delivery with celecoxib and placebo in the relief of knee OA, the investigators randomized patients for at least 6 months to either 110 mg epicutaneous ketoprofen in 4.8 g Transfersome plus oral placebo (138 patients), 100 mg oral celecoxib plus placebo gel (132 patients), or both placebo formulations (127 patients) twice a day for 6 weeks.

Efficacy was assessed by measuring the changes in the Western Ontario and McMaster Universities (WOMAC) Index of Osteoarthritis pain subscale, physical function subscale, and patient global assessment (PGA) of response from baseline to the end of the study, in the index knee.

Overall, the mean WOMAC pain subscale scores were reduced by 18.2 in patients who received IDEA-033, by 20.3 in patients who received celecoxib, and by 9.9 in those patients who received placebo.

The mean physical function subscale score was reduced by 14.6 in patients who received IDEA-033, 16.6 in those receiving celecoxib, and 10.2 in the placebo group.

The mean PGA of response scores were 1.8 in the IDEA-033 group, 1.7 in the celecoxib group, and 1.3 in the placebo group.

The differences in change between IDEA-033 and placebo were statistically significant for pain subscale ($P = .0041$) and PGA of response ($P = .0015$).

Gastrointestinal adverse events with IDEA-033 were similar to placebo, the investigators wrote. No GI bleeding occurred. The rate of nonserious GI adverse events for IDEA-033, at 9.4%, was similar to placebo and numerically lower than for celecoxib (13.6%).

One patient treated with celecoxib had a myocardial infarction, one patient treated with placebo had angina, and no serious cardiovascular events occurred in patients treated with IDEA-033.

The IDEA-033 patients had more erythema and more skin irritations than the group receiving placebo gel, the investigators added (ARD Online First, published online by the British Medical Journal on March 15, 2007, as 10.1136/ard.2006.065128).

Systemic exposure in the IDEA-033 group was between 1% and 5%, compared with that of celecoxib, Dr. Rother said. ■