Some osteoarthritis treatments are less effective than previously thought, judging from findings from a review of research conducted since 2006. The goal of the update of published evidence is to determine whether the current Osteoarthritis Research Society International’s (OARSI) recommendations for the treatment of OA, published in 2008, needs to be modified. After reviewing this update and collecting feedback, the OARSI Treatment Guidelines Committee will determine whether changes are needed in 2010.

Acetaminophen use and surgical lavage and debridement were among the therapies that may be falling out of favor to treat knee and hip OA, but evidence supporting weight reduction is on the upswing, said Dr. Weiya Zhang, a rheumatologist at the University of Nottingham (England), and colleagues.

The researchers identified 64 systematic reviews, 266 randomized controlled trials, and 21 economic evaluations related to hip and knee OA that were published between January 2006 and January 2009. “Of the 51 modalities of treatment addressed in the OARSI recommendations, 35 have now been systematically reviewed with 16 new or updated systematic reviews in the last 3 years,” the researchers wrote (Osteoarthritis Cartilage 2010 Feb. [Epub doi: 10.1016/j.joca.2010.01.013]). The reviewers assessed the best available evidence for effect size (ES) with 95% confidence intervals for improving function and relieving pain and stiffness associated with OA.

The new evidence for non-pharmacological therapies included several studies supporting weight reduction. Pooled data from two new systematic reviews showed improvements in pain (ES, 0.20) and physical function (ES, 0.23) after an average weight loss of 6.1 kg (approximately 13 pounds). The ES for pain relief for hip and knee OA were not significantly changed for acupuncture, education, exercise, and self-management.

New research on electromagnetic therapy showed a relatively small improvement in ES (0.13) and no significant effect on pain reduction (ES, 0.16), in contrast to data from a 2002 Cochrane review showing an ES of 0.77 that almost led to electromagnetic therapy’s inclusion in the 2008 OARSI guidelines (it was not included). The review also yielded changes in evidence for pharmacological treatments for OA, notably for acetaminophen.

A review of five new studies of acetaminophen for knee OA showed no significant reductions in effect size for pain relief (pooled ES, 0.14). Other recent studies showed an increased risk of hospitalization due to gastrointestinal, peptic ulceration, and bleeding when acetaminophen doses of more than 3 grams per day were used to treat OA (hazard ratio 1.20). No data from recent studies identified significant changes in the risks and benefits of oral or topical nonsteroidal anti-inflammatory agents, diacerein, or interarticular corticosteroid injections for treating OA.

For surgical treatments, pooled results showed no benefit for lavage, debridement, or a combination of the two for treating OA compared with placebo. Effect sizes for pain relief, improvement in function, and reduction in stiffness were 0.21, 0.12, and 0.05, respectively.

For alternative medicine treatments, recent studies showed a reduced effect size for pain relief of OA with treatments including glucosamine sulphate, chondroitin sulphate, intra-articular hyaluronidase, and avocado soybean unifomposibles. Recent studies of these treatments also showed increased evidence of publication bias and heterogeneous outcomes.

The results of the review were limited by their being continuously updated, making it difficult to make comparisons across treatments when meta-analyses and systematic reviews had different inclusion and exclusion criteria than randomized controlled trials.

The researchers noted that there is a need for a more continuously updated, comprehensive, and coherent database of well-characterized trials of all modalities of treatment of OA.”

But they emphasized that treatment guidelines must be based on the best evidence, not simply on updated cumulative evidence.

Data Show Weight Loss Cuts Osteoarthritis Pain

BY HEIDI SPLETE

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New Osteoarthritis Measures May Encourage New Therapies

BY BRUCE JANCIN

SNOWMASS, Colo. — The Food and Drug Administration appears to be poised to redefine osteoarthritis progression as its required pivotal outcome measure in clinical trials aimed at earning approval for disease-modifying osteoarthritis drugs.

Since 1999, the FDA has defined osteoarthritis (OA) progression as evidence of joint-space narrowing on serial x-rays of the knee or hip. It’s an antiquated and unreliable metric that has probably resulted in nonapproval of some therapies that truly are disease modifying, and it has caused pharmaceutical companies to steer clear of OA and focus their research and development efforts elsewhere, Dr. Joanne M. Jordan said at a symposium sponsored by the American College of Rheumatology.

A critical reappraisal of the definition of OA progression and how best to evaluate drugs, devices, and biologics for the prevention and treatment of OA is in the works. It’s the culmination of a 2-year OARSI (Osteoarthritis Research Society International) initiative that was carried out in partnership with industry and patient organizations at the FDA’s request. The massive report will be submitted to the FDA in the next few months, and then published as a series of papers in the journal Osteoarthritis and Cartilage, according to Dr. Jordan, chief of rheumatology, allergy, and immunology, and director of the Thurston Arthritis Research Center at the University of North Carolina, Chapel Hill.

“We think that we’ll be able to convince the FDA, sooner rather than later, that maybe joint-space narrowing on x-ray is not the best way to decide if a treatment is disease modifying or not. What we’re hoping to accomplish is to change hearts and minds—not to look at osteoarthritis just as the person who comes in with an end-stage knee, or even moderate radiographic osteoarthritis. Rather, we hope to be able to predict these developments at an earlier point in time with improved technologies such as MRI, functional MRI, and biomarkers. We want to be able to screen the high-risk phenotype and then to be able to intervene to avoid or delay osteoarthritis,” explained the rheumatologist, who chaired the OA prevention/reduction working group as part of the larger OARSI initiative.

Joint-space narrowing on x-ray is a poor pivotal measure of OA progression. It’s a laborious, error-prone measurement with poor reproducibility. Changes may not be evident for at least 2 years. As a result, clinical trials have a high dropout rate and thus must be large and very expensive.

Furthermore, joint-space narrowing on x-ray probably isn’t even a good surrogate for OA progression. Originally, the FDA adopted it as its yardstick under the assumption that it reflects cartilage loss, which can’t be seen directly on x-ray, but it’s now clear from MRI studies that joint-space narrowing can also be caused by meniscal extrusion, bone-marrow edema, and inflamed synovium.

In the future, OA clinical trials will feature a more fine-nomed preselection of study participants in order to maximize the likelihood of positive results, Dr. Jordan predicted. Also coming will be the eagerly anticipated results of clinical trials of two promising potential disease-modifying OA agents: calcetin and vitamin D.

The vitamin D study is a 2-year, double-blind, placebo-controlled, randomized trial involving 2,000 IU of vitamin D per day. It has two major outcomes: change in cartilage volume as assessed by MRI, functional MRI, and biomarkers. The results of the review were limit-