Weight Loss Helps Modify Cartilage Structure

ARTICLES BY BRUCE JANCIN

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — Weight loss in obese patients with knee osteoarthritis has been shown for the first time in a prospective study to have beneficial structure-modifying effects upon knee cartilage.

This finding has major public health implications. Weight loss now becomes the only therapy ever shown to have salutary structural effects on knee articular cartilage. No drug has yet been shown to have such a benefit, said presenter Dr. Ana Ananda, a rheumatologist at the University of Sydney.

"We found that with a mean weight loss of 9%, which is fairly achievable… we can make meaningful, clinically important differences in terms of cartilage structure," she said in an interview. Focusing on weight loss might "prevent or delay the need for knee replacement down the line."

She presented the results of MRI studies conducted before and 12 months after a weight-loss intervention in a group of patients with knee OA and a body mass index greater than 35 kg/m^2.

Patients who achieved at least a 9% reduction in body weight at the 1-year mark had a significantly lower rate of loss in cartilage thickness in the medial compartment, vs. those who had weight gain or lesser weight loss at follow-up.

Moreover, patients with significant weight loss also showed improvement in cartilage quality, as reflected in increased proteoglycan content seen on delayed gadolinium-enhanced MRI. Evidence from other studies suggests that loss in proteoglycan is perhaps the earliest OA-induced change in cartilage, and might be potentially reversible with early intervention, she said.

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In all, 78 patients had baseline and follow-up measurements of knee cartilage thickness as a proxy for cartilage volume. Of these, 28 underwent bariatric surgery involving laparoscopic adjustable gastric banding with a mean 1-year weight loss of 17.5%, vs. the mean 2.5% weight loss in patients who participated in a dietary weight-loss program.

The MRIs showed a graded inverse relationship between the percent weight loss and the rate of loss in cartilage thickness in the medial compartment, through which most of the load on the knee joint is transmitted. This relationship remained significant in a multivariate analysis adjusted for age, sex, baseline BMI, and knee range of motion.

The MRI studies were done in 54 patients. The 24 with surgical weight loss had a mean 56-msec increase in delayed gadolinium-enhanced MRI index in the medial compartment during 1 year of follow-up, reflecting a substantial increase in cartilage proteoglycan content. In contrast, the 30 patients with lesser, nonsurgical weight loss had a mean 23-msec decrease in the index. In a multivariate analysis, the correlation between percentage of body weight loss and increase in the index remained significant. For every 10% loss in body weight, a patient's cartilage proteoglycan index improved by about 40 msec.

A second study presented at the congress concluded that substantial weight loss has a chondroprotective effect. The study assessed changes in pain scores, joint biomarkers, and markers of systemic inflammation as outcomes.

Dr. Pascal Richette of Lariboisière Hospital, Paris, reported on 44 obese patients with knee osteoarthritis who underwent bariatric surgery, with a resultant 20% decrease in BMI.

At 6 months post surgery, the group's mean osteoarthritis pain scores had dropped from a baseline of 50 out of a possible 100 points to 24.5 points. This was accompanied by significant functional improvement as measured on the WOMAC (Western Ontario and McMaster Universities) osteoarthritis index subscales.

Serum levels of N-propeptide of type IIA procollagen, a biomarker of cartilage type II collagen synthesis, increased by 32%. Serum levels of cartilage oligomeric matrix protein, a biomarker for cartilage degradation, were down by 36%. Serum levels of interleukin-6 decreased by 26% from baseline, high-sensitivity C-reactive protein was down by 46%, and fibrinogen decreased by 5%, all indicative of reduced systemic inflammation. In addition, serum lipids and insulin resistance were significantly reduced. ■

Disclosures: *Dr. Richette and Dr. Ananda reported having no conflicts of interest.*

Osteoarthritis Patients Are at Substantial Cardiovascular Risk

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — Cardiovascular risk profiles in osteoarthritis patients are, on average, comparable to those in patients with rheumatoid arthritis, according to a Dutch study.

In recent years, much attention has been focused on the elevated risk of cardiovascular events in patients with rheumatoid arthritis, as a consequence of their increased prevalence of the standard cardiovascular risk factors coupled with a further boost in risk resulting from the chronic systemic inflammatory disease process. The cardiovascular risk associated with osteoarthritis has received far less attention, Dr. Inger Meek said.

She determined the cardiovascular risk profiles of 285 consecutive rheumatoid arthritis patients and 112 consecutive osteoarthritis patients using the SCORE (Systematic Coronary Risk Evaluation) system, which is routinely employed in Europe in lieu of the Framingham risk score. The two groups were similar in terms of mean age and sex. The mean disease duration of the rheumatoid arthritis patients was 6.8 years.

In all, 18% of the osteoarthritis patients had a greater-than-10% estimated 10-year risk of a fatal cardiovascular event by SCORE, as did 15% of rheumatoid arthritis patients, according to Dr. Meek of the University of Twente in Enschede, the Netherlands.

Hypercholesterolemia was significantly more prevalent in the osteoarthritis patients (45%) than in the rheumatoid arthritis patients (29%).

The two groups did not differ significantly in terms of the other elements of SCORE (smoking status, systolic blood pressure, age, and sex).

The SCORE system, developed by the European Society of Cardiology, is based upon 3 million person-years of observation, and doesn't factor in body mass index, Dr. Meek noted. The prevalence of obesity is greatly increased in osteoarthritis patients. Thus, SCORE likely underestimates their cardiovascular mortality risk.

Recent evidence-based recommendations by the European League Against Rheumatism advise physicians to apply a 1.5 multiplication factor to the conventional cardiovascular mortality risk SCORE in rheumatoid arthritis patients who meet two of three criteria: disease duration greater than 10 years, rheumatoid factor or anti–cyclic citrullinated peptide positivity, or extra-articular disease manifestations (Ann. Rheum. Dis. 2010;69:325-31). This is designed to account for the heightened cardiovascular risk imposed by a high degree of systemic inflammation.

The high percentage of osteoarthritis patients in this study with a greater-than-10% estimated likelihood of cardiovascular death within 10 years is of concern, Dr. Meek stressed, because the prevalence of osteoarthritis is expected to mushroom as a result of the graying of the baby boom generation.

Dr. Johannes W.J. Bijlsma of the University Medical Center Utrecht (the Netherlands) commented that the take-home message of Dr. Meek's study is that physicians need to be aware that not only rheumatoid arthritis patients but also osteoarthritis patients are at increased cardiovascular risk. ■

Disclosures: *Dr. Meek declared that she had no financial conflicts.*

Oral Tasocitinib Shows Continued Promise in RA

FROM THE ANNUAL EUROPEAN CONGRESS OF RHEUMATOLOGY

ROME — The investigational oral Janus kinase 3 inhibitor tasocitinib, in combination with methotrexate, showed impressive dose-dependent efficacy for rheumatoid arthritis in a phase II study.

If the results of the ongoing phase III trials are positive, tasocitinib could become the first JAK3 inhibitor licensed for a nononcology indication, and the first new oral disease-modifying antirheumatic drug for RA in more than a decade.

In the phase II RA study presented by Dr. Yoshiya Tanaka, 136 patients with active disease (defined as six or more tender and swollen joints and a C-reactive protein level greater than 7 mg/dL) despite standard-dose methotrexate were randomized to add-on oral tasocitinib at 1, 3, 5, or 10 mg b.i.d. in double-blind fashion for 12 weeks.

Tasocitinib demonstrated a rapid, strong effect; significant benefit was seen within the first week, noted Dr. Tanaka, chair of internal medicine at the University of Occupational and Environmental Health in Kitakyushu, Japan.

In patients with a lower baseline DAS (Disease Activity Score) of 5.1 or less, the tasocitinib 1- and 3-mg b.i.d. arms showed a mean 1.5-point drop from baseline, whereas the 5- and 10-mg b.i.d. groups had decreases of 2.2 and 2.3 points, respectively, compared with a 0.7-point reduction with placebo.

In patients with a high baseline DAS (greater than 5.1), the mean reductions over 12 weeks of treatment with 1, 3, 5, and 10 mg b.i.d. were 2.3, 2.4, 2.8, and 3.4 points, respectively. But only the 10-mg b.i.d. dose was significantly better than placebo in achieving the key end points of DAS remission (a score lower than 2.6) and low disease activity state (a DAS of 3.2 or less). By week 12, roughly 70% of patients with a high baseline DAS and 90% of those with a lower baseline DAS had achieved LDAS on 10 mg b.i.d. of tasocitinib, compared with 10% and 20% of those on placebo. ■

Disclosures: *The study was funded by Pfizer Inc. Dr. Tanaka disclosed that he serves as a consultant to Pfizer and is on the speakers bureaus for Mitsubishi Tanabe Pharma Corp. and several other Japanese pharmaceutical companies.*