Questions Linger About Steroid Injections and Knee Arthritis

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Patients with mild to moderate knee osteoarthritis (KOA) who used intra-articular corticosteroids (IACs) experienced substantially faster disease progression than those in a matched group who had not received IACs.

However, experts caution that the difference in progression rates might reflect underlying differences that influenced the decision to treat with IACs. Thus, the analysis, published online January 28 in *Osteoarthritis and Cartilage*, adds to the literature but does not resolve previous questions over potential detrimental effects of IACs on cartilage.

"In this cohort study, IACs were associated with significant acceleration of knee OA progression, assessed as KL [Kellgren and Lawrence] grade worsening (ie, an increase in KL grade by ≥1 grades or having a knee replacement) or JSW [joint space width] worsening (ie, a decrease in JSW by ≥0.7 mm or having a knee replacement)," lead author Chao Zeng, MD, PhD, told *Medscape Medical News.*

"However, since our findings were based on an observational study, we could not rule out the potential residual confounders," continued Zeng, a postdoctoral fellow in the Division of Rheumatology, Allergy, and Immunology, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, and associate professor, Department of Orthopaedics, Xiangya Hospital, Central South University, Hunan, China.

He acknowledged being "a little bit surprised" about the results. "However, our findings agree with a trial published in *JAMA* recently, which showed that repeated IACs resulted in greater loss of cartilage volume compared with intra-articular saline. In that trial, repeated IACs were administered to participants during the study period regardless of the flare of pain or inflammatory signs, which are the usual indications for such injections in clinical practice. Thus, a pragmatic trial is needed."

David T. Felson, MD, director of clinical epidemiology and professor of medicine and public health, Boston University School of Medicine, Massachusetts, agreed that a randomized trial is needed. He told *Medscape Medical News* that, on the basis of these data, he is not convinced that IACs accelerate joint deterioration.

"Persons undergoing intra-articular corticosteroid injection have more severe pain and worse disease than persons not undergoing this procedure," Felson said. "Despite [the authors'] attempts to adjust for these differences, they can't really be adjusted for. The pain measure 'adjusted for' was drawn after the steroid injection for those who underwent the shot and therefore underestimates their pain at the time of the shot. Pain is a main driver of OA outcomes."

A Matter of Debate

Zeng and colleagues examined the relation of IACs to radiographic KOA progression in a "real-world" setting using data from patients with mild to moderate KOA who were enrolled in the Osteoarthritis Initiative, a natural history study. The cohort includes 1329 patients with symptomatic tibial-femoral KOA who have osteophytes and who experience frequent symptoms in one or both knees. Among those, the researchers identified 148 patients for whom IACs were initiated during follow-up and matched them with 546 patients who did not receive IACs during a 4-year period.

Patients for whom IACs were initiated had three to four times the risk for KL grade worsening vs the comparison group, who did not receive IACs (hazard ratio, 3.02 for IAC initiation and 4.67 for continuous IACs).

The authors write, "In this cohort study of knee ROA [radiographic osteoarthritis], we found that IACs may be associated with an increased risk of knee ROA progression, and the risk appeared larger with continuous IACs use. These results agree with the recent RCT [randomized controlled trial], which found that repeated IACs led to larger cartilage volume loss, compared with intra-articular saline. Our findings were independent of the effect of the major confounders, and remained stable in various sensitivity analyses, suggesting that the initiation of IACs and continuous IACs may have a detrimental effect on knee ROA progression."

Felson disagreed. He said, "The study has no implications for treatment. Intra-articular steroids are effective treatments for

pain in osteoarthritis. They are among the most effective treatment modalities that we have. Of two large randomized trials testing intra-articular steroids and examining cartilage loss or joint space loss, one showed no effect of steroids vs placebo, and the other [referred to by Zeng and colleagues] showed a trivial effect that was not clinically important. These results are the ones that are most likely to be true."

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