CLINICAL UPDATE

Glucosamine: A potential disease-modifying agent in osteoarthritis?

Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet* 2001;357:251-6.

Background: Osteoarthritis is a prevalent disease and a major cause of pain and disability. Conventional treatments aim to relieve pain and to improve function, but none is known to alter the course of the disease. Glucosamine is a natural constituent of glycosaminoglycans in joint cartilage and appears to alleviate osteoarthritic pain. However, its role as a disease-modifying drug for osteoarthritis is speculated but unproven.[1]

Question: In patients with osteoarthritis of the knee, does glucosamine sulfate reduce progressive joint damage and symptoms?

Design: This randomized controlled trial was conducted in a university hospital clinic in Belgium. Eligible patients were those over 50 years of age with osteoarthritis of the knee that met the diagnostic criteria of the American College of Rheumatology. Patients with most other diseases were excluded. The active treatment consisted of 1500-mg tablets of glucosamine sulfate, produced commercially by the company that sponsored the study. Patients were randomly assigned to receive 1 tablet of either glucosamine or placebo daily for 3 years. Rescue analgesia with acetaminophen or NSAIDs, or both, was permitted. The primary outcome measures were joint-space narrowing in the affected knee and symptom relief. The width of the joint space was assessed using 2 methods: visually by a radiologist unaware of the patient's treatment assignment, and automatically by means of a computer analysis of digitized radiographs. A validated index addressed symptoms of pain, stiffness and disability using visual analogue scales. Secondary outcomes included treatment tolerability and safety.

Results: A total of 212 patients were enrolled in the study (106 assigned to each group). The baseline characteristics were similar for the 2 groups. The mean age of the patients was 66 years, and about 80% were women. Only 71 patients (67%) in the glucosamine group and 68 (64%) in the placebo group completed the 3 years of follow-up. Intention-to-treat analysis revealed that the mean joint-space narrowing was –0.06 mm in the glucosamine group and –0.31 mm in the placebo group, for a difference of 0.24 mm (95% confidence interval [CI] 0.01 to 0.48, $p = 0.043$). The minimum joint-space narrowing was –0.07 mm with glucosamine, as compared with –0.40 mm with placebo, for a similar difference of 0.33 mm (95% CI 0.12 to 0.54, $p = 0.003$). A preservation of about 0.3 mm in joint-space width over 3 years may not seem clinically significant, but the authors cite a rate of natural joint-space narrowing of –0.1 mm per year in other studies. The change in overall symptom score using visual analogue scales was –11.7% with glucosamine and 9.8% with placebo, for a difference of –21.6% ($p = 0.02$). Glucosamine was well tolerated.

Commentary: Although this was described as a double-blind study, there were no data on the success of allocation concealment, a criticism of earlier studies of glucosamine.[2] If patients knew their treatment assignment, then the subjective perception of symptom relief with glucosamine may have been exaggerated. The measurements of joint-space narrowing, however, were objective and raise the possibility of a disease-modifying effect.

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Practice implications: Glucosamine sulfate appears to be well tolerated and may have a role as a disease-modifying agent in the treatment of osteoarthritis of the knee. More studies are needed to determine the true magnitude of benefit of glucosamine sulfate, its optimum dose and the role of other putative chondroprotective agents such as chondroitin. — *Benjamin H. Chen*

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References

1. Walker-Bone K, Javaid K, Arden N, Cooper C. Medical management of osteoarthritis. *BMJ* 2000;321:936-40.
2. McAlindon TE, LaValley MP, Gulin JP, Felson DT. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA* 2000;283:1469-75.