

# Glucosamine Sulfate Ineffective for the Treatment of Hip Osteoarthritis

Rozendaal R, Koes BW, van Osch G, et al. Effect of glucosamine sulfate on hip osteoarthritis: a randomized trial. *Ann Intern Med* 2008;148:268–77.

## Study Overview

**Objective.** To determine whether glucosamine sulfate is effective for reducing symptoms and radiographic progression of hip osteoarthritis.

**Design.** Randomized, blinded, placebo-controlled trial.

**Setting and participants.** Participants from Rotterdam, Netherlands, were recruited by their general practitioners if they met American College of Rheumatology criteria for hip osteoarthritis during a screening examination. Individuals were excluded if they had or were awaiting a hip replacement, were already taking glucosamine, were unable to fill out questionnaires, had very severe osteoarthritis (Kellgren and Lawrence score = 4), or had renal disease, diabetes, liver disease, or any other disabling condition that would limit their ability to visit the study site. Eligible participants were randomized to glucosamine sulfate 1500 mg daily or matching placebo for 2 years.

**Main outcome measures.** Western Ontario and McMaster Universities Osteoarthritis Index 3.1 (WOMAC) pain and function scores and joint space narrowing at 24 months. Secondary outcome measures included WOMAC pain, function, and stiffness scores at 3, 12, and 24 months; overall stiffness (based on WOMAC score); pain measured by a visual analogue scale; and pain medication use.

**Main results.** Of 386 patients screened, 222 were randomized (111 patients in each group). Most of those not randomized

chose not to participate in the study. 20 patients were not fully adherent to therapy (8 in the glucosamine group, 12 in the placebo group), and 20 patients underwent total hip arthroplasties during the course of the trial. At 24 months, there was no significant difference in WOMAC scores or improvements in joint space narrowing between the glucosamine and placebo groups. There also were no differences between groups in secondary outcome measures. Subsequent adjustments for nonadherence and sensitivity analyses did not substantially alter the results.

**Conclusion.** Glucosamine sulfate was ineffective for treating symptoms associated with hip osteoarthritis and did not alter joint space narrowing over 2 years.

## Commentary

In the United States, glucosamine is a commonly used over-the-counter supplement for osteoarthritis. Prior research on the effectiveness of glucosamine has been mixed. A Cochrane Collaboration meta-analysis of glucosamine for the treatment of osteoarthritis (mostly involving the knee) found a small benefit when compared with placebo; however, less than half of the studies showed a significant effect [1]. Since that meta-analysis was published, several studies have evaluated the efficacy of glucosamine. Clegg et al [2] recently conducted a large, multicenter, randomized controlled trial of 1583 patients with knee osteoarthritis. Participants were assigned to 1 of 5 arms: glucosamine hydrochloride, chondroitin sulfate, celecoxib, a combination of glucosamine/chondroitin, or placebo. This trial found no significant difference between

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the placebo group and any of the supplement groups (chondroitin or glucosamine alone or in combination) over 6 months except among patients with moderate to severe osteoarthritis. An accompanying editorial raised some concerns about the study by Clegg et al because of the use of glucosamine hydrochloride instead of glucosamine sulfate [3]. Another recently published randomized trial of 317 patients with moderate to severe knee osteoarthritis compared glucosamine sulfate or acetaminophen with placebo [4]. This study was funded by Rottapharm, the original manufacturer of glucosamine sulfate, and found a small but possibly clinically insignificant benefit of glucosamine compared with placebo over 6 months (there was no difference between acetaminophen vs. placebo).

Most studies to date have evaluated the efficacy of glucosamine in knee osteoarthritis, and this study by Rozendaal et al is the first to assess its effect on hip osteoarthritis. This study was adequately powered to evaluate a clinically relevant difference in WOMAC scores (a difference of  $\geq 10$  points) and improvements in joint space narrowing (change of 0.25 mm) between intervention and control groups, and baseline characteristics of the groups were equivalent (except for an imbalance between unilateral vs. bilateral disease). No differences in symptomatic or radiographic progression of hip osteoarthritis were found between the glucosamine and placebo arms.

The major limitation of this study was the nearly 10%

rate of total hip arthroplasty, which limits the availability of complete follow-up data. Only 15 patients were lost to follow-up by the end of the trial, and data were missing for 23 patients.

### Applications for Clinical Practice

Glucosamine sulfate was not effective for the treatment of hip osteoarthritis. As a result of these findings, it would be difficult to recommend glucosamine for the routine care of patients with hip osteoarthritis.

—Review by Jason P. Block, MD, MPH

### References

1. Towheed TE, Maxwell L, Anastassiades TP, et al. Glucosamine therapy for treating osteoarthritis. *Cochrane Database Syst Rev* 2005;(2):CD002946.
2. Clegg DO, Reda DJ, Harris CL, et al. Glucosamine, chondroitin sulfate, and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006;354:795–808.
3. Hochberg M. Nutritional supplements for knee osteoarthritis—still no resolution [editorial]. *N Engl J Med* 2006;354:858–60.
4. Herrero-Beaumont G, Ivorra JA, Del Carmen Trabado M, et al. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: a randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. *Arthritis Rheum* 2007;56:555–67.

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