Lack of Benefit of Glucosamine for Knee Osteoarthritis

McAlindon T, Formica M, LaValley M, et al. Effectiveness of glucosamine for symptoms of knee osteoarthritis: results from an internet-based randomized double-blind controlled trial. Am J Med 2004;117:643–9.

Study Overview

Objective. To determine the safety and effectiveness of glucosamine for symptoms of knee osteoarthritis.

Design. Double-blind, randomized, placebo-controlled trial with an intention-to-treat analysis.

Setting and participants. Participants were solicited through advertisements posted on the study center's (Boston University School of Medicine) Web site, and recruitment and outcome assessments were performed entirely through the internet. Inclusion criteria included age ≥ 45 years, self-reported use of analgesics for knee osteoarthritis on most days, and having at least 1 knee meet the American College of Rheumatology clinicoradiologic criteria for knee osteoarthritis. Participants were excluded if they had a knee intra-articular steroid injection within 60 days of baseline assessment, were currently using glucosamine or chondroitin, had arthroplasty in the study knee, participated in other clinical trials, or had an allergy to shrimp or shellfish. Inclusion and exclusion criteria were determined through both patients' self-report and medical record review.

Intervention. Participants allocated to the treatment arm received glucosamine. Initially this was in the form of a capsule containing on average 496 mg of glucosamine sulfate per capsule. Capsules were taken 3 times/day. Over the course of the study, the industry supplier of glucosamine changed and subjects in the intervention group received glucosamine hydrochloride 1.5 g in powder form. The powder was taken once daily. Both forms of the intervention had corresponding matching placebos.

Main outcome measures. Participant responses on the pain subscale of the Western Ontario and McMaster University Osteoarthritis Index (Likert version). This instrument has been validated and consists of 24 items assessing 3 different subscales (pain, stiffness, and function). A secondary outcome was change in analgesic use. Participants were prompted periodically to report any adverse events.

Main results. 205 individuals were randomized to either glucosamine (n = 101) or placebo (n = 104). In the glucosamine group, 75% (n = 76) of participants completed the 12-week trial compared with 74% (n = 77) in the control group. At baseline, fewer women were randomized to the glucosamine group versus the control group (57% versus 71%; P = 0.04). Participants randomized to the glucosamine group were also less likely to be using nonsteroidal anti-inflammatory drugs (75% versus 90%; P = 0.03) and had lower body mass indices (mean BMI, 31.0 kg/m^2 versus 34.1 kg/m^2; P = 0.01). Over the course of the trial, pain scores decreased in both groups. There was no statistically significant difference in the mean change of outcome scores between the 2 study groups (pain subscale mean change, –0.5 [95% confidence interval {CI}, –1.7 to 0.7]; P = 0.41; overall score mean change, 0.6% [95% CI, –4.0 to 5.2]; P = 0.81). These results did not change after adjusting for sex, BMI, and baseline score. Subgroup analysis also revealed no significant differences between groups when stratified by radiographic severity or analgesic requirements. Adverse events were similar between the 2 groups.

Conclusion. Glucosamine does not appear to be efficacious in reducing pain associated with knee osteoporosis over a 12-week period.

Commentary

Osteoarthritis of the knee is a common and disabling condition [1]. Even though total knee replacement is indicated in certain cases of osteoarthritis [2], most patients are managed primarily through analgesic therapy. Much excitement was generated when early studies suggested that glucosamine might not only result in better pain control [3], but could actually be a disease-modifying agent [4]. Subsequent trials evaluating glucosamine have had mixed results. This study by McAlindon et al adds to the growing consensus that glucosamine is probably not more efficacious than placebo at treating osteoarthritis symptoms. Another notable achievement of this study is that it was conducted almost entirely over the internet.

Although investigators demonstrated the feasibility of a clinical trial conducted over the internet, this design limits the validity of their overall findings. Most importantly, the

trial was likely underpowered to detect small differences between the study groups. Another limitation related to the study's online design is the lack of direct observation of the outcome measures. The choice of a applying a validated instrument that has previously been administered in a computer format, however, should help alleviate some of these concerns. Furthermore, the randomization procedure did not result in a balanced allotment of baseline study characteristics. Whether this is related to the internet-based design of the study or just the small sample size is indeterminate. The formulation of the study drug was also changed over the course of the study (from glucosamine sulfate to glucosamine hydrochloride), which could markedly limit the validity of the study results.

Applications for Clinical Practice

This study suggests that glucosamine is no more effective than placebo in treating osteoarthritis of the knee; however, concerns about the overall study design limit the overall validity of the trial.

–Review by Harvey J. Murff, MD, MPH

References

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