Review: both glucosamine and chondroitin are effective for osteoarthritis, but the magnitude of effect is unclear

McAlindon TE, LaValley MP, Guhlin JP, et al. *Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis*. JAMA 2000 Mar 15;283:1469-75.

QUESTION: In patients with osteoarthritis (OA), are glucosamine and chondroitin effective for relieving symptoms and improving function?

Data sources

Studies were identified by searching Medline (1966 to June 1999) and the Cochrane Controlled Trials Register. Handsearches were done of bibliographies of articles and meeting abstracts published in supplements of *Arthritis and Rheumatism*, the *British Journal of Rheumatology*, and *Osteoarthritis and Cartilage* (1978-98). Authors, content experts, and drug manufacturers were contacted to identify unpublished studies.

Study selection

Studies in any language were selected if they were randomised, double blind, controlled trials that compared oral or parenteral glucosamine sulphate, glucosamine hydrochloride, or chondroitin sulphate with placebo for ≥ 4 weeks in patients with knee or hip OA. Studies also had to include ≥ 1 outcome measure from a list compiled by the reviewers.

Data extraction

2 reviewers assessed the quality of studies (14 item quality scale) and resolved disagreements by discussion. Data were extracted on patients, route of administration, joint with OA, outcomes, funding, allocation concealment, and use of intention to treat analysis. Effect sizes were calculated.

Main results

17 studies met the inclusion criteria. 2 of these studies did not provide sufficient data for extraction and were excluded from the meta-analysis. The mean quality score was 36%. 1 study reported adequate allocation concealment, and 1 study used intention to treat analysis. No studies were funded by government or non-profit organisations, and most were sponsored by companies that produced glucosamine or chondroitin. 6 studies of glucosamine, which involved 911 patients, had quality scores ranging from 12-52%. Outcome measures were the Lequesne Index (a disability score on a questionnaire) (3 studies), global pain scores (2 studies), and the Western Ontario and McMaster Universities Osteoarthritis Index pain subscale score (1 study). Combined results showed a moderate benefit for glucosamine (effect size 0.44, 95% CI 0.24 to 0.64). 9 studies of chondroitin, which involved 799 patients, had quality scores ranging from 14-55%. Outcome measures were the Lequesne Index score (2 studies), global pain scores (5 studies), mobility scores (1 study), and use of non-steroidal anti-inflammatory drugs (1 study). Chondroitin had a large benefit (effect size 0.96, CI 0.63 to 1.3), but studies were heterogeneous ($p < 0.001$). When the study with the largest effect size (4.56) was removed, heterogeneity was no longer significant, and the effect size decreased to 0.78 (CI 0.60 to 0.95).

Conclusions

In patients with osteoarthritis, both glucosamine and chondroitin are effective for improving outcomes. The magnitude of effect is unclear, however, because of inconsistencies in study quality and dependence on industry support for study execution.

COMMENTARY

The review by McAlindon *et al* addresses a void in the literature about the efficacy of glucosamine and chondroitin in the treatment of patients with osteoarthritis. Because these substances are classified as nutritional supplements, they are readily available without prescription. Alone or in combination, each has been touted in lay publications as beneficial in relieving painful arthritis symptoms. Positive effects are attributed to anti-inflammatory action and cartilage protection and repair. Few side effects have been identified, and neither supplement has the gastrointestinal toxicity of the non-steroidal anti-inflammatory drugs.

Using meta-analysis, this review intended to provide the reader with a scientific, state of the art assessment on the effectiveness of glucosamine and chondroitin as shown in clinical trials. 15 investigations meeting study criteria were included in the meta-analysis; all but 1 were limited to osteoarthritis of the knee. No study was included that used glucosamine and chondroitin in combination. The results showed that both supplements are likely to be of benefit in patients with osteoarthritis. A greater benefit was found for chondroitin than for glucosamine; substantial methodological problems, however, were identified that had the net effect of inflating estimates of treatment effectiveness. Publication bias and the number of studies sponsored by drug manufacturers were particularly problematic. Descriptions of participants in the studies were not provided, which makes generalisation difficult.

Alternative treatments, such as glucosamine and chondroitin, are increasingly accepted and used by those who have chronic diseases for which there is no cure. Because of public demand, a National Institutes of Health study on these supplements will begin soon. In the interim, issues of concern are the association of glucosamine with insulin resistance, whether glucosamine and chondroitin are more effective individually or in combination, optimal therapeutic doses, long term effects, the degree of risk for those with shellfish allergies who take glucosamine, and standardisation among commercial preparations of these products.

Although available evidence indicates that overall risks are low and that benefits are at least moderate, definitive results and clinical recommendations for use have not yet been adequately determined. In the interim, informed choice and judicious decision making by consumers are required.

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