Review: Based on evidence from higher-quality trials, chondroitin does not reduce pain in knee or hip osteoarthritis

Reichenbach S, Sterchi R, Scherer M, et al. **Meta-analysis: chondroitin for osteoarthritis of the knee or hip.** Ann Intern Med. 2007;146:580-90.

Clinical impact ratings: Rheumatology ★★★★★☆☆

QUESTION

In patients with knee or hip osteoarthritis (OA), is chondroitin an effective treatment for pain?

METHODS

Data sources: MEDLINE, EMBASE/Excerpta Medica, CINAHL, Cochrane Central Register of Controlled Trials, Science Citation Index, and 4 online clinical trial registries (to November 2006); conference proceedings; reference lists; and experts.

Study selection and assessment: Randomized controlled trials (RCTs) or quasi-RCTs that compared chondroitin with placebo or no treatment in patients with OA of the knee or hip. Groups given low-dose chondroitin (< 400 mg/d) were excluded. 22 RCTs (n = 4056; range of mean ages 50 to 67 y, median age 61 y; 27% to 94% women, median 62% women) met the selection criteria. The median (range) oral dose was 1000 (800 to 2000) mg/d, treatment duration was 25 (6 to 103) weeks, and duration of follow-up was 31 (13 to 132) weeks. Quality assessment of individual trials was based on allocation concealment, blinding, and intention-to-treat analysis. Most trials had poor methodological quality or inadequate reporting.

Outcomes: Pain measurements at the end of the trial or ≤ 3 months after chondroitin therapy was stopped (whichever came first), change in minimum and mean radiographic joint space width, and adverse events.

MAIN RESULTS

Meta-analysis of all trials showed that chondroitin reduced pain more than placebo or no treatment (Table). The effect size of –0.75 is equivalent to a reduction of 1.6 cm on a 10-cm visual analogue scale (an effect size of –0.30 or 0.6 cm is considered clinically relevant). However, a high degree of heterogeneity existed across trials, related to sample size and methodological quality. 3 recent, large trials with intention-to-treat analysis (and allocation concealment in the 2 larger RCTs) and low heterogeneity across trials showed no effect of chondroitin on pain (Table). Chondroitin increased joint space width more than placebo or no treatment (Table). Groups did not differ for adverse events (12 RCTs).

CONCLUSION

Based on evidence from higher-quality trials of patients with knee or hip osteoarthritis, chondroitin does not reduce pain more than placebo or no treatment.

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Chondroitin vs placebo or no treatment for osteoarthritis of the knee or hip at median 31 weeks*

Outcomes	Number of trials (n)	Effect size (95% CI)†	I^2‡
Pain	20 (3846)	–0.75 (–0.99 to –0.50)	92%
	3 trials with ITT analysis (1553)	–0.03 (–0.13 to 0.07)	0%
	17 trials without ITT analysis (2293)	–0.88 (–1.13 to –0.64)	86%
Minimum joint space width (mm)	5 (1192)	0.16 (0.08 to 0.24)	8%
Mean joint space width (mm)	5 (1192)	0.23 (0.09 to 0.37)	21%

*ITT = intention-to-treat; CI defined in Glossary.

†Effect size for pain was calculated by dividing the differences in mean values between groups by the pooled standard deviation; effect size for joint space width was calculated as difference in change between groups. All results favor chondroitin.

‡I^2 is a measure of heterogeneity among trials; values of 25%, 50%, and 75% represent low, moderate, and high heterogeneity, respectively.

COMMENTARY

Because no currently available medical therapy can reverse or slow the progression of knee and hip OA, many patients use nutriceuticals, such as glucosamine and chondroitin, to treat their pain. Expectations for these agents are based on the fact that OA involves loss of articular cartilage, and chondroitin is the predominant glycosaminoglycan (GAG) component of articular cartilage and glucosamine is an important GAG precursor.

In clinical trials of hip and knee OA, patients often have a wide range of disease severity and disability, and the control group may have considerable placebo response, making it difficult to estimate the true magnitude of medication efficacy (1). Several small, industry-sponsored studies found chondroitin to be effective for painful OA. In contrast, a large National Institutes of Health trial found no benefit for either chondroitin or glucosamine compared with placebo (1). Therefore, Reichenbach and colleagues performed a systematic review to determine the efficacy of chondroitin for pain in OA.

The review raised critical issues about potential biases in clinical trials (resulting from small sample sizes, no intention-to-treat analysis, no placebo controls, no blinding, unequal receipt of co-interventions, short follow-up duration, and industry sponsorship) that can lead to inaccurate estimates of the efficacy of an intervention. 17 of the 20 RCTs in this review had some of these potential biases. Therefore, it was appropriate for the authors to pool only the 3 RCTs that had strong methodology to minimize bias (2).

Reichenbach and colleagues concluded that the symptomatic benefit of chondroitin, if any, is small, and they discouraged routine use. However, the doses and preparations of chondroitin varied across trials, and the outcomes measured were mainly symptomatic. Whether this supplement can conclusively slow joint structural deterioration, as has been suggested in studies using standard radiography, will require additional studies with such advanced imaging modalities as magnetic resonance imaging.

To date, high-quality RCTs generally do not support using nutriceuticals for OA pain. Current evidence does support recommendations for conservative treatment of OA pain, including analgesics, antiinflammatory agents, physical and occupational therapy, assistive devices, weight loss, and low-impact exercise (3); however, these approaches are usually only modestly effective. Clearly, more research is needed to develop therapies to better control pain and prevent disease progression.

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References

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