The rate of decline of joint space width in patients with osteoarthritis of the knee: a systematic review and meta-analysis of randomized placebo-controlled trials of chondroitin sulfate

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CRD summary
The review concluded that chondroitin sulphate was effective for slowing the rate of decline in minimum joint space width in patients with osteoarthritis of the knee. The authors’ conclusions appeared appropriate. However, due to potential for bias and errors during the process these must be treated with some caution.

Authors’ objectives
To assess the efficacy of orally administered chondroitin sulphate as a structure-modifying drug for osteoarthritis of the knee.

Searching
MEDLINE (from January 1996 to October 2007) and abstracts from scientific presentations at annual meetings of American College of Rheumatology and European League of Associations of Rheumatology were searched without language restrictions. Search terms were reported. Reference lists of relevant systematic reviews and meta-analyses were checked for additional studies. Manufacturers and an author from all the identified trials were contacted for unpublished studies.

Study selection
Randomised controlled trials (RCTs) that evaluated orally administered chondroitin sulphate compared to placebo were selected for review. Trial duration needed to be at least 52 weeks. Change in minimum joint space width was required to be reported.

Chondroitin sulphate dose used in all studies was 800mg. Follow-up period was either 52 weeks or 24 months.

One author performed study selection.

Assessment of study quality
One author assessed study validity using the Jadad scale of 0 to 5 points based on randomisation, blinding and reporting of withdrawals.

Data extraction
Data were extracted in order to calculate change in minimum joint space width (mm) per year, standardised mean difference (SMD) and associated 95% confidence intervals (CI). Rate of change was assumed to be constant in trials of two-year duration. Authors were contacted for additional data, where appropriate.

One author performed data extraction.

Methods of synthesis
Differences in change in minimum joint space width in mm/year between chondroitin sulphate and placebo groups were combined in fixed-effect meta-analyses. I² statistic was used to assess heterogeneity.

Results of the review
Four RCTs (n=1,088) were included in this review. All trials scored 3 or higher on the Jadad scale.

There was a small but significant reduction in annual rate of joint space width decline of 0.07mm/year (95% CI 0.03 to 0.10; four RCTs) in patients treated with oral chondroitin sulphate compared to placebo treated patients (SMD 0.26,
95% CI 0.14 to 0.38). Heterogeneity was not statistically significant.

Sensitivity analyses that assessed influence of excluding unpublished studies (0.07mm/year, 95% CI 0.01 to 0.12; three RCTs) and studies of different durations (0.13mm/year, 95% CI 0.06 to 0.20; two RCTs) showed no substantial changes in the pooled estimate. Heterogeneity was not statistically significant.

**Authors' conclusions**

Chondroitin sulphate at a dose of 800mg orally per day was effective in slowing the rate of joint space narrowing in patients with osteoarthritis of the knee and may have a role as a structure-modifying agent in management of such patients.

**CRD commentary**

This review focused on a clear research question and was supported by well-defined inclusion criteria. Several sources were searched (including conference abstracts). Attempts were made to identify unpublished studies. No language restrictions were applied in selecting eligible studies, which minimised risk of language bias. However, study selection, validity assessment and data extraction were performed by only one reviewer. Therefore, this review may have been vulnerable to bias and errors. Methods of synthesis appeared appropriate. Robustness of review findings was explored in sensitivity analyses. The authors' conclusions appeared to reflect data presented. However, due to potential for bias and errors during the review process these must be treated with some caution.

**Implications of the review for practice and research**

*Practice:* The authors did not state any implications for practice.

*Research:* The authors did not state any implications for research.

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