Effects of low-dose corticosteroids on the bone mineral density of patients with rheumatoid arthritis: a meta-analysis

CRD summary
This review concluded that low-dose corticosteroid treatment reduced bone mineral density in patients with rheumatoid arthritis. These conclusions were supported by the data presented, but should be interpreted with some caution due to a lack of details on the review methods.

Authors’ objectives
To assess the effects of low-dose corticosteroids on bone mineral density in patients with rheumatoid arthritis.

Searching
MEDLINE and Cochrane Central Register of Controlled Trials were searched to December 2007. Key words were reported. References in retrieved studies were reviewed to identify additional relevant studies. The review was restricted to published studies.

Study selection
Randomised controlled studies (RCTs) that compared prednisolone (10mg/day or less) with placebo in patients with rheumatoid arthritis and reported on bone mineral density following treatment were eligible for inclusion. Studies had to include follow-up of at least 12 weeks.

All studies were performed in European countries. Mean daily prednisolone dose ranged from 6mg to 10mg. Duration of follow up ranged from 20 weeks to three years. Mean age of included patients ranged from 51 to 69 years. Bone mineral density was measured in the lumbar, femur and neck; measurements were expressed as g/cm², mg/mL, bone mineral content or as T scores.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
Studies were assessed for methodological quality using the Jadad scale to assign studies a score out of 5. The authors did not state how many reviewers performed the validity assessment.

Data extraction
Data were extracted on mean and standard deviation of bone mineral density at end of follow up or change from baseline at the longest treatment duration point separately for prednisolone and placebo groups. Standardised mean differences were calculated for each study by dividing the difference between the corticosteroid and placebo groups by the baseline variance. Where there was no standard deviation data available this was imputed by using the mean proportional standard deviation of the other studies.

The authors did not state how many reviewers performed the data extraction.

Methods of synthesis
Standardised mean differences were pooled separately for each skeletal site. Methods used to pool data were not reported. Heterogeneity was assessed using the Q and I² statistics. Sensitivity analysis was conducted by limiting the meta-analysis to studies that used prednisolone alone, reported end of period data, reported change from baseline data, reported different durations of follow up, included calcium supplements and that reported standard deviations.

Publication bias was assessed using funnel plots and the Egger test and trim and fill method.
**Results of the review**

Seven RCTs were included in the review (n=696). Study quality scores ranged from 1 to 3 out of 5.

Lumbar bone mineral density was reduced in patients with rheumatoid arthritis who took low-dose prednisolone (standardised mean difference 0.48, 95% CI: -0.82 to -0.15; seven studies). There was substantial heterogeneity between studies (p<0.001, $I^2=74\%$). Findings were similar for all subgroups investigated.

There was no difference in femoral bone mineral density between the groups (standardised mean difference -0.22, 95% CI: -0.66 to 0.22; six studies). There was substantial heterogeneity between studies (p<0.001, $I^2=83\%$). When the meta-analysis was restricted to the three studies that analysed data as change from baseline femoral bone, mineral density was found to be reduced in patients with rheumatoid arthritis who took low-dose prednisolone (standardised mean difference -0.49, 95% CI: -0.91 to -0.07). The only other subgroup to show decreased bone mineral density in patients with rheumatoid arthritis taking prednisolone were the four studies that did not give calcium supplements (standardised mean difference -0.58, 95% CI: -0.86 to -0.30).

There was no evidence of publication bias based on the Egger test (p>0.1), and adjusting for publication bias did not change the pooled estimates.

**Authors' conclusions**

Bone mineral density was reduced after low-dose corticosteroid treatment in patients with rheumatoid arthritis.

**CRD commentary**

The review addressed a narrow, focused question supported by clearly defined inclusion criteria. The literature search was adequate, but the review was restricted to published studies and so there was a possibility of publication bias, which was addressed in the review. Study quality was assessed using appropriate criteria and the results of the quality assessment were clearly reported, but they were not considered in the synthesis of results. Review methods were poorly reported, so it was not possible to determine whether appropriate steps were taken to minimise bias and errors. Details were not reported on methods used to pool data, so the reliability of the summary measures was unclear. Heterogeneity was formally assessed and appropriate subgroup analysis was carried out to investigate differences between studies. The authors' conclusions were supported by the data presented, but should be interpreted with some caution due to the lack of details of review methods.

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

**Practice:** The authors stated that the finding that low-dose corticosteroid treatment reduced bone mineral density in patients with rheumatoid arthritis had practical implications for the long-term management of patients with rheumatoid arthritis.

**Research:** The authors stated that further research was required to determine whether the benefits of low-dose corticosteroids outweighed their disadvantages in rheumatoid arthritis.

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