Review: 9 drugs prevent an increase in radiographic scores of bone erosion in joints in adult rheumatoid arthritis

Jones G, Halbert J, Crotty M, et al. **The effect of treatment on radiological progression in rheumatoid arthritis: a systematic review of randomized placebo-controlled trials.** Rheumatology. 2003;42:6-13.

QUESTION

In patients with adult rheumatoid arthritis, are pharmacologic interventions effective for preventing an increase in radiographic scores of bone erosion in joints?

DATA SOURCES

Studies were identified by searching the Cochrane Controlled Trials Register, MEDLINE (1966 to 2000), EMBASE/Excerpta Medica, and Proceedings of the American College of Rheumatology. Bibliographies of relevant articles were reviewed, and pharmaceutical companies and authors were contacted for unpublished data.

STUDY SELECTION

Studies published in English were selected if they were randomized controlled trials (RCTs) of adults with rheumatoid arthritis, compared ≥ 1 pharmacologic intervention with placebo (or equivalent control group), reported radiographic scoring of joints as an outcome, and had at least a 24-week interval between start of the trial and last X-ray.

DATA EXTRACTION

2 reviewers independently extracted data on sample size, follow-up, patient characteristics, duration of disease, details of the intervention, study quality, and outcomes. For each RCT, the main outcome (bone erosion scores in joints) was converted into the standardized mean difference (difference between the mean change from baseline in erosion scores between the intervention and control groups divided by the standard deviation of the difference) and the odds of worsening X-ray results before meta-analysis.

MAIN RESULTS

25 RCTs (3907 patients) met the selection criteria. Pharmacologic interventions included corticosteroids, parenteral gold, sulfasalazine, leflunomide, auronofin, hydroxychloroquine, chloroquine, pamidronate, cyclosporin, minocycline, methotrexate, cyclophosphamide, D-penicillamine, interleukin-1–receptor antagonist, and infliximab. Cyclosporin, infliximab, sulfasalazine, leflunomide, methotrexate, parenteral gold, corticosteroids, auranofin, and interleukin-1–receptor antagonist were better than placebo at preventing an increase in radiographic scores of bone erosion in joints (Table).

CONCLUSION

In patients with adult rheumatoid arthritis, 9 pharmacologic interventions prevent an increase in radiographic scores of bone erosion in joints.

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Pharmacologic interventions vs placebo in adult rheumatoid arthritis at 6 to 24 months*

Outcome	Number of RCTs (Number of patients)	Intervention	Standardized mean difference (95% CI)†
Change from baseline in erosions scores	1 (60)	Cyclosporin	–0.74 (–1.28 to –0.20)
	1 (349)	Infliximab	–0.67 (–0.84 to –0.49)
	2 (210)	Sulfasalazine	–0.50 (–0.77 to –0.22)
	2 (365)	Leflunomide	–0.49 (–0.70 to –0.27)
	1 (221)	Methotrexate	–0.36 (–0.63 to –0.08)
	2 (182)	Parenteral gold	–0.33 (–0.62 to –0.03)
	4 (302)	Corticosteroids	–0.32 (–0.54 to –0.09)
	2 (198)	Auranofin	–0.30 (–0.58 to –0.02)
	1 (347)	IL-1R antagonist	–0.27 (–0.44 to –0.10)

*IL-1R = interleukin-1 receptor; RCTs = randomized controlled trials. Meta-analyses were done using a fixed-effects model; CI defined in Glossary.
†All significant differences favor the intervention.

COMMENTARY

The review by Jones and colleagues showed that several antirheumatic drugs were better than placebo for retarding radiologic progression in rheumatoid arthritis. However, it is difficult to compare the effectiveness of different pharmacologic interventions using meta-analysis of several trials involving different populations, time frames, and scoring methods. It has been argued that the scoring methods of Sharp (1) and Larsen (2) are not comparable in the locations and abnormalities assessed (3, 4). Furthermore, radiographic scoring methods might not be able to give comparable results early and later in rheumatoid arthritis because of a ceiling effect (5).

Jones and colleagues have presented a good overview of selecting effective drugs to retard radiologic progression in rheumatoid arthritis. In addition, the data suggest that some drugs are stronger and others are weaker. However, to confirm the rank list constructed by the standardized mean difference method, all X-rays from the trials (or a random sample of them) should be collected and assessed by one (or both) methods. In addition, every effort should be made to exclude a sampling error caused by different inclusion criteria. Furthermore, while acknowledging that there might be ethical restraints on future placebo-controlled trials in rheumatoid arthritis, it needs to be recognized that the individual RCT is still the most robust way to compare drug effects.

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