Should tetracycline treatment be used more extensively for rheumatoid arthritis? Metaanalysis demonstrates clinical benefit with reduction in disease activity.


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Abstract

OBJECTIVE:
To compare the effectiveness of tetracycline antibiotics versus control (placebo or conventional treatment) in rheumatoid arthritis (RA) for the reduction of disease activity as defined by American College of Rheumatology criteria.

METHODS:
We searched Medline (1966-February 2002), Embase (1980-February 2002), and the Cochrane Controlled Trials Register (Issue 1, 2002 Cochrane Library). Reference lists of published trials were searched by hand for further identification of published reports and presentations at scientific meetings. Randomized controlled trials comparing tetracyclines to control (placebo or conventional disease modifying antirheumatic therapy) were selected for inclusion if at least one of the following outcomes was reported: tender joint count (TJC), swollen joint count, patient pain score by visual analog scale, patient global assessment of disease activity, physician global assessment of disease activity, eosinophil sedimentation rate (ESR) and C-reactive protein (CRP), joint space narrowing and erosions, adverse events, and quality of life as measured by the Health Assessment Questionnaire. Subjects were required to have RA as defined by the 1987 ARA criteria.

RESULTS:
Ten randomized controlled trials including 535 individuals were reviewed. Only 3 trials were considered high quality; elements of bias could not be excluded in the remainder.
Tetracyclines, when administered for \( > \) or \( = 3 \) months, were associated with a significant reduction in disease activity in RA as follows: for TJC, standardized mean difference (SMD) = -0.39, 95% CI -0.74, -0.05; and for acute phase reactants, ESR, SMD = -8.96, 95% CI -14.51, -3.42. The treatment effect was more marked in the subgroup of patients with disease duration < 1 year who were seropositive. There was no absolute increased risk of adverse events associated with tetracyclines: absolute risk difference = 0.10, 95% confidence interval (CI) -0.01, 0.21. No beneficial effect was seen on radiological progression of disease: for erosions, SMD = 0.17, 95% CI -0.29, 0.64. In addition, subgroup analysis excluding trials with doxycycline showed that minocycline alone had a greater effect on reduction of disease activity: for TJC, SMD = -0.69, 95% CI -0.89, -0.49; and for ESR, SMD = -10.14, 95% CI -14.72, -5.57.

CONCLUSION:

Tetracyclines, in particular minocycline, were associated with a clinically significant improvement in disease activity in RA with no absolute increased risk of side effects. Unfortunately, the information available was inadequate to allow a detailed analysis of individual side effects in the studies. Further research is warranted to compare these agents to newer disease modifying drugs for comparable safety, efficacy, and cost-effectiveness.

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