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LACK OF EFFECT OF DOXYCYCLINE ON DISEASE ACTIVITY AND PYRIDINOLINE EXCRETION RATES IN RHEUMATOID ARTHRITIS. A DOUBLE-BLIND PLACEBO-CONTROLED STUDY

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Matrix metalloproteinases (MMPs) have been implicated in the degradation of articular cartilage and bone in rheumatoid arthritis (RA). Independent of their antibiotic effects, tetracyclines are capable of inhibiting MMPs. Previous work shows that doxycycline treatment resulted in a reduction of urinary release of markers of joint destruction in adjuvant arthritis. Minocycline has been shown to suppress disease activity in RA. To study the effects of doxyxcline in RA, the effects of 12, 24, and 36 weeks of doxycycline therapy on parameters of disease activity and joint destruction were investigated.

The study was set up as a double-blind placebo-controlled study. Patients received 100 mg doxycycline (50 mg BID) during 12 weeks (n = 15), 24 weeks (n = 16), 36 weeks (n = 16) or a placebo (n = 17). Patient assessments were performed before, at 6, 12, 24, and 36 weeks of treatment, and finally at 4 weeks after cessation of treatment. ESR and the Modified Disease Activity Score (mDAS) were used as parameters of disease activity; urinary excretion rates of pyridinolines hydroxylysylpyridinoline (HP) and lysylpyridinoline (LP) were used as parameters of joint degradation.

In doxycycline-treated and placebo-treated patients gastrointestinal complaints were reported: 8 (17%) and 3 (18%) respectively. Six patients treated with doxycycline (13%) and 3 (18%) patients in the placebo-group discontinued the study because of lack of effect or an exacerbation of the arthritis. Doxycycline treatment during 12, 24 or 36 weeks did not show any significant changes in ESR, mDAS, or morning stiffness, nor in urinary HP or LP excretion rates.

In **conclusion,** in contrast to minocycline, no effect of short term or long term doxycycline treatment was found on disease activity. In addition, no effect was observed on markers of joint destruction. These results indicate that 100 mg daily doxycycline does not contribute to the treatment of RA.