## **Minocycline Therapy for Rheumatoid Arthritis**

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Tetracyclines are group of antibiotic drugs. One of them is called minocycline. It has certain interesting properties. Firstly, it is obviously anti-bacterial being an antibiotic. Secondly, it has the ability to inhibit enzymes which digest and degrade cartilage and the tissues of the joint. Third, it may also be able to inhibit the function of T lymphocytes and macrophages (a specialised white blood cell) which are involved in initiating and perpetuating the inflammation in rheumatoid arthritis. For these reasons, several randomised, controlled, placebo clinical trials have been carried out.

In 1994, Kloppenburg and colleagues, Leiden, Holland treated 40 patients with established rheumatoid arthritis with 200 mg daily of minocycline for 26 weeks. At the end of this time there was significant improvement in the laboratory aspects of rheumatoid arthritis but less so for the clinical features. The adverse side-effects were minimal and mainly involved gastrointestinal upset and dizziness.

In 1995, Tilley and colleagues, Detroit, USA treated 109 patients with rheumatoid arthritis with 200 mg daily of minocycline for 48 weeks. There were significant improvements in both laboratory and clinical features of rheumatoid arthritis.

O'Dell and his colleagues, Nebraska, USA in 1997 carried out the first controlled study of minocycline in patients with rheumatoid arthritis of less than one year duration. The study was for six months and this again confirmed the fact that minocycline has a positive effect on laboratory and clinical features of rheumatoid arthritis. The same group in 1999, reported a 4 year follow up on patients with early rheumatoid arthritis, again treated with 200 mg daily of minocycline. They found that remissions were more frequent and the need for other disease modifying drugs less likely in the minocycline treated group.

Finally, O'Dell and his colleagues in 2001 compared 200 mg minocycline daily in 30 patients with early rheumatoid arthritis (less than 1 year duration) with hydroxychloroquine 400 mg daily in another 30 patients. These patients were followed up for two years. The finding was quite impressive in that 60% of the patients treated with minocycline had reached an American College of Rheumatology 50% response rate, as compared with 33% in patients with hydroxychloroquine. An American College of Rheumatology 50% response is a very marked response. The difference between the minocycline and hydroxychloroquine was significant. There were two further fascinating findings from this study. Firstly, minocycline reduced the amount of steroid the patients were taking. Secondly, patients taking minocycline were more likely to be able to stop steroids all together.

There is, therefore, no doubt that minocycline has a laboratory and clinical effect in rheumatoid arthritis. The question is whether minocycline also has a beneficial effect on the rate of progression of joint damage and on the appearance of new joint damage as seen on X-ray examination. Here the result is not so clear cut. The effects seen have been small.

It may be concluded, therefore, that minocycline is a good drug in terms of symptom relief and joint swelling relief and improvement in laboratory measures of inflammation, but that it has no important affect on joint damage. It is joint damage that is important for the long-term functional outcome in rheumatoid arthritis. Thus, on the present evidence, minocycline should not be recommended as the treatment of choice for early rheumatoid arthritis and not as monotherapy. What is needed are combination therapy studies of minocycline with other disease modifying drugs to see if they can bring additional benefit without increased side effects. Such investigation should particularly focus on the affect on bone damage as detected by X-rays.