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Sustained effect after lowering high-dose infliximab in patients with rheumatoid arthritis

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BACKGROUND

Infliximab is a chimeric monoclonal antibody that neutralises the biological activity of tumour necrosis factor (TNF). Several studies with infliximab in rheumatoid arthritis (RA) demonstrate that infliximab provides rapid and sustained clinical response, delays radiographic progression and improves quality of life. The adverse effects reported in clinical trials are generally mild.

In clinical trials, only a small subset of patients with rheumatoid arthritis (RA) benefits from higher than standard dose of infliximab (3 mg/kg for 8 weeks), but in practice doctors tend to use high doses of infliximab. A possible solution for avoiding individual overdosing of anti-TNF could be titration of the infliximab dose based on actual disease activity scores. ❑

PURPOSE

The aim of the presented study was to evaluate the effects of progresively lowering infliximab doses in patients with stable RA. ❑

METHODS

The study included 18 patients over 6 months. Inclusion criteria were: RA according to the ACR 1987 revised criteria, treated with 5 mg/kg infliximab (irrespective of dose frequency), stable disease activity and stable treatment The patients were initially treated with 3 mg/kg, but had their dose escalated to 5 mg/kg based on the clinical judgement of the treating doctor.

The primary end point was defined as the proportion of patients in whom infliximab dosages could not be lowered without inducing a persistent flare of disease activity within the timeframe of two lowered dosages of infliximab. ❑

RESULTS

At dose-reduction study start and at the second and third low infusion, the mean DAS28 in the infliximab group was 3.2, 3.2 and 3.3 respectively. The difference in DAS28 score between the first and the last visit was not significant (p=0.91). The primary end point, was met in one patient. In this patient, lowering the infliximab dose resulted in an increase of 1.2 (3.30 to 4.65) in DAS28 before the second low dose infusion. This increase sustained until the next infusion. After restarting with 5 mg/kg infliximab this patient responded positively (DAS28 2.47). Three other patients flared at the third visit. One had to stop infliximab because of a ''lupus-like reaction'', the other two

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recovered spontaneously without medical intervention after the next visit. All other patients remained in stable disease activity.

The median serum infliximab level was at baseline 4.7 (0.48–12) mg/litre. After the dose was decreased the infliximab serum trough level decreased to 3.1 (0.59–6.2) mg/litre and 3.1 (0.17–8.2) mg/litre, before the second and third 3 mg/kg infliximab infusion. Detectable anti-infliximab antibodies were found in two and four patients, respectively, before and after dose decrease. ❑

CONCLUSION

The study indicates that a dose of 5 mg/kg infliximab could be lowered in the majority of patients with RA without persistent increase of disease activity. Individual dose titration of infliximab should be considered in daily practice to reach the best individual dose. ❑