Comment on: Use of parenteral methotrexate significantly reduces the need for biological therapy

Sir, We read with interest Bharadwaj et al’s letter [1] demonstrating encouraging responses to parenteral MTX in a retrospective analysis of 32 patients with RA. We conducted a prospective study to investigate the effectiveness of parenteral MTX in a cohort of patients with RA [2] for whom oral MTX was ineffective or not tolerated. In addition, we assessed whether the change from oral to parenteral MTX prevented the need for a biologic agent. This study was conceived as an audit of our standard practice in RA management and as such did not require explicit ethical approval. All patients, however, provided informed consent to the use of parenteral MTX.

Thirty consecutive patients (26 females, 4 males) with mean disease duration of 15.3 yrs (range 2-46 yrs) were recruited between October 2004 and March 2006 from our rheumatology clinics. They were assessed at baseline, 3 and 6 months after the introduction of subcutaneous (s.c.) MTX. We measured tender joint score (TJC), swollen joint score (SJC), patient’s global assessment of disease activity (PGA), CRP and 28-joint disease activity score (DAS28) at each visit. Oral MTX was discontinued due to lack of efficacy (23) and intolerance (7). Patients were started on s.c. MTX at a mean dose of 14.25 mg (range 7.5–17.5 mg). At 6 months the mean dose was 19.9 mg (range 12.5–25 mg). Three patients discontinued treatment at 3 months due to leucopenia (1) and poor compliance (2); a further two stopped s.c. MTX at 6 months due to lack of efficacy (1) and nausea (1). Five reported minor side-effects (nausea in four, an injection site reaction in the other).

Compared with baseline, there was a significant improvement in DAS28 at both 3 and 6 months with a mean reduction of 2.34 (mean DAS28 5.2–2.95±7.5%; n=27, P<0.001) at 3 months and 2.09 (mean DAS28 5.2–3.05±8.9%; n=25, P<0.001) at 6 months. At 3 months, 20/27 patients showed a good response (using EULAR response criteria) and 13/25 maintained this at 6 months. Moreover, of the 11 patients who met BSR criteria for anti-TNF-α therapy at baseline, 8 had a good response at 3 months. None needed anti-TNF-α therapy at 6 months, although two of the three patients who failed to respond at 3 months needed it at 6 months.

Our results provide further evidence of the efficacy of parenteral MTX in controlling active RA in patients who fail to respond to, or are intolerant of, oral MTX. In a cohort who fulfilled NICE criteria for treatment with anti-TNF-α therapy the majority responded to the switch to parenteral MTX (8/11). Whilst parenteral MTX is an under-utilized therapy in the UK its superiority over oral MTX has recently been demonstrated in a prospective randomized controlled trial comparing oral and s.c. MTX in 375 patients [3]. Whilst it is tempting to suggest that patients should receive a trial of parenteral MTX prior to biologics, the lack of comparative outcome data of biologic agents and parenteral MTX makes this debatable; however, the increasing evidence of the superior efficacy of parenteral MTX over the oral route does support the need for further studies.

Disclosure statement: The authors have declared no conflicts of interest.

C. THORNTON1, V. ONG1, J. WARD1, N. KENNEDY1, A. STEUER1

1Department of Rheumatology, Wexham Park Hospital, Slough, UK

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Correspondence to: A. Steuer, Department of Rheumatology, Wexham Park Hospital, Wexham Street, Slough, Berkshire SL2 4HL, UK. E-mail: alan.steuer@hwph-tr.nhs.uk

1 Bharadwaj A, Agrawal S, Batley M, Hammond A. Use of parenteral methotrexate significantly reduces the need for biological therapy. Rheumatology 2006;47:222.

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Comment on: Use of parenteral methotrexate significantly reduces the need for biological therapy: reply

Sir, We are interested to note Dr Thornton’s reply to our letter [1]. The additional data she presents supports our argument that the deployment of intramuscular MTX is a helpful therapeutic step in the RA treatment algorithm and may avoid the necessity for progression to anti-TNF-α treatments. Presumably, in this they are highly cost effective. The safety profile of the treatment in this reported study seems acceptable. The fact that this is a prospective study adds additional weight to the conclusion though, like our study, the numbers of patients are low. We also note a recently published study by Braun et al [2] whose conclusions are in line with our own and those of Thornton and colleagues. For our part, we believe that careful consideration should be given to the introduction of subcutaneous MTX in the formulation of guidelines for the treatment of rheumatoid disease.

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A. BHARADWAJ1, M. BATEY1, A. H. HAMMOND1

1Department of Rheumatology, Maidstone Hospital, Maidstone, UK

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Correspondence to: A. Bharadwaj, Department of Rheumatology, Rheumatology Maidstone Hospital, Hermitage Lane, Maidstone ME16 9QQ, UK. E-mail: anurag_bharadwaj@hotmail.com; anurag_bharadwaj@nhs.net


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Comment on: Intravenous immunoglobulin therapy in pregnant patients affected with systemic lupus erythematosus and recurrent spontaneous abortion

Sir, As rheumatologists practicing in a developing country where the birth rate is relatively high, pregnancy with SLE constitutes a major problem for us. We have encountered a growing number of