## Tolerance of parenteral, higher dose methotrexate in children with juvenile chronic arthritis

Sir,

We read with interest the article by Ravelli *et al.* (1), in which the authors compared the efficacy and safety of oral and parenteral low dose (10 mg/m$^2$/week) methotrexate (MTX) therapy in patients with juvenile chronic arthritis (JCA). We wish to report our experience with a higher parenteral dose (> 20 mg/m$^2$/week) of MTX in a single center.

We performed an observational, longitudinal, retrospective study of the tolerance of this treatment in children with JCA. A consecutive series of patients attending the Pediatric Rheumatology Clinic at our tertiary facility between September 1988 and June 1999 were included in the study. Data concerning side effects from medications are routinely scrutinized and clearly recorded in the clinical charts. Clinical evaluation is performed monthly or bimonthly. Laboratory monitoring includes complete blood cell count, MCV, platelet count, SGOT, SGPT, plasma creatinine, albumin, and urinalysis.

Twenty patients received the higher parenteral dose of MTX: 14 patients with systemic arthritis, 3 with rheumatoid factor (RF)-negative polyarthritis, and 3 with RF-positive polyarthritis. Their mean age was 10.6 (range: 4-16) years and the mean duration of their disease was 3.4 (range: 0.5-10) years. They received the higher dose (mean 23.25 mg/m$^2$/week, range 20-33 mg/m$^2$/week) for an average of 51 (range: 8-104) weeks, and they all had been treated with oral low dose MTX for 52 (range: 12-180) weeks. All patients were treated concomitantly with NSAIDs, 3 with oral cyclosporine, and 9 received folic acid 7.5 mg/week.

**Table I.** Demographic data and side effects of MTX treatment.

| | Oral, low dose | Parenteral, higher dose |
|---|---|---|
| Number | 124 | 20 |
| Sex M | 42 (34%) | 8 (40%) |
| F | 82 (66%) | 12 (60%) |
| Age (years, mean) | 9.9 | 10.6 |
| Dis. dur. (yrs., mean) | 2.3 | 3.4 |
| Folic acid | 58 (47%) | 9 (45%) |
| Total side effects | 70 (56%) | 8 (40%) |
| Elevated SGOT/SGPT | 27 (22%) | 5 (25%) |
| Nausea, vomiting | 27 (22%) | 1 (5%) |
| Abdominal pain | 26 (21%) | 1 (5%) |
| Loss of appetite | 12 (10%) | 2 (10%) |
| Pain at injection site | - | 4 (20) |
| Stomatitis | 1 (1%) | - |

Eight patients (40%) (5 with systemic and 3 with polyarthritis) experienced some form of toxicity: the most common was transient raised liver enzymes (SGOT and SGPT), which occurred in 5 patients. There were 9 episodes of increased plasmatic levels; in 7 these were more than twice the upper normal limit.

In all cases, liver enzyme levels returned to normal after the drug was withheld for 2 weeks. Four patients reported pain at the site of the injection; loss of appetite and stomach discomfort occurred in 2 patients; 1 patient each experienced abdominal pain, vomiting, headaches, and sleepiness. No patient needed to permanently discontinue the drug due to side effects. The time between the treatment onset and the occurrence of toxicity was 31 (range 4-60) weeks.

We then compared these results with those obtained for a cohort of 124 consecutive patients who received low dose MTX (< 15 mg/m$^2$/week) for their JCA (48 with systemic arthritis, 26 RF-positive polyarthritis, 21 RF-negative polyarthritis, 17 enthesitis-related, 8 extended oligoarthritis, and 4 psoriatic arthritis). Their features and adverse effects are summarized in Table I. The children in the two study groups (low and high dose MTX) were demographically similar, the only significant difference being the MTX dose itself. The frequency and type of side effects was similar in both groups, although the parenteral higher dose MTX group experienced a much lower occurrence of complaints related to the gastrointestinal (GI) system. Of interest, 19 (15%) patients on oral low-dose MTX had to permanently discontinue the treatment due to side effects, which were related to GI intolerance in 17 of them.

Despite the fact that these observations suffer from the disadvantages of retrospective studies, our data show that higher dose parenteral MTX therapy is safe, and is not associated with more frequent side effects than low-dose oral MTX, at least during the first year of treatment. Some authors have already pointed out this issue (2, 3), and an international multicenter study coordinated by PRINTO (Pediatric Rheumatology International Trials Organization) will address this subject, as well as the question of efficacy. The long-term, prospective follow-up of patients on this regime will eventually confirm our observations.

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### References

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## Visual recovery after retinal stroke due to giant cell arteritis

Sir,

Giant cell arteritis (GCA) is the most common form of vasculitis in Western countries (1- 3). In this respect, although in most series long-term mortality due to GCA is low (4), vascular complications overshadow the good outcome observed in most patients (5, 6). Among these, vision loss remains the most common complication of this vasculitis and has been observed in up to 17% of cases (4-8). Indeed, recovery of visual function is uncommon and generally depends on the duration of the vision loss prior to the start of corticosteroid therapy (6). We describe the case of a patient with GCA who experienced an unexpected visual recovery after 6 days of central retinal artery stroke due to GCA.

An 82-year-old woman was referred to the emergency unit of the Hospital Xeral-Cies (Vigo) because of headache and complete visual loss in her right eye. Symptoms started 2 weeks earlier with severe right-sided headache, jaw claudication and asthenia. Six days before admission she suffered acute and complete unilateral visual loss in her right eye. At that time an ophthalmologist examined the patient and made a diagnosis of retinal stroke. At that time, due to a previous history of allergy to aspirin, antiaggregation treatment with Triflusal 300 mg/12 hrs/p.o. was started, without further changes. However, because of persistent and severe headache, she was referred to our hospital for further evaluation. On examination, besides thickening and tenderness to palpation of both temporal arteries, the patient's visual acuity was 20/30 in the left eye and no light perception in the right. In addition, the right pupil did not react to light. However, motility and intraocular tension were normal in both eyes. Fundos-