

## Low Dose Cyclosporin A and Methotrexate in the Treatment of Psoriasis

Sir,

Cyclosporin A (CsA) and methotrexate are both effective drugs when used alone in the treatment of psoriasis. Few reports in the literature have documented the combined therapy of both drugs for this inflammatory skin disorder. We describe a patient with severe psoriasis and psoriatic arthritis who showed a clinically significant improvement on combined therapy with low dose CsA and regular dose methotrexate.

### CASE REPORT

A 37-year-old male pharmacist presented with longstanding psoriasis of 16 years' duration and arthritis affecting mainly the axial skeleton and peripheral joints. On initial presentation the patient had severe psoriasis (PASI=15) and psoriatic arthritis, the latter treated with methotrexate. Methotrexate however had no therapeutic effect on the skin manifestations of his psoriasis. Subsequently methotrexate was weaned and CsA (3 mg/kg/day) was started for his psoriasis. Over the next several months there was marked clinical improvement of his psoriasis (PASI=3.7) but CsA failed to control his associated arthritis. Therefore a combination of CsA and methotrexate was begun. The patient has been maintained on low dose CsA (mean 2 mg/kg/day) in addition to intramuscular methotrexate (7.5–20 mg/week) for almost 24 months (although a CsA-free period of 3 months occurred after 12 months of combined therapy at the request of the patient). This drug combination has achieved a relatively stable control of his skin and arthritic symptoms. Serum creatinine did not rise above 30% of baseline and the patient experienced no other documented side-effects whilst on this combined oral therapy.

### DISCUSSION

This case is unusual in that methotrexate was ineffective in controlling the psoriatic skin manifestations, while CsA had no therapeutic effect on the arthritic symptoms. However, when both drugs were used in a combination of low dose CsA and regular dose methotrexate, good therapeutic control of both skin and joint symptoms was achieved. Few reports in the current literature document the combined use of CsA with other anti-psoriatic treatments. Mazzanti et al. reported the effectiveness of combination low dose CsA and methotrexate in the treatment of 8 patients with severe psoriatic arthritis (1). The side-effects documented were only a mild increase in serum creatinine in one patient and reversible hypertension in another. Korstanje et al. highlighted the increase in risk of serious side-effects when CsA and methotrexate were used concomitantly in psoriasis, mainly that each drug decreased elimination of the other, leading to an increase in blood levels of each drug. The study also reported increases in serum creatinine as well as liver transaminases (2). However, their study comprised only 4 patients and since then considerably more data have been generated on the use of this drug combination, specifically in the area of rheumatology.

Bensen et al. reported 20 patients with rheumatoid arthritis who had a partial response to conventional dose oral methotrexate and then had CsA (mean dose 2.5 mg/kg/day) added

to their regimen for 6 months (3). There was a significant clinical improvement on this therapeutic combination with no significant increase in adverse reactions. In a recent open study of 14 patients with refractory rheumatoid arthritis who received both CsA (mean dose 2.5–3.9 mg/kg/day) and methotrexate (10–15 mg/week) all clinical variables significantly improved with this treatment regimen over a 6-month period (4). In addition, the combination treatment showed no greater toxicity than can be expected on treatment with single agents over this period. Tugwell et al. compared combination therapy with CsA (2.5–5 mg/kg/day) and methotrexate (at the maximal tolerated dose) to methotrexate and placebo in 148 patients with severe rheumatoid arthritis in a large double-blind 6-month study (5). The study concluded that patients who had only partial responses to methotrexate had clinically important improvement after combination therapy with CsA and methotrexate. In addition, the side-effects were not significantly increased.

From the evidence available in the current literature it appears that potential side-effects are not substantially increased when CsA and methotrexate are used in combination, as is illustrated in our case. Minimal side-effects were observed with low dose CsA and conventional dose methotrexate treatment for psoriasis over a period of 24 months. The lower doses of CsA administered in our patient and in the above studies probably reduced the side-effects of combined CsA and regular dose methotrexate therapy. Both serum creatinine and folate should be monitored when this combination is used. Future large-scale studies may be warranted to assess the safety of this combined therapy in the treatment of psoriasis and associated psoriatic arthritis.

### REFERENCES

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