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Short-term "Cyclosporin A" Therapy for Psoriatic Arthritis

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The usefulness of low-dose cyclosporin A (CsA) in psoriatic skin lesions is well known (4) and during the treatment an improvement of the sometimes associated arthritis has been noted (6).

There are few published studies on psoriatic arthritis (PA) patients treated with CsA, showing variable experiences both on effectiveness and safety (5, 8, 9).

We investigated the efficacy and safety of low-dose CsA therapy in a 6-month open study on 13 patients with PA to assess the main clinical and laboratory changes.

MATERIALS AND METHODS

13 patients affected by PA, according to Moll and Wright criteria (7), 9 men and 4 women aged 30 to 62 (mean age 45), were recruited for the study. All of them had active polyarthritis with a mean duration of 9 years (range 1–32 yrs). All patients had already been treated unsuccessfully with other disease-modifying antirheumatic drugs, but had not taken these drugs for at least 3 months prior to starting CsA therapy. They all were heated by non-steroidal anti-inflammatory drugs (NSAIDs), while 4 of them were also taking low-dose steroids (6-methylprednisolone 4 mg/daily). Patients were excluded for any of the following reasons: abnormal hepatic and renal function, recent major surgery, hypertension, concomitant uncontrolled infections, history or presence of malignancy, pregnancy.

The starting oral dose of CsA was 3 mg/kg daily administered twice a day for 6 months. If the articular improvement was then unsatisfactory, increments of 1 mg/kg daily were permitted at monthly intervals to a maximum dose of 5 mg/kg. A reduction of the dose by 1 mg/kg daily was made if the serum creatinine concentrations increased by more than 50% over the baseline value, or for any other significant side effects.

Each patient was examined by the same rheumatologists at entry, and then monthly throughout the trial. The rheumatological evaluation included number of painful joints; Ritchie articular index; patient's pain using a 10 cm visual analogue scale, and duration of morning stiffness (min). Blood pressure was measured at each visit.

The following laboratory investigations were carried out at entry and at each visit: complete blood cell count; Westergren erythrocyte sedimentation rate (ESR); C-reactive protein (CRP), serum urea nitrogen; creatinine; uric acid; electrolytes; albumin; transaminases; alkaline phosphatase; total bilirubin, and urine analysis. Creatinine clearance was measured before therapy began and again every other month. At entry, all the patients lacked rheumatoid factor and antinuclear antibodies.

Statistical analysis differences between paired data were analysed using the Wilcoxon signed rank test. The significance of correlations was determined using the Spearman rank correlation test. *P*-values less than 0.05 were considered significant.

RESULTS

Table I shows the main clinical data of the 13 patients on entry. Ten patients (77%) completed the 6-month study period, while 3 of them (23%) interrupted CsA treatment, owing to gastrointestinal problem in one case, uncontrolled elevation of blood pressure in another and poor compliance in the third.

Table II shows the changes in main clinical and laboratory parameters.

At the end of the trial, all the patients showed an improvement in their arthritis and in one case a complete remission of articular disease was achieved. Statistical analysis showed a significant improvement in the number of painful joints, Ritchie index, and subjective pain. Regarding laboratory investigations, reductions in ESR and CRP were detected in the study period, but a significant laboratory change occurred only in serum creatinine levels, although it was not over 50% from baseline value and did not require any reduction.

Steroid therapy was discontinued in all cases but one, while all the patients were encouraged to reduce their intake of NSAIDs during CsA treatment.

DISCUSSION

Our short-term study of CsA in PA patients showed that the number of painful joints, Ritchie index and patient's assessment of pain improved significantly during the treatment. However, no significant decrease in ESR was found, as already reported by other authors (3, 11, 12). It is questionable whether ESR can be considered a reliable variable for considering CsA a remittive

Table I. *Demographic and clinical features of the study patients* (N = 13).

Sex (M/F)	9/4
Mean age (yrs)	45±12
(range)	(30–62)
Mean age of onset of arthritis (yrs)	36±10
(range)	(23–57)
Mean duration of arthritis (yrs)	9±9
(range)	(1–32)
Steroid treatment (no. of pts)	4

Table II. *Outcome at baseline (T_0) and after 6-months (T_6) of CsA therapy in 10 PA patients.*

	T_0 M±SEM	T_6 M±SEM	p
Painful joints (no.)	9.9±1.2	4.9±1.4	0.001
Ritchie index	18.8±4.7	6.8±2.4	0.005
Pain analogue scale (cm)	5.2±0.6	3.4±0.6	0.01
Morning stiffness (min)	27±30	9±6	n.s.
ESR (mm/1 hr)	41.8±9.7	27.1±5.3	n.s.
CRP (mg/l)	19.2±6	10.8±4.9	n.s.
Serum creatinine (mg/dl)	0.9±0.1	1.1±0.1	0.05
6-methylprednisolone (mg/daily)	1.6±0.5	0.2±0.2	0.05

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agent, since these studies report that other acute-phase reactive proteins decrease during CsA treatment.

In our group of patients a significant rise in serum creatinine was found at the end of the 6-month study, although the values were still within the normal range and no other renal functional parameters revealed any significant modification. Hypertension occurred in one patient which led to withdrawal within the first month of therapy, despite the concomitant antihypertensive therapy.

However, the side effects, occurring only in 16% of cases, were mild and similar to those reported by others (3). The major problem with CsA is undoubtedly nephrotoxicity, even if it is conceivable that the duration of the treatments as well as the drug dosage are contributory factors for the renal damage (2, 10). The risk of interaction with other potentially nephrotoxic agents such as NSAIDs has been pointed out (1). We underline the significantly successful reduction of steroid consumption achieved quite soon in our trial. In fact, in all cases the reduction of 6-methylprednisolone dose was made within the first 3 months of CsA therapy.

In this study, low-dose CsA proved to be highly effective in the improvement of articular involvement in active PA, but in our opinion, the criterion of an aimed selection of the subjects to be treated must be followed, in order to avoid the most common side effects. Furthermore, larger double-blind studies and longer treatments will also be required to make a better assessment of the efficacy and tolerability of CsA in PA.

REFERENCES

1. Altman RD, Perez GO, Sfakianakis GN. Interaction of cyclosporin A and nonsteroidal anti-inflammatory drugs on renal function in patients with rheumatoid arthritis. Am J Med 1992; 93: 396–402.
2. Boers M, Dijkmans BAC, Van Rijthoven AWAM, Goei The HS, Cats A. Reversible nephrotoxicity of cyclosporin in rheumatoid arthritis. J Rheumatol 1990; 17: 38–42.
3. Dougados M, Awada H, Amor B. Cyclosporin in rheumatoid arthritis: a double-blind placebo controlled study in 52 patients. Ann Rheum Dis 1988; 47: 127–133.
4. Ellis CN, Gorsulowsky DC, Hamilton TA et al. Cyclosporin improves psoriasis in double-blind study. JAMA 1986; 256: 3110–3116.
5. Gupta AK, Matteson EL, Ellis C et al. Cyclosporin in the treatment of psoriatic arthritis. Arch Dermatol 1989; 125: 507–510.
6. Harper JL, Keat ACS, Staughton RCD. Cyclosporin for psoriasis. Lancet 1984; ii: 981–982.
7. Moll JM, Wright V. Familial occurrence of psoriatic arthritis. Ann Rheum Dis 1973; 32: 181.
8. Salvarani C, Macchioni P, Boiardi L et al. Low dose cyclosporin A in psoriatic arthritis: relation between soluble interleukin 2 receptors and response to therapy. J Rheumatol 1992; 19: 74–79.
9. Steinsson K, Jonsdottir I, Valdimarsson H. Cyclosporin A in psoriatic arthritis: an open study. Ann Rheum Dis 1990, 49: 603–606.
10. Tugwell P, Bombardier C, Gent M et al. Low-dose cyclosporin in rheumatoid arthritis: a pilot study. J Rheumatol 1987, 14: 1108–1114.
11. Weinblatt ME, Coblyn JS, Fraser PA et al. Cyclosporin A treatment of refractory rheumatoid arthritis. Arthritis Rheum 1987, 30: 11–17.
12. Yocum E, Klippel JH, Wilder RL et al. Cyclosporin A in severe, treatment-refractory rheumatoid arthritis. Ann Intern Med 1988; 109: 863–869.