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Intermittent Cyclosporin A Treatment of Severe Plaque Psoriasis

Long-term follow-up of 26 patients

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The aim of this study was to evlauate the long-term effects of intermittent Cyclosporin A treatment of severe plaque psoriasis. For this purpose we considered the clinical records of 26 patients who had been intermittently treated with Cyclosporin A for 2 to 4 years. All 26 patients had severe plaque-type psoriasis (PASI score >18) that was unresponsive to conventional treatment. The initial Cyclosporin A dosage was 5 mg/kg/day in 8 cases and 3 mg/kg/day in 18 cases. In all patients, Cyclosporin A treatment was prolonged until complete or nearly complete remission of psoriasis (mean 2 months; range 1–4 months). All patients subsequently underwent a 2–4 months maintenance treatment with Cyclosporin A dosages that were gradually reduced until tapering off. In order to maintain clinical improvement after Cyclosporin A withdrawal, patients were treated with topical steroids, topical tar, emollients and UVA exposure and/or eliotherapy. Cyclosporin A treatment (2.5–3 mg/kg/day) was reintroduced only when clinical relapses reached a PASI score of 12 or more. Duration and dosages of Cyclosporin A cycles were always adapted for the purpose of obtaining an improvement acceptable to the patient (PASI <8) rather than total clearance of psoriasis. So far, the 26 patients have undergone 3–5 cycles of therapy with low doses of Cyclosporin A. None of these 26 patients interrupted Cyclosporin A treatment because of side effects. In conclusion, in our experience cyclic CyA treatment is effective for the long-term treatment of psoriatic patients.

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The efficacy of oral Cyclosporin A (CyA) in inducing remission of severe psoriasis has been widely demonstrated in a number of open and blind studies (1–9). However, optimal modalities of long-term management of psoriatic patients using CyA, as well as the side-effect profile of prolonged or intermittent administration of the drug, are still under discussion. The aim of this study was to evaluate the long-term effects of CyA cyclic treatment in severe plaque psoriasis. For this purpose we scrutinized the clinical records of 26 patients who had been periodically treated with CyA over a period of 2 to 4 years. These 26 patients formed part of an original cohort of patients who entered two multicentre Italian studies regarding the safety and efficacy of CyA in severe plaque psoriasis (8, 9).

PATIENTS AND METHODS

All 26 patients (11 females and 15 males) aged 22–65 years (mean 47.92 years) had severe plaque-type psoriasis (defined by a PASI score >18) which had been unresponsive to conventional treatment. They were otherwise in good health. Previous treatments included 1–3 courses of methotrexate (8 patients), etretinate (5 patients), PUVA therapy (7 patients) and both methotrexate and etretinate (7 patients). Patients had interrupted all systemic therapies at least 4 weeks before entering the study. None were taking drugs known to interact with CyA. Women of childbearing age were using effective contraception during CyA treatment.

The initial CyA dosage was 5 mg/kg/day in 8 patients and 3 mg/kg/day in 18 patients. In all patients, initial CyA dose was prolonged until complete or nearly complete remission of psoriasis (mean 2.53 months; range 1–3 months). All patients subsequently underwent 2 to 4 months of maintenance treatment with CyA dosages that were gradually reduced until tapering off. In order to maintain clinical improvement after CyA suspension, the patients were treated with topical therapies: steroids, tar, emollients and UVA exposure and/or eliotherapy. Since June 1992, 2 patients have been utilizing topical calcipotriol.

CyA treatment (2.5–3 mg/kg/day) was reintroduced only when clinical relapses reached a PASI score of 12 or more. Duration and dosages of CyA were always adapted to the purpose of obtaining an improvement acceptable to the patient (PASI <8), rather than total clearance of psoriasis.

Clinical and laboratory monitoring

During CyA therapy, patients were examined every 1 to 4 weeks, depending on drug dosages. A complete laboratory monitoring, including serum CyA levels, was performed at each visit. Twelve-hour whole-blood levels of CyA were measured using a radio-immunoassay (RIA) with a specific monoclonal antibody. Target range was 50–275 ng/ml and dosages were adjusted if levels were outside these values. Glomerular renal function was checked at pretherapy, and at the end of each cycle of CyA therapy. In patients who exhibited a rise of >30% in their baseline creatinine levels, the dose of CyA was reduced by 0.5–1 mg/kg/day and creatinine levels were monitored every 2 weeks.

During the CyA-free period, patients were examined every 1–2 months according to their clinical state and response to adjuvant treatments.

RESULTS

Initial CyA treatment produced a reduction of more than 85% in PASI score in 15 patients and a reduction of 75% in 11 patients. Psoriasis relapsed gradually in all patients 2 to 4 months after interruption of CyA (mean 3.19). PASI scores of relapses were always below baseline PASI. In 12 patients, adjuvant therapies permitted maintenance of a PASI score <12 for a period ranging from 3 to 4 months. Four of them did not require CyA reintroduction for 5 to 6 months.

Nine patients, on the other hand, required reintroduction of CyA, 2 to 3 months after interruption, to control their psoriasis despite of regular use of adjuvant therapies.

In all our patients, an acceptable control of psoriasis was obtained by using 2–5 cycles of CyA treatment in 24 months. During the 1st cycle of CyA reintroduction, 4 of the 8 patients who had started CyA therapy with 5 mg/kg/day required more than 3 mg/kg/day in order to control their psoriasis (3.5 to 4 mg/kg/day). However, dosages of 3 mg/kg/day were always sufficient in successive CyA cycling.

Side effects

None of the 26 patients interrupted CyA treatment because of

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side effects. Four of the 26 patients developed hypertension, 5 transient renal impairment and 5 both. Hypertension occurred during the first 2–4 weeks of treatment in 12 patients. In 5 patients, hypertension was only transient and controlled by reducing the CyA dosage.

Seven of the 12 patients developed mean blood pressure values (160/95 Hg) that required treatment with hypotensive agents. In all these patients, blood pressure returned to normal values when CyA therapy was stopped. In 4 of these 7 patients, hypertension reoccurred with every cycle of CyA. In 6 patients, after a slight increase in serum creatinine within normal range during 1–2 months of treatment, no significant change was subsequently detected.

A transient rise of more than 30% in serum creatinine level occurred in 14 patients, including 5 patients treated with CyA 5 mg/kg/day and 9 patients treated with CyA 3 mg/kg/day. The rises occurred within the first 3 months of treatment in all the 5 patients taking 5 mg/kg/day. Three of the 9 patients treated with 3 mg/kg/day showed a rise in serum creatinine after 4 months of therapy, whereas the remaining 6 patients developed a transient rise of creatinine after the third cycle of treatment. In all cases, serum creatinine value returned to pretreatment level within 1–2 months of CyA reduction.

Renal dysfunction was seen only 5 out of 12 patients with hypertension. No correlations were apparently detected between of creatinine increase above baseline, or incidence of hypertension and previous systemic antipsoriatic treatment.

Minor side effects noted during our study included headache (48%) and paresthesias (34%).

DISCUSSION

Our study indicates that intermittent treatment with low dosages of CyA was effective in maintaining an acceptable control of psoriasis in all our patients. During the follow-up period, however, the frequency and duration of cycles varied considerably in one and the same patient. Furthermore, a considerable variation in the minimal CyA dosage capable of maintaining adequate disease control was observed among the different patients. CyA dosages of 3 mg/kg/day were, however, effective in controlling psoriasis recurrences in most of our cases. This indicates that modalities and dosages of CyA treatment in the long-term management of psoriatic patients are strongly related to the clinical response of the individual patient.

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