TREATMENT OF CHRONIC PLAQUE TYPE PSORIASIS WITH SYSTEMIC MYCOPHENOLATE MOFETIL

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Abstract- Chronic plaque-type psoriasis may be difficult to control without the use of potent systemic therapies that are accompanied by systemic toxicity. Mycophenolate mofetil is a novel agent that may be effective in the treatment of chronic plaque type psoriasis. Our purpose was to investigate of the safety and efficacy of oral mycophenolate mofetil in the treatment of chronic plaque-type psoriasis. Four patients with severe stable plaque-type psoriasis and a psoriasis area and severity index (PASI) between 7.2 and 30.4 (mean 19) were included in the study. They received oral mycophenolate mofetil 1 g twice daily for 3 months. The PASI were determined at baseline (week 0) and every two weeks thereafter. Within 4 weeks of this therapy, there was a reduction in PASI of between 52% and 68% in patients (mean PASI: 7.45). The mean PASI was 3.7 and a PASI decrease of 62.5-90% obtained after 3 month of therapy. The drug was tolerated by all the patients and severe side-effects especially hematological and liver toxicity, were not observed in any of them. Oral mycophenolate mofetil might be a safe and effective drug to treat chronic plaque type psoriasis. We think that randomized controlled trials are needed to clarify this opinion.

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Key words: Mycophenolate mofetil, psoriasis, systemic treatment

INTRODUCTION

Chronic plaque type psoriasis sometimes becomes a severe intractable disease associated with considerable morbidity (1). It may be difficult to control the disease without the use of potent systemic therapies. However, it is not uncommon to face with many systemic toxicities which may limit their continued use.

Mycophenolate mofetil (MMF) is an immunosuppressive agent presented primarily for the prevention of organ rejection in transplant patients (2). More recently it has been reported to be beneficial in the treatment of psoriasis and other immune dermatoses (3). MMF has a favorable side effect profile compared with other commonly used systemic drugs used in dermatology such as cyclosporine, methotrexate and acitretin. Reported adverse effects of MMF are mainly gastrointestinal and hematological with little effect on the hepatic and renal functions of the patients (2). The frequency of malignant disorders is considerably higher than healthy control population (4). There is currently no reason to suppose an increased carcinogenic or mutagenic risk due to MMF monotherapy, but a potential risk to develop malignancies cannot be completely ruled out based on the existing data (3). Mycophenolic acid (MPA), the active metabolite of MMF, reversibly blocks the de novo biosynthesis of guanine nucleotides required for DNA and RNA synthesis. Therefore, all cell types that rely predominantly on the de novo biosynthetic pathway rather than the purine salvage pathway, such as T and B lymphocytes, are most significantly affected by MPA (5).

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MATERIAL AND METHODS

Four patients (all women, aged 17-57 years, mean 36.5 years) with severe stable plaque-type psoriasis were included in the trial. Informed consent was obtained from all patients after complete written and oral explanation. All the patients had different topical antipsoriatic therapies (emollients, keratolytics, dithranol, corticosteroids or calcipotriol), two of them had broad-band ultraviolet B (UVB), psoralen plus UVA (PUVA) and two of four patients reported systemic antipsoriatic treatments (methotrexate and acitretin) with partial success during the therapies or their withdrawal due to adverse effects; however, none of the patients received any antipsoriatic treatment for 4 weeks before entering into this study.

All patients underwent a pretreatment evaluation consisting of clinical assessment, determination of Psoriasis Area and Severity Index (PASI) and laboratory tests including full blood count, serum biochemistry, liver enzymes (aspartate aminotransferase, alanine aminotransferase), renal function tests (urea, creatinine), markers for viral hepatitis and Gravindex for premenopausal patients. The PASI was determined at baseline (week 0) and every two weeks thereafter, by the same clinician. The patients received oral mycophenolate mofetil (CellCept®) 1 g twice daily. During the study period, no other topical or systemic antipsoriatic therapy was allowed except for petrolatum.

The patients were visited every other week and at each visit, patient's general medical condition and laboratory values regarding adverse effects were reviewed and PASI scores were determined. Therapy was continued for three months. Treatment efficacy or response to treatment is defined as reduction more than 50% in the baseline PASI score and marked improvement as reduction more than 75% in this score.

RESULTS

PASI scores during the treatment period are shown in table 1. At baseline, the PASI of the patients ranged between 7.2 and 30.4 (mean PASI: 19). During mycophenolate mofetil therapy, the PASI decreased within 4 weeks by 52-68% in patients (mean PASI: 7.45, range of PASI: 3.5-9.9). Overall, the mean PASI was 3.7 (range: 2-5.2) and a PASI decrease of 62.5-90% was obtained after 3 month of therapy.

Table 1. PASI scores during the treatment period in patients treated with mycophenolate mofetil.

	Before treatment	At one month	After 3 months
Patient 1	19.3	8.6	5.2
patient 2	7.2	3.5	2.7
Patient 3	30.4	9.9	4.8
Patient 4	19.3	7.8	2

In order to demonstrate the effect of mycophenolate mofetil in more detail, the mean scores of erythema, infiltration, scaling and area were calculated for the four patients (Fig. 1). Although the reduction in the desquamation of psoriatic plaques was more prominent, erythema, infiltration, and surface area were also reduced.

All patients completed the study. Except for one patient who complained of mild gastrointestinal disturbances following mycophenolate mofetil intake, no side effects were observed in any of the patients treated. There were no changes in full blood counts, biochemistry, liver or renal blood tests.

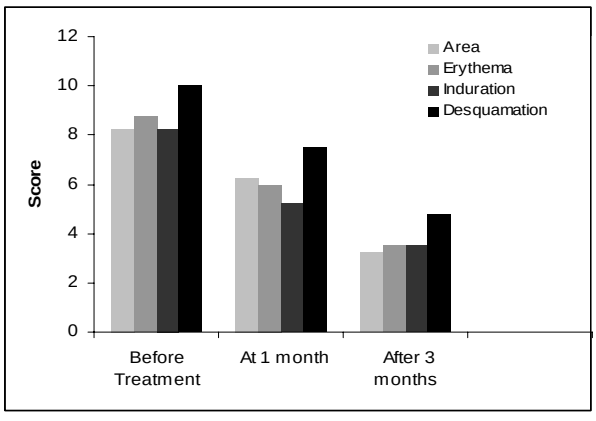

Fig. 1. Mean scores of surface area, erythema, induration and desquamation in patients treated with mycophenolate mofetil during the course of therapy.

DISCUSSION

Several systemic immune-suppressants have been used to treat psoriasis. Many of these agents have considerable adverse effects on the renal, hepatic or hematological functions but MMF has little side effect on the renal and hepatic systems (6).

The results of the present study indicate the effectiveness of the oral treatment of psoriasis with MMF. The assumption that, in psoriasis, activated T lymphocytes either directly or indirectly stimulate the proliferation of keratinocytes, suggests a selective mechanism of action of MPA in this disease, because *de novo* purine biosynthesis of lymphocytes is the main target of this drug. Inhibition of lymphocyte proliferation reduces the predominant inflammatory cell type in psoriatic lesions and possibly reduces the increased proliferation of epidermal keratinocytes (7, 8).

Haufs *et al*. described the first case of a man with severe psoriasis treated successfully with oral MMF. The psoriasis area and severity index score decreased during therapy (5 weeks) from 22.0 to 11.4. They concluded that MMF appears to be an effective therapeutic alternative in the treatment of severe psoriasis (9). Geilen *et al.* reported two patients with severe erythrodermic psoriasis that were treated with oral mycophenolate mofetil and good responses were seen after 3 weeks and after 6 weeks (10).

Until now in the largest study on the effectiveness of MMF in psoriasis treatment, 23 patients with moderate to severe psoriasis (mean PASI of 21.7) were treated with MMF 2-3 g/daily for 12 weeks. Eighteen patients completed the study. The PASI was reduced by 24% at 6 weeks and by 47% at 12 weeks. At the end of the treatment, 77% of patients responded well to MMF with significant reduction in PASI. Five patients experienced mild nausea. One case had periorbital edema and pruritus (2). One patient had transient leukopenia.

In another study, 11 psoriatic patients were treated with MMF 2g daily. Within 3 weeks of therapy, there was a reduction in PASI between 40% and 70% in seven of 11 patients. No significant side effect especially hematological or gastrointestinal was seen despite muscle pain in one patient (3).

In one case report, a woman with a long history of wide spread plague psoriasis unresponsive or intolerant to systemic treatment was successfully treated with MMF. Remission was maintained on doses between 1 and 1.5 g/day for 18 months (6).

Grundmann-Kollmann *et al.* described 5 patients with moderate to severe chronic plaque psoriasis and 6 patients with psoriatic arthritis that was refractory to conventional systemic and/or topical treatment who were treated with MMF. Only patients with moderate psoriasis and psoriatic arthritis improved with therapy, whereas patients with severe psoriasis did not respond to MMF. They suggested that MMF may develop into an interesting therapeutic alternative for patients with psoriatic arthritis (11).

In conclusion oral MMF has been shown to be safe and effective in the treatment of recalcitrant psoriasis as is shown in our study. However, it is recommended that a randomized placebo-controlled clinical trial with more cases confirm these findings to use MMF as an alternative therapy for psoriasis.

Conflict of interests

We have no conflict of interests.

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