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EFFICACY OF MYCOPHENOLATE MOFETIL (MMF) IN THE TREATMENT OF CHRONIC PLAQUE TYPE PSORIASIS

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Summary

One to two percent of world population is suffering from psoriasis and treating moderate and severe psoriasis is a huge challenge as most of the systemic anti-psoriatics cause long term toxicities. The aim of the study was to see the efficacy and of Mycophenolate mofetil (MMF) in the treatment of moderate to severe plaque type psoriasis. It was an open prospective study conducted in the department of Dermatology and Venereology, Dhaka Medical College, Dhaka and Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Seven patients with moderate to severe plaque type psoriasis were treated with MMF 1 gm twice daily for twelve weeks. Outcome was measured with Psoriasis Area and Severity Index (PASI) and adverse effects were recorded. Baseline PASI was 10.8 to 30 and PASI reduction after 4, 8 and 12 weeks treatment was 23.70% to 43.75%, 49.5% to 70.37% and 75.0% to 88.89% respectively. PASI-75 (PASI reduction >75.0%) was achieved in all seven cases. No adverse effect was found. Mycophenolate Mofetil (MMF) is a effective treatment option for moderate to severe plaque type psoriasis.

Key words

Mycophenolate mofetil; psoriasis; plaque

Introduction

Psoriasis is a chronic, inflammatory skin disease with a remitting /recurring course that requires active, lifelong management in most patients. Approximately 20–30% of affected individuals require continuous, long-term, systemic therapy to achieve effective symptom control[1]. The burden of psoriasis is substantial, with effects on quality of life (QoL) comparable with those observed with major chronic diseases such as cancer, arthritis and depression[2]. Although conventional systemic treatments for psoriasis [e.g. methotrexate, ciclosporin, oral retinoids, psoralen ultraviolet A (PUVA)] may be effective for short-term symptom relief, they are associated with serious toxicities that limit their long-term use,[3] and patients using such treatments are faced with the inconvenience of rotational, intermittent or step-wise treatment regimens and regular safety monitoring[4]. Furthermore, symptom control with conventional agents is often suboptimal. For example, extended follow-up of patients treated with PUVA, a standard agent in clinical practice that is generally considered effective, and intermittent methotrexate revealed no long-term improvements in disease severity and that 50% of patients still had moderate-to-severe psoriasis despite treatment[5]. Additionally, patient dissatisfaction with current treatments is high,[6,7] and a substantial proportion of patients with moderate-to-severe psoriasis do not receive any systemic treatment[8].

Further elucidation of the molecular and cellular pathways involved in psoriasis has led to the development of target specific biological therapies[9,10].

Mycophenolate mofetil (MMF), a widely used immunosuppressant in organ transplantation, is a recent addition to the therapeutic armamentarium of autoimmune and inflammatory skin disorders in dermatology. It is a salt form of the immunosuppressive drug mycophenolic acid selectively and noncompetitively inhibits inosine monophosphate dehydrogenase (IMPDH) in the de novo purine synthesis pathway. This enzyme facilitates the conversion of inosine monophosphate to xanthine monophosphate, an intermediate metabolite in the production of guanosine triphosphate. As MMF results in the depletion of guanosine nucleotides, it impairs RNA, DNA and protein synthesis.[11] Very few studies has been conducted to see the efficacy of MMF in the treatment of psoriasis.[12-16] Here is a series of seven patients of chronic plaque type psoriasis treated with MMF and the response was observed in terms PASI.

Materials and methods

To see the efficacy of MPM in chronic plaque type psoriasis this prospective open study was done in the department of Dermatology & Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka and Dhaka Medical college, Dhaka. Seven patients of severe (PASI>10) plaque type psoriasis, diagnosed clinically and histopathologically were enrolled purposively in the study. Patients aged 18 years who were not well

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responsive to topical therapy and had not taken other systemic anti-psoriatics for last three months were selected for treated with Mycophenolate Mophetil. Complete blood count (CBC), urine routine and microscopic examination, serum creatinine, AST, ALT, pregnancy test (female) and chest radiography were done before starting therapy. All seven patients were treated with Mycophenolate Mophetil 1 gm (two 500 mg tablets) twice daily for 12 weeks. Disease severity was assessed by serial photograph and measured by Psoriasis Area and severity Index (PASI) at baseline and every four weeks interval. Assessed by general physical examination and laboratory tests (CBC, Urine analysis, T and serum creatinine) every two weeks.

Results

Age of the seven patients (six male and one female) were 38 to 60 years and duration of the disease were from 5 to 20 years. Five of those patients had past history of treated with systemic anti-psoriatic therapy (methotrexate) for a duration of 2 to 7 years. At base line PASI of the patients were 10.8 to 30, PASI reduction after 4, 8 and 12 weeks treatment from 23.70% to 43.75%, 49.5% to 70.37% and 75.0% to 88.89%. PASI-75 (PASI reduction >75.0%) was achieved in all seven cases (Table-1).

Discussion

Moderate to severe psoriasis is treated with phototherapy and a variety of systemic therapies, which are often used either singly or in combination, very few of those current therapies are capable to induce remissions, and most patients do not achieve prolonged, disease-free periods without continued maintenance therapy[17-18]. Most of those are associated with different severe systemic adverse effects and long-term toxicities which limits their long-term use. Many of those are also associated generalized immune-suppression and malignancy [18-19]. So, there is an unmet need for less toxic and more effective psoriasis treatments that produce long-lasting remissions.

In the current study, seven patients of age ranging from 38 to 60 years having moderate to severe psoriasis were evaluated. Base line PASI were from 10.8 to 30, after 4 weeks treatment disease severity (PASI) was reduced from 23.70% to 43.75%, after 8 weeks reduced from 49.5% to 70.37% and after 12 weeks of treatment it was reduce from 75.0% to 88.89% ($p<0.001$). In a similar type of study[20], patients initially received MMF 1g twice daily for 3 weeks followed by 0.5g twice daily. Within 3 weeks of therapy, there was a reduction in PASI of between 40% and 70% in seven of the 11 patients.

Table 1 : Demographic and clinical characteristics of the patients

Characteristics	Patient-1	Patient-2	Patient-3	Patient-4	Patient-5	Patient-6	Patient-7
Age (years)/Sex	56 /Male	45 /Male	40 /Male	60 /Male	38 /female	58 /Male	55 /Male
Duration of disease (years)	12	10	7	17	5	10	20
History of pustule psoriasis	No	No	No	No	No	Yes	No
History of erythroderma	No	Yes	No	Yes	No	Yes	No
Palmoplantar involvement	Yes	Yes	No	Yes	No	Yes	Yes
Previous therapies							
Topical	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Phototherapy	No	No	No	No	No	No	No
Systemic /drug /duration	Yes/Methotrexate/ 5 years	Yes/Methot rexate/3 years	No	Yes/Methot rexate/5 years	No rexate/2 years	Yes/Methot rexate/7 years	Yes/Methot
PASI							
At baseline	13.4	21.3	21.6	19.2	30	10.8	27
After 4 weeks treatment	9.5	12.9	14.0	10.8	21.8	7.9	20.6
(reduction) of PASI	(29.10%)	(39.43%)	(35.19%)	(43.75%)	(27.33%)	(26.86%)	(23.70%)
After 8 weeks treatment	6.9	9.9	9.6	7.0	16.1	3.2	12.1
(reduction) of PASI	(49.5%)	(53.52%)	(55.56%)	(63.54%)	(53.0%)	(70.37%)	(55.19%)
After 12 weeks treatment	4.7	5.1	2.4	3.7	7.5	1.8	4.8
(reduction) of PASI	(75.77%)	(76.06%)	(88.89%)	(80.72%)	(75.0%)	(83.3%)	(82.22%)
Adverse effects	No	No	No	No	No	No	No

Only one patient achieved a reduction in PASI of <25% from baseline. After 6 weeks, there was further improvement in six patients. However, PASI increased in four patients when MMF was tapered to the lower dosage[20]. In another two-center, prospective, open-label clinical trial,[21] patients with moderate to severe psoriasis were treated with MMF 2-3g/day for 12 weeks. In the 18 patients who completed the study, the PASI was reduced by 24% ($p < 0.001$) at 6 weeks and by 47% ($p < 0.001$) at 12 weeks[21]. In a comparatives study[22], after 12 weeks of treatment PASI -75 were achieved in 58.8% of patients in MMF group and comparable ($P > 0.05$) with Methotrexate (73.3%). Three months after discontinuing the treatment, PASI-75 remained in 33.3% of patients in MMF and 53.3% of MTX group ($P > 0.05$)[22] and in the current study all seven patients achieved PASI-75. None of the patients reported any adverse effect during treatment period, although the post-treatment follow-up was not done.

Conclusion

MMF is a very effective treatment option for chronic moderate to severe plaque type psoriasis and further long term comparative study is needed to be conducted to see its safety and efficacy.

Disclosure

All the authors declared no competing interestes

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