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-psoratics 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 Venerology, 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 an 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 control1. 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 depression2. 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 use3, and patients using such treatments are faced with the inconvenience of rotational, intermittent or step-wise treatment regimens and regular safety monitoring4. 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 treatment5. Additionally, patient dissatisfaction with current treatments is high6,7, and a substantial proportion of patients with moderate-to-severe psoriasis do not receive any systemic treatment8. Further elucidation of the molecular and cellular pathways involved in psoriasis has led to the development of target specific biological therapies9,10.

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. Very few studies have been conducted to see the efficacy of MMF in the treatment of psoriasis. 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 & Venerology, 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
responsive to topical therapy and had not taken other systemic anti-psoriatics for last three months were selected for treatment 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. 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. 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. Baseline 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 reduced from 75.0% to 88.89% (p<0.001). In a similar type of study, 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**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patient-1</th>
<th>Patient-2</th>
<th>Patient-3</th>
<th>Patient-4</th>
<th>Patient-5</th>
<th>Patient-6</th>
<th>Patient-7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)/Sex</td>
<td>56/Male</td>
<td>45/Male</td>
<td>40/Male</td>
<td>60/Male</td>
<td>38/female</td>
<td>58/Male</td>
<td>55/Male</td>
</tr>
<tr>
<td>Duration of disease (years)</td>
<td>12</td>
<td>10</td>
<td>7</td>
<td>17</td>
<td>5</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>Prior history of psoriasis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Prior history of erythema</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Prior history of psoriasis</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Prior history of rheumatoid arthritis</td>
<td>Yes/Methotrexate</td>
<td>Yes/Methotrexate</td>
<td>No</td>
<td>Yes/Methotrexate</td>
<td>No</td>
<td>Yes/Methotrexate</td>
<td>Yes/Methotrexate</td>
</tr>
<tr>
<td>Methotrexate duration (years)</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>PASI At baseline</td>
<td>13.4</td>
<td>21.3</td>
<td>21.6</td>
<td>19.2</td>
<td>30</td>
<td>10.8</td>
<td>27</td>
</tr>
<tr>
<td>After 4 weeks treatment</td>
<td>(29.10%)</td>
<td>(39.43%)</td>
<td>(35.19%)</td>
<td>(43.75%)</td>
<td>(27.33%)</td>
<td>(26.86%)</td>
<td>(23.70%)</td>
</tr>
<tr>
<td>(reduction) of PASI</td>
<td>69</td>
<td>9.9</td>
<td>9.6</td>
<td>7.0</td>
<td>16.1</td>
<td>3.2</td>
<td>12.1</td>
</tr>
<tr>
<td>After 8 weeks treatment</td>
<td>(49.5%)</td>
<td>(55.52%)</td>
<td>(55.56%)</td>
<td>(63.54%)</td>
<td>(53.0%)</td>
<td>(70.37%)</td>
<td>(55.19%)</td>
</tr>
<tr>
<td>(reduction) of PASI</td>
<td>47</td>
<td>5.1</td>
<td>2.4</td>
<td>3.7</td>
<td>7.5</td>
<td>1.8</td>
<td>4.8</td>
</tr>
<tr>
<td>After 12 weeks treatment</td>
<td>(75.77%)</td>
<td>(76.06%)</td>
<td>(88.89%)</td>
<td>(80.72%)</td>
<td>(75.0%)</td>
<td>(83.3%)</td>
<td>(12.22%)</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

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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. In another two-center, prospective, open-label clinical trial, 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. In a comparative study, 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) 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 interests.

References
4. Shear NH. Fulfilling an unmet need in psoriasis: do biologicals hold the key to improved tolerability? Drug Saf 2006; 29:49–66