**Background:** Pemphigus vulgaris is a potentially life-threatening autoimmune disease. Although combination therapies with prednisone and azathioprine are usually effective in controlling the disease, some patients either do not respond to this treatment or show early relapses.

**Objective:** To find out whether mycophenolate mofetil would be an effective drug in controlling pemphigus vulgaris in patients who failed initial treatment with azathioprine and prednisone.

**Results:** Twelve patients who were initially diagnosed as having pemphigus vulgaris and had relapsed while undergoing treatment with azathioprine (1.5-2 mg/kg of body weight) and prednisolone (2 mg/kg of body weight) subsequently received combination therapy with mycophenolate mofetil (2 x 1 g/d) and prednisolone (2 mg/kg of body weight per day). Eleven of the 12 patients responded to therapy and showed no relapse of their disease even after tapering of the steroid dose. One patient did not respond. Toxic effects were low with only mild gastrointestinal symptoms in 5 patients and mild lymphopenia (World Health Organization grade I) in 9 patients. During the 9- to 12-month follow-up, none of the 11 patients showed reappearance of pemphigus lesions.

**Conclusion:** Treatment of pemphigus vulgaris with mycophenolate is a safe and effective treatment.

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PATIENTS AND METHODS

PATIENTS

Twelve patients with PV who had relapsed after prior treatment with azathioprine and prednisolone (Table 1) were selected for treatment with mycophenolate. All diagnoses were confirmed by histologic findings and direct immunofluorescent staining.

MATERIALS

Patients were treated initially with prednisolone 2 mg/kg of body weight, and mycophenolate mofetil, 2 g. When appearance of new blisters stopped, steroid doses were rapidly reduced by 50% and then gradually tapered during the follow-up period. Mycophenolate mofetil doses were kept at 2 g/d throughout the treatment period of 9 to 12 months. After this period, all patients were either kept at 5 mg/d of prednisolone or did not receive any steroids at all.

INDIRECT IMMUNOFLUORESCENCE

To better assess clinical efficacy of the treatment, indirect immunofluorescence was performed from patients’ serum samples on regular and salt-split skin before and during treatment with mycophenolate.

BLOOD TESTS

Regular blood tests were performed, including erythrocyte sedimentation rate, blood cell counts, liver and renal function tests, and electrolyte levels.

Additionally, MPA treatment of peripheral blood mononuclear cells not only reduced their guanosine triphosphate levels but also decreased the mannosylation of high- and low-molecular-weight glycoproteins involved in intercellular adhesion and leukocyte trafficking. Although this has not formally been shown, this may affect the recruitment of leukocytes to sites of inflammation.

Meanwhile, the efficacy of mycophenolate to suppress immunologic processes has led to the approval of the drug for acute renal graft rejection. Also, mycophenolate has been used in the treatment of vasculitis and in autoimmune disorders such as bullous pemphigoid. Thus far there has only been 1 report that mycophenolate has efficacy in the treatment of PV. This report extends our previously limited experience with mycophenolate in PV to an additional, previously unreported 12 patients who received treatment in our hospital.

RESULTS

Twelve patients with histologically confirmed PV were initially treated with a combination therapy of prednisolone (2 mg/kg of body weight per day) and azathioprine (1.5-2 mg/kg of body weight per day). Despite thorough examinations (eg, chest radiograph or ultrasonography), no underlying disease was detectable. Although all patients experienced improvement of their disease initially, reduction of steroids doses led to early relapses in all cases.

Treatment with azathioprine was discontinued and all patients were subjected to a combination therapy with 2 g/d of mycophenolate mofetil and 2 mg/kg per day of prednisolone. When induction of new blisters ceased, steroid doses were reduced by 50% and then slowly tapered during the follow-up period. Eleven of 12 patients responded to treatment. One patient immediately relapsed after steroid reduction and was withdrawn from the study. All patients responding were slowly reduced to either no steroids or 5 mg/d of maintenance therapy during the follow-up period. The median dose of prednisolone after 9 months was 2.5 mg/d. Mycophenolate dosage was not reduced and treatment was continued for the whole study period (median, 12 months per patient). None of the initial responders experienced a relapse during the median follow-up period of 12 months. All responding patients were clinically free of disease within 2 months.

Toxic effects from treatment were moderate (Table 2). Besides mild lymphopenia of 250 to 300/µL that was observed in 9 of 11 patients, only moderate gastrointestinal symptoms were observed in 5 of 11 patients. Transient rises in transaminases were observed in 3 patients.

Monitoring of serum titers of pemphigus autoantibodies as a mirror of disease activity revealed a rapid decrease of positive titers during therapy with mycophenolate and steroids (Table 3).

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>Weight, kg</th>
<th>Disease Duration, mo</th>
<th>Prior Treatment, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/42/M 25/M 55/M 65/M 75/M 85/M 95/M 105/M</td>
<td>72 63 58 53 72 5 72 63</td>
<td>6 4 4 8 7</td>
<td>Prednisolone, 150 Azathioprine, 150 Prednisolone, 120 Azathioprine, 100 Prednisolone, 100 Azathioprine, 120 Azathioprine, 100 Azathioprine, 100 Azathioprine, 100</td>
</tr>
</tbody>
</table>

Table 2. Toxic Effects of Mycophenolate

<table>
<thead>
<tr>
<th>Toxic Effect</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild lymphopenia</td>
<td>9/11</td>
</tr>
<tr>
<td>Gastrointestinal symptoms</td>
<td>5/11</td>
</tr>
<tr>
<td>Transient rises in transaminases</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 3. Serum Titters of Pemphigus Autoantibodies

<table>
<thead>
<tr>
<th>Patient No./Age, y/Sex</th>
<th>Disease Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior to Treatment</td>
<td>After Therapy</td>
</tr>
<tr>
<td>Serum titter</td>
<td>Serum titter</td>
</tr>
<tr>
<td>Prednisolone, 150</td>
<td>Azathioprine, 100</td>
</tr>
<tr>
<td>Prednisolone, 120</td>
<td>Azathioprine, 100</td>
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<tr>
<td>Prednisolone, 100</td>
<td>Azathioprine, 100</td>
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</table>

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Pemphigus vulgaris is a dermatologic autoimmune disorder that was characterized by a usually fatal outcome before the advent of immunosuppressive therapies. Although death rates due to PV are significantly lower today, some patients remain difficult to treat and show a relapsing course of the disease whenever immunosuppressive therapies are reduced. These relapses often require the repeated use of high doses of steroids and immunosuppressive drugs. Patients occasionally die because of the adverse effects of these aggressive therapeutic approaches.

Mycophenolate has been approved for acute renal transplant rejection due to its immunosuppressive effects primarily exerted on lymphocytes. Besides being a potent drug in the transplantation situation, mycophenolate has also been used in the treatment of autoimmune disorders such as vasculitis and bullous pemphigoid. This study extends our earlier experience on the efficacy of mycophenolate in PV with 12 new, previously unreported patients.

Our study demonstrates that mycophenolate in combination with prednisolone is an effective drug in the treatment of patients suffering from PV. Due to the effectiveness of mycophenolate in patients relapsing under conventional treatment with azathioprine and prednisolone, one can conclude that mycophenolate is superior to azathioprine in the treatment of PV. In addition to being a highly effective drug in the treatment of PV, mycophenolate is also characterized by a low toxicity profile, causing only moderate adverse effects. Therefore, a combination therapy of prednisolone and mycophenolate might become standard therapy in patients with PV. Larger, randomized trials are necessary to carefully address this issue.

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REFERENCES