The effect of mycophenolate mofetil on patients with active non-renal SLE

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Controlled trials have demonstrated that Mycophenolate mofetil (MMF) is effective for lupus nephritis (1-5), but its efficacy in non-renal systemic lupus erythematosus (SLE) has not been as well-studied. We performed a six-month, prospective study, examining the effect of MMF on patients with mild to moderately active non-renal SLE.

We recruited adult patients meeting the 1997 revised American College of Rheumatology Classification Criteria for SLE (6), who had active SLE despite use of prednisone in doses of 7–20 mg/day and an immunomodulating medication. Active disease was defined as at least one clinical feature of active SLE, plus at least one laboratory abnormality of active lupus. Patients also had at least 2 of the following: patient global assessment of disease as active, physician global assessment of disease as active, and/or Systemic Lupus Activity Measure (SLAM) score of > 6 (7).

Subjects had to have failed or been intolerant of hydroxychloroquine. Patients who were on other agents were eligible after a six-week washout period.

Patients with active lupus nephritis, significant renal disease, prior use of MMF, active infection, use of cyclophosphamide in the past year, a serious concomitant illness, inability to give informed consent, or women who were pregnant or breast feeding were excluded.

All patients were examined by one rheumatologist at entry and at three and six months. At each visit, CBC, ESR, creatinine, dsDNA, complements, urinalysis, patient and physician global assessment scores, and SLAM score were assessed.

MMF was initiated at 500 mg daily and gradually increased to 1000 mg twice daily, if tolerated. The prednisone dose was kept stable for at least the first month but then could be tapered if the patient improved.

This was an investigator (KGM) initiated protocol which was approved by our IRB and subjects provided informed consent. Funding was provided by Roche Pharmaceuticals.

A significant response to MMF treatment was defined as at least a 20% improvement in the abnormal laboratory parameters measured, patient/physician global assessment, SLAM score, or a 20% reduction in mean daily prednisone dose.

Paired *t*-tests were used to compare baseline and follow-up measures when paired differences were normally distributed and the signed rank test was used otherwise. Assuming a placebo effect of 20%, with enrollment of 23 patients, we could detect a minimum of 25% difference between baseline and follow-up measures with a power of 0.8 and $p < 0.05$.

Of the 23 patients enrolled, one was male. The mean age (± SD) of the patients was 45 ± 14 years (range 23-71 years) with a mean disease duration (± SD) of 8.2 ± 10.9 years (range 0.5-45 years).

Three patients withdrew within the first month of study because of adverse reactions to MMF (one with rash and two with gastrointestinal upset). Another patient was withdrawn within the first month secondary to a subarachnoid hemorrhage that was unrelated to her SLE or treatment. Other adverse events were infrequent (four minor infections in three patients).

There were statistically significant improvements in the dsDNA levels, patient and physician global assessments, and SLAM score, as well as significant reductions in the mean daily dose of prednisone with MMF treatment (Table I). Only one patient was considered a treatment failure due to lack of efficacy after more than 3 months of MMF treatment, and was withdrawn from the study before the 6-month follow-up, as per study protocol.

Improvement (by at least 20% over follow-up), despite reduced prednisone doses, was noted for skin involvement (5/7 patients (73%)), oral ulcers (2/4, (50%)) and inflammatory arthritis (4/7 (57%)).

In summary, we found that MMF was a well-tolerated and effective steroid sparing agent in non-renal SLE patients.

Table I. Baseline and follow-up data of SLE patients treated with mycophenolate mofetil.

	Baseline	3 months	6 months	*p* value*
		(mean ± standard deviation)		
Number of patients	23	19	18	
Hemoglobin (g/dl)	12.7 ± 1.7	12.8 ± 1.3	13 ± 1.4	NS
WBC (x 10^9/L)	6.4 ± 3.8	7.3 ± 3.1	6.3 ± 3.3	NS
Platelets (x 10^9/L)	234 ± 117	238 ± 133	248 ± 145	NS
ESR (mm/hr)	23 ± 30	13 ± 11	13 ± 12	NS
dsDNA (IU/ml)	224 ± 204	160 ± 177	101 ± 124	0.02
Total Complement (units)	47 ± 14	53 ± 12	52 ± 14	NS
C3 (mg/dl)	92 ± 33	95 ± 36	105 ± 38	NS
C4 (mg/dl)	17 ± 14	15 ± 7	16 ± 8	NS
Patient global (VAS, 0-10)	5.3 ± 2.1	3.8 ± 2.3	3.3 ± 2.3	0.014
Physician global (VAS, 0-10)	4.5 ± 1.6	3.1 ± 1.6	2.0 ± 1.8	0.003
SLAM (0-85)	10.4 ± 3.4	7.7 ± 3	7.3 ± 2.6	0.009
Prednisone dose (mg/day)	12.7 ± 5.3	12.4 ± 6.4	7.3 ± 4.5	0.0001

*Statistical significance based on differences between the baseline value at study entry compared to the value at the last follow-up for 19 patients who completed at least 3 months of treatment (6-month follow-up data used for 18 patients and 3-month follow-up data used for 1 patient).
NS: not statistically significant; WBC: white blood cell count; ESR: erythrocyte sedimentation rate; dsDNA: double-stranded DNA; VAS: visual analogue scale; SLAM: Systemic Lupus Activity Measure.

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