Mycophenolate Mofetil for Chronic Inflammatory Demyelinating Polyradiculoneuropathy

An Open-Label Study

A.J. Radziwill^a K. Schweikert^b T. Kuntzer^a P. Fuhr^b A.J. Steck^b

^aDepartment of Neurology, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, and

^bDepartment of Neurology, University Hospital Basel, Basel, Switzerland

Dear Sir,

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), an immune-mediated heterogeneous progressive or relapsing disorder, is considered as the chronic variant of the Guillain-Barré syndrome that differs from the latter disease by its temporal evolution over at least 2 months, by its relative absence of cranial nerve implication or autonomic disorder, by its relative absence of previous infection and by treatment response to corticosteroids. There are several effective evidence-based therapies, but not all patients improve with these treatments. Around 30% of patients do not respond to immunotherapy such as intravenous immunoglobulin (IVIg), plasma exchange, corticosteroids, azathioprine, cyclophosphamide or interferon- β [1].

Mycophenolate mofetil (MM), a non-competitive reversible inhibitor of inosine 5'-monophosphate dehydrogenase, is now widely used in transplantation medicine and in immune-mediated diseases. Its antiproliferative effect acts by inhibition of the de novo purine synthesis of activated T and B lymphocytes. MM can improve several neurological disorders such as myasthenia gravis, inflammatory myopathy or CIDP [2–4].

We conducted an open-label study in 7 patients with CIDP diagnosed according to common guidelines [5]. Two women and 5 men with a mean age of 57.6 years (44–67 years), a mean disease duration of 9 years (2–23 years), 4 relapsing courses and 3 progressive courses were enrolled after oral informed consent because of insufficient response to previous therapies or because of a high frequency of IVIg therapy (at least every 4 weeks). Two patients had predominantly sensory signs, 2 predominantly motor signs and 3 motor and sensory signs. Superimposed axonal loss was demonstrated by electroneuromyography in 2 out of 7 cases. One gram of MM was administered twice daily, in 3 patients in association with prednisone and/or IVIg (table 1). Efficacy was defined as stability or improvement of disability after 6 months and/or reduction of IVIg dose within 12 months. The disability was measured by the disability grade (0–5 points; 0 = healthy, 1 = minor signs, 2 = able to walk without assistance but unable to run, 3 = able to walk 5 m only with help, 4 = chair/bed bound, 5 = death), the Neurological Disability Scale (NDS; 0–202 points; 0 = healthy, 202 = worst situation) [6], the Hammersmith Motor Ability Test

(HMAT; 0–40 points; 0 = unable to move, 40 = normal) [7] and the timed 10-meter walk test [8]. Physical and neurological examinations associated with laboratory tests were performed at defined regular intervals.

Seven patients received MM with a mean duration of 13.7 months (6–24 months). All of them had previous treatments without significant and longstanding amelioration. No spontaneous improvement was seen (table 1). Two patients had adverse events (gastrointestinal disorder, infection with leukopenia). The dosage of MM had to be decreased in 1 patient with improvement because of adverse events and treatment was stopped in the other one because there was no effect. Neurological signs and function improved in 3 patients (table 1); 1 patient had pain relief. An improvement was seen in 1 of the 3 patients despite superimposed axonal loss, starting already after 2 months of treatment and was sustained up to 10–24 months. One patient (patient 4) continued to be treated with IVIg with the same interval and dosage, but the relapses presented a lesser degree of disability.

In the literature the long-term efficacy of MM in CIDP is unknown. One out of 3

Table 1. Summary of clinical course

Pa-tient	Disease duration years	Type/course	Previous treatments	Addition therapy	Follow-up months	Disability grade ¹	NDS ¹	HMAT ¹	10-meter walk test ¹	Reasons to stop MM
1	2	sensory/progressive, painful, demyelinating	IVIg	no	14	1/1	17/14	40/40	7.0/7.0	continued (relief of pain)
2	23	sensory/relapsing, demyelinating	prednisone, interferon- β , azathioprine, cyclophosphamide	IVIg	12	1/1	48/52	39/34	7.4/7.3	no benefit
3	7	motor/progressive, demyelinating	IVIg, azathioprine	no	12	2/2	55/72	22/19	18.2/19.0	no benefit
4	2	sensory-motor/relapsing, demyelinating	interferon- β , azathioprine, IVIg	IVIg, prednisone	18	2/1	50/19	22/40	9.3/5.0	continued
5	14	motor/progressive, axonal-demyelinating	IVIg	no	6	2/2	46/46	24/24	-/8.0	no benefit, AE
6	14	sensory-motor/relapsing, demyelinating	prednisone, azathioprine, IVIg, cyclophosphamide, interferon- β	no	24	1/1	26/16	33/40	6.9/5.1	continued , AE
7	2	sensory-motor/relapsing, axonal-demyelinating	IVIg	prednisone	10	2/1	47/26	38/37	10.4/8.8	continued

The 4 patients with an improvement are shown in bold (1 with relief of pain). AE = Adverse events; HMAT = Hammersmith Motor Ability Test; NDS = Neurological Disability Scale.

¹ At baseline/at the end of follow-up.

patients responded after 4 months in one study [2]. In another study, 2 patients with additional IVIg or plasma exchange 'rapidly' recovered strength and sensation under MM, with a relapse after discontinuing and improvement after resuming MM [3]. Four patients had no benefit in another small study [4]. The dosage of IVIg in 2 other patients receiving simultaneously MM could be reduced by 50% [9]. Three out of 8 patients with idiopathic CIDP improved in a recently published study, whereas the 5 patients who had a secondary CIDP showed no response (4 associated with IgG or IgA monoclonal gammopathies of uncertain significance (MGUS), 1 with a POEMS syndrome) [10].

There might be subgroups of CIDP patients who respond to MM (e.g. relapsing course, CIDP without MGUS, predominantly sensory or motor-sensory signs). MM could be more effective if started early in the disease before axonal degeneration. A large prospective randomized trial is needed.

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