Ciclosporin A in Lupus Nephritis

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Dear Sir,

Renal involvement is the major cause of morbidity and mortality in patients with systemic lupus erythematosus (SLE) despite immunosuppressive therapy since up to 60-70% of patients with lupus nephritis progress to end-stage renal disease [1]. The most widely used therapeutic regimens include steroid plus azathioprine or cyclophosphamide [2]. The activation of disease under immunosuppressive therapy poses a great problem. Certain clinical approaches had been proposed to improve the survival. Plasmapheresis seems to be ineffective and did not improve the prognosis of patients under standard immunosuppressive treatment [3]. Ciclosporin A (CSA; Sandimmun®, Sandoz), by inhibiting interleukin-2 production, suppresses the helper T cells and has been shown to reduce anti-DNA production in an experimental animal model of SLE [4]. Ten patients (3 male, 7 female, mean age 29.5 ± 10.01 years, range 19-50) showing serologic or clinical activation of SLE under the immunosuppressive treatment with prednisolone and azathioprine were enrolled in the study. Patients with uncontrolled hypertension and a serum creatinine level above 2 mg/dl were excluded. All patients fulfilled 4 or more of the American Rheumatism Association revised criteria. In 2 patients, renal biopsy was performed showing diffuse proliferative nephritis. Daily protein excretion was above 0.5 g in all patients. CSA (3-5 mg/kg/day) divided into 2 doses, was added to treatment of patients and dosage was then adjusted according to serum

CSA levels. The mean follow-up duration before and after CSA was 49 and 29 months, respectively. Each patient was followed regularly and at each visit blood pressure, serum creatinine, AST, ALT, 24-hour urinary protein excretion along with ANA and anti-DNA were recorded. An informed consent was obtained from all patients.

In 5 patients, marked clinical and serologic improvements were seen and continued to the end of the study. One patient died because of CNS involvement, and another was initiated to a chronic hemodialysis program. In the remaining 3 patients clinical or serologic activation persisted. Hypertension was observed in 3 of 10 patients and controlled with antihypertensive therapy. Mean anti-DNA titers of patients were significantly decreased at the end of study (from 87.2 ± 9.8 to $49.6 \pm 16.7 \text{ IU/ml}$, $p < 0.05$). There were no significant changes in proteinuria and serum creatinine levels.

Although there were some encouraging results, there was no controlled trial with CSA as a treatment of lupus nephritis. Effects of CSA in SLE were evaluated in some uncontrolled trials and anecdotal reports [5-7]. Favre et al. [8] showed decrement in proteinuria and clinical improvement in 26 patients. No change in anti-DNA production was reported. We observed decrement in the anti-DNA titers and clinical improvement in 5 of 10 patients showing clinical or serologic activation of disease. Controlled trials are needed to clarify the role of CSA in the treatment of lupus nephritis.

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