Steroid-Resistant Idiopathic Nephrotic Syndrome and Cyclosporin

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Dear Sir,

Steroid-resistant idiopathic nephrotic syndrome carries a poor prognosis since about half of the patients progress to end-stage renal disease. Immunosuppressive agents, namely alkylating agents, may be efficient in only a few steroid-resistant patients. Conflicting results have been reported with the use of cyclosporin given as mono-therapy [1–5]. However, it seems that only a small proportion of patients attain complete remission. We report our experience on the effects of cyclosporin in association with prednisone in 31 children with idiopathic nephrotic syndrome. All patients, 13 girls and 18 boys, aged 1 month to 14.3 years at the onset of nephrotic syndrome, had failed to respond to daily prednisone 60 mg/m² for 1 month, followed by three methylprednisolone pulses 1 g/1.73 m². Four patients had in addition received chlor-ambucil without beneficial effect. Renal biopsy had shown minimal-change disease (MCD) in 19 cases, and focal and segmental glomerulosclerosis (FSGS) in 12 cases. The treatment with cyclosporin was undertaken after informed consent of the parents. Children who had a creatinine clearance of less than 50 ml/min/1.73 m² or who had had the disease for more than 2 years were excluded from the study. Cyclosporin, 150–200 mg/m², was given in combination with daily prednisone, 30 mg/m², for 1 month, and with alternate-day prednisone, 30 mg/m², thereafter for 5 months. Fourteen patients went into complete remission, 9 of them during the first 2 months of therapy. Three patients had a partial remission with a rise of serum albumin > 30 g/l but persistent proteinuria. The remaining 14 patients failed to respond to the treatment. The response to cyclosporin and prednisone was not correlated to the histopathological findings, since among the 14 patients who responded to the treatment, 9 had MCD and 5 FSGS, whereas among the 14 patients who failed to respond to the treatment, 9 had MCD and 5 had FSGS. There was no relationship between the response to the treatment and either the dose of cyclosporin which did not exceed 200 mg/m² or the trough cyclosporin whole blood levels as measured by radioimmunoassay using the monoclonal antibody (between 100 and 200 ng/ml).

Among the side effects of the treatment, 1 patient with FSGS progressed rapidly to end-stage renal failure after 2 months of treatment. The responsibility of cyclosporin, although not proven, may be suspected. Cyclosporin was withdrawn after 2 months in another patient because of a reduction in creatinine clearance which returned to normal values afterwards. High blood pressure was observed in 12 patients, hypertrichosis in 18, gum hypertrophy in 11, vomitings or diarrhea in 2, headaches in 1, and gynecomastia in 1 patient.

These preliminary data suggest that cyclosporin in combination with prednisone may be efficient in patients with steroid-resistant nephrotic syndrome with either MCD or FSGS. This combined

treatment seems therefore to optimize the therapeutic effects of ciclosporin and we are currently assessing the eventual reduction of its nephrotoxicity.

References

Waldo FB, Kohaut EC: Therapy of focal segmental glomerulosclerosis with cyclosporine A. *Pediatr Nephrol* 1987; 1:180–182.

Niaudet P, Habib R, Tête MJ, Hinglais N, Broyer M: Cyclosporin in the treatment of idiopathic nephrotic syndrome in children. *Pediatr Nephrol* 1987;1:566–573.

Garin EH, Orak JK, Hiott KL, Sutherland SE: Cyclosporine therapy for steroid-resistant nephrotic syndrome. *Am J Dis Child* 1988;142:985–988.

Brandis M, Burghard R, Leititis J, Zimmer-Hackl B, Hildebrandt F, Helmcher U: Cyclosporine A for treatment of nephrotic syndromes. *Transplant Proc* 1988;20(suppl 4): 275–279.

Brodehl J, Hoyer PF: Ciclosporine in idiopathic nephrotic syndrome of children. *Am J Nephrol* 1989;9(suppl 1):61–64.