

The Efficacy of Cyclosporine in Minimal Change Disease

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Introduction

MCD remains the most common pattern of idiopathic nephrotic syndrome in children involving 80% of all cases and its prevalence in adult patients is also far from negligible. Studies reveal that a 10-15% of adults having idiopathic nephrotic syndrome is due to this type of glomerulonephritis and 22% of all cases of nephrotic syndrome in adults is caused by MCNS (1). Since 1950 first line treatment choice of MCNS was established to be glucocorticoids therapy (2). Long lasting experience of this treatment choice in clinical arena showed that response rates and remissions tend to develop slower than in children (3) and this difficulty often leads to prolonged treatment with steroids bringing in light the multiple known serious unfavorable side effects of this therapy (3,4).

Patients who fail to appear complete remission (SR: steroid resistance), patients who appear relapses at a certain level of steroids dose during the tapering process (SD: steroid dependence) and patients who appear relapses repeatedly after the cessation of corticosteroids therapy on multiple occasions require alternative treatment approach (FR: frequent relapses). In 1985 at the 18th Annual Meeting of the American Society of Nephrology, Tejani et al and Meyrier et al introduced the first alternative treatment option, cyclosporine in children and adults with MCNS (5,6).

Table 1. Clinical data of 7 patients with MCNS before cyclosporine therapy

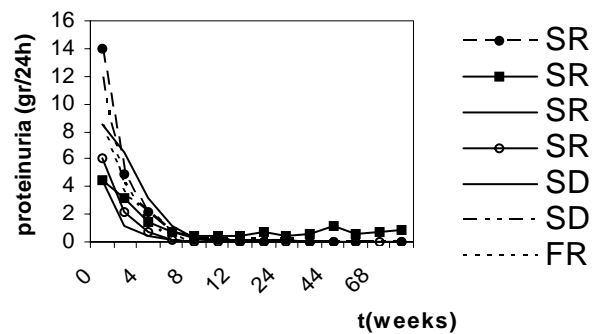
Patient s	Age	Sex	Status	Proteinuria (gr/24 h)	BP	Plasma Albumin (gr/dL)	Serum Creatinine (mg/dL)
1	22	M	SR	14	110/80	2.2	1.2
2	37	F	SR	4.5	125/85	3	0.9
3	44	F	SR	8.5	130/80	2.8	1
4	66	F	SR	6	130/80	2.7	1.2
5	30	M	SD	4.5	110/70	2.6	0.8
6	19	M	SD	12	100/65	2.2	1
7	68	F	FR	8.5	160/95	2.4	1.4

Patients and methods

We followed the long-term efficacy of CsA treatment in 7 adult patients with MCNS who previously were treated with classic corticosteroid therapy. Median age of the patients was 41 years (range 19-68) and sex ratio 4.3(female-male). At entry into the study we used oral administration of corticosteroids (16 mg/ day) and CsA (2.5mg/Kgr/day). The prior steroid responses of these patients were: four (4) of them were SR (steroid resistant), 2 were steroid dependent

(SD) and 1 was FR (frequent relapsed). Mean duration of therapy to attain complete remission in SD and FR patients was 5.8(±1.2) weeks and 8.4 (±3.4) weeks in SR patients. Treatment after complete remission continued for 12 weeks while the tapering period was 18 months. Blood pressure, serum creatinine, serum albumin and proteinuria, were checked every two weeks and CsA levels were measured during cyclosporine full treatment period every 2 weeks.

Figure 1. Course of proteinuria during cyclosporine therapy in 7 patients with MCNS



Rational basis for the treatment with this new antilymphocytic agent was that loss of negative charges in the glomerular polyanionic structures was probably due to secretion of lymphokines by T-lymphocytes (7,8).

Later on action of CsA was best established by its clear-cut effect on IL-2 secretion and other lymphokines from T-cells so that the recruitment of T-cells is attenuated while inflammatory effector mechanisms are diminished in the absence of other lymphokines and this leads to decrease proteinuria in this form of nephrotic syndrome (9).

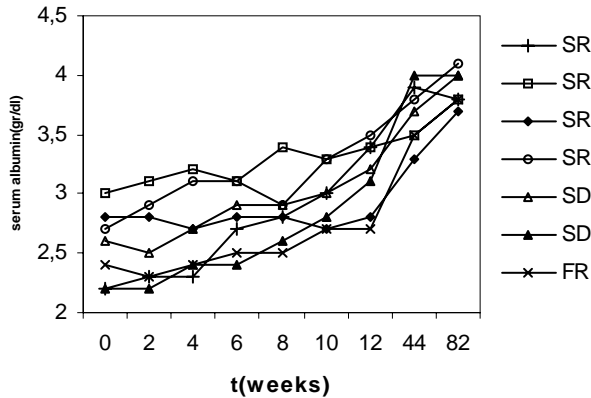
By this time there was also enough experience of CsA treatment to organ transplantation to control the safety of the drug.

In recent years CsA had been used in steroid sensitive and in steroid resistant nephrotic syndrome, particularly in combination with steroids and best results were seen in SD, SR and FR patients (10). Although CsA is strongly nephrotoxic the overall risk of nephropathy is dose-dependent and it is more often observed in steroid dependent syndrome (11).

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Figure 2. Course of serum albumin level during cyclosporine therapy in 7 patients with MCNS



In our study treatment induced complete remission rapidly in all patients apart from one of the SR patients in whom proteinuria was significantly diminished (initial proteinuria 4.5 gr and final 820 mg)

Mean duration of CsA therapy to attain complete remission in SD and FR patients was 5.8 ± 1.2 weeks and 8.4 ± 3.4 in SR patients.

Treatment after complete remission continued for 12 weeks while the tapering period was 18 months.

Mean 2 hours CsA levels were 570 ng/ml with range (478-666 ng/ml).

Serum creatinine wasn't deteriorated and Blood Pressure did not present any significant alterations from their initial level. Other evidence of CsA toxicity weren't observed.

In conclusion though cyclosporine cannot replace corticosteroids as first-line agent for most patients with minimal

change disease, the present data suggest that long-term maintenance treatment in combination with CsA and low dose-of prednisolone are efficacious and safe in adult patients in whom classic steroid therapy was not successful.

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