Cyclosporine (CYA) in Combination with Low Dose Methylprednisolone (MP) in Patients with Idiopathic Membranous Nephropathy (IMN) and Nephrotic Syndrome (NS)

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Introduction

Membranous nephropathy remains the most common cause of adult-onset nephrotic syndrome. Most patients do well with long-term natural history studies reporting a 10-year renal survival of 70% to 90% but the remainder progress to end stage renal failure (1). IMN is characterized by thickening of glomerular basement membrane (GBM) on light microscopy and by the presence of immune-complex deposits along the subepithelial side of the GBM. Corticosteroids and cytotoxic agents have been used widely in membranous nephropathy. (3) CYA may reduce proteinuria to non-nephrotic range in approximately two thirds of patients (4).

Apart from its immunosuppressive properties, CYA exerts its beneficial effects on proteinuria through changes in the properties of the glomelular barrier, resulting in increased charge and size selectivity (5,6).

In the present study we evaluate the effects of CYA in combination with low dose of methylprednisolone (MP) in patients with idiopathic membranous nephropathy and nephrotic syndrome.

Materials and methods

Eight patients, six males and two females, of mean age 49,12±16,5 years with IMN and NS were studied. The diagnosis of IMN was established by renal biopsy and all secondary causes of membranous nephropathy were excluded by extensive clinical and laboratory examination.

The patients were receiving oral CYA at a dose of 3,0-3,5 mg/kgBW/d and oral MP at dose 12,5 mg/d for 9 months. In all patients we determined the serum levels of creatinine, albumine, total cholesterol, urate, potassium, 24-hour urinary protein excretion and mean arterial pressure (MAP). None of the patients received antihypertensive medication except diuretics.

The baseline mean creatinine levels were 1,09±0,2 mg/dl, while the mean albumin levels were 2,65±0,80 mg/dl, the total cholesterol levels 445±98 mg/dl, the urate levels 7,2±1,9 mg/dl, the potassium levels 4,2±0,5 mEq/L, urinary protein excretion levels were 11,45±4,80 g/24hr and MAP 100±12 mmHg . Statistical analysis was performed using the SPSS program. ANOVA for repeated measures was performed to test the timing effect of the studied parameters during the study. A paired t-test was used to compare the differences between the studied parameters at the different time intervals along the study and p values less than 0,05 were considered to be statistically significant.

Results

Renal function, as judged by serum creatinine remained stable during the nine months of therapy. It was 1,16±0, 2 mg/dl at first month, 1,06 ±0,3 mg/dl at second month, 1,10±0,34 mg/dl at third month, 1,18±0,38 mg/dl at sixth month and 1,29±0,45 mg/dl at ninth month (p NS vs baseline).

Serum albumin levels were statistically increased since first month of therapy and remained so until the end of the ninth month. It was 3,05±0,90 mg/dl at first month, 3,38±0,89 mg/dl at second month, 3,56±0,61 mg/dl at third month, 3,87±0,84 mg/dl at sixth month and 3,96±0,83 mg/dl at ninth month (p=0,015 vs baseline).

Serum total cholesterol levels were significantly decreased from the second month and remained so until the end of the study. It was 402±86 mg/dl at first month, 382±87 mg/dl at second month, 379±111 mg/dl at third month, 336±88 mg/dl at sixth month and 318±83 mg/dl at ninth month (p=0,026 vs baseline).

Serum uric acid was significantly increased since the first month of therapy (p=0,03) and remained so until the end of the ninth month. It was 7,2±1,9 mg/dl at first month 7,6±2,0 mg/dl at second month, 8,2±1,7 mg/dl at third month, 8,8±2,0 mg/dl at sixth month and 9,5±1,6 mg/dl at the endpoint.

Serum potassium was unchanged during the therapy (p=NS). It was 4,6±0,6 mEq/L at first month, 4,7±0,7 mEq/L at second month, 4,6±0,5 mEq/L at third month, 4,7±0,7 mEq/L at sixth month and 4,7±0,5 mEq/L at the end of the study.

Proteinuria was significantly reduced from the first month (p=0,01) and remained so until the endpoint. It was 6,34±3,51 g/24hr at first month, 4,37±2,35 g/24hr at second month, 5,17±2,89 g/24hr at third month, 3,42±2,64 g/24hr at sixth month and 3,47±2,78 g/24hr at the end of the ninth month. Of note, four patients despite the decrease of proteinuria continued to present nephrotic range proteinuria at the end of the study.

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MAP was unchanged during the therapy (p=NS). It was 101±8 mmHg at first month, 102±8 mmHg at second month, 102±8 mmHg at third month, 108±11 mmHg at sixth month and 109±13 mmHg at ninth month.

Conclusions

In patients with IMN and NS, the administration of CYA and low dose MP results in substantial reduction of proteinuria and improvement of hypoalbuminaemia and hyperlipidaemia without changing the renal function and arterial pressure.

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