EFFECT OF THYMUS FACTOR AND LEVAMISOLE TREATMENT IN PATIENTS WITH PERSISTENT NEPHROTIC SYNDROME

S Czekalski, D Sulima, G Strzelecka

Academy of Medicine, Szczecin, Poland

Summary

The effects of thymus factor (TFX) and levamisole on the clinical picture and some indices of cellular immunity have been evaluated in 10 patients with nephrotic syndrome due to membranoproliferative glomerulonephritis Type I. The patients revealed decreased T-lymphocyte number and impaired responsiveness to phytohaemagglutinin (PHA) stimulation before treatment. An association between the slight diminution of proteinuria and the increase of E-rosette forming lymphocytes, increased responsiveness to PHA and return to normal of previously elevated B-cell percentages, was observed in four patients treated with TFX and one patient treated with levamisole.

Introduction

In 1974 Shalhoub [1] proposed the hypothesis of altered T-cell function as the basis of lipoid nephrosis. Peters and Lachman [2] suggest that in glomerulonephritis there is a state of immune deficiency, caused by complement depletion, leading to defective clearance of antigen-antibody complexes by the reticuloendothelial system and glomerular trapping of these complexes. Hoffstein et al [3] demonstrated T-cell deficiency in experimental immune complex glomerulonephritis represents a state of immune deficiency, some patients reveal a decreased and functional impairment of T-lymphocyte numbers. The approach to treatment of such patients may require the use of agents which stimulate the immune response.

This study evaluates the effect of two immunostimulants: thymus factor and levamisole treatment in two comparable groups of five patients with persistent nephrotic syndrome due to chronic Type I membranoproliferative glomerulonephritis, who had T-lymphocyte deficiency and impairment of T-lymphocyte function and refused the proposal of combined immunosuppressive-glucocorticoid therapy.

Patients and methods

Ten patients with nephrotic syndrome due to chronic Type I membranoproliferative glomerulonephritis were the subject of the study. Their urine protein excretion exceeded 3.5g/24hr (mean 5.3 ± 1.6g/24hr) lasted from 6–20 months (mean 12 ± 6 months). The patients revealed normal total lymphocyte numbers (2021 ± 667/mm^3), decreased T-lymphocyte number detected as E rosette-forming cells (E-RFC; 56 ± 9%; normal, 68 ± 9%), impaired T-lymphocyte response to phytohaemagglutinin (PHA) stimulation (stimulation index 42.5 ± 26%; normal: 83 ± 7%). B-lymphocyte numbers were evaluated by EA rosettes (EA-RFC; 33 ± 10%) and EAC rosettes (EAC-RFC; 32 ± 9%) was elevated (normal: 22 ± 7% and 22 ± 5%, respectively). The patients refused the proposal of combined immunosuppressive-glucocorticoid therapy, but accepted the trial of either thymus factor (TFX-Polfa, Poland) or levamisole treatment. Patients were hospitalised one to three months before the beginning of treatment and their urine protein excretion was monitored daily, the mean value of urinary protein loss was calculated (basal values). Then TFX or levamisole treatment was started. Some clinical data of patients included in both groups are presented in Table I.

Thymus factor (TFX-Polfa, the preparation from calf thymus glands, possessing the immunostimulatory properties, elaborated by J Czarniecki, MD) was

TABLE I. Some clinical data of patients included in the groups treated with TFX or levamisole

		TFX	Levamisole
Number of patients		5	5
Sex (Female/Male)		2/3	2/3
Age (years)	Mean ± SD (Range)	25.4 ± 11.3 (17 – 45)	31.6 ± 9.5 (25 – 48)
Duration of nephrotic syndrome before treatment (months)	Mean ± SD (Range)	9.8 ± 4.2 (9 – 16)	11.8 ± 5.5 (6 – 19)
Protein excretion during 1–3 months preceding treatment (g/24hr)	Mean ± SD (Range)	5.8 ± 1.7 (3.5 – 7.6)	5.0 ± 1.6 (3.5 – 7.2)
Serum albumin (g/100ml)	Mean ± SD (Range)	2.8 ± 0.3 (2.3 – 3.1)	2.9 ± 0.3 (2.3 – 3.1)
Plasma creatinine (mg/100ml)	Mean ± SD (Range)	1.1 ± 0.3 (0.8 – 1.6)	2.0 ± 1.0 (1.2 – 3.6)
Creatinine clearance (ml/min)	Mean ± SD (Range)	89 ± 33 (32 – 114)	71 ± 43 (29 – 138)

administered daily in a dose of 20mg i.v. for one to two months. Levamisole (Decaris, Richter, Hungery) was given orally 150mg for two consecutive days, repeated every week for one to three months. Urinary protein excretion during treatment was monitored daily and mean value calculated and compared to basal value. Serum albumin concentration, plasma creatinine and creatinine clearance were measured weekly. The determination of total lymphocyte number, E-RFC, stimulation index after PHA, EA-RFC and EAC-RFC were repeated at the end of treatment.

Results

Four patients from the group treated with TFX had decreased protein excretion during the drug administration ranging 7–39 per cent of basal value, while in one case slight increase of protein excretion was noted. In patients treated with levamisole, only one demonstrated a decline (21 per cent of basal value) of mean daily protein excretion. Four other patients from this group revealed a slight increase in urinary protein excretion. No significant changes in serum albumin, plasma creatinine or creatinine clearance were found in either group. No side effects have been observed during treatment. As presented in Table II, five patients who responded to treatment with slight diminution of protein excretion the increase of total lymphocytes number accompanied by an increase of E-RFC, increased PHA induced-stimulation index and normalisation of previously augmented per cent of EA-RFC and EAC-RFC have been found. In five patients who did not respond to treatment with diminution of protein excretion no marked changes in the indices of cellular immunity were found.

TABLE II. Effect of treatment on some indices of cellular immunity in patients with and without diminution of proteinuria

	Patients with diminution of proteinuria		Patients without diminution of proteinuria	
	Before treatment	After treatment	Before treatment	After treatment
Lymphocytes n/mm^3	1883 ± 829*	2622 ± 1054†	2195 ± 484	2053 ± 350
E-rosettes %	57 ± 6	68 ± 5‡	60 ± 13	51 ± 12
Blastic transformation index after PHA stimulation %	44 ± 24	63 ± 13†	45 ± 30	51 ± 29
EA-rosettes %	34 ± 6	21 ± 5†	29 ± 14	35 ± 9
EAC-rosettes %	35 ± 5	20 ± 4‡	30 ± 14	37 ± 13

*Mean ± SD, † $p < 0.05$, ‡ $p < 0.01$, paired Student's t-test

Discussion

Most investigators have concluded that no therapeutic regimen yet devised is effective in modifying the natural history of Type I membranoproliferative glomerulonephritis [4]. Persistent nephrotic syndrome is one of the factors which confer an ominous prognosis in this disease [5]. The rationale for the treatment of our patients with immunostimulants was the presence of indices of decreased T-lymphocyte numbers and their impaired function. The mechanism of action of TFX, like the other preparations with thymic activity, is believed to promote T-cell differentiation which may induce immunologic changes with or without clinical improvement. Four patients out of five responded to TFX treatment with an increase of T-lymphocyte numbers and the augmentation of blastic transformation index after PHA stimulation. Only these patients experienced slight beneficial clinical effect of treatment manifested as a moderate diminution of urinary protein excretion. The effect of levamisole treatment both on the clinical picture and some indices of cellular immunity was markedly less pronounced. Only one patient responded to treatment with an improvement of T-lymphocyte function associated with slight diminution of protein excretion. In the patients who did not respond to treatment with an increase of T-cell number and improvement in their function, but no beneficial effect on clinical picture has been found.

The results of this preliminary report suggest that the improvement of impaired T-lymphocyte function in patients with nephrotic syndrome due to Type I membranoproliferative glomerulonephritis treated with TFX is associated with only slight diminution of proteinuria, while levamisole treatment was generally without beneficial effect.

References

1 Shalhoub RJ. *Lancet 1974; ii:* 556
2 Peters DK, Lachman DJ. *Lancet 1974; i:* 58
3 Hoffstein PE, Villalobos R, Hill C, Klahr S. *Kidney Int 1977; 11:* 318
4 Glassock RJ. In Wilson CB, Brenner BM, Stein JH, eds. *Immunologic Mechanisms of Renal Disease 1979;* 255. New York: Churchill Livingstone
5 Barbiano di Belgiojoso G et al. *Nephron 1977; 19:* 250

Address for correspondence: S Czekalski, Academy of Medicine, Szczecin, Poland