

LOW-PROTEIN DIET INCREASES SERUM ALBUMIN BY REDUCING PROTEINURIA IN SOME NEPHROTIC PATIENTS

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Summary

A reduction in protein intake was associated with a fall in proteinuria without lowering serum albumin in eight patients with an idiopathic glomerulopathy. If the proteinuria was reduced to ≥ 25 per cent, serum albumin rose with this regimen. Unfortunately, the decrease in creatinine clearance was not mitigated by this low protein intake.

Introduction

Severe proteinuria with subsequent hypoalbuminaemia due to membranous nephropathy, membranoproliferative glomerulonephritis and focal segmental glomerulosclerosis is generally not improved by corticosteroid or other immunosuppressive agents. Non-steroidal anti-inflammatory drugs, i.e. prostaglandin synthesis inhibitors may relieve symptoms by reducing protein excretion but do probably not affect the course of the disease [1]. Recent studies on experimental glomerulonephritis suggest that a protein-restricted diet reduces proteinuria, increases serum albumin and might stop the progression of renal failure [2]. This study investigated whether such a regimen has a similar effect on patients with severe proteinuria.

Patients and methods

The group consisted of eight patients (age 22-70 years). Proteinuria in all of them was more than 3.5g/24hr. Histological diagnoses were: membranous nephropathy in three, membranoproliferative glomerulonephritis in three and focal segmental sclerosis in two. All were on a diuretic and the prescribed diet contained 50mmol sodium/day. Five patients were taking non-steroidal anti-inflammatory drugs. The above therapy was continued for the duration of the study.

Proteinuria, creatinine clearance in 24-hour urine specimens and serum albumin were assessed according to the following scheme. The first two measurements with an interval of 12–18 weeks while the patients were still on a 70 gram protein diet in seven patients. Subsequently all eight patients went over to a 30 gram protein diet for four to six weeks, after which the above parameters were measured again. Depending on the patient's subjective sense of well-being four patients continued the 30 gram protein diet and four patients returned to a 70 gram protein diet, again for a period of four to six weeks. Thereafter and 12–18 weeks later all parameters were assessed again.

Selectivity [3] was defined as the slope with the horizontal axis of the regression line relating the logarithm of renal clearance of proteins, expressed in percentages of the transferrin clearance (vertical axis), to the logarithm of their molecular weights (horizontal axis). Besides transferrin (mol wt 88,000), the plasma and urinary concentration in 24-hour specimen of α_1 -acid glycoprotein (mol wt 40,000), albumin (mol wt 67,000), IgG (mol wt 150,000) and α_2 -macroglobulin (mol wt 840,000) were measured by nephelometry. Selectivity was assessed when the patients were on the 70 gram protein diet and once when they were on the 30 gram protein diet.

Data were presented as median values. To analyse differences between consecutive measurements Wilcoxon's signed rank test for paired observations was used. Spearman rank correlation coefficient was calculated to assess whether a low protein diet correlated with a decreased proteinuria.

Results

The median value of proteinuria of the first two measurements (patients on a 70g protein diet) was 9.5 and 9.9g/24hr. Four to six weeks after start of the 30g protein diet the proteinuria in all patients had fallen to a median value of 7.2g/24hr ($p < 0.05$). Since the fall in protein loss did not result in a direct increase of serum albumin, it was decided that the continuation of the low protein diet should depend on the patient's coping with the diet. Four patients felt hungry and weary on the 30g protein intake and wished to resume the 70g protein diet. When the proteinuria was assessed in these patients four to six weeks later, an increase was found. On the basis of this finding, the patients were persuaded to go back to a 30g protein diet. At the final measurement all eight patients had had a protein restriction for a minimum of 12 consecutive weeks. In all patients a decrease in proteinuria was found as shown in Figure 1.

The median value of serum albumin of the first two measurements was 25 and 27g/L respectively and creatinine clearance 70 and 61ml/min. Four to six weeks after reducing the protein intake to 30 gram the median value of serum albumin was 24g/L due to a drop of serum albumin in two patients. However, in four patients serum albumin increased. Because of the different response to protein restriction in the individual patients, four patients started again with a 70g protein diet. In three of them serum albumin rose, in one it declined. Almost the same effect was seen in the four patients continuing the 30g protein diet. In two patients serum albumin rose and in two patients it remained stable.

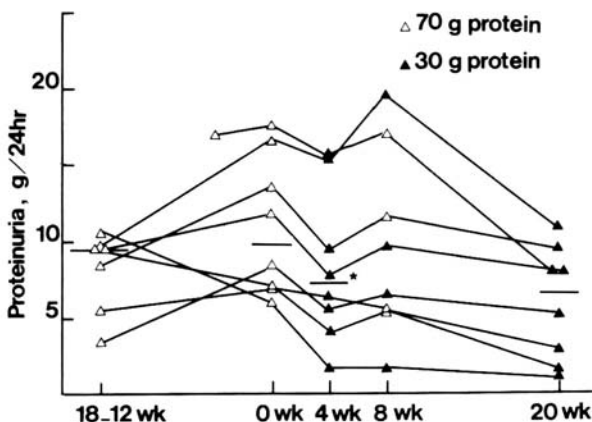


Figure 1. Proteinuria (g/24hr) in eight nephrotic patients after a 70g and a 30g protein diet. The horizontal bar represents the median value. The asterisk indicates a significant ($p < 0.05$ Wilcoxon test for paired observations) with the previous measurement

So it was decided that all patients should continue with a 30g protein diet. Serum albumin, measured after all patients had a protein restriction for a minimum of 12 consecutive weeks, showed a persistent rise in six of them (Table I). When the reduction in proteinuria was expressed as a percentage of previous values, a significant inverse correlation with the rise of albumin could be established ($r=0.86$).

TABLE I. Effect on serum albumin and creatinine clearance in eight nephrotic patients on 70 and 30g protein diets. The results shown are expressed as median values

	18-12 weeks	0 weeks	4 weeks	8 weeks	20 weeks
Protein intake	70	70	30	30/70	30
Serum albumin (g/L)	25	27	24	27/26	29
Creatinine clearance (ml/min)	70	61	54	52/50	43

Reduction of the protein intake was followed by a decrease of creatinine clearance in seven patients. The median value of the creatinine clearance after four to six weeks protein restriction was 54ml/min. In three of the four patients resuming the 70g protein intake the creatinine clearance increased again. On the protein restricted diet for at least 12 weeks the creatinine clearance decreased to 43ml/min as shown in Table I.

The median value of the selectivity during the 70g protein diet measured in seven patients was 45° and 58° when it was repeated during the 30g protein diet ($p < 0.05$). This finding implies a greater selectivity of the proteinuria.

Discussion

Our findings agree with those of El Nahas [4] in that a low protein diet is followed by a reduction in proteinuria. The ratio of serum urea to creatinine fell during the period with a low protein diet, indicating the adherence to the diet by the patients. The reduction in proteinuria was in all but one patient associated with a decrease of the creatinine clearance. This could be an expression of a decrease in the glomerular compensatory hyperfusion and hyperfiltration which seems to exist in primary nephropathics [5]. Another sign of a diminished glomerular hyperfusion after lowering the protein intake is the increased selectivity of the proteinuria [6]. From our data it could be concluded that patients with a steroid resistant nephrotic syndrome might benefit, besides sodium restriction and a diuretic, from a protein restricted diet. This effect is seen, whether or not in combination with non-steroidal anti-inflammatory drugs. This regimen might reduce proteinuria and in case proteinuria does decrease 25 per cent or more serum albumin will rise.

The hypothesis that protein restriction results in prevention of the progression towards renal failure is difficult to prove because progression towards renal failure is frequently defined as decline in creatinine clearance. However, protein restriction in itself causes such a decline, so one parameter of progression loses its significance. Only long-term randomized studies may provide the answer to this question. This group of patients shows, however, that protein restriction even in cases of severe proteinuria is feasible.

References

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