

PERMEABILITY OF THE PERITONEUM TO PROTEINS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS PATIENTS WITH SYSTEMIC DISEASE

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Summary

Peritoneal loss and clearances of five serum proteins were determined in 13 continuous ambulatory peritoneal dialysis (CAPD) patients with renal failure due to a primary renal disease, four with systemic lupus, 15 with diabetic nephropathy and four with generalized amyloidosis. Proteins measured in serum and dialysate were albumin, transferrin, IgG, C₃ and α_2 -macroglobulin. Albumin was quantitatively the most important protein in the dialysate. Peritoneal protein losses and clearances were higher in the patients with amyloidosis or diabetes than in those with systemic lupus or with a primary renal disease. This increased permeability may be a consequence of vascular basement membrane alterations in the former conditions. In all patient groups protein clearances were lower, the higher the molecular weight of the protein. This relationship was linear when plotted on a double logarithmic scale. The observed restriction in transport of macromolecules was more than could be attributed to differences in free diffusion in water.

Introduction

Proteins in peritoneal dialysate mainly originate from the blood by passage through the peritoneal membrane. During their transport various structures have to be passed, such as the capillary endothelium, capillary basement membrane, interstitium, mesothelial basement membrane and mesothelium. It is conceivable that alterations in the peritoneal microcirculation, as could occur in patients with generalized vascular diseases, might influence the peritoneal permeability to proteins. Previous reports [1,2] in a limited number of patients on intermittent peritoneal dialysis showed reduced clearances of urea, creatinine and phosphate in two patients with malignant hypertension, one with diabetic nephropathy, one with systemic lupus erythematosus (SLE) and one with progressive systemic sclerosis.

In an earlier study Weber [3] found very large peritoneal protein losses in a patient with Alport's syndrome. As this hereditary glomerulonephritis is characterized by splitting and lamelling of the glomerular basement membrane, this again suggested to us that continuous ambulatory peritoneal dialysis (CAPD) patients with systemic disease involving the capillary wall of various organs, could have altered peritoneal permeability to proteins.

This study describes peritoneal protein losses and peritoneal protein clearances in CAPD patients with SLE, diabetic nephropathy and amyloidosis. The results are compared with those in a group of CAPD patients with a primary renal disease.

Patients and methods

Thirty-six CAPD patients volunteered for the study. Fifteen of them suffered type 1 diabetes mellitus with diabetic nephropathy, four SLE, four amyloidosis and 13 renal failure due to a primary renal disease. Mean age was 42 years in the diabetic, 32 in the SLE patients, 55 in the patients with amyloidosis and 41 in those with a primary renal disease. Nineteen of the patients were male, all SLE patients were female. The diabetic patients were studied on 27 occasions, those with a primary renal disease on 24 occasions. Each patient with amyloidosis and SLE was studied once. All studies were performed in the absence of any sign of peritonitis.

During each study period the patients collected all CAPD bags for three consecutive days. The dialysate volume of each bag was measured and samples were taken for determination of protein concentrations. At least once during each study period a blood sample was taken for determination of serum protein concentrations. Proteins measured were albumin, transferrin, IgG, complement C₃ and α_2 -macroglobulin. The molecular weight varied from 69,000 for albumin to 820,000 for α_2 -macroglobulin. Standard immunoturbidimetric and radial immunodiffusion methods were used.

The dialysate loss of the proteins (mg/24hr) was calculated by taking the sum of the quantity per bag for all dialysate collections during the study period, divided by the number of collection days. Protein clearances (ml/24hr) were calculated by dividing the dialysate loss per day by the serum concentration. This clearance was adjusted for variations in body surface area by expressing it as ml/24hr/1.73m². As the minimal dialysate/serum ratio was only 0.01 for albumin and even lower for the other proteins, the clearances were assumed to be equal to mass transfer area coefficients and therefore to represent peritoneal permeability.

If more than one study was done in a patient, mean values were used in further statistical analysis. The four patient groups were compared using the unpaired 't' test for two means.

Results

The peritoneal losses of the five proteins are shown in Table I. Albumin was most important quantitatively. In general, the patients with diabetes and amyloidosis had higher losses than those with a primary renal disease and SLE.

Figure 1 shows the peritoneal protein clearances in the four patient groups.

TABLE I. Comparison of protein loss (mg/24hr) into the dialysate of the five proteins according to their molecular weight (MW) in the patients with a primary renal disease (PRD), systemic lupus (SLE), diabetic nephropathy (DM) and amyloidosis (AMY) (mean \pm SEM)

	PRD	SLE	DM	AMY
albumin (MW 69,000)	3259 \pm 202	2115 \pm 248*	3959 \pm 265	4642 \pm 776*
transferrin (MW 90,000)	194 \pm 17	149 \pm 29	277 \pm 26*	269 \pm 47
IgG (MW 150,000)	511 \pm 56	569 \pm 97	695 \pm 64*	1580 \pm 492**
C ₃ (MW 184,000)	36 \pm 4	22 \pm 6	62 \pm 8**	64 \pm 19*
α_2 -macroglobulin (MW 820,000)	44 \pm 5	30 \pm 9	87 \pm 7***	64 \pm 19

't' test * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$, when compared to PRD patients

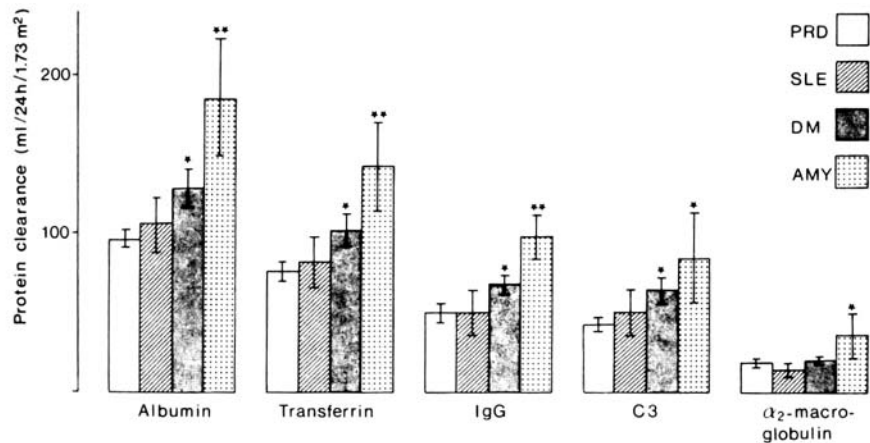


Figure 1. Peritoneal protein clearances (mean \pm SEM) in 13 CAPD patients with renal failure due to a primary renal disease (PRD), four with systemic lupus (SLE), 15 with diabetic nephropathy (DM) and four with amyloidosis (AMY). Clearances are higher in DM and AMY when compared to PRD (* $p < 0.05$; ** $p < 0.01$)

Patients with SLE had protein clearances similar to patients with a primary renal disease, but patients with diabetes or amyloidosis were found to have increased clearances for all investigated proteins, the only exception being α_2 -macroglobulin in the diabetic patients. Furthermore, the figure clearly shows that protein clearances were lower, the higher the molecular weight of the protein. This

relationship was linear when plotted on a double logarithmic scale. The mean (\pm SEM) of the slopes of the individual regression lines was -0.70 ± 0.02 in the patients with a primary renal disease, -0.86 ± 0.04 in those with SLE, -0.75 ± 0.02 in the diabetic patients and -0.72 ± 0.08 in the patients with amyloidosis. Only the slope of the regression line in the SLE patients was significantly different from that of the patients with a primary renal disease ($p < 0.01$).

TABLE II. Comparison of serum concentrations (g/L) of the five proteins in the four patient groups. See Table I for the description of the abbreviations

	PRD	SLE	DM	AMY
albumin	34 \pm 1	27 \pm 3*	32 \pm 1	26 \pm 2**
transferrin	2.6 \pm 0.1	2.3 \pm 0.1	2.7 \pm 0.1	1.9 \pm 0.2*
IgG	10.7 \pm 1.0	15.8 \pm 2.7	10.5 \pm 0.6	16.2 \pm 4.0
C ₃	0.84 \pm 0.06	0.55 \pm 0.05*	0.95 \pm 0.04	0.77 \pm 0.06
α_2 -macroglobulin	2.6 \pm 0.2	2.9 \pm 0.3	4.3 \pm 0.2***	2.1 \pm 0.3

In Table II the mean serum concentrations are given. Patients with SLE and amyloidosis had lower serum albumin concentrations than the other patients. Complement C₃ was lower in the SLE patients and α_2 -macroglobulin in the diabetic patients, when compared to the group with a primary renal disease.

Discussion

In this study we have shown that peritoneal protein losses and peritoneal protein clearances were increased in CAPD patients with diabetes mellitus or amyloidosis, when compared to patients with a primary renal disease or SLE. Patients with diabetic microangiopathy have increased microvascular permeability to proteins [4]. This may be the consequence of the conspicuous changes in the structure and thickness of the capillary basement membranes, reported in the capillaries of diabetic patients, for instance in muscles [5,6]. Especially basement membrane thickening with areas of loosening of the fibrillar meshwork has been described [7]. It is tempting to speculate that the increased peritoneal permeability to macromolecules in diabetic CAPD patients may be a consequence of peritoneal microangiopathy.

In the four patients with amyloidosis a peritoneal biopsy was done during catheter placement. In all biopsy specimens amyloid was found in the vessel walls of their peritoneal capillaries. This may explain their high permeability to proteins. In the SLE patients we found no evidence of an abnormal high or low peritoneal permeability.

The concentration of most serum proteins was in the normal range. The low serum albumin and transferrin concentrations in the patients with amyloidosis may be a consequence of the large peritoneal loss of the proteins. No obvious explanation is present for the low serum albumin in the SLE patients. The

observed low C_3 concentrations in these patients and the high α_2 -macroglobulin concentrations in the diabetic patients are known from the literature [8,9].

In all four patient groups the clearances of the investigated serum proteins from the blood to the peritoneal cavity were dependent on their molecular weight. The slopes of the regression lines between clearances and molecular weight varied from -0.70 in the patients with a primary renal disease to -0.86 in those with SLE. These slopes represent the permeability of the peritoneal membrane to macromolecules: the steeper the slope, the less permeable to proteins with a high molecular weight. As all slopes were well below -0.36 , which is the expected slope for free diffusion in water of the proteins [10], a mechanism of restricted diffusion in the transport of macromolecules through the peritoneum is likely.

This study has shown that CAPD patients with diabetic nephropathy and with amyloidosis have increased peritoneal permeability to proteins, when compared to patients with a primary renal disease and SLE. This is probably due to alterations in the capillary basement membranes. In all patients the protein clearances were a function of their molecular weight, indicating a size selective barrier for macromolecules in the peritoneal membrane.

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