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Factors influencing serum levels and peritoneal clearances of low molecular weight proteins in continuous ambulatory peritoneal dialysis

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Factors influencing serum levels and peritoneal clearances of low molecular weight proteins in continuous ambulatory peritoneal dialysis. To identify the factors influencing the serum concentrations and the peritoneal clearances of low molecular weight proteins (LMWP), fourteen patients on continuous ambulatory peritoneal dialysis (CAPD) for 1 to 57 (mean 9.4) months were examined. LMWP [β_2-microglobulin (β_2m, molecular wt 11.8 kD), cystatin C (cyst C, molecular wt 13.2 kD), Clara cell protein (CC16, molecular wt 15.8 kD), retinol-binding protein (RBP, molecular wt 21 kD) and alpha 1-microglobulin (α_1m, molecular wt 33 kD)] and high molecular weight proteins (HMWP) [albumin (Alb, molecular wt 66 kD), immunoglobulins (IgG, molecular wt 170 kD and IgM, molecular wt 600 kD) and alpha 2-macroglobulin (α_2m, molecular wt 718 kD)] were determined by latex immunoassay in the serum and dialysate collected during the peritoneal equilibration test (PET) with 2.27% dextrose (N = 14), and in dialysate from 56 standard exchanges, performed the day preceding PET, with 1.36% (N = 21), 2.27% (N = 23) and 3.86% (N = 12) dextrose. Determinants of serum concentrations and transperitoneal clearances of the proteins were traced by stepwise regression analysis using as possible contributors age, sex, residual diuresis, duration of the therapy (for serum concentrations), molecular radius of the protein and peritoneal membrane characteristics (for peritoneal clearances). LMWP serum concentrations were markedly increased whereas serum concentrations of HMWP were within the normal range. Residual diuresis, age and duration of dialysis emerged as significant determinants of serum concentration of some proteins, whereas transperitoneal clearance was dependent mainly on the size of the protein and, only for HMWP, on the dwell time. Residual diuresis was inversely related to the serum concentrations of four LMWP. Age was negatively correlated to the serum concentrations of β_2m, CC16 and RBP. RBP and Alb were the only proteins whose serum concentration significantly decreased with time on CAPD. The relationship between peritoneal clearance and M_r shows two slopes suggesting the existence of two populations of pores in the peritoneal capillary wall: small pores of about 20 to 25 Å radius and large pores exceeding 100 Å radius. A long dialysis cycle is associated with significant loss of HMWP only. Daily peritoneal protein losses, in mg (mean ± SD), were as follows: β_2m 43.4 ± 4.5; cyst C 9.6 ± 1.8; CC16 1.8 ± 0.3; RBP 58.9 ± 11.1; α_1m 149.5 ± 15.7; Alb 6570 ± 530; IgG 750 ± 111; IgM 46.4 ± 14.9; and α_2m 67.0 ± 12.7. In conclusion, LMWP concentrations in the serum of patients on CAPD were markedly increased and influenced mainly by patient-related factors (residual diuresis and age). Serum albumin and RBP declined with the duration of dialysis. Peritoneal protein loss was determined by the size of the protein and, for large proteins, by the dwell time. The peritoneum behaves as a membrane with at least two populations of pores.

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The class of low molecular weight proteins (LMWP) includes a great variety of proteins with different biological functions. These proteins are characterized by their small size (<40 kD) leading to their rapid elimination from plasma by glomerular filtration and subsequent catabolism in proximal tubular cells. Recently, we demonstrated that (1) their serum concentration was elevated in hemodialyzed patients, and (2) the determinants of the predialysis serum level are patient-related (residual diuresis, age and sex), whereas those of the dialysis induced change in serum concentration are related to the protein size, permeability of the dialysis membrane and the degree of hemoconcentration [1]. Similar data are not available in patients who are on peritoneal dialysis. Available information is limited to the loss and the peritoneal transport characteristics of β_2m, high molecular weight proteins (HMWP) such as albumin, immunoglobulins, complement metabolites, and to the peritoneal transport characteristics of neutral dextrans [2–7]. In the present study we determined the serum concentrations and the peritoneal losses of five LMWP [β_2-microglobulin (β_2m, molecular wt 11.8 kD), cystatin C (cyst C, molecular wt 13.2 kD), protein 1 or Clara cell protein (CC16, molecular wt 15.8 kD), retinol-binding protein (RBP, molecular wt 21 kD) and alpha 1-microglobulin (α_1m, molecular wt 33 kD)] and four HMWP [albumin (Alb, molecular wt 66 kD), immunoglobulins (IgG, molecular wt 170 kD; IgM, molecular wt 600 kD) and alpha 2-macroglobulin (α_2m, molecular wt 718 kD)] in patients who were on continuous ambulatory peritoneal dialysis (CAPD). The factors influencing these parameters were also examined. The results demonstrate a marked elevation of the serum concentrations of LMWP in patients on CAPD, which is similar to that reported for hemodialyzed patients [1]. These serum levels are determined by patient-related factors (residual diuresis and age) and, only for albumin and RBP, related to the duration of dialysis. Peritoneal clearance of individual proteins is a function of their size.

Methods

Patients

Fourteen patients (6 females and 8 males) with a mean (± SD) age of 52.5 ± 13.6 (females) and 51.0 ± 12.9 (males) years,

Table 1. Patient characteristics

Patient no.	Sex	Age *yr*	Weight *kg*	Dialysis duration *months*	Diagnosis	Residual diuresis *ml/24 hr*
1.	m	64	65.0	57	Amylosis	0
2.	m	26	70.4	8	Ig A GN	0
3.	m	46	71.5	7	Sarcoidosis	135
4.	m	56	59.6	14	Wegener	450
5.	w	59	59.2	1	HTA	1180
6.	w	70	57.8	18	CIN	420
7.	w	47	50.5	9	Diabetes	400
8.	m	52	67.5	3	MPGN	140
9.	m	57	68.1	1	CGN	160
10.	w	33	54.8	3	CIN	1300
11.	w	44	69.9	1	PKD	0
12.	w	62	37.5	5	HTA	0
13.	m	42	62.5	2	HTA	125
14.	m	65	70.1	3	Diabetes	400

Abbreviations are: IgA GN, IgA glomerulonephritis; PKD, polycystic kidney disease; HTA, hypertension; CIN, chronic interstitial nephritis; MPGN, membranoproliferative glomerulonephritis; CGN, crescentic glomerulonephritis.

undergoing CAPD for 1 to 57 (mean 9.4) months were included. Their clinical characteristics, primary kidney disease and residual diuresis are presented in Table 1. At the time of the study, none had nephrotic syndrome or other pathological conditions such as chronic liver or lung disease, malignancy or inflammatory disorders, likely to interfere with protein metabolism. All patients had been free from peritonitis for at least one month prior to the study.

Dialysis procedure

The CAPD catheters were of the straight Missouri swan-neck type. They were surgically inserted through an infra-umbilical midline incision, with the exit-site about 6 cm above and 30 degrees off center from the original incision.

Patients were dialyzed continuously with four exchanges daily (3 in the daytime, 1 overnight), with 2 liters of dialysate containing 1.36%, 2.27% or 3.86% dextrose (Baxter Healthcare, Round Lake, IL, USA). The dwell time ranged from 3 to 6 (mean 4.45) hours during daytime and 9 to 12 (mean 10.50) hours during overnight exchanges. For the latter, only a 1.36% dextrose solution was used. The total dialysate effluent volume was recorded for all cycles of varying dwell time.

The recommended daily protein intake was 1.2 to 1.5 g/kg of body wt. Diet was supplemented whenever necessary with vitamins, calcium carbonate and aluminium hydroxide.

Study protocol

Samples were obtained during a standard four-hour peritoneal equilibration test (PET) [8], with 2.27% dextrose ($N = 14$). Serum samples were drawn at two hours, samples of dialysate were taken at the end of inflow and after two and four hours of PET. The total effluent volume was recorded at the end of the test. During the 24 hours preceding the PET, additional samples were obtained from each drained exchange whose volume was measured [$N = 56$, including 1.36% ($N = 21$), 2.27% ($N = 23$) and 3.86% ($N = 12$) dextrose]. All samples were frozen at −20°C until the day of analysis.

Analytical methods

All the proteins were determined in serum and dialysate samples by a sensitive immunoassay relying on the agglutination of latex particles (latex immunoassay) [9], using the antibodies from Dakopatts (Glostrup, Denmark). Creatinine was measured in serum and dialysate by the Jaffé's technique; dialysate values were corrected for glucose concentration, as previously described [8]. Urea nitrogen was measured by a modified carbamidodiacetyl reaction (Technicon SMAC System). Serum and dialysate glucose concentrations were determined by oxidation using the Beckman Glucose Analyzer 2.

Calculations and statistical analysis

PET data. Peritoneal mass transfer (PMT, mg/4 hr) and peritoneal clearance (Cl, ml/min) of creatinine, urea and of proteins were calculated from PET data as follows: $V_e \cdot C_e/T$ and $V_e \cdot C_e/t \cdot P$, respectively, where: V_e = total dialysate effluent volume (ml), C_e = dialysate effluent concentration of solute or protein, T and t = dwell time in hours and minutes, respectively, and P = serum concentration of the solute or protein [10]. Cl and PMT data were normalized for the body surface area (BSA) of 1.73 m^2 and expressed as the arithmetic mean ± SE.

Log transformation of the data were used if necessary (abnormal distribution) before statistical analysis. Factors influencing the serum levels or peritoneal loss of the proteins were analyzed by stepwise regression analysis using as dependent variable the log of the serum concentration or of the peritoneal clearance of the proteins, and as independent variables age, sex, residual diuresis as an indirect marker of residual glomerular filtration rate, duration of the therapy (for serum levels), molecular radius (M_r) of the protein (for peritoneal clearances) and peritoneal membrane characteristics. Sex was introduced in the model categorized as female 0 and male 1. Peritoneal membrane characteristics were determined on the basis of the PET results [8] and categorized as low 0 ($N = 2$), low-average 1 ($N = 6$), high-average 2 ($N = 4$) and high 3 ($N = 2$) permeable membrane.

Dialysate data

Daily loss of each protein (mg) was calculated from the protein concentration and the measured effluent volume of the exchanges collected during the 24 hours preceding PET. The influence of dextrose concentration and dwell time on the loss of proteins was evaluated in patients with low average and high average peritoneal permeability characteristics ($N = 10$), excluding those with either high or low peritoneal permeability ($N = 4$).

The influence of dextrose levels was examined by comparing the protein loss during a five-hour two liter exchange with 1.36% ($N = 8$), 2.27% ($N = 12$) and 3.86% ($N = 8$) dextrose. The influence of dwell time was assessed by comparing creatinine and protein peritoneal loss during short (5 hr, $N = 8$) and long (10 hr, $N = 10$) time exchange with two liters of 1.36% dextrose. All these samples were obtained from the exchanges performed the day preceding PET. Comparisons between the groups were performed by analysis of variance followed by the Scheffé's multiple comparison test, or by multiple linear regression analysis with $P < 0.05$ considered as statistically significant.

Table 2. Serum concentrations, peritoneal mass transfer, clearances and daily loss of solute and proteins (mean ± SE) in patients on CAPD (N = 14)

Parameters	M_r Å	Serum concentration, *mg/liter*	Peritoneal mass transfer *mg/4 hr · 1.73 m²*	Peritoneal clearance *μl/min · 1.73 m²*	Daily peritoneal loss *mg*
Urea	2.6	1272 ± 48	267.6 ± 15.8	15,100 ± 500	—
Creatinine	4.0	97.1 ± 3.5	98.7 ± 6.0	7,600 ± 500	—
LMWP[a]					
cyst C	15.1	8.8 ± 0.4	2.0 ± 0.3	1559 ± 126	9.6 ± 1.8
β_2m	16.0	33.4 ± 1.3	10.5 ± 1.5	1330 ± 165	43.4 ± 4.5
CC16	19.0	2.8 ± 0.2	0.4 ± 0.1	656 ± 110	1.8 ± 0.3
RBP	17.5	260.1 ± 12.5	14.2 ± 3.6	459 ± 56	58.9 ± 11.1
α_1m	27.7	508.9 ± 25.4	40.4 ± 7.8	168 ± 33	149.5 ± 15.7
HMWP[a]					
Albumin	36.0	37,100 ± 500	1657 ± 277	190 ± 33	6570 ± 530
IgG	54.0	12,700 ± 900	141.3 ± 16.1	65 ± 17	750 ± 111
α_2M	89.0	2526 ± 166	13.1 ± 2.2	35 ± 10	67.0 ± 12.7
IgM	96.0	1629 ± 204	8.4 ± 2.4	22 ± 3	46.4 ± 14.9

Abbreviations are: Mr, molecular radius; LMWP, low molecular weight proteins; HMWP, high molecular weight proteins.
[a] Normal range in serum, LMWP (mg/liter): cyst C, 0.6–1.6; β_2m, 1–2; CC16, 0.05–0.1; RBP, 50–80 and α_1m, 20–100; HMWP (g/liter): Alb, 35–50; IgG 5–14; α_2m, 1.5–3.5 and IgM, 0.6–2.5.

Results

Serum levels

The serum concentrations of LMWP were markedly increased, with mean values 4 to 40 times above normal; those of HMWP were within the normal range (Table 2).

Peritoneal transfer characteristics

The dialysate over serum concentration ratios observed for proteins and solutes at two and four hours during the PET are depicted in Figure 1. It is noteworthy that it increased continuously over time, a trend towards equilibrium being observed only for urea. The ratio at four hours decreased as M_r increased (Fig. 1).

The peritoneal clearances and the peritoneal mass transfer of solutes and proteins during the four hours PET are given in Table 2.

Peritoneal loss of proteins

The daily loss of proteins calculated on the basis of protein concentrations and drained volume of each exchange collected during the 24 hours preceding the PET is described in Table 2. It ranges (mean ± SE) from 1.8 ± 0.3 (CC16) to 149.5 ± 15.7 (α_1m) mg for LMWP and 46.4 ± 14.9 (IgM) to 6,570 ± 530 (Alb) mg for HMWP.

Determinants of serum levels and peritoneal transport of the proteins

Serum levels. Residual diuresis was inversely related to the serum concentrations of the four LMWP. It emerged as the most important determinant of the serum LMWP concentration. Age was inversely related to the serum concentrations of β_2m, CC16 and RBP. RBP and Alb were the only proteins whose serum concentration significantly decreased with time on peritoneal dialysis. Other factors such as peritoneal membrane characteristics and sex were without influence on the protein serum levels (Table 3).

Peritoneal transport. The peritoneal transport of proteins is influenced by the M_r of the protein. Indeed, by stepwise regression analysis using clearance data of all proteins as dependent variable and age, sex, residual renal function, duration of therapy, M_r of the protein and peritoneal membrane characteristics as possible predictors, only M_r emerges as significant determinant (inversely related to the peritoneal clearance, $r^2 = 0.54$, $P = 0.0001$). The relationship between peritoneal clearance and Mr shows a hyperbolic regression, constituted by two slopes [(a) $y = 5.646 - 2.728x$, $r^2 = 0.86$, $P = 0.0001$; (b) $y = 0.238$ to $0.023x$, $r^2 = 0.85$, $P = 0.0001$), suggesting the existence of two different populations of pores, a small one allowing proteins with $M_r < 25$ Å and another much larger accommodating proteins with M_r above 25 Å radius (Fig. 2).

The influence of dialysate dextrose concentration on protein loss is assessed during five hours exchanges. Results, presented in Figure 3, demonstrate that protein losses are virtually identical for each of three tested dextrose concentrations (1.36%, 2.27% and 3.86%), although the ultrafiltrate volume proved significantly higher for 3.86% than for 1.36% dialysate (results not shown).

The influence of dwell time was assessed by the ratio of protein loss at 10 over that of the five hour dwell with 1.36% dextrose dialysate. The average drained volume was identical for the two dwell times (2020 ± 540 ml during 10 hr and 2045 ± 750 ml during 5 hr dwell exchange). As shown in Figure 4, the ratio increases with the M_r of the protein, the difference with the creatinine ratio reaching significance for albumin and other larger HMWP.

Discussion

Our results demonstrate that, in CAPD patients, LMWP serum concentrations are markedly elevated, within the range reported previously in hemodialyzed patients [1], whereas serum concentrations of all large proteins are within the normal range. Taking into account the biological activities of some of these LMWP, such as β_2m, CC16 and cyst C [11–16], it is suggested that their

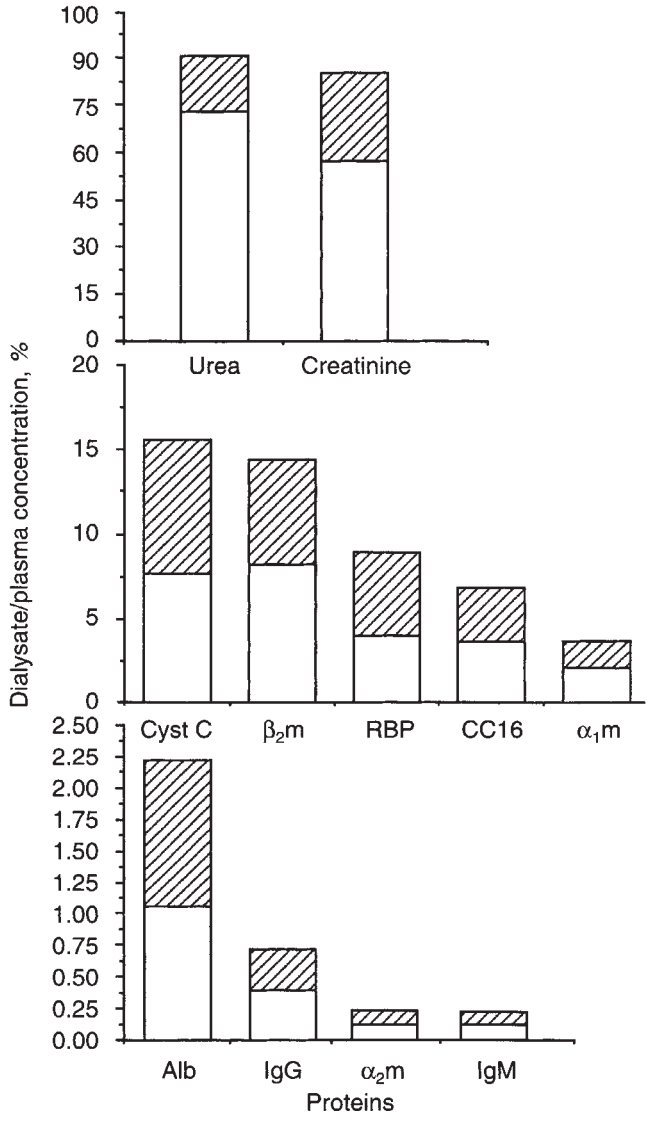

Fig. 1. *Equilibration between dialysate and plasma, expressed as % of dialysate to plasma concentration ratios (D/P), for creatinine, urea and proteins during peritoneal equilibration test (N = 14).* Symbols are (□) the first two hours and (▨) the following two hours of PET. Note the differences in scale for the three parts of the Figure.

Table 3. Determinants of serum LMWP and albumin (Alb) in CAPD patients ($N = 14$)

Dependent variable	Independent variables	Partial regression coefficient	Partial r^2
β_2m	Age	−0.267	0.11[a]
	Sex	0.031	0.03
	Residual diuresis	−0.0012	0.37[b]
	Duration of therapy	−0.008	0.05
	Peritoneum characteristics	0.22	0.06
Cyst C	Age	−0.271	0.04
	Sex	0.123	0.06
	Residual diuresis	−0.0003	0.30[b]
	Duration of therapy	−0.0021	0.06
	Peritoneum characteristics	0.30	0.04
CC16	Age	−0.589	0.09[a]
	Sex	−0.11	0.06
	Residual diuresis	−0.0003	0.29[b]
	Duration of therapy	0.21	0.01
	Peritoneum characteristics	−0.03	0.004
RBP	Age	−0.219	0.16[a]
	Sex	0.188	0.03
	Residual diuresis	−0.0002	0.10[a]
	Duration of therapy	−0.062	0.39[b]
	Peritoneum characteristics	−0.03	0.01
Alb	Age	−0.070	0.04
	Sex	0.035	0.05
	Residual diuresis	0.0002	0.02
	Duration of therapy	−0.002	0.32[b]
	Peritoneum characteristics	0.30	0.06

[a] $P < 0.01$, [b] $P = 0.0001$, otherwise statistically not significant

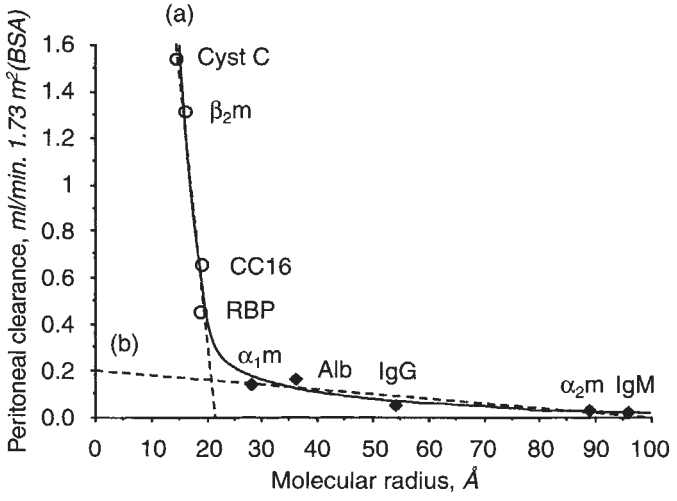

Fig. 2. *Transperitoneal protein clearances (ml/min/1.73 m^2 BSA) as a function of molecular radius (Å) of the proteins.* Symbols are: (○) low molecular weight proteins; (◆) alpha1-microglobulin and high molecular weight proteins.

retention contributes to the uremic syndrome of patients on CAPD.

The serum concentrations of LMWP in long-term CAPD patients are significantly influenced by residual renal function. Residual diuresis, used as a surrogate of residual renal function [17], is indeed inversely correlated with all LMWP serum levels. Taken together with similar observations made in patients given hemodialysis [1], these results confirm the major role of the residual kidney function in the catabolism of LMWP. Our results are in agreement with those obtained by others for β_2m in CAPD patients [18–20].

Advancing age is associated with a progressive fall of the serum concentrations of β_2m, CC16 and RBP. This observation is of special interest for β_2m, since age is considered a risk factor in the development of β_2m amyloidosis in dialyzed patients [21]. Decreased serum levels in aged patients could reflect an enhanced removal of β_2m into synovial amyloid deposits. Alternatively it may result from a decreasing synthesis of LMWP. The latter hypothesis, unlike the former, also accounts for the effect of age on the serum level of the other LMWP whose precipitation has never been documented in dialyzed patients.

In contrast to the observations made in hemodialyzed patients

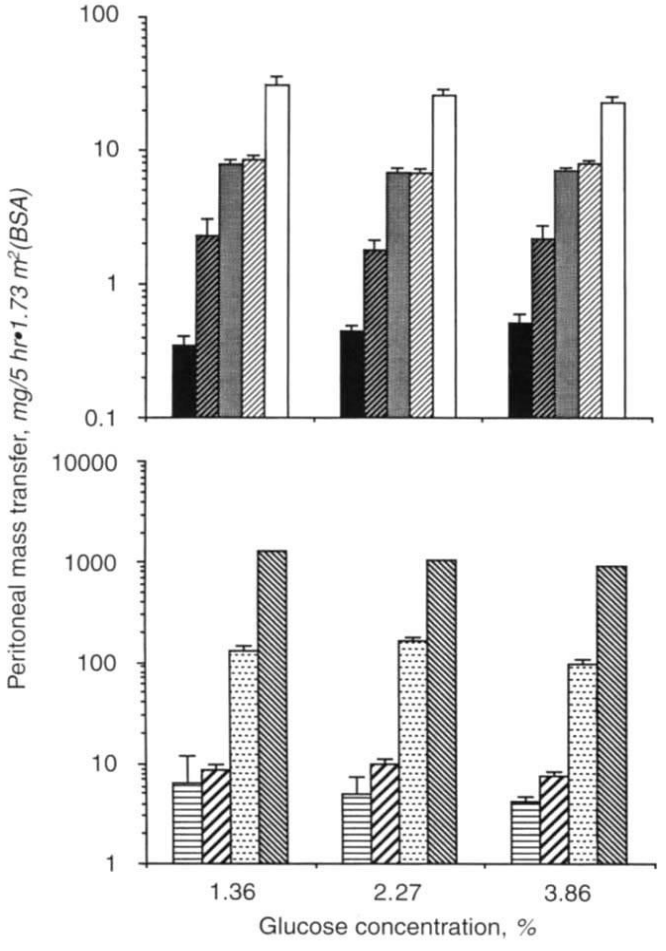

Fig. 3. *Protein losses during five hours dwell with 1.36%, 2.27% and 3.86% dextrose.* Symbols are: (■) Clara cell protein; (▨) cystatin C; (▩) β_2-microglobulin; (▨) retinol-binding protein; (□) alpha 1-microglobulin; (▤) IgM; (▨) alpha 2-microglobulin; (▭) IgG; and (▧) albumin.

[1], serum RBP and Alb significantly decrease in patients on long-term peritoneal dialysis. Interestingly, these two proteins are synthesized mainly by the liver. Peritoneal losses of RBP and Alb might therefore exceed their synthesis by the liver. Whether RBP is–despite its elevated level–like albumin, a good indicator of the nutritional status in peritoneal dialysis patients remains to be demonstrated. These data have to be taken with caution since duration of therapy with CAPD did not exceed 12 months in the majority of our patients.

Protein loss into dialysate is a major drawback with peritoneal dialysis [2–7]. It may indirectly contribute to various nutritional and metabolic disturbances in patients on CAPD such as hypercholesterolemia or altered amino acid metabolism [22]. Our study not only confirms the important daily losses of HMWP, but quantifies for the first time the daily losses of specific LMWP such as RBP, cyst C, CC16 and α_1m in peritoneal dialysis. The peritoneal transport of the proteins being related to their serum concentrations and to the dwell time (mainly for HMWP), the comparison of results between different studies requires that patients should be matched for these determinants. However that may be, the values of daily protein losses observed by us are within the range reported in the literature for albumin or other large proteins [2, 3, 6] and β_2m [18–20].

Peritoneal transport of the various proteins is significantly related to their molecular radius: the higher the radius, the lower the peritoneal clearance. This finding is in agreement with those made previously by others [6, 7, 10, 23], who mainly used larger proteins or dextrans. We extend this concept by relying on a larger range of LMWP. The use of representative proteins of the LMWP class [M_r from 15.1 (cyst C) to 27.7 Å (α_1m)] in addition to HMWP [M_r from 36.0 (Alb) to 96.0 Å (IgM)] allows an analysis of the peritoneal membrane characteristics. Our results suggest the existence of at least two populations of pores in the peritoneal capillary walls. As illustrated in the Figure 2, the relationship between peritoneal clearance and molecular radii exhibits two slopes. The first slope suggests the presence of small pores of about 20 to 25 Å radius through which LMWP with a $M_r < 25$ Å diffuse. The second slope is compatible with the existence of larger pores exceeding 100 Å radius, through which proteins with M_r above 25 Å radius are cleared. This observation fits the two-pore theory for transcapillary transport of the proteins [24–26]. In the peritoneal capillary wall, Nakamura and Wayland [24] have suggested the existence of small pores of approximately 30 Å radius and larger pores exceeding 150 Å radius. Rippe and Stelin [27], using a computer simulation, report a large number of small pores in the 40 to 50 Å range, and a small number of larger pores in the 200 to 300 Å range. Imholz et al [28] propose a radius of less than 40 Å for the small pores. None of these three studies evaluates the peritoneal handling of proteins with a M_r in the critical 16 to 35 Å range. In our study, the availability of three LMWP in the latter range provides a better definition of the smaller pore sizes. Of special interest is the observation that α_1m, although classified among LMWP, behaves as a HMWP as a result of its M_r (27.7 Å), just above the proposed size of the small pores.

The presence of a third ultrasmall pore (<5 Å) that is only involved in fluid transport has been postulated [29]. Its existence could not be tested with the proteins evaluated in the study.

Although an increased transcapillary ultrafiltration induced by hypertonic dialysate (3.86%) during the first hour dwell might influence the convection of macromolecules [30], we were unable to detect any influence of dextrose concentration on the loss of the various tested proteins after a five hour dwell. Similar observations were made by others on the loss of small solutes and total protein after a six hour dwell [31, 32] or HMWP during the overnight or daytime exchanges [6]. Imholz et al [28] evaluated the effect of dialysate tonicity on the peritoneal clearance rather than on the mass transfer of proteins. Raising dextrose concentration from 1.36% to 3.86% did not modify the clearance of HMWP but was associated with a small, but significant increase of β_2m clearance for 1.17 to 1.34 ml/min.

Dwell time also influences transperitoneal transport of proteins but the effect is significant only for HMWP. Indeed, the protein loss ratio of 10 over a five hour exchange indicates that the loss of large proteins, such as albumin, immunoglobulins and alpha 2-macroglobulin, increases when dwell time is extended. In contrast, dwell time influences LMWP removal to a smaller but not statistically significant extent. Comparing peritoneal protein loss between short (4 hr) and long (8 hr) cycles, Kagan et al [10] also found that LMWP and small solutes clearances were unchanged

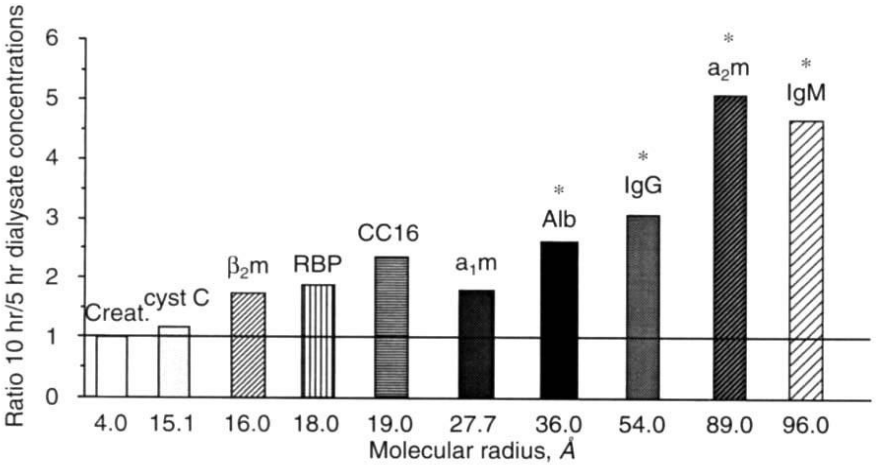

Fig. 4. *Concentration ratios of creatinine and protein losses at 10 over a five hour dwell with dextrose 1.36% as a function of molecular radius.* Symbols are: (□) creatinine; (▨) cystatin C; (▨) β_2-microglobulin; (▥) retinol-binding protein; (▤) Clara cell protein; (▩) alpha 1-microglobulin; (■) albumin; (▩) IgG; (▨) alpha 2-macroglobulin; and (▨) IgM. *Statistically significant compared to creatinine.

or decreased, while they are significantly increased during the long cycle for Alb, IgG and IgM.

Other factors such as residual renal function, age, sex and dialysis duration do not influence the peritoneal transport of the proteins. The peritoneal membrane characteristics, assessed on the basis of the PET results, apparently fail to influence the protein peritoneal transport, a finding to be interpreted with caution as the number of patients included in the extreme groups is small.

From this study, we conclude that in CAPD patients serum LMWP concentrations are markedly increased. Their level is influenced mainly by patient-related factors (residual diuresis and age). Serum albumin and RBP are the only proteins where the concentration is inversely related to duration of dialysis. Proteins are lost through the peritoneum according to their molecular radius. It may be inferred from this relationship that the peritoneal membrane behaves like a two-pore model in the handling of proteins. The fact that extending the dwell time to 10 hours influences only the loss of HMWP equal to or larger than albumin suggests that substitution of short cycle to long cycle dialysis might reduce the loss of HMWP without affecting the clearance of small and middle size molecules.

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