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High peritoneal residual volume decreases the efficiency of peritoneal dialysis

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High peritoneal residual volume decreases the efficiency of peritoneal dialysis.

Background. Wide variation in peritoneal residual volume (PRV) is a common clinical observation. High PRV has been used in both continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis to minimize the time of a dry peritoneal cavity and to achieve better dialysis. However, the impact of PRV on peritoneal transport is not well established. In this study, we investigated the effect of PRV on peritoneal transport characteristics.

Methods. Peritoneal effluents were collected in 32 male Sprague-Dawley rats after a five-hour dwell with 1.36% glucose solution. Forty-eight hours later, a four hour dwell using 25 ml of 3.86% glucose solution and frequent dialysate and blood sampling was done in each rat with ^{125}I-albumin as a volume marker. Before the infusion of the 3.86% glucose solution, 0 (control), 3, 6, or 12 ml (8 rats in each group) of autologous effluent (serving as PRV) was infused to the peritoneal cavity.

Results. After subtracting the PRV, the net ultrafiltration was significantly lower in the PRV groups as compared with the control group: 13.4 ± 0.5, 12.0 ± 1.0, 11.7 ± 1.7, and 8.9 ± 0.4 ml for 0, 3, 6, and 12 ml PRV groups, respectively ($P < 0.001$). The lower net ultrafiltration associated with higher PRV was due to (*a*) a significantly lower transcapillary ultrafiltration rate (Q_u) caused by a lower osmotic gradient, and (*b*) a significantly higher peritoneal fluid absorption rate (K_E) caused by an increased intraperitoneal hydrostatic pressure. No significant differences were found in the diffusive mass transport coefficient for small solutes (glucose, urea, sodium, and potassium) and total protein, although the dialysate over plasma concentration ratios values were higher in the high-PRV groups. The sodium removal was significantly lower in the PRV groups as compared with the control group ($P < 0.01$).

Conclusion. Our results suggest that a high PRV may decrease net ultrafiltration through decreasing the Q_u, which is caused by a decreased dialysate osmolality, and increasing the K_E caused by an increased intraperitoneal hydrostatic pressure. The high volume of PRV also decreased the solute diffusion gradient and decreased peritoneal small solute clearances, particularly for sodium. Therefore, a high PRV may compromise the efficiency of dialysis with a glucose solution.

Key words: dialysate osmolality, CAPD, peritoneal effluents, ultrafiltration, intraperitoneal hydrostatic pressure, glucose.

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It is generally accepted that it is difficult for many continuous ambulatory peritoneal dialysis (CAPD) patients to achieve the recently recommended clearance targets [1] with four two-liter CAPD exchanges when the residual renal function becomes negligible. Although the relevance of the new targets is still debated [2, 3], most people believe that the adequacy of peritoneal dialysis needs to be improved. Increasing the dialysate flow rate (by increasing dialysate fill volume or by increasing the number exchanges or by automated peritoneal dialysis) is a common way to increase peritoneal small solute clearances [1, 4, 5]. This, however, may adversely impact patients' quality of life and also lead to increased cost [6]. Better utilization of the dialysis fluid by optimizing the dwell time without changing the dialysate flow rate is an important area that to date, however, has not been extensively explored. For example, prolonging the dwell time (especially in high peritoneal transport rate patients) may not only worsen the fluid balance, but may also decrease the efficiency of small solute removal [7]. On the other hand, shortening the dwell times, especially the overnight dwell, has been shown to improve fluid and solute removal [8].

It was proposed that the drainage time in both CAPD [9] and automated peritoneal dialysis [10] should be minimized to increase the contact between dialysate and the peritoneum (effective dialysis time), which may presumably increase the efficiency of peritoneal dialysis. Shortening the drainage time in general increases the peritoneal residual fluid volume (PRV). This is, in fact, the rationale for tidal peritoneal dialysis (TPD), which uses a constant PRV of dialysate that remains in the peritoneal cavity throughout the night plus an additional volume that is continuously exchanged. Although the efficiency of shortening the drainage time in CAPD patients is not clear, a recent study showed that TPD, in fact, resulted

in lower solute clearances than the conventional intermittent peritoneal dialysis at the same dialysate flow rate [11], indicating that the high PRV may not be beneficial.

In fact, PRV may often vary significantly between CAPD patients with a well-functioning catheter [12], especially in pediatric peritoneal dialysis patients [13]. Incomplete drainage of peritoneal fluid and thus high PRV is one of the causes of inadequate fluid removal in CAPD patients [14]. However, little is known about the impact of PRV *per se* on the peritoneal fluid and solute transport characteristics during the subsequent exchange. The impact of PRV is also of importance when interpreting the results of peritoneal equilibration tests or other peritoneal function tests.

Therefore, in this study, we investigated the effect of PRV on peritoneal fluid and solute transport characteristics.

METHODS

Thirty-two male Sprague-Dawley rats with an average body weight of 300 g (range 290 to 310 g) first underwent a five-hour intraperitoneal dialysis dwell with 25 ml of Dianeal® 1.36% glucose dialysis solution. The solution was infused intraperitoneally through a multiholed silastic catheter (0.8 mm internal diameter; Venoflon, Helsingborg, Sweden) with the animal under light ether anesthesia. The rats were then let free. Five hours later, under light ether anesthesia, the peritoneal fluid was drained through the multiholed silastic catheter and was centrifuged ($150 \times g$, 10 min) to remove cells. The fluid was then filtered through a 0.45 μm sterilized filter and stored at –20°C for future use. Forty-eight hours later, the rats were randomly divided into four groups with eight rats in each group, and they underwent a four-hour dwell study modified from our previous study [15]. Briefly, each rat was anesthetized initially with a single intramuscular injection of 60 mg/kg pentobarbital sodium. After two hours, the rat was given 25 mg/kg of pure pentobarbital sodium subcutaneously every hour to maintain the intensity of anesthesia during the experiment. The fur over the abdominal wall was closely shaved. The animal was laid in a supine position and was kept at 37°C with a heating pad (CMA/Microdialysis, Stockholm, Sweden). Isotonic saline (2 ml/hr) was injected subcutaneously to prevent hypovolemia. A multiholed silastic catheter was inserted percutaneously in the left lower quadrant of the abdomen for dialysis fluid infusion and sampling. Then 0 (control group), 3 (R3 group), 6 (R6 group), or 12 (R12 group) ml of autologous effluent (prewarmed to 37°C, serving as PRV) was infused to the peritoneal cavity via a three-way valve (Viggo; Connecta, Helsingborg, Sweden) connected to the end of a 0.8 mm catheter, followed immediately by intraperitoneal infusion of 25 ml of Dianeal® 3.86% glucose dialysis fluid. The 3.86% dialysis solution was prewarmed to 37°C and contained 18.5 KBq ^{131}I-human serum albumin (RISA; Isopharma AS, Kjeller, Norway). A priming dose of 0.2 g/liter of human serum albumin was added in the 3.86% dialysis solutions to minimize the adhesion of tagged albumin to the surface of the catheter. After infusion, the dialysis solution was mixed thoroughly with the residual solution and allowed to remain in the peritoneal cavity for four hours. The intraperitoneal hydrostatic pressure (IPP) was measured after the infusion using a water manometer connected to the peritoneal catheter, setting the reference level at the heart of the rat. Dialysate samples (0.35 ml) were taken at 0-, 3-, 15-, 30-, 60-, 90-, 120-, 180-, and 240-minutes postinfusion. Prior to each sampling, 1 ml of the dialysate was flushed back and forth five times through the catheter. Blood samples were drawn at 0, 120, and 240 minutes from the tail artery. After 240 minutes, the peritoneal cavity was opened, and the dialysate was collected using syringe and preweighed gauze tissues. The volume was then recorded. The experimental study was approved by the Animal Ethical Committee of the Karolinska Institute at Huddinge Hospital.

Dialysate samples (0.1 ml) and blood samples (0.1 ml of plasma) were analyzed for RISA activity on a gamma counter (Packard Instrument Company, Meriden, CT, USA) for 10 minutes each. Dialysate including the residual fluid and plasma concentrations of urea (urease-glutamate dehydrogenase method), protein (Coomassie Brilliant Blue Dye binding method), and glucose concentration (hexokinase method) were analyzed using a Monarch™ 1000 autoanalyzer (Instrumentation Laboratory, Lexington, MA, USA). Dialysate and plasma concentrations of sodium and potassium were analyzed using a flame photometer (Instrumentation Laboratory). Dialysate and blood osmolality were measured by a Vapro® vapor pressure osmometer 5520 (Wescor Inc., Logan, UT, USA).

Intraperitoneal dialysate volume was estimated from the dilution of RISA with corrections made for the elimination of RISA from the peritoneal cavity and the sample volume [16]. Note that the intraperitoneal volume at the end of the dwell was directly measured. The peritoneal fluid absorption rate was estimated as the coefficient of RISA elimination from the peritoneal cavity, K_E (ml/min), and the transcapillary ultrafiltration rate was calculated as net volume change plus K_E. Because only a very small amount of free iodine was found in the RISA solution [17], we did not take the free iodine into account in the K_E calculation.

The direct lymphatic absorption of fluid from the peritoneal cavity was assessed as the clearance of RISA from the dialysate to the blood, K_{EB} (ml/min). K_{EB} was calculated from the rate of increase of RISA amount in plasma divided by the average intraperitoneal RISA concentration [18]. The plasma volume was set at 3.6

ml/100 g body wt [18, 19]. The K_{EB} values were also corrected for the RISA "spill over" from plasma to the body interstitium during the dwell using a constant of 0.0018 min^{-1} as described previously [19]. The remaining part of fluid absorption to the peritoneal tissue interstitium and capillaries, K_{ET} (ml/min), was calculated as K_E minus K_{EB}.

The dialysate over plasma concentration ratios (D/P) for all of the investigated solutes were calculated by dividing the dialysate concentrations of the investigated solutes at a certain time with the aqueous concentrations of the investigated solutes in plasma [20]. If no blood sample was taken at the same time as a dialysate sample, then the blood concentration of the solute was linearly interpolated from the blood sample taken before and after this moment [21]. The D/D_0 for glucose was calculated as the dialysate glucose concentration (D) divided by the glucose concentration in the fresh dialysis solution (D_0). The diffusive mass transport coefficients (K_{BD}, ml/min) were estimated using the modified Babb-Randerson-Farrell (BRF) model as described previously [22, 23] using the computer program PERTRAN (Baxter Novum, Karolinska Institute, Stockholm, Sweden). The model describes the net change of the amount of solute in the peritoneal dialysate over a time increment equal to the rate of solute flow between blood and dialysate due to the combined diffusion, convective transport, and peritoneal absorption of the solute. In addition, in this study, we set the sieving coefficients (S) for glucose, urea, sodium, and potassium to be 0.55 [15, 24]. The clearance of each investigated solute was calculated as the total amount of the solute in the dialysate minus the infused amount (including the amount in the residual fluid) and divided by the mean blood concentration of the solute and the dwell time. The absorbed glucose amount was calculated as the total infused amount minus the amount left in the dialysate.

Two-way analysis of variance with repeated measurements and one-way analysis was applied to compare intraperitoneal volume, K_E, K_{EB}, K_{ET}, D/P ratios, and K_{BD}. When analysis of variance showed a significant difference among the three groups, then Scheffe's *F*-test was used to compare the difference between different groups. The results are expressed as mean ± SD. A *P* value of less than 0.05 was considered significant.

RESULTS

Fluid transport

The increase in intraperitoneal volume (net ultrafiltration volume) was significantly lower in the R12 group as compared with all of the other groups (all $P < 0.001$) and was significantly lower in the R3 and R6 groups compared with the control group (both $P < 0.05$; Fig. 1, two-way analysis of variance repeated measurements). No significant difference was found in the net ultrafiltration volume between the R3 and R6 groups. Not surprisingly, the increase in the PRV volume was associated with an increase in IPP ($P < 0.01$; Table 1) and an increase in the peritoneal fluid absorption (as assessed by the RISA elimination rate, K_E; Table 1). However, there was no significant difference in the direct lymphatic fluid absorption rate (as assessed by the RISA appearance rate in blood, K_{EB}) during the dwell among these four groups (Table 1). Therefore, the differences in fluid absorption rates among the four groups were due to differences in the fluid absorption to peritoneal tissue, as assessed by the RISA elimination rate to peritoneal tissue, K_{ET} (Table 1). The transcapillary ultrafiltration rate was significantly lower in the R12 group as compared with the other groups (all $P < 0.01$), whereas no significant differences were found among the other groups (Table 1).

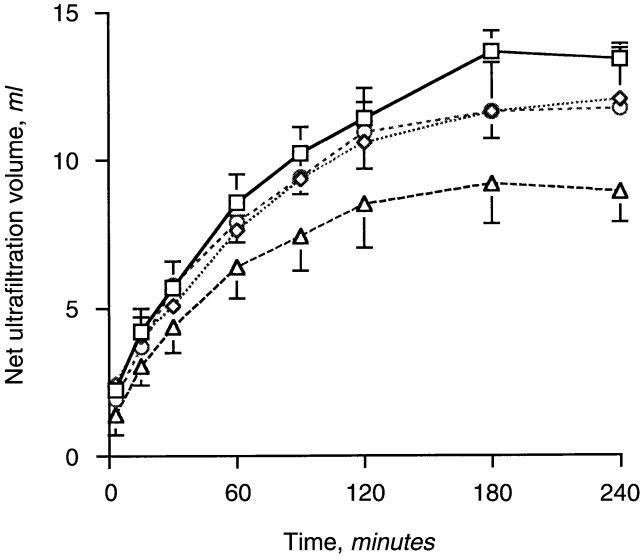

Fig. 1. Changes in intraperitoneal volume (net ultrafiltration) versus time. Symbols are: (□; control) R0 group ($N = 8$); (◇; 3 ml) R3 group ($N = 8$); (○; 6 ml) R6 group ($N = 8$); (△; 12 ml) R12 group ($N = 8$). Data are mean ± SD.

Glucose transport

There was no significant difference in the glucose concentration in the PRV among the four groups. The D/D_0 of glucose was significantly lower in the higher PRV groups as compared with the lower residual fluid groups and the control group (all $P < 0.01$, analysis of variance, repeated measurements; Fig. 2). Note that the D/D_0 of glucose decreased markedly slower in the high residual fluid volume groups as compared with the lower residual fluid volume groups and the control group, resulting in

Table 1. Fluid and RISA transport parameters and intraperitoneal hydrostatic pressure among the four groups

	N	RV ml	IPP cm H_2O	Q_u μl/min	Net UF ml	K_E	K_{EB}	K_{ET}
						μl/min		
R0	8	0	1.58 ± 0.21	74.8 ± 2.2	13.4 ± 0.5	19.0 ± 3.0	3.3 ± 1.0	15.7 ± 2.5
R3	8	3	1.70 ± 0.36	75.2 ± 3.3	12.0 ± 1.7[b]	25.1 ± 6.4[b]	3.6 ± 1.2	21.5 ± 6.5[b]
R6	8	6	2.21 ± 0.24[b]	73.1 ± 3.3	11.7 ± 0.4[b]	24.3 ± 2.2[b]	3.4 ± 2.4	21.0 ± 1.7[b]
R12	8	12	3.95 ± 0.53[a]	68.4 ± 4.1[a]	8.9 ± 1.0[a]	31.3 ± 4.8[a]	3.7 ± 1.5	27.6 ± 3.6[a]

Data are mean ± SD. Abbreviations are: RISA, ^{131}I-human serum albumin; RV, residual fluid volume; IPP, intraperitoneal hydrostatic pressure after infusion; Q_u, mean transcapillary ultrafiltration rate between 0 min and 240 min; Net UF, net ultrafiltration volume at 4 hours of the dwell; K_E, total RISA elimination rate representing the fluid absorption rate from the peritoneal cavity; K_{EB}, RIA elimination rate to the blood from the peritoneal cavity representing the peritoneal lymphatic absorption; K_{ET}, RISA elimination rate to peritoneal tissue.

[a] $P < 0.05$ compared with all the other groups

[b] $P < 0.05$ compared with the control group

no significant difference at the end of the dwell. However, the diffusive mass transport coefficient for glucose did not differ among the four groups (Table 2, discussed later in this article). Concurrently, the dialysate osmolality was significantly lower in the high residual fluid groups compared with the low residual fluid groups and the control group (only up to 90 min of the dwell; Fig. 2). There was no significant difference in the total absorbed amount of glucose during the dwell, despite the higher glucose load and lower ultrafiltration in the high residual fluid groups (Fig. 2).

Transport of other solutes

There was no significant difference in the dialysate urea, potassium, sodium, and total protein concentration in the residual fluid. The D/P urea was significantly higher in the R12 group as compared with the R3 and the control group, and higher in the R6 group as compared with the control group (all $P < 0.05$; Fig. 3). No significant difference was found between the other groups. The D/P potassium was significantly higher in the R12 and R6 groups as compared with the R3 and the control group (all $P < 0.01$; Fig. 3), whereas no significant difference was found between the R12 and the R6 groups. Note that the differences in the D/P of urea and potassium were mainly in the initial two hours of the dwell. There was no significant difference in these parameters at the end of the dwell. The D/P of sodium was significantly higher in the higher residual volume groups as compared with the lower residual volume groups and the control group (all $P < 0.01$; Fig. 3), except that no difference was found between the R6 and R3 groups. The D/P of total protein was significantly higher in the R12 group as compared with all of the other groups (all $P < 0.05$; Fig. 3), whereas no significant differences were found between the other groups.

There were no significant differences in the diffusive mass transport coefficient, K_{BD}, for glucose, urea, sodium, and potassium among the four groups, as estimated with the BRF model (Table 2).

The peritoneal clearances for urea did not differ among the four groups. However, the potassium and sodium clearances were significantly lower in the R12 groups as compared with the control group. The total protein clearance, on the contrary, initially was significantly higher in the R12 group as compared with the control group, although no significant difference was found at the end of the dwell (Fig. 4).

DISCUSSION

This study shows that increased PRV has a significant impact on peritoneal fluid and solute transport, as it may decrease peritoneal fluid removal and small solute clearances.

Fluid transport

It is well known that the processes of peritoneal transcapillary ultrafiltration (Q_u) and peritoneal fluid absorption (K_E, which can be estimated with the elimination rate of intraperitoneal albumin) occur simultaneously during peritoneal dialysis [25, 26]. The net fluid removal depends on the balance between these two processes [25]. During peritoneal dialysis, significant Q_u can be achieved only when osmotic agents are being added to the dialysis solution, creating an osmotic gradient between dialysate and blood. K_E, on the other hand, is mainly driven by the IPP [27], and IPP is strongly dependent on the intraperitoneal dialysate volume [15, 28]. This study shows that PRV affects both peritoneal fluid absorption and transcapillary ultrafiltration. The decreased net ultrafiltration volume with higher PRV in this study is due to the combined effect of increased fluid absorption and decreased transcapillary ultrafiltration, and is in agreement with a previous computer simulation by Rippe, Stelin and Haraldsson, although varied fluid absorption rates were not taken into account in the computer simulation [29].

The significantly higher peritoneal fluid absorption associated with higher IPP in the R6 and R12 groups is in agreement with our previous studies in rats [15, 30], showing that increasing dialysate fill volume of 3.86 or 1.36% glucose dialysis solution from 25 ml to 30 ml or 40 ml

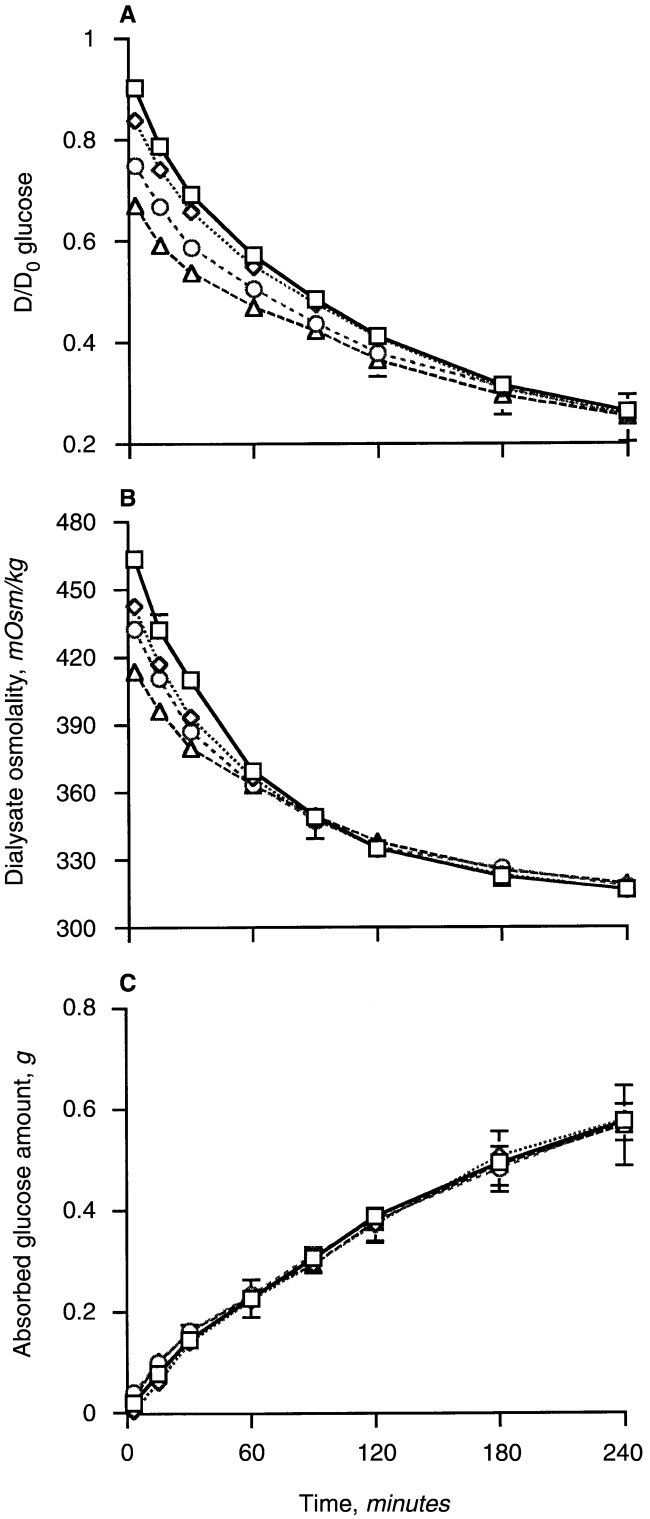

Fig. 2. Dialysate glucose concentration (D) to fresh dialysate glucose concentration (D_0) ratio (*A*), dialysate osmolality (*B*) and total absorbed glucose amount (*C*) versus dwell time. Symbols are: (□; control) R0 group ($N = 8$); (◇; 3 ml) R3 group ($N = 8$); (○; 6 ml) R6 group ($N = 8$); (△; 12 ml) R12 group ($N = 8$).

significantly increased the IPP and peritoneal fluid absorption rate [15, 30]. Zakaria and Rippe also found that the intraperitoneal fluid loss rate and the loss of an intraperitoneally administered macromolecular tracer were proportional to the IPP [19]. Flessner and Schwab reported that a steady rise in the rate of fluid movement from the cavity into the body and into the abdominal wall occurs with increasing intraperitoneal pressure above 2 cm H_2O [31]. Our results also show that a higher intraperitoneal volume and higher IPP do not alter the direct peritoneal lymphatic fluid absorption rate, in support of previous reports by others and us [15, 19, 30]. The significant increase in peritoneal fluid absorption rate in the R3 group as compared with the control group (although no difference was observed in the IPP between the two groups) suggests that another mechanism(s) than IPP may also contribute to the peritoneal fluid absorption process.

Glucose transport

The significantly decreased transcapillary ultrafiltration rate in the R12 group was due to a high degree of dilution of glucose by the residual fluid. However, it is interesting to note that despite the dilution of dialysate glucose concentrations in the R3 and R6 groups, the transcapillary ultrafiltration rate did not differ significantly as compared with the control group. This may be due to the higher intraperitoneal volume (as compared with the control group) in these groups, resulting in a slower decline of glucose concentration after mixing with the residual fluid, as shown by the slower decrease in D/D_0 of glucose after three minutes of the dwell, which compensated, to some extent, for the impact of glucose dilution by the residual fluid. In fact, the dialysate osmolality was similar among the four groups after 90 minutes of the dwell, and the dialysate glucose concentration did not differ among the four groups after two hours of the dwell. The slower decline in glucose concentration after three minutes in the residual fluid groups is similar to previous studies using different dialysate fill volumes [28, 32]. It may partially be explained by less dilution by the transcapillary ultrafiltration. In addition, as the diffusive mass transport coefficient, K_{BD}, for glucose did not significantly increase with the high intraperitoneal volume associated with high residual volume, the ratio of maximal diffusive transport (as estimated by K_{BD}) to the volume that should be cleared (fill volume) decreased with high dialysate volume, resulting in a slower decrease in dialysate glucose caused by diffusive transport [15, 30]. Furthermore, the lower glucose diffusion gradient (especially during the initial two hours of the dwell) in the high residual fluid volume group may also contribute to the slower changes in the D/D_0 of glucose, which also explains the almost identical glucose amount absorbed

Table 2. Diffusive mass transport coefficients (K_{BD}) for glucose, urea, sodium and potassium estimated using the modified Babb-Randerson-Farrell (BRF) model by setting sieving coefficient to 0.55, and clearance for total protein

		K_{BD} *ml/min*				
	N	Glucose	Urea	Sodium	Potassium	Total protein[a]
R0	8	0.180 ± 0.014	0.144 ± 0.032	0.140 ± 0.016	0.178 ± 0.026	0.0024 ± 0.0002
R3	8	0.184 ± 0.018	0.163 ± 0.079	0.140 ± 0.057	0.181 ± 0.033	0.0025 ± 0.0007
R6	8	0.186 ± 0.022	0.183 ± 0.050	0.156 ± 0.037	0.195 ± 0.042	0.0027 ± 0.0004
R12	8	0.189 ± 0.04	0.196 ± 0.079	0.204 ± 0.080	0.145 ± 0.039	0.0033 ± 0.0012

Data are mean ± SD.
[a] Total protein clearance calculated from 0 min to 240 min with the protein contents in the residual fluid subtracted

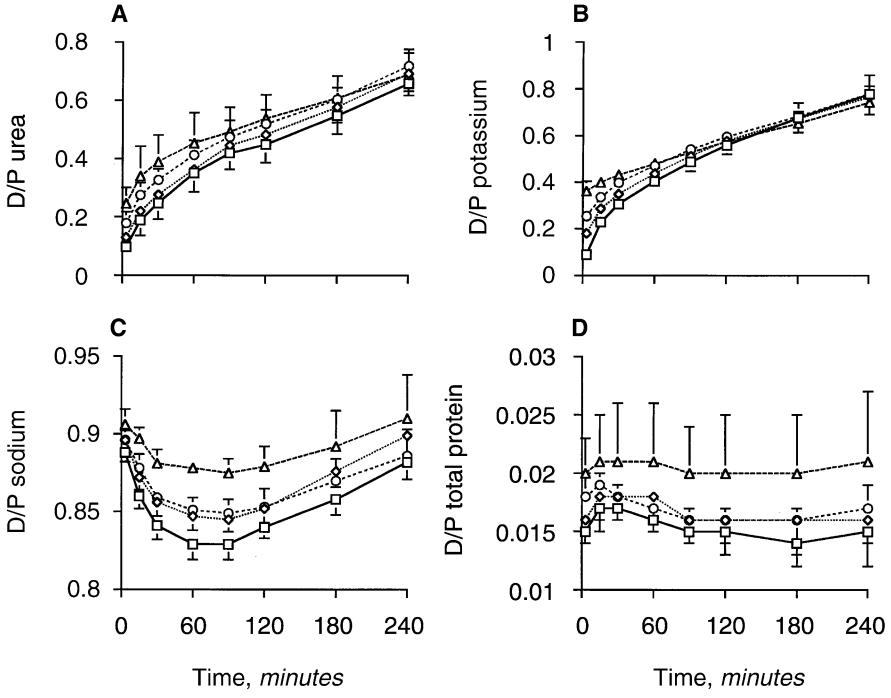

Fig. 3. Dialysate to plasma concentration ratio (D/P) for urea (*A*), potassium (*B*), sodium (*C*), and protein (*D*) versus dwell time. Symbols are: (□; control) R0 group ($N = 8$); (◇; 3 ml) R3 group ($N = 8$); (○; 6 ml) R6 group ($N = 8$); (△; 12 ml) R12 group ($N = 8$).

among the four groups. The discrepancy between dialysate osmolality and dialysate glucose concentration may be due to the difference in the dialysate sodium (presumably chloride as well) concentration.

The changes in peritoneal fluid kinetics with different PRV are of particular importance when new dialysis fluids or new dialysis regimens are investigated. In a multicenter study by Imholz et al on the use of an oligopeptide solution, the authors did not observe a presumed higher net ultrafiltration with the oligopeptide solution over the conventional glucose dialysis solution. However, they noted that a significantly higher PRV was present in the oligopeptide solution group [33]. It is not clear whether the high residual fluid may have affected the observed results.

Transport of other solutes

Higher D/P values in the high PRV groups for all of the investigated solutes are expected, as the residual peritoneal fluid contains high solute concentrations. However, it is interesting to note that the differences in D/P values for urea and potassium became less significant with the time on the dwell, and no significant differences were found in these parameters at the end of the dwell. We have previously reported that higher dialysate fill volume resulted in lower D/P values for small solutes [15]. Therefore, the slower increase in D/P values for urea and potassium in the high residual fluid volume group is partly the result of the principle governed by the geometry of diffusion, stating that equilibration of a solute occurs rapidly when the dialyzed solute diffuses into a relatively small volume, whereas relatively slower equilibration occurs in association with diffusion into a larger volume [15]. In addition, as the solute concentration gradient between dialysate and blood was lower with a high volume of residual fluid, the small solute diffusion process would be slower in the high residual volume groups. Although the difference in the initial dialysate sodium concentration between R12 and the

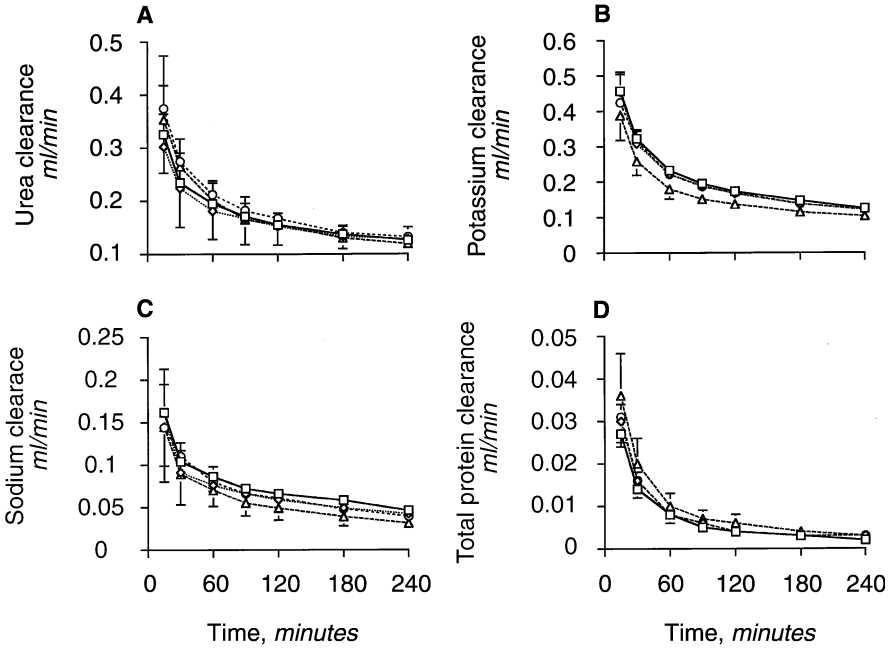

Fig. 4. Peritoneal clearances for urea (*A*), potassium (*B*), sodium (*C*), and total protein (*D*) versus dwell time. Symbols are: (□; control) R0 group ($N = 8$); (◇; 3 ml) R3 group ($N = 8$); (○; 6 ml) R6 group ($N = 8$); (△; 12 ml) R12 group ($N = 8$).

control group was less than 1 mmol/liter, the D/P of sodium was markedly higher in the R12 group as compared with the control group. The significantly lower transcapillary ultrafiltration rate and less sieving in the R12 group may be the major reason. Sodium removal in CAPD is well known to be strongly related to the fluid removal. Ultrafiltration not only increases sodium removal by convection but also increases the sodium concentration gradient (because of sodium sieving), and therefore results in increased diffusive transport of sodium [34]. The difference in D/P of sodium between the R3, R6, and control groups may, however, be due mainly to the difference in intraperitoneal volume because the transcapillary ultrafiltration rate did not differ among these groups. With a higher intraperitoneal volume and similar ultrafiltration rate, the dilution effect will be smaller because of the large volume. The changes in D/P values in this study suggest that the impact of PRV should be taken into consideration when interpreting the peritoneal equilibration test (PET) results or other peritoneal functional tests, in particular when interpreting the D/P values from the early part of the exchange.

The details of peritoneal protein transport mechanisms are not well established. Our results show that D/P protein increased initially and then remained stable or even slightly decreased in all of the four groups. This is in agreement with our recent finding showing that the initial protein flux from the peritoneal interstitium may be the major determinant of dialysate protein content (abstract; Waniewski et al, *Perit Dial Int* 18:109, 1998). Note, however, that a protein appearance in the dialysate of our rats may be different from its appearance in CAPD patients, as the rats were not on continuous dialysis therapy. In this study, the clearance of total protein was initially significantly higher in the R12 group as compared with the control group, although no significant difference was found at the end of the dwell. The reason, however, is not clear.

Our results also show that a high PRV and thus a high intraperitoneal volume may not increase the small solute clearances. In fact, the clearances for potassium and sodium were significantly lower in the R12 group in comparison with the control group. This may be due to the lower peritoneal fluid removal and the lower (at least during the initial period of the dwell) solute diffusion gradient. These findings are in contrast to the effects of different dialysate fill volumes (with fresh dialysis fluid) [15, 30]. Note, however, that in our previous studies, high dialysate fill volumes were associated with a higher transcapillary ultrafiltration rate (irrespective of the net ultrafiltration) and increased solute diffusion gradients [15, 30].

Note that urea clearance did not significantly decrease in the R12 group despite the lower net peritoneal fluid removal in this group. This result is in agreement with our previous study [30], suggesting that high peritoneal urea clearances could be achieved without adequate peritoneal fluid removal [5]. Urea and creatinine clearances were usually used to define the outcome in most of the studies dealing with various peritoneal dialysis modalities, whereas fluid removal and/or dialysate sodium clearance were often neglected [35, 36]. However, adequacy of dialysis is not only a matter of reaching target Kt/V_{urea} or creatinine clearance, but also, and maybe even more importantly, is a matter of removing enough

fluid and sodium [37, 38]. Inadequate fluid removal and inadequate blood pressure control are common problems in CAPD patients [39, 40] that may contribute to technique failure and mortality. The possible discrepancy between urea clearance and peritoneal fluid removal and sodium removal should thus be borne in mind in future studies on new peritoneal dialysis regimens.

Automated peritoneal dialysis aiming at higher small solute clearances has been increasingly used in recent years and now ranks as the fastest growing home dialysis modality [41]. However, the best method of automated peritoneal dialysis has not been determined. Various forms of automated peritoneal dialysis imply high PRV, especially in TPD [35, 42]. In this study, the net ultrafiltration volume was significantly lower in the R12 group in comparison with the control group, even during the initial three minutes. Although the PRV we used in this study differed from the PRV used in automated peritoneal dialysis, a recent report showing that TPD with 50% intraperitoneal volume exchange achieved significantly lower net fluid removal as well as small solute clearances as compared with the standard intermittent peritoneal dialysis (IPD) with the same dialysis fluid flow rate (with a relatively low flow rate) is in general agreement with our results [11]. However, when a high flow rate is used, TPD yields similar solute clearances as IPD if the same flow rate and same intraperitoneal volume are used in both treatments [43]. Further studies are therefore needed to evaluate the practical advantages of TPD [42] versus its possible disadvantages in dialysis efficiency.

In summary, this study shows that a high volume of PRV may decrease peritoneal fluid removal and also lower the clearances for some small solutes. The decreased peritoneal fluid removal associated with high volume of residual fluid was due to an increased peritoneal fluid absorption (because of an increased IPP) and a lower transcapillary ultrafiltration rate (because of the dilution of dialysate glucose concentration). A high volume of PRV also decreased the solute diffusion gradient and decreased the peritoneal small solute clearances, particularly for sodium. Our results suggest that PRV may have adverse effects on adequacy of peritoneal dialysis, especially on adequate peritoneal fluid removal. Also, the impact of PRV should be taken into account when interpreting the PET results or results from other peritoneal function tests, as a high volume of PRV may interfere markedly with the results of the tests. However, our results do not justify prolonging the drainage time in order to achieve a completely empty peritoneal cavity. Our results also suggest that the efficiency of peritoneal dialysis modalities such as tidal peritoneal dialysis that use a high volume of PRV should be carefully re-evaluated.

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APPENDIX

Abbreviations used in this article are: BRF model, Babb-Randerson-Farrell model; CAPD, continuous ambulatory peritonal dialysis; D, dialysate glucose concentration; D_0, glucose concentration in fresh dialysate; D/P, dialysate over plasma concentration ratio; IPP, intraperitoneal hydrostatic pressure; IPV, intermittent peritoneal volume; K_{BD}, diffusive mass transport coefficient; K_E, fluid absorption rate; K_{EB}, clearance of RISA from the dialysate to the blood; K_{ET}, fluid absorption to the peritoneal tissue interstitium and capillaries; NUF, net ultrafiltration; PD, peritoneal dialysis; PRV, peritoneal residual volume; Q_u, transcapillary ultrafiltration rate; RISA, ^{125}I-human serum albumin; S, sieving coefficient; TPV, tidal peritoneal volume.

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