

Sodium Removal in Peritoneal Dialysis: The Role of Icodextrin and Peritoneal Dialysis Modalities

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One of the main goals of dialysis is the control of extracellular volume, because inadequate sodium and fluid removal result in fluid overload and increased mortality. In the present study, we evaluated the roles of continuous ambulatory peritoneal dialysis (CAPD), continuous cycling peritoneal dialysis (CCPD), and the use of icodextrin on sodium removal in 29 patients (n = 18 on CAPD, n = 11 on CCPD). Daily removal of sodium by each modality and dialysis adequacy by Kt/V and creatinine clearance were evaluated.

A significantly higher amount of sodium was removed in CAPD patients than in CCPD patients, although peritoneal dialysis clearances were lower in CAPD, and no difference in daily ultrafiltration was observed between the modalities. In the CAPD group, patients using icodextrin for the long dwell showed significantly increased 24-hour sodium removal (218 ± 65 mmol/L) as compared with patients not using icodextrin (96.3 ± 58 mmol/L, $p < 0.001$); they also showed increased daily ultrafiltration (1685 ± 302 mL vs. 717 ± 440 mL, $p < 0.001$). In the CCPD group, 8 patients were using icodextrin for the long dwell, and they showed significantly increased sodium removal only for the day exchange (43 ± 49 mmol/L) as compared with patients not using icodextrin (-60 ± 6 , $p < 0.001$). Hypertension was less common in the CAPD patients than in the CCPD patients.

These results indicate that CAPD is a more efficient modality than CCPD for sodium removal. Icodextrin is an effective tool not only for increasing adequacy, but also for removing more sodium in both modalities.

Key words

Automated peritoneal dialysis, continuous ambulatory peritoneal dialysis, icodextrin, sodium

Introduction

One of the main goals of dialysis therapy is the control of extracellular volume, because inadequate sodium and fluid removal result in fluid overload, hypertension, and increased cardiovascular mortality (1–3). Many patients undergoing peritoneal dialysis (PD) are frequently overloaded. A low-sodium diet and adequate sodium removal by PD are important steps in avoiding overhydration.

Only a few studies have examined sodium removal rates in PD patients (4–9). It has been argued that automated PD (APD) may be less effective than continuous ambulatory PD (CAPD) for sodium removal because of its frequently lower capacity for ultrafiltration (UF) and also because of the short dwell schedule, which may result in significant sodium sieving and less efficient sodium removal (3). The problem of sodium removal becomes even more complicated when the heterogeneity of APD prescription is considered (high- versus low-volume APD with varying dwell times), with potentially highly variable sodium and fluid removal (6–8). Icodextrin, a glucose polymer, has been shown to increase sodium removal, essentially mediated by an increase in UF; icodextrin does not induce sodium sieving (3,10,11).

The aim of the present study was to evaluate the role of two PD modalities—CAPD and continuous cycling peritoneal dialysis (CCPD)—and the use of icodextrin solution on sodium removal in PD patients.

Patients and methods

We studied 29 stable PD patients aged 51 ± 13 years, who were undergoing CAPD ($n = 18$) using 7.9 ± 0.2 L dialysate daily or CCPD ($n = 11$) using 19 ± 1.4 L dialysate daily for 47.5 ± 42 months (Table I).

TABLE I Patient demographics, peritoneal dialysis (PD) prescription, and adequacy indices for continuous ambulatory peritoneal dialysis (CAPD) and continuous cycling peritoneal dialysis (CCPD)

	CAPD	CCPD
Patients (<i>n</i>)	18	11
Age (years)	56±11	43±12
Sex (men/women)	9/9	7/4
Time on PD (months)	48±49	46±32
Body surface area (m ²)	1.8±0.1	1.9±0.2
Dialysate-to-plasma (D/P) creatinine	0.67±0.12	0.72±0.1
Daily total infused volume (L)	7.9±0.2	19±4.7
Daytime exchanges (<i>n</i>)	3	0–1
Nighttime exchanges (<i>n</i>)	1	4–10
Icodextrin for long dwell (<i>n</i>)	7	8
Kt/V urea	1.9±0.5	2.2±0.3
Weekly creatinine clearance (L)	81±36	84±23
Daily ultrafiltration (mL)	1093±618	954±542
Systolic blood pressure (mmHg)	123±13	125±±14
Diastolic blood pressure (mmHg)	73±10	78±10

Selection of PD modality was based on social issues and on medical criteria (peritoneal membrane characteristics and adequacy indices). The main adequacy targets of PD prescription for both modalities were a total Kt/V urea over 2 and a total weekly creatinine clearance over 60 L/1.73 m². The daily UF target was more than 700 mL daily for anuric patients.

The CAPD patients were prescribed 4 daily exchanges of 2 L dialysate (1 patient was on 4 exchanges of 1.5 L because of small body size). Icodextrin was being used by 7 patients for the long nighttime dwell (Table I).

The CCPD patients used a cycler during the night for 7–9 hours with a total dialysate volume ranging from 8 L to 20 L, and dwell times ranging from 40 minutes to 100 minutes. For the daytime long dwell, 8 patients were using icodextrin. In 5 patients, a second daytime exchange was prescribed [1.5–2 L of 1.36% glucose in 4 patients, and 1.5 L of 1.1% amino-acid solution in 1 patient (Table I)].

Samples of 24-hour urine (where applicable) and spent dialysate (daytime and nighttime) were collected and analyzed for the CAPD and CCPD patients separately, to define the relative roles in sodium removal of the short (daytime for CAPD, nighttime for CCPD) and long (nighttime for CAPD, daytime for CCPD) dialysis dwell phases. Sodium removal was calculated as the difference between the sodium concentration in the drained dialysate multiplied by the total drain volume and the sodium concentration in the instilled dialysate multiplied by the total inflow volume (6). A

peritoneal equilibration test with 2.27% dextrose dialysate (standard PET) was also performed for each patient after a 2- to 4-week interval. No patient received loop diuretics.

Statistical analysis

All values are expressed as mean ± standard deviation. The Student *t*-test for unpaired data or linear regression analysis was used as appropriate. Values of $p < 0.05$ were considered statistically significant.

Results

Sodium removal and PD modalities

A significantly higher amount of sodium (143 ± 84 mmol/L) was removed in CAPD patients than in CCPD patients (62 ± 69 mmol/L, $p < 0.01$; Table II), although the PD Kt/V in the CAPD patients was lower (1.5 vs. 1.9 ± 0.2 , $p < 0.05$). There was no difference between the groups in daily UF (1093 ± 618 mL vs. 954 ± 542 mL; Table I). Daily sodium removal was significantly correlated with daily UF in CAPD ($r = 0.868$, $p < 0.001$), but not in CCPD.

Icodextrin and sodium removal in CAPD

In the CAPD group, 7 patients were using icodextrin for the long dwell. These patients showed significantly greater 24-hour sodium removal (218 ± 65 mmol/L) than did patients not using icodextrin (96 ± 58 , $p < 0.001$); they also showed greater daily UF (1685 ± 302 mL vs. 717 ± 440 mL, $p < 0.001$).

TABLE II Sodium removal in continuous ambulatory peritoneal dialysis (CAPD) and continuous cycling peritoneal dialysis (CCPD) patients

	CAPD	CCPD	p Value
Daily peritoneal Na, long dwell (mmol)	38±59	22.4±61	NS
Daily peritoneal Na, short dwell (mmol)	105±61	42±62	<0.01
Daily peritoneal Na, total (mmol)	143±84	62±69	<0.01
Daily urinary Na (mmol)	27±43	31±50	NS

NS = nonsignificant.

Icodextrin and sodium removal in CCPD

In the CCPD group, 8 patients were using icodextrin for the long dwell. These patients showed significantly greater sodium removal during the daytime exchange (43 ± 49 mmol/L) than did patients not using icodextrin (-60 ± 6 mmol/L, $p < 0.001$), but the 24-hour removal difference did not reach statistical significance (67 ± 69 mmol/L vs. 49 ± 82 mmol/L). Patients using icodextrin also had greater, but not statistically significantly greater, daily UF (1075 ± 536 mL vs. 633 ± 503 mL) and higher, but not statistically significantly higher, Kt/V values (2 ± 0.2 vs. 1.7 ± 0.4).

In patients receiving icodextrin, daily sodium removal was significantly correlated with daily UF for both PD modalities ($r = 0.516$, $p < 0.05$).

Hypertension in CAPD and CCPD

Hypertension was less common in CAPD (38%) than in CCPD (54%) patients.

Discussion

Cardiovascular disease is the leading cause of death in patients with end-stage renal disease (1,2). Although earlier studies reported excellent short-term blood pressure control with CAPD, after 2–3 years of therapy (and especially when residual renal function was lost), patients presented signs of volume overload and hypertension. The initial sense that CAPD patients might have a more liberal salt and fluid intake was proven wrong (3).

Fluid and salt removal depend on residual renal function and ultrafiltration by PD. Although the importance of residual renal function can not be neglected, we do not usually prescribe loop diuretics for our PD patients. The other proposed steps to avoid volume overload and hypertension that we apply include a low-salt diet, use of icodextrin solution, or CCPD with 1 or 2 daytime exchanges. The proposed

new low-sodium PD solutions are not yet commercially available (3).

Because of the phenomenon of sodium sieving, sodium removal is lower in APD than in CAPD despite the equal UF rates that can be achieved with the use of more hypertonic exchanges (3). In our study, sodium removal was greater in our CAPD patients than in our CCPD patients despite approximately equal UF rates.

Ortega *et al.* (5) reported higher sodium removal in CAPD than in APD, but that removal was accompanied by higher net UF. Sodium removal correlated with UF only for their CAPD group. We also observed a strong correlation between sodium removal and UF only for the CAPD population studied. Rodríguez-Carmona and Pérez Fontán (6) reported equal results and suggested that the main determinants of sodium removal are UF and the mode of PD, because standard APD schedules are associated with poor sodium removal rates. Demetriou *et al.* (8), in an open-label randomized controlled crossover study in 18 APD patients, reported that increasing nightly dialysate flow resulted in a 10% increase in solute clearances and a 27% fall in sodium removal as compared with an APD regimen with an extra daytime exchange. Notably, some of our CCPD patients presented a negative net sodium removal (for the short or the long dwell, or sometimes for both), a finding that has also been previously reported (5–7).

All of the foregoing results have important clinical implications, especially for the steadily increasing population of patients undergoing APD. Sodium sieving does not occur with icodextrin, because icodextrin causes UF by colloid osmosis and not by crystalloid osmosis as glucose does (3,10). Icodextrin has been proven to increase UF and sodium removal for both CAPD and APD in many studies (3). Its superiority over glucose-containing solutions in CCPD has been

proven (11), and it also contributes to a lower glucose load when offered in PD patients.

The advantages of icodextrin solution for sodium removal were more pronounced in our CAPD population. In our CCPD patients, although icodextrin increased sodium removal during the day, total daily sodium removal was not statistically different from that in patients not using icodextrin. This finding might be explained not only by the small number of patients studied, but also by our policy to strive for maximum solute clearances and UF when targets are not achieved. In our program, anuric and larger CCPD patients are therefore more likely to receive icodextrin.

Hypertension in PD is strongly related to volume overload (3), and most studies report a higher incidence in APD than in CAPD (4–6). Our results accord with those findings. Increased fluid and sodium removal has also been associated with better outcomes in PD patients. Ates *et al.* (4) studied a cohort of 125 PD patients for 3 years and found significantly better survival in patients with higher levels of total fluid and sodium removal. Although attempts to prove the importance of volume management in improving clinical outcomes have been difficult, the European Best Practice Guidelines for Peritoneal Dialysis suggest that a net fluid removal of 1 L daily should also be included in the adequacy targets of PD therapy (12). However, this approach has been criticized, with the suggestion of a reverse-causation phenomenon, because fluid removal depends on fluid intake (13). According to that concept, healthier patients might have a higher fluid intake and so a higher fluid removal.

Recent large randomized controlled studies in both hemodialysis (14) and PD (15) that focused on increased solute clearances reported rather disappointing results: no improvement in the survival of patients with end-stage renal disease. Management of hypervolemia deserves major attention. Changes in the therapeutic approach, such as dietary advice in limiting sodium and fluid intake, and optimal prescription of PD, taking into consideration not only solutes clearances but also efficient sodium and fluid removal, will improve survival rates in patients undergoing PD.

Conclusions

Our results indicate that, despite of lower solute removal as reflected in Kt/V urea and creatinine clearance, CAPD is a more efficient modality for sodium removal than is high-volume CCPD. This phenomenon

may be explained by the sodium sieving effect that results from the short dwell times applied by cyclers in high-volume CCPD.

The use of icodextrin solution is an effective tool not only to achieve adequacy targets, but also to remove more sodium in both modalities. However, optimal control of extracellular volume necessitates patient compliance with a low-salt diet and reduced fluid intake.

References

- 1 Gokal R. Fluid management and cardiovascular outcome in peritoneal dialysis patients. *Semin Dial* 1999;12:126–32.
- 2 Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis* 1998;32(Suppl 3):S112–19.
- 3 Khandelwal M, Kothari J, Krishnan M, *et al.* Volume expansion and sodium balance in peritoneal dialysis patients. Part II: Newer insights in management. *Adv Perit Dial* 2003;19:44–52.
- 4 Ateş K, Nergizođlu G, Keven K, *et al.* Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. *Kidney Int* 2001;60:767–76.
- 5 Ortega O, Gallar P, Carreño A, *et al.* Peritoneal sodium mass removal in continuous ambulatory peritoneal dialysis and automated peritoneal dialysis: influence on blood pressure control. *Am J Nephrol* 2001;21:189–93.
- 6 Rodríguez–Carmona A, Pérez Fontán M. Sodium removal in patients undergoing CAPD and automated peritoneal dialysis. *Perit Dial Int* 2002;22:705–13.
- 7 Rodríguez–Carmona A, Pérez–Fontán M, García–Naveiro R, Villaverde P, Peteiro J. Compared time profiles of ultrafiltration, sodium removal, and renal function in incident CAPD and automated peritoneal dialysis patients. *Am J Kidney Dis* 2004;44:132–45.
- 8 Demetriou D, Habicht A, Schillinger M, Hörl WH, Vychytil A. Adequacy of automated peritoneal dialysis with and without manual daytime exchange: a randomized controlled trial. *Kidney Int* 2006;70:1649–55.
- 9 Struijk DG, Krediet RT. Sodium balance in automated peritoneal dialysis. *Perit Dial Int* 2000;20(Suppl 2):S101–5.
- 10 Rippe B, Levin L. Computer simulations of ultrafiltration profiles for an icodextrin-based peritoneal fluid in CAPD. *Kidney Int* 2000;57:2546–56.
- 11 Plum J, Gentile S, Verger C, *et al.* Efficacy and safety of a 7.5% icodextrin peritoneal dialysis solution in patients treated with automated peritoneal dialysis. *Am J Kidney Dis* 2002;39:862–71.

- 12 Dombros N, Dratwa M, Feriani M, *et al.* European Best Practice Guidelines for Peritoneal Dialysis. 7. Adequacy of peritoneal dialysis. *Nephrol Dial Transplant* 2005;20(Suppl 9):ix24–7.
- 13 Sharma AP, Blake PG. Should “fluid removal” be used as an adequacy target in peritoneal dialysis? *Perit Dial Int* 2003;23:107–8.
- 14 Eknoyan G, Beck GJ, Cheung AK, *et al.* Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med* 2002;347:2010–19.
- 15 Paniagua R, Amato D, Vonesh E, *et al.* Effects of in-

creased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. *J Am Soc Nephrol* 2002;13:1307–20.

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