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257

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Original Paper

Routine Monitoring of Sodium and Phosphorus Removal in Peritoneal Dialysis (PD) Patients Treated with Continuous Ambulatory PD (CAPD), Automated PD (APD) or Combined CAPD+APD

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Key Words

APD • CAPD + APD • CAPD • Phosphorus • Peritoneal dialysis • Sodium

Abstract

Background: Adequate removal of sodium (Na) and phosphorus (P) is of paramount importance for patients with dialysis-dependent kidney disease can easily quantified in peritoneal dialysis (PD) patients. Some studies suggest that automated PD (APD) results in lower Na and P removal. **Methods.** In this study we retrospectively analysed our data on Na and P removal in PD patients after implementation of a routine monitoring in 2011. Patients were stratified in those treated with continuous ambulatory PD (CAPD, n=24), automated PD (APD, n=23) and APD with one bag change (CAPD+APD, n=10). Until 2015 we collected time-varying data on Na and P removal from each patient (median 5 [interquartile range 4-8] values). **Results:** Peritoneal Na and P removal (mmol per 24h ± standard deviation) was 102 ± 48 and 8 ± 2 in the CAPD, 90 ± 46 and 9 ± 3 in the APD and 126 ± 39 and 13 ± 2 in the CAPD+APD group (ANOVA P=0.141 and <0.001). Taking renal excretion into account total Na and P removal (mmol per 24h) was 221 ± 65 and 16 ± 5 in the CAPD, 189 ± 58 and 17 ± 6 in the APD and 183 ± 38 and 16 ± 6 in the CAPD+APD group (P=0.107 and 0.764). Over time, peritoneal removal of Na but not that of P increased in all groups. In patients with modifications of PD treatment, Na but not P removal was significantly increased over-time. **Conclusions:** Overall

V. Moor and R. Wagner contributed equally and therefore share first authorship.

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Na and P removal were similar with different PD modalities. Individualized adjustments of PD prescription including icodextrin use or higher glucose concentration can improve Na removal while P removal is mainly determined by the dialysate volume.

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Introduction

Chronic kidney disease (CKD) leads to disturbance of whole-body sodium (Na) and phosphorus (P) balance and typically results in Na and P retention in advanced renal disease, particularly in those with dialysis-dependent end-stage renal disease (ESRD). Na and P retention are key elements in the pathogenesis of cardiac impairment and secondary hyperparathyroidism, both important predictors of mortality in ESRD patients [1-4]. Hence, adequate Na and P removal is of paramount importance for dialysis-dependent ESRD patients [5]. In contrast to hemodialysis patients, removal of Na and P can easily be quantified in peritoneal dialysis (PD) patients. A recent study suggested that PD results in higher P retention due to reduced clearance compared to HD [6]. This could be particularly true for patients treated with automated PD (APD) that has been reported to result in lower Na and P removal [7-9]. For Na, lower removal during APD can be explained by sodium sieving during the first hour of the dwell time due to transcellular water transport by aquaporins [10, 11]. Net Na mass transfer takes place thereafter through small pores driven by chemical gradient and solvent drag. For P, transport across the peritoneum also involves small pores and is hindered by the intracellular distribution of P and the large radius of the hydrated phosphate ions [12]. Hence, adequate peritoneal Na and P removal is expected to be higher with an increasing dwell time and a higher P transporter status [9, 13].

Given these caveats, Na and P removal can still be influenced by the PD prescription such as adapting dialysate volume, glucose concentration, usage of icodextrin or number of exchanges [14]. As residual renal function deteriorates adequacy of Na and P removal by PD becomes even more important. Measuring Na and P removal PD helps to assess the efficacy of the current regimen and to adapt the PD prescription when there is evidence of Na and P retention, particularly in APD patients. It furthers helps to illustrate how much of Na and P the patient can orally ingest to maintain balance. For these reasons, we have implemented a routine monitoring of Na and P removal in our center that is measured in addition to measurement of Kt/V and weekly creatinine clearance. Here we report on the results of this monitoring during a 4-year time span (2011-2015) with emphasis on the PD modality and time trends.

Materials and Methods

Study design and subjects

All incident and prevalent PD patients treated in our department since implementation of routine monitoring of Na and P removal in October 2011 were enrolled in the study. This routine monitoring was done at the outpatient visits of each patient every 3 months in addition to measurement of Kt/V and weekly creatinine clearance from the effluent and urine that had been collected on the previous day. Na and P removal were calculated from the measured Na (using ion-selective electrodes) and P concentrations and the effluent and urine volumes. For Na, values had to be corrected for the Na content of the dialysate volume. GFR was taken as the average of creatinine and urea clearance that were calculated from the 24 h urine. Measurements of the urine and effluent Na and P concentration were done on the same day of the outpatient visit and then transferred to the dialysis software Nephro 7 (Medvision, Bad Soest, Germany) that was programmed to compute the peritoneal and renal Na and P removal. Data for this retrospective study were extracted from the electronic file until September 1st 2015.



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51 patients were

those

CAPD,

PD

combined

in

with

CAPD+APD. 6 patients

modality were analysed per modality resulting in group sizes of 24 patients in the CAPD,

group. Patients were treated with glucose and/or

3.86%

double-chamber bags), acids

and icodextrin 7.5% as clinically needed. CAPD was performed with 3 to 4 manual bag changes per day. APD was done with a cycler

Illinois, USA) over 7.5-9 hours with 4-6 cycles, 75-85 % tidal volume

changed

patients in the APD and 10 patients

CAPD+APD

2.27

(only

1.1%

Deerfield,

and

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treated

APD

who

23

in

1.36%

amino

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and/or

the

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	CAPD	4.00		D		
	CAPD	APD	CAPD+APD	Р		
1.11	(n=24)	(n=23)	(n=10)			
renal diseases	0	_	-			
- diabetic/hypertensive	9	5	5	n.a.		
nephropathy	_	_				
- glomerulonephritis	5	7	3			
 polycystic kidney disease 	2	3	2			
- obstructive	0	2	0			
- toxic	5	4	0			
- cardiorenal	3	1	0			
- unknown/other	0	1	0			
gender ratio 9:0	14:10	6:17	3:7	0.061		
age at study inclusion	52 ± 15	54 ± 16	57 ± 19	0.715		
time on PD, years	2.7 ± 2.2	2.4 ± 1.8	4.7 ± 2.4	0.014		
time in study, years	1.8 ± 1.0	1.6 ± 0.9	3.0 ± 1.5	0.005		
GFR	4.7 ± 2.7	4.0 ± 3.3	1.1 ± 1.1	0.005		
$(mL/min/1.73m^{2})$						
dialysate volume.	5.8 ± 1.8	10.4 ± 2.0	12.6 ± 2.1	< 0.001		
L per pro 24h						
glucose concentration. %	1.73 ± 0.34	2.01 ± 0.43	2.12 ± 0.39	0.014		
patients with icodextrin	12/24	19/23	10/10	0.003		
D/P creatinine	0.76 ± 0.15	0.82 ± 0.09	0.71 ± 0.11	0.095		
ultrafiltration during PET-	441 ± 268	341 ± 277	420 ± 286	0.514		
test. mL/4 h						
total Kt/V	2.25 ± 0.43	2.38 ± 0.69	1.91 ± 0.16	0.066		
total creatinine clearance.	115 ± 48	97 ± 41	57 ± 17	0.002		
$L/week/1.73m^2$						
peritonitis episodes	4	8	4	n.a.		
peritonitis rate (natient	259	125	114	na		
months per enisode)	200	120		ma		
hemoglobin g/dl	101+12	105 ± 10	102 ± 05	0 5 2 7		
albumin g/dl	37 ± 0.5	38 ± 0.5	38 ± 0.7	0.853		
C-reactive protein mg/dl	3.7 ± 0.3 3.3 ± 2.9	3.0 ± 0.3 3.4 ± 3.3	5.0 ± 0.7 5.0 ± 4.7	0.000		
PFT: peritoneal equilibration test done with 2 L 3 86 % glucose CFP: averaged						
from 24 h urinary creatining	and urea clears	1213.0070 giu	nlicable	ageu		
nom 24 n urmary creatinne and urea clearance, n.a. not applicable						

and a last fill of 1.5-2 L during daytime. CAPD+APD was similarly performed as usual APD except for an additional 3-5 hours daytime fill with 2 L at 6 pm until begin of overnight APD. The decision about treatment modality CAPD vs. APD primarily related to the patient's preference and secondly to transporter status. High transporters with low ultrafiltration were treated with APD. CAPD+APD was commenced when residual renal function strongly declined and adequacy goals were not achieved. Volume status was measured with the bioimpedance spectroscopy (BCM monitor, Fresenius Medical Care Homburg, Germany). Blood pressure data were derived

from self-measurements with a uniform oscillometric device provided by Baxter (Deerfield, Illinois, USA).

Statistical analysis

The study was approved the local ethics committee.

Each studied parameter was arithmetically averaged per patient over the whole study period and this average value was used in final analyses. The median number of replicates per patient was 5 (interquartile range 4-8) values during a median study period of 1.4 (1.1;2.6) years per patient. Differences between the groups were analysed with one-way analysis of variance (ANOVA) with Tukey-Kramer post-test. To account for differences in patient characteristics (table 1), groups were additionally compared with oneway analysis of covariance (ANCOVA) with adjustments made for time on PD, glucose concentration, usage of icodextrin (yes or no), dialysate volume and residual GFR. To analyse the time trend of the parameters, all single replicate values of a patient were entered by treatment group into a mixed model with time as fixed effects and patient identifier as random effects. To test group-specific differences in the time trend, the mixed model was repeated with group as an interaction term. Variables entering multivariable linear regression were selected from stepwise approach (enter when p < 0.2, remove when p > 0.21). Statistical analyses were done with MedCalc Statistical Software version 16.4.2 (MedCalc Software byba, Ostend, Belgium) and JMP 11 (SAS Institute Inc., Cary, NC, USA).

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Fig. 1. Removal of fluid (A) by ultrafiltration and residual diuresis as well as peritoneal and renal removal of Na (B) and P (C). Total removal is derived from the sum of peritoneal and renal excretion. Arithmetic means with SD.

Results

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Table 1 shows the characteristics of the groups that significantly differed with respect to time on PD, average glucose concentration, usage of icodextrin, dialysate volume and residual GFR. Patients with CAPD+APD were longer on PD, had lower residual GFR, highest dialysate volume and glucose concentration as well as icodextrin usage. Transporter status was not different across the groups. Total Kt/V and weekly creatinine clearance were highest among CAPD patients followed by APD patients. CAPD+APD patients had the lowest clearance values, particularly weekly creatinine clearance (table 1).

As shown in Fig. 1A, CAPD+APD patients had the highest ultrafiltration and inversely the lowest urine volume. CAPD patients had the lowest ultrafiltration, yet the highest urine volume resulting in the highest total fluid excretion. Peritoneal, renal and total Na removal is shown Fig 1B. Peritoneal Na removal was slightly lower in the APD group reaching statistical significance after adjusting for group differences with ANCOVA. In the CAPD+APD group, peritoneal Na removal was highest while renal Na excretion was the lowest. Total Na removal was similar across all groups with a tendency to highest values in the CAPD group. Peritoneal, renal and total P removal is shown Fig 1C. Peritoneal P removal was significantly higher and renal P excretion lower in the CAPD+APD group compared to the other groups. Total P excretion was similar across the groups.

Table 2 shows the time- and group-dependent changes in peritoneal and renal clearance as analysed with a mixed linear regression model. GFR was lost in the CAPD and APD groups with a similar rate, in the CAPD+APD the value was somewhat lower which may be explained with a very low baseline GFR. Similarly, urine volume fell in all groups by 236-266 ml per year. Inversely, dialysate volume increased in all groups, particularly in the APD and CAPD+APD group. As a result, ultrafiltration also increased with time which was, however, less pronounced in the APD group. While renal Na removal decreased, peritoneal Na removal increased with time and a tendency towards group-specific differences. Interestingly, peritoneal P removal remained stable throughout the study period, while renal P excretion decreased in all groups with time.

During the study period PD treatment was modified in 6 (12%) patients who changed PD modality, mainly from CAPD to APD, and in 33 (58%) patients whose PD treatment was changed (table 3). The median number of treatment changes were on average two per patient and similar across the groups (table 3, p=0.22). During the first regimen, patients with and without treatment changes had a similar glucose concentration (1.74 [1.36; 1.97] vs. 1.82 % [1.59; 2.10], p=0.31) and dialysate volume (7.76 [4.5; 10.0] vs. 7.91 L [5.0; 10.0],

260

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Moor/Wagner/Sayer et al.: Na and P Removal During PD

Table 2. Time dependence of studied parameters, Results of a mixed model with time as independent variable and group as an interaction term. Slope values of individual patients were averaged to give a quantitative estimate of the change with time

GFR, mL/min/1.73m ² CAPD APD -0.8 (-2.3; -0.3) 135 (-2.5; -0.1) 0.94 (-0.0001) change with time groups dialysate volume, mL / 24 h APD (-APD + APD) -0.5 (-0.3; -0.2) 92 (-0.0001) 0.92 (-0.0001) -0.0001 (-0.0001) urine volume, mL / 24 h APD (-APD + 4PD) +1049 (81; 3394) 138 (-0.0001) 0.81 (-0.0001) <0.0001 urine volume, mL / 24 h APD (-APD + 266 (-691; -159) 153 (-479; 94) 0.81 (-0.0001) <0.0001 urine volume, mL / 24 h APD (-APD + 266 (-691; -159) 153 (-401; -153) 0.82 (-401; -153) 0.82 (-0.0001) <0.0001 ultrafiltration, mL / 24 h APD (-APD + 474 (-362; 428) 138 (-67 (-0.0156) 0.0043 peritoneal Na elimination, mmol / 24 h CAPD + 4PD (-APD + 472 (-41; 50) 137 (-52 (-54); -77) 0.78 (-0.0001) 0.0001 peritoneal P elimination, mmol / 24 h CAPD (-APD + 4PD -27 (-43; -11) 89 (-144; 449) 0.81 (-0.0001) <0.0001 peritoneal P elimination, mmol / 24 h APD (-APD + 4PD -27 (-43; -11) 89 (-12 (-41; 15) 0.21 (-47 (-52; 0.1) 0.48 (-0.0001) <0.0001 renal P elimination, mmol / 24 h	parameter	group	median slope	Ν	R ²	P for	P for
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$			per year			change	difference
$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$						with time	between
GFR, ml/min/1.73m ² CAPD APD (CAPD+APD) -1.3 (-2.5; -0.1) 147 0.93 <0.0001 0.0437 dialysate volume, mL / 24 h CAPD +0.0 (-79; 433) 137 0.92 <0.0001							groups
$\begin{array}{cccc} \mathrm{ML}, \\ \mathrm{mL}/\mathrm{min}/1.73\mathrm{m}^2 & \mathrm{APD} & -1.3 \ (-2.5; -0.1) & 147 & 0.93 & <0.0001 & 0.0437 \\ \mathrm{CAPD} + \mathrm{APD} & -0.5 \ (-0.8; -0.2) & 92 & 0.92 & <0.0001 \\ \mathrm{dialysate volume,} & \mathrm{CAPD} & +0 \ (-79; 433) & 137 & 0.92 & <0.0001 \\ \mathrm{ML} / 24 \ \mathrm{h} & \mathrm{APD} & +1049 \ (81; 3394) & 138 & 0.81 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & +606 \ (41; 1239) & 123 & 0.81 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & -256 \ (-691; -159) & 153 & 0.82 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & -266 \ (-691; -159) & 153 & 0.82 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & -226 \ (-691; -153) & 95 & 0.86 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & -226 \ (-401; -153) & 95 & 0.86 & <0.0001 \\ \mathrm{CAPD} + \mathrm{APD} & -226 \ (-401; -153) & 95 & 0.86 & <0.0001 \\ \mathrm{CAPD} + 162 \ (-133; 332) & 136 & 0.67 & 0.0156 \\ \mathrm{CAPD} & +162 \ (-133; 332) & 138 & 0.63 & 0.1693 & 0.0043 \\ \mathrm{CAPD} & +74 \ (-362; 428) & 138 & 0.63 & 0.1693 & 0.0043 \\ \mathrm{CAPD} & +74 \ (-362; 428) & 138 & 0.63 & 0.1693 & 0.0043 \\ \mathrm{CAPD} & +74 \ (-362; 428) & 138 & 0.63 & 0.1693 & 0.0043 \\ \mathrm{CAPD} & +12 \ (-41; 50) & 137 & 0.52 & 0.4584 & 0.0521 \\ \mathrm{Peritoneal Na} & \mathrm{CAPD} & +12 \ (-41; 50) & 137 & 0.52 & 0.4584 & 0.0521 \\ \mathrm{CAPD} & +APD & -27 \ (-43; -11) & 80 \ 0.81 & <0.0001 & <0.0001 \\ \mathrm{CAPD} & +110 \ (-14; 40) & 123 & 0.32 & 0.0032 \\ \mathrm{renal Na \ elimination, mmol / 24 \ h & \mathrm{APD} & -27 \ (-43; -11) & 80 \ 0.81 & <0.0001 & <0.0001 \\ \mathrm{CAPD} & +113 \ (-0.5; 2.6) & 135 & 0.64 & 0.1782 & 0.5377 \\ \mathrm{CAPD} & +0.2 \ (-1.1; 1.5) & 122 & 0.21 & 0.4580 \\ \mathrm{renal P \ elimination, mmol / 24 \ h & \mathrm{APD} & -1.0 \ (-2.8; 0) & 135 & 0.85 & 0.0496 \\ \mathrm{renal P \ elimination, mmol / 24 \ h & \mathrm{APD} & -1.0 \ (-2.8; 0) & 135 & 0.82 & <0.0001 \\ \mathrm{CAPD} & \mathrm{APD} & -0.23 \ (-0.5; 0.25) \ 142 & 0.78 & <0.0001 & 0.0787 \\ \mathrm{CAPD} & \mathrm{APD} & -0.23 \ (-0.5; 0.25) \ 142 & 0.78 & <0.0001 & 0.0787 \\ \mathrm{CAPD} & \mathrm{APD} & -0.23 \ (-0.5; 0.25) \ 142 & 0.78 & <0.0001 \\ \mathrm{CAPD} & \mathrm{APD} & -0.23 \ (-0.5; 0.25) \ 142 & 0.78 & <0.0001 & 0.9813 \\ \mathrm{CAPD} & \mathrm{APD} & -0.01 \ (-0.08; 0.07) \ 100 & 0.20 \ 0.2404 \\ \mathrm{CAPD} & \mathrm{APD} & -10 \ (-15; -1) \ 139 & 0$	CEP	CAPD	-0.8 (-2.3; -0.3)	135	0.94	< 0.0001	
$\begin{array}{cccc} \mbox{IIII} / \mbox{IIIII} / \mbox{IIIIII} / \mbox{IIIII} / \mbox{IIIIII} / \mbox{IIIII} / \mbox{IIIII} / \mbox{IIIII} / \mbox{IIIII} / \mbox{IIIIII} / \mbox{IIIIII} / \mbox{IIIIII / \mbox{IIIIII} / \mbox{IIIIII} / \mbox{IIIIII} / \mbox{IIIII} / \mbox{IIIIII} / IIIIIIII / \mbox{I$	mI /min /1 $73m^2$	APD	-1.3 (-2.5; -0.1)	147	0.93	< 0.0001	0.0437
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		CAPD+APD	-0.5 (-0.8; -0.2)	92	0.92	< 0.0001	
	dialysata volumo	CAPD	+0 (-79; 433)	137	0.92	< 0.0001	
$ \begin{array}{c} \mbox{IIII } / 24 \mbox{IIII } / 24 \mbox{IIII } \\ \mbox{CAPD } + 253 (-479; 94) & 146 & 0.81 & <0.0001 \\ \mbox{CAPD } -253 (-479; 94) & 146 & 0.81 & <0.0001 \\ \mbox{CAPD } + 266 (-691; -159) & 153 & 0.82 & <0.0001 \\ \mbox{CAPD } +206 (-401; -153) & 95 & 0.86 & <0.0001 \\ \mbox{CAPD } +162 (-133; 322) & 136 & 0.67 & 0.0156 \\ \mbox{APD } +74 (-362; 428) & 138 & 0.63 & 0.1693 & 0.0043 \\ \mbox{CAPD } +284 (124; 489) & 124 & 0.61 & <0.0001 \\ \mbox{CAPD } +8 (-24; 46) & 135 & 0.67 & 0.0150 \\ \mbox{CAPD } +8 (-24; 46) & 135 & 0.67 & 0.0150 \\ \mbox{CAPD } +8 (-24; 46) & 135 & 0.67 & 0.0150 \\ \mbox{CAPD } +12 (-41; 50) & 137 & 0.52 & 0.4584 & 0.0521 \\ \mbox{CAPD } +27 (-45; 5) & 146 & 0.81 & <0.0003 \\ \mbox{CAPD } -27 (-45; 5) & 146 & 0.81 & <0.0001 \\ \mbox{CAPD } -27 (-45; 5) & 146 & 0.81 & <0.0001 \\ \mbox{CAPD } +1.1 (0.3; 2.9) & 135 & 0.78 & 0.1230 \\ \mbox{CAPD } +1.1 (0.3; 2.9) & 135 & 0.64 & 0.1782 & 0.5377 \\ \mbox{CAPD } +1.3 (-0.5; 2.6) & 135 & 0.64 & 0.1782 & 0.5377 \\ \mbox{CAPD } +0.2 (-1.1; 1.5) & 122 & 0.21 & 0.4580 \\ \mbox{CAPD } -1.0 (-2.8; 0) & 135 & 0.85 & 0.0496 \\ \mbox{CAPD } +0.2 (-1.1; 1.5) & 122 & 0.21 & 0.4580 \\ \mbox{CAPD } -0.05 (-0.23; 0.08) & 138 & 0.83 & <0.0001 \\ \mbox{CAPD } -0.05 (-0.23; 0.08) & 138 & 0.83 & <0.0001 \\ \mbox{CAPD } -0.05 (-0.23; 0.08) & 138 & 0.83 & <0.0001 \\ \mbox{CAPD } -10 (-15; -1) & 139 & 0.89 & <0.0001 \\ \mbox{CAPD } -10 (-15; -1) & 139 & 0.89 & <0.0001 \\ \mbox{CAPD } -10 (-15; -1) & 139 & 0.89 & <0.0001 \\ \mbox{CAPD } -10 (-15; -1) & 139 & 0.89 & <0.0001 \\ \mbox{CAPD } -10 (-15; -1) & 139 & 0.89 & <0.0001 \\ \mbox{CAPD } -15 (-37; 8) & 142 & 0.86 & <0.0001 & 0.1824 \\ \mbox{CAPD } -7 (-9; -2) & 100 & 0.90 & <0.0001 \\ \end{tabular}$	mL / 24 h	APD	+1049 (81; 3394)	138	0.81	< 0.0001	< 0.0001
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	IIIL / 24 II	CAPD+APD	+606 (41; 1239)	123	0.81	< 0.0001	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	uring volume	CAPD	-253 (-479; 94)	146	0.81	< 0.0001	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	mL / 24 h	APD	-266 (-691; -159)	153	0.82	< 0.0001	< 0.0001
	IIIL / 24 II	CAPD+APD	-236 (-401; -153)	95	0.86	< 0.0001	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	ultrafiltration	CAPD	+162 (-133; 332)	136	0.67	0.0156	
$\begin{array}{cccc} \mbox{Int} / 24 \mbx$	mL/24 b	APD	+74 (-362; 428)	138	0.63	0.1693	0.0043
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	IIIL / 24 II	CAPD+APD	+284 (124; 489)	124	0.61	< 0.0001	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	paritonaal Na	CAPD	+8 (-24; 46)	135	0.67	0.0150	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	alimination mmol / 24 h	APD	+12 (-41; 50)	137	0.52	0.4584	0.0521
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	emmation, millor / 24 m	CAPD+APD	+16 (-14; 40)	123	0.32	0.0032	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	ronal Na elimination	CAPD	-27 (-54; -7)	137	0.78	0.0003	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	mmol / 24 h	APD	-27 (-45, 5)	146	0.81	< 0.0001	< 0.0001
$ \begin{array}{c ccccc} & CAPD & +1.1 \left(0.3; 2.9 \right) & 135 & 0.78 & 0.1230 \\ \hline APD & +1.3 \left(-0.5; 2.6 \right) & 135 & 0.64 & 0.1782 & 0.5377 \\ \hline CAPD + APD & +0.2 \left(-1.1; 1.5 \right) & 122 & 0.21 & 0.4580 \\ \hline CAPD + APD & -1.0 \left(-2.8; 0 \right) & 135 & 0.85 & 0.0496 \\ \hline APD & -2.4 \left(-5.2; 0.1 \right) & 142 & 0.86 & <0.0001 & 0.0787 \\ \hline CAPD + APD & -1.5 \left(-2.6; 0.6 \right) & 87 & 0.82 & <0.0001 \\ \hline CAPD & -0.05 \left(-0.23; 0.08 \right) & 138 & 0.83 & <0.0001 \\ \hline CAPD & -0.23 \left(-0.51; 0.25 \right) & 142 & 0.78 & <0.0001 \\ \hline CAPD + APD & -0.01 \left(-0.08; 0.07 \right) & 100 & 0.20 & 0.2404 \\ \hline CAPD & -15 \left(-37; 8 \right) & 142 & 0.86 & <0.0001 \\ \hline CAPD & -15 \left(-37; 8 \right) & 142 & 0.86 & <0.0001 \\ \hline CAPD + APD & -7 \left(-9; -2 \right) & 100 & 0.90 & <0.0001 \\ \hline \end{array} $	1111101 / 24 11	CAPD+APD	-27 (-43; -11)	89	0.81	< 0.0001	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	noviton col D olimination	CAPD	+1.1 (0.3; 2.9)	135	0.78	0.1230	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	mmal (24 h	APD	+1.3 (-0.5; 2.6)	135	0.64	0.1782	0.5377
renal P elimination, mmol / 24 h CAPD APD -1.0 (-2.8; 0) 135 0.85 0.0496 APD -2.4 (-5.2; 0.1) 142 0.86 <0.0001	1111101 / 24 11	CAPD+APD	+0.2 (-1.1; 1.5)	122	0.21	0.4580	
APD -2.4 (-5.2; 0.1) 142 0.86 <0.0001 0.0787 mmol / 24 h CAPD+APD -1.5 (-2.6; 0.6) 87 0.82 <0.0001	wanal Dalimination	CAPD	-1.0 (-2.8; 0)	135	0.85	0.0496	
$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	mmol / 24 h	APD	-2.4 (-5.2; 0.1)	142	0.86	< 0.0001	0.0787
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total Kt/V APD -0.23 (-0.51; 0.25) 142 0.78 <0.001 0.9813 CAPD+APD -0.01 (-0.08; 0.07) 100 0.20 0.2404 - total creatinine clearance, L/week/1.73m ² CAPD + APD -10 (-15; -1) 139 0.89 <0.0001	total Kt/V	CAPD	-0.05 (-0.23; 0.08)	138	0.83	< 0.0001	
CAPD+APD -0.01 (-0.08; 0.07) 100 0.20 0.2404 total creatinine clearance, L/week/1.73m ² CAPD -10 (-15;-1) 139 0.89 <0.0001		APD	-0.23 (-0.51; 0.25)	142	0.78	< 0.0001	0.9813
total creatinine clearance, L/week/1.73m ² CAPD APD -10 (-15;-1) 139 0.89 <0.0001 0.15 (-37;8) 142 0.86 <0.0001		CAPD+APD	-0.01 (-0.08; 0.07)	100	0.20	0.2404	
total creatinine clearance, APD -15 (-37;8) 142 0.86 <0.0001 0.1824 L/week/1.73m ² CAPD+APD -7 (-9;-2) 100 0.90 <0.0001		CAPD	-10 (-15;-1)	139	0.89	< 0.0001	
CAPD+APD -7 (-9;-2) 100 0.90 <0.0001	$L_{\rm run old} (1.72 m^2)$	APD	-15 (-37;8)	142	0.86	< 0.0001	0.1824
	L/week/1./3m ²	CAPD+APD	-7 (-9;-2)	100	0.90	< 0.0001	

p=0.74). In patients with treatment changes, glucose concentration and dialysate volume were significantly increased to 2.04 % ([1.36; 2.27], p=0.008) and 8.7 L ([4.5; 10.0], p=0.03). To analyse if the treatment changes resulted in increased solute removal we reanalysed the time-dependent data after stratification of patients with or without treatment changes. As shown in table 4, patients with treatment changes had significantly higher time-dependent changes in dialysate volume, ultrafiltration and peritoneal Na but not P removal compared to patients without treatment changes (table 4). Time-dependent changes of peritoneal Kt/V and creatinine clearance were not significantly different between the groups, although they tended to increase in the patients with treatment changes.

We also assessed the surrogates for Na and P retention such as increased blood pressure, overhydration, hyperphosphatemia and secondary hyperparathyroidism. As shown in Fig. 2A, systolic and diastolic blood pressure was not different between groups although patients with APD and CAPD+APD tended to have higher systolic and diastolic blood pressure. Overhydration as surrogate of Na retention was common in all groups and was highest in the CAPD group (Fig. 2B). Inversion of extracellular to intracellular water (E/I) was uniformly found across all groups. The number of antihypertensives including diuretics was 3–5 drug classes per patient with a great variability and no significant difference (Fig.2C).

Patients in the CAPD+APD group had the highest plasma phosphorus concentration (Fig. 3A) while plasma calcium values were very similar in all groups (2.2-2.3 mM, P=0.108; data not shown). Parathyroid hormone concentration was similar across all groups (Fig.

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Moor/Wagner/Sayer et al.: Na and P Removal During PD

3A). CAPD+APD patients took the highest number of pills to bind phosphorus (Fig. 3B). However, the great variability precluded significant differences. Native and active vitamin D usage was identical in all groups (10 000 IE native vitamin D per week and 0.23 μ g per day, P=0.728 and 0.667).

Table 5 shows the results of a multivariate linear regression analysis to identify independent predictors of peritoneal Na and P removal. For Na, glucose concentration and usage of icodextrin were independent predictors, while for P dialysate volume and plasma phosphate concentrations were independent predictors.

Discussion

This study shows that different PD modalities can achieve fairly high and comparable removal of 80-120 mmol Na and 8-12 mmol P through the

Table 4. Time dependence of peritoneal solute elimination according to treatment changes . Results of a mixed model with time as independent variable stratified according to treatment changes (yes/no). Treatment modality was not entered into the model. Slope values of individual patients were averaged to give a quantitative estimate of the change with time

Table 3. Course of PD treatment duringstudy period

study completed on single	17		
PD modality			
terminated PD	25		
death	13		
transplanted	6		
switched to HD	4		
recovered renal function	2		
changed dialysis provider	4		
/lost to follow-up			
changed PD modality	6		
CAPD to APD	4		
APD to CAPD	1		
APD to APD+CAPD	1		
median number of	2		
treatment changes per			
patient			
CAPD	2		
APD	2		
CAPD+APD	3		
patients without			
treatment changes	24*		
CAPD	11**		
APD	11***		
CAPD+APD	2****		
* (42% of all patients); ** (42% of all			

(42% of all patients); (42% of all APD patients); **** (43% of all APD patients); ****(20% of all CAPD+APD patients)

parameter	group	median slope per	Ν	\mathbb{R}^2	P for	P for
		year			change	differenc
					with	e
					time	between
						groups
dialucata valuma	no	1202 (166.012)	126	0.76	0.0065	
ularysate volume,	changes	+365 (-466; 942)	120	0.76	0.0905	0.0034
ml / 24 n	changes	+1113 (0; 1376)	272	0.85	< 0.0001	
ultrafiltration	no	-79 (-464: 358)	126	0.66	0.7027	
mL / 24 h	changes	, , (101, 550)	120	0.00	0.7027	< 0.0001
1112/2111	changes	+259 (-16; 429)	272	0.60	< 0.0001	
peritoneal Na	no	-15 (-61: 27)	125	047	0 4607	
elimination,	changes	10 (01, 27)	120	0.17	0.1007	0.0001
mmol / 24 h	changes	13 (-8; 46)	270	0.50	0.0254	
peritoneal P	no	+3(0.4)	124	044	0 8946	
elimination,	changes		121	0.11	0.0710	0.5500
mmol / 24 h	changes	+2 (0; 3)	268	0.58	0.0726	
	no	-0.07 (-0.22; 0.11)	143	0.82	0.0035	0.0040
peritoneal Kt/V	changes				0.0004	0.3240
	changes	+ 0.19 (0.00; 0.27)	280	0.71	< 0.0001	
peritoneal	no	-1 (-2.0)	128	0.86	0 1070	
creatinine	changes	1 (2, 0)	120	0.00	0.1070	0.3510
clearance,	changes	-1 (-2.1)	295	058	0.0225	
L/week/1.73m ²		-1 (-2,1)	295	0.50	0.0223	

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Fig. 2. Surrogates for Na retention and use of antihypertensive drugs, A Systolic and diastolic blood pressure, B Overhydration and ratio of extra- to intracellular water (E/I) from bioimpedance spectroscopy, C Number of classes of antihypertensive drug including diuretics (torasemid and xipamide counted separately). Arithmetic means with SD

peritoneum per day. Peritoneal Na removal was slightly higher in CAPD than in APD, while there CAPD tended to have lower peritoneal P removal compared to APD. The combination of CAPD+APD achieved the highest values for both peritoneal Na and P removal compensating for the low residual renal function in these patients. Overall total Na and P removal were similar in the groups (180-220 mmol Na and 14-16 mmol P per day). The superiority of the peritoneal removal rates achieved with CAPD+APD is not a new finding and was characterized by Blake et al. in 1996 [15]. In that study, CAPD+APD with a mid-day change lead to higher clearance rate

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Fig. 3. Surrogates for P retention and use of phosphorus binders, Hyperphosphatemia (A), secondary hyperparathyroidism (B) and number of pills to bind phosphorus (C) including lanthan, calcium-containing, sevelamer and aluminium. Arithmetic means with SD

Table 5. Determinants of peritoneal Na and P removal as analysed by multivariable regression. All patients irrespective of the group were entered into the same model. SE standard error

independent	model strength	covariate	coefficient	p-value
variable			with SE	
peritoneal	adjusted $r^2 = 0.25$	y-intercept	-22	-
Na removal	P=0.0004	gender (1=male, 2=female)	24±12	0.0563
		glucose concentration, %	31±15	0.0497
		icodextrin (1=yes)	43±14	0.0051
peritoneal P	adjusted $r^2 = 0.59$	y-intercept	-1.70	-
removal	P<0.0001	glucose concentration, %	1.37 ± 0.85	0.1148
		icodextrin (1=yes)	1.30 ± 0.81	0.1177
		dialysate volume, mL	0.36 ± 0.11	0.0030
		plasma phosphate, mM	2.55±0.80	0.0024

263

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Moor/Wagner/Sayer et al.: Na and P Removal During PD

across all transporter types compared to APD with or without daytime filling which can be explained with the time-dependence of Na and P removal. In our center we commence this intensive treatment when residual function is strongly reduced in an APD patient, such as after several years on PD. Instead of a mid-day exchange we prescribe a 3-5 hours dwell time at the evening which is well feasible in patients after returning from their work. Our data show that this approach ensures high peritoneal removal rates compensating for reduced renal excretion that occurred in all groups over time. With combined CAPD+APD adequate PD can be re-accomplished in an APD patient enabling to continue PD and to benefit from the advantages of this home dialysis method.

Our study shows that treatment changes had an impact on peritoneal solute removal over time (table 4). These were most pronounced for ultrafiltration and Na elimination and to a lesser extent in peritoneal urea or creatinine elimination suggesting that routine Na monitoring helped to guide treatment and ensure adequate sodium balance. Treatment changes encompassed increased dialysate volume, higher glucose concentration and use of icodextrin. In patients with APD, cycler settings were optimized on an individual basis e.g. taking into account transporter status. Some patients were transferred to APD or CAPD+APD. Our data confirm that using icodextrin is of particularly great importance for peritoneal Na and to a lesser extent for P removal [10]. In APD patients and in those with reduced residual renal function icodextrin seems to be essential. Increasing glucose concentration could also work as it was also a determinant of higher peritoneal Na and to a lesser extent P removal. However, this will be limited by side effects of high glucose such as exacerbated hyperglycemia in diabetic patients, glucose overfeeding or peritoneal injury. In addition, high dialysate volume was found to be associated with damage to erythrocytes and eryptosis [16]. Interestingly, dialysate volume was an independent predictor only for P but not for Na removal. For P, plasma phosphorus concentration was also a highly significant predictor of peritoneal P removal that was has been reported earlier [17] and could be explained by an increased chemical gradient. This would also explain the highest peritoneal P removal in patients treated with CAPD+APD who at the same time had the highest plasma phosphorus values. This constellation indicates P retention in these patients despite higher removal. With regard to Na, CAPD+APD patients had the lowest values for overhydration measured with BCM (Fig. 2) that fit to the highest Na removal values. Therefore, it is important to analyse data on removal in combination with markers of retention such as overhydration or plasma P concentration to adequately assess solute homeostasis.

Weekly P removal on PD in our study was comparable to other studies [9, 13, 17]: we achieved 8-12 mmol (248-372 mg) per day corresponding to a weekly P dialysate clearance of 37 L/week in CAPD and 44 L/week in APD and CAPD+APD patients. These values are higher than that reported in a recent study comparing PD with HD [6]. The authors reported a weekly P dialysate clearance of only 33 L/week in a pooled sample of CAPD and APD patients that was significantly lower than in HD patients. This was driven by the extraordinary low clearance achieved with APD of 28 L/week whereas CAPD patients had a weekly clearance of 38 L/week. The reason for the low clearance on APD compared to our values must be related to the prescription. Unfortunately, that study did not report details on APD settings such as number of cycles, tidal volume or others or patient characteristics of the patients treated with APD. It mentions a high ultrafiltration suggesting a high number of cycles with short dwell times which is expected to result in lower P clearance. It is also conceivable that APD patients despite higher creatinine transporter status had low phosphorus transporter status and reduced phosphate transport [9, 13]. With our data, we can convincingly show that P removal is not necessarily inferior in APD patients and can be increased using CAPD+APD. Despite removal of 14-16 mmol P per day, dietary intake often exceeds this amount and was found to 20 mmol per day or higher in a peritoneal dialysis patient [18]. To avoid P retention this difference must be absorbed by phosphate binders. Thus, determination of P removal helps to calculate the required dose of P binders which also has to take into account binding capacity of the used P binders and the dietary intake.



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Moor/Wagner/Sayer et al.: Na and P Removal During PD

The limitations of this study are due to its retrospective and character, its single-center character and the low number of PD patients. PD modality was not controlled and subject to confounding by indication such as CAPD+APD in those with reduced residual function. Therefore, the groups had significant differences in their characteristics which we adjusted for using ANCOVA. We are aware that an interventional study with a crossover design would have been superior to study the efficacy of each modality as done by Demetriuo et al. [19], but our goal was to analyse the values obtained in a real-life setting. Therefore, we were able to follow the time dependence from begin of the monitoring. Values for both peritoneal and renal Na and P removal showed great intra- and interindividual variability which is commonly encountered in studies examining solute clearance in PD [20, 21]. We addressed this by using a mixed model with time as independent variable and taking into account each replicate values of a patient.

Conclusion

Routine monitoring of Na and P removal increases awareness of maintaining Na and P balance in PD patients. Individualized adjustments of PD prescription including icodextrin use or higher glucose concentration can improve Na removal while P removal is mainly determined by the dialysate volume.

Disclosure Statement

The authors of this manuscript state that they do not have any conflict of interests and nothing to disclose.

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