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Determinants of Sodium Removal with Tidal Automated Peritoneal Dialysis

In a comprehensive evaluation of dialysis adequacy, major attention has been recently paid to fluid and Na balance. Removal of Na has been reported to be significantly poorer with automated peritoneal dialysis (APD) than with continuous ambulatory peritoneal dialysis. Only limited data on Na removal with tidal APD have been published.

We analyzed peritoneal Na mass balance in 122 separate nightly tidal APD sessions performed by 7 peritonitis-free, clinically stable, patients with negligible residual renal function (<100 mL urine daily). Correlations with other efficiency measures [ultrafiltration (UF) and small-solute clearances], prescriptive parameters [duration of treatment, initial intraperitoneal fill volume (IPV) and its tidal percentage, and dialysate flux] and peritoneal transport status were tested in univariate and multivariate linear regression models.

Removal of Na was 89 ± 55 mmol per treatment, which correlated with UF (r = 0.29, p = 0.001) and was higher in patients with high-average transport (118 ± 41 mmol vs. 81 ± 56 mmol in low-average transporters, p = 0.0004), in whom a significant positive correlation was found with initial IPV and duration of treatment (r = 0.55; 95% confidence interval: 0.21 to 0.77; p = 0.0029; and r = 0.66; 95% confidence interval: 0.38 to 0.83; p = 0.0002 respectively).

Removal of Na correlated weakly with UF in tidal APD and showed wide inter-patient variability. It should therefore be measured rather than roughly estimated from UF. Its magnitude exposes the anuric patient on nightly APD with a “dry” day to the risk of Na retention, unless controlled Na intake or dialytic strategies aimed at enhancing Na removal, or both, are implemented.

Key words
Peritoneal transport, prescription, removal, sodium, tidal

Introduction
Fluid and Na removal have been found to correlate better with outcome in chronic kidney disease patients on long-term peritoneal dialysis (PD) than have traditional adequacy targets (1,2). Compared with patients on continuous ambulatory PD, patients on automated PD (APD) have been reported to have significantly poorer Na removal (3,4) and faster decline of residual renal function and urinary Na excretion (5). Few data on tidal APD have been published (6–9). In the present study, we aimed to quantify Na removal during nightly tidal treatment and to investigate correlations with UF, the commonly measured solute clearances, and the most relevant parameters of the tidal APD prescription.

Methods
In the context of an ongoing prospective interventional trial aimed at individually optimizing nightly APD treatments in our patients, comprehensive kinetic studies, including Na removal, are being routinely performed monthly at the time of the patient’s visit to the PD clinic. Patients who agreed to participate to the study by signing a written consent have been trained to adequately sample spent dialysate. Throughout the study period, the tidal APD prescription was managed and modified to meet the accepted minimal solute clearance (weekly urea Kt/V > 1.7, creatinine clearance > 45 L/1.73 m² body surface area) and ultrafiltration (UF) targets. A low-Na diet was regularly recommended to every APD patient without residual renal function. A blood sample was drawn 1 – 3 hours after the end of the APD session, and total volume infused and drained was recorded from the cycler. Standard laboratory methodology

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was used to measure urea, creatinine, and phosphate, and plasma and dialysate Na was determined by direct ion-selective electrode potentiometry (Vitros: Ortho Clinical Diagnostics, Raritan, NJ, U.S.A.). Peritoneal solute clearance was calculated as usual, and Na removal was calculated as

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\text{(effluent Na concentration } \times \text{ total effluent volume) } - \text{ (infused dialysate Na concentration } \times \text{ total volume infused)}.
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Duplicate samples of both infused dialysate and peritoneal effluent were randomly sent to the laboratory to check for variability. All patients used Gambrosol Trio PD fluids (Gambro Lundia, Lund, Sweden) in 5-L bags and a Serena cycler 7.0 (Gambro Lundia). From a database of 289 kinetic studies, we extracted sessions performed by clinically stable, peritonitis-free patients with negligible residual renal function (<100 mL urine output daily). To minimize case-mix, only patients who had completed at least 12 kinetic studies were included. All patients had undergone a standard peritoneal equilibration test within 1 year of each study session. Data are presented as mean ± standard deviation or median and 95% confidence interval (CI). Correlation with Na removal was tested by univariate and stepwise multivariate regression analysis. A Student t-test (or a Welch test whenever unequal variance was present) was used to compare continuous variables. The statistical analysis used MedCalc for Windows (version 11.1.6.1: MedCalc Software, Mariakerke, Belgium).

Results

Table I shows the characteristics of the 7 patients included in the analysis. Table II summarizes the main tidal APD prescription parameters and the resulting urea, creatinine, and phosphate clearances, UF, and Na removal from the 122 kinetic studies performed by those 7 patients.

Figure 1 shows the scatter plot of Na removal in the study sessions, averaging 89.5 mmol with wide (63%) overall variability. The inter-assay variability for the laboratory analyses of Na was remarkably low (0.94%). The within-subject variability in Na removal ranged from 19% to 87%, with higher values being observed in patients with low-average (LA) transport.

Figure 2 shows the correlations between Na removal and other measured solute clearances and UF. In stepwise multivariate regression analysis, the model retained UF, creatinine, and urea clearance, but the resultant adjusted $R^2$ was a rather low 0.226. Despite a significantly shorter treatment duration (26 minutes, $p = 0.002$), lower dialysis dose (0.3 L/h, $p < 0.0001$), and intraperitoneal fill volume (IPV: 93 mL, $p = 0.035$), solute clearances and Na removal were both significantly higher in the 3 patients with high-average (HA) transport than in the 4 patients with LA transport, but UF did not vary significantly (Figure 3). None of the prescription parameters correlated with Na removal in LA transporters, but treatment duration and IPV correlated positively in

| Table I: Demographic and clinical characteristics of the study patients |
|-----------------|-------|---------|------|----------|--------|
| Pt ID | Sex | Age (years) | BMI (kg/m$^2$) | BSA (m$^2$) | Months on PD | D/P Cr |
| 1 | Female | 38 | 24.2 | 1.7 | 41 | 0.69 |
| 2 | Female | 65 | 28.7 | 1.9 | 18 | 0.71 |
| 3 | Female | 41 | 24.8 | 1.7 | 21 | 0.67 |
| 4 | Female | 28 | 23.1 | 1.5 | 32 | 0.63 |
| 5 | Male | 33 | 27.9 | 2 | 55 | 0.62 |
| 6 | Female | 52 | 20.5 | 1.5 | 62 | 0.61 |
| 7 | Male | 38 | 25.9 | 2 | 51 | 0.65 |

Mean±SD: 42±12 | 25±2.8 | 1.75±0.21 | 39±17 | 0.65±0.03 |

95% CI: 30 to 58 | 21 to 28 | 1.5 to 2 | 18 to 58 | 0.61 to 0.7 |

| Table II: Automated peritoneal dialysis prescription parameters and observed results |
|-----------------|-------|---------|------|----------|--------|
| Variable | Mean±SD | Median | 95% CI |
| Duration (min) | 497±39 | 500 | 486 to 505 |
| Initial IP volume (mL) | 2287±200 | 2200 | 2200 to 2400 |
| Qd (L/h) | 2.1±0.34 | 2.1 | 1.9 to 2.2 |
| Tidal (%) | 68±17 | 68 | 58 to 74 |
| Ultrafiltration (mL/min) | 2.97±0.77 | 2.93 | 2.7 to 3.1 |
| Clearance (mL/min) | | | |
| Urea | 16.3±1.63 | 16.2 | 15.7 to 16.6 |
| Creatinine | 10.1±2.1 | 9.86 | 9.3 to 10.4 |
| Phosphate | 7.7±2 | 7.47 | 7 to 7.9 |
| Na$^+$ removal (mmol) | 89.5±55 | 93.5 | 79 to 105 |

SD = standard deviation; CI = confidence interval; IP = intraperitoneal; Qd = dialysis dose.
HA patients (adjusted $R^2 = 0.42, p < 0.001$). In 21 paired observations in 3 patients (1 HA and 2 LA transporters), a 5-L nightly increase in the dialysis dose resulted in a comparably significant increase in UF and urea clearance, but no appreciable effect on creatinine and phosphate clearances and Na removal (Figure 4). During the study period, 2 patients were prescribed a daytime dwell, and 1 patient performed a daytime exchange for overall adequacy purposes. Their results were not included in this study.

**Discussion**

Removal of Na has been reported to be lower with nightly APD than with continuous ambulatory PD (3–5), raising concerns about the possibility of achieving a neutral Na balance when residual renal function is lost. In the foregoing comparative studies, no details of the APD prescription were given, but

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**FIGURE 1** Removal of Na with tidal automated peritoneal dialysis (122 sessions).

**FIGURE 2** Correlation of Na removal with ultrafiltration (UF) and with urea, creatinine, and phosphate clearances. CI = confidence interval; NS = nonsignificant.
non-tidal (3,4) or tidal volumes exceeding 80% (5) were used. The lower Na removal was attributed to less UF with APD and to the short dwell time typical of nightly APD and the resulting magnification of Na sieving. Although adding a daytime dwell may help, that strategy has obvious drawbacks.

Removal of Na with tidal APD has been little investigated in published studies (6–9). In 8 anuric patients (4 HA and 4 LA transporters), Amici reported Na removal to be about 120 mmol over 24 hours with nightly tidal PD plus a daytime dwell with polyglucose, which accounted for 40% – 65% of the total Na removed. No differences with the non-tidal modality were found, and no appreciable increase in Na removal was obtained with a 5-L increase in the nightly APD dose. In a population consisting mainly of high and HA transporters, substantially higher Na removal was found (7), with a trend toward higher removal in tidal compared with non-tidal APD. In re-analyzing data from a previously published study, Vychytil and Hörl found an actual reduction in Na removal when the dialysis dose was increased (and the dwell time consequently shortened), with both tidal and non-tidal APD, the negative impact being more marked in LA transporters when a non-tidal modality was used (8). In a crossover study in 18 patients (8 HA and 10 LA transporters) that compared high-dose nightly 75% tidal APD plus
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a daytime dwell with low-dose nightly tidal APD plus a daytime exchange, urea and creatinine clearances were found to be higher and phosphate and β₂-microglobulin clearances to be not different, but Na removal to be about 50 mmol lower with the former regimen (9).

Our data accord with the findings of the above-mentioned studies, and they highlight the wide inter-patient and daily within-subject variability. Removal of Na was consistently higher in HA transporters, in whom positive correlations with both treatment duration and IPV were found. Dialysis dose increase had no appreciable effect on Na removal, but at least to some extent, that finding might have been influenced by the higher number of sessions performed by LA transporters in the present study.

Conclusions
Total Na removal warrants monitoring in APD patients, and efficient strategies to enhance Na balance need to be defined. Reducing Na concentration in PD fluids for APD appears to be a rational way to promote Na removal during nightly APD. Despite advocacy for such solutions having already begun more than a decade ago (10), none are yet commercially available.

Disclosures
The authors have no financial conflicts of interest to disclose.

References

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