Nocturnal ultrafiltration profiles in patients on APD: Impact on fluid and solute transport

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In order to prevent morbidity and mortality in peritoneal dialysis (PD), sodium and water balance as well as a minimal level of small-solute clearances are needed. The impact of three nocturnal peritoneal ultrafiltration (UF) profiles on UF and small solute clearance in patients on automated PD (APD) was studied: constant glucose concentration of 1.36% (flat) or modifying the glucose concentration of the heater bag (descendant: 3.86–1.36%; ascendant: 1.36–3.86%). Sixty-two patients were enrolled in the study and received each profile within a four-month period, thus serving as their own controls. UF was lower with the flat profile (367 ± 420 ml; *P* < 0.01), but no difference was seen between the two higher glucose concentration profiles. Peritoneal *Kt/V* (*pKt/V*) and peritoneal creatinine clearance (CrpC) showed statistically higher values from the descendant vs ascendant vs flat profiles (*pKt/V*: 1.54 ± 0.30 vs 1.45 ± 0.30 vs 1.38 ± 0.27, and CrpC: 36.9 ± 7.9 vs 33.5 ± 7.48 vs 29.92 ± 7.5 ml min^{-1}). Multivariate analysis showed statistical significance for the following: in the intrasubject comparisons, the profile for *pKt/V* (F=9.109, *P* < 0.001) and CrpC (F=11.697, *P* < 0.001), and in the intersubjects comparisons, the effects of both gender (F=14.334, *P* < 0.01) for *pKt/V* and peritoneal permeability for both parameters (*pKt/V*: F=4.37, *P* < 0.05; CrpC: F=11.697, *P* < 0.001). In conclusion, the application of ascendant and descendant UF profiles in automated PD is feasible and results in better UF and small solute clearances, thus preventing inadequate dialysis and volume overload.

Kidney International (2008) **73,** S94–S101; doi:10.1038/sj.ki.5002609

KEYWORDS: ultrafiltration; profiles; adequacy; peritoneal dialysis

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An increasing number of peritoneal dialysis (PD) patients are using automated PD (APD) as first-line renal replacement therapy, which now accounts for 80% of patients who choose PD in Spain.[1] One reason for this growth has been the recognition that an adequate dialysis dose has a significant impact on the clinical outcome of PD patients, as shown by various studies; among them is CANUSA[2] from which reference guidelines of dialysis adequacy have been derived. Although it is now recognized that the effects of residual renal function and peritoneal clearance are not equivalent,[3] the National Kidney Foundation Kidney Disease Quality Initiative (NKF KDOQI) guidelines have been widely used as a reference for PD adequacy.[4]

The Adequacy of Peritoneal Dialysis in Mexico (ADEMEX) study, although performed in continuous ambulatory PD patients, has changed the perception of PD prescription as it showed that survival is less dependent on small-solute clearance, emphasizing the importance of clinical assessment, maintenance of residual renal function, and optimization of salt and water balance. However, it should be emphasized that there must be a minimum level of small-solute clearances needed to prevent uremia-related morbidity and mortality, as the highest uremia-related death rate occurred in the lowest clearance group.[5]

The ADEMEX results confirm those of previous studies regarding the importance of the adequate balance of sodium and water and its effects on PD patients' morbidity and survival.[6,7] Whereas only a few studies comprising a limited number of patients have studied the survival of patients on APD,[8,9] it is quite likely that APD may help to improve some of the comorbidity factors associated with PD by increasing both ultrafiltration (UF) and small-solute clearances. However, as experience has grown with this technique, new questions for its optimization have arisen. In this modality, it is the policy to delay the use of PD solutions with greater glucose concentration and, therefore, greater osmolarity, with the aim of protecting and maintaining the function of the peritoneal membrane as long as possible. This overall strategy may be applied as long as the residual renal function is preserved and the peritoneal transport characteristics allow us to do so.

New PD cyclers have allowed us to analyze UF profiles for each session, which is determined by the scheduled prescription of osmolar PD solutions to each patient. In Dr Negrín Hospital, 1.36% glucose has always been used in the heater bag to minimize the osmolarity of the PD solution resulting from the mixture of the various bags to reach the desired UF. With this strategy, a flat (constant glucose concentration) or ascendant (increasing glucose concentration) UF profile is always obtained. If instead, the sequence of the heater bag is reversed (descendant profile), one would start with a high osmolarity of the dialysis solution, yielding maximum UF initially, which during the first hours of treatment should contribute to greater peritoneal clearances. However, the impact of these UF profiles on fluid and solute removal rates has not previously been systematically evaluated.

The aim of this study was, therefore, to assess the impact of these three different UF profiles on UF and on the amount of dialysis received by the patient on APD during the nocturnal period, using different dialysis adequacy indices.

RESULTS

The classification of transport type according to peritoneal equilibrium test (PET) and dialysate/plasma (D/P) creatinine at baseline showed high ($n=8$), high average ($n=22$), low average ($n=13$), and low ($n=19$) transporters. As assessed by the mass transfer coefficients (MTCs), the peritoneal transport characteristics did not change substantially throughout the study period. Thus, creatinine (Cr) and glucose (G) MTCs showed no significant differences between the baseline and final studies (Cr: 7.04 ± 4.35 vs $7.31 \pm 2.34\,\mathrm{ml\,min^{-1}}$; G: 7.00 ± 3.32 vs $6.94 \pm 1.92\,\mathrm{ml\,min^{-1}}$), whereas MTC for urea (U) differed significantly between baseline and final evaluation (U: 19.73 ± 7.08 vs $16.90 \pm 4.46\,\mathrm{ml\,min^{-1}}$, $P<0.05$).

Table 1 shows global average values of weekly creatinine clearance (CrC) and *Kt/V* as well as the sum of peritoneal and renal clearances for all 62 patients at each study time point; it is broken down according to the fractions contributed by the nocturnal and diurnal periods, the sum of both, and the renal clearance.

As the objective of this study was to assess the impact of the three UF profiles on the dose of dialysis received by the patient during the nocturnal period, only this aspect is reported in the following results. Table 2 summarizes the results of the univariate analysis of the parameters obtained in all 62 patients, being the flat, descendant, and ascendant profiles, expressed as mean $\pm$ s.d. There were no differences among the three profiles in relation to body surface area (BS), total body water (TBW), mean dwell time per cycle, total dwell time, non-useful time, and the infusion volume corrected for BS.

Urea and creatinine D/P ratios were significantly higher in the descendant profile vs the flat and ascendant profiles. UF was significantly lower only when comparing the flat profile (with lower glucose concentration) to the other two profiles. The results for weekly peritoneal urea clearance (pUC), *Kt/V* of weekly peritoneal urea (p*Kt/V*), peritoneal creatinine clearance (CrpC), weekly CrpC corrected for BS ($\mathrm{CrpC_{BS}}$), and glucose absorption showed significant differences between the descendant, ascendant and flat profiles, with highest values for the descendant profile and lowest values for the flat profile. Protein loss in the dialysate (Prot Dial) was also higher with the descendant profile. Urea maximum clearance per cycle (U MCpc) was higher with the descendant profile compared to the ascendant profile and the flat profile, whereas creatinine MCpc (Cr MCpc) was higher with the descendant profile compared to the ascendant profile, but not to the flat profile.

Multivariate analyses were performed, where in addition to intrasubject factors (profiles), intersubject factors such as gender, underlying disease, and peritoneal permeability, were taken into account. When grouping patients by gender (male vs female), underlying disease (diabetic vs non-diabetic), or peritoneal permeability (high + high average vs low + low average), no significant interactions were observed between the intrasubject and intersubject factors, but statistical significance was observed in the intersubject effects between both genders and both permeability groups. Between genders, BS ($P<0.01$), TBW ($P<0.01$), U D/P ($P<0.01$), U MCpc ($P<0.05$), and pUC ($P<0.01$) were higher in men, whereas filling volume corrected for BS (IVBS) ($P<0.01$) and *Kt/V* ($P<0.01$) were greater in women in spite of U D/P and pUC being lower. There was no difference in MCpc, CrpC, and $\mathrm{CrpC_{BS}}$, nor in the ratio of Cr D/P and U D/P (Cr/U D/P) or UF. Between both permeability groups, there were significant differences ($P<0.01$), in U D/P and Cr D/P rates, U/Cr D/P, U MCpc, Cr MCpc, pUC, CrpC, $\mathrm{CrpC_{BS}}$, and glucose absorption (G Abs). IVBS, *Kt/V*, and UF showed no significant differences.

For the dialysis adequacy parameters p*Kt/V* and CrpC, the results of intrasubject comparisons and intersubject effects of the combination of each and every factor in the multivariate analysis are shown in Table 3.

DISCUSSION

The association between low-molecular-weight solute clearances and the clinical outcome of patients on PD is still a point of interest and controversy. According to several

Table 1 | Characterization of weekly CrC and *Kt/V*

	Flat profile	Descendant profile	Ascendant profile
CrC pcycler ($\mathrm{l\,wk^{-1}1.73\,m^{-2}}$)	29.1 ± 8.1	35.9 ± 9.2	32.6 ± 8.6
CrC pday ($\mathrm{l\,wk^{-1}1.73\,m^{-2}}$)	22.8 ± 5.9	23.0 ± 5.0	22.5 ± 5.2
CrC ptotal ($\mathrm{l\,wk^{-1}1.73\,m^{-2}}$)	51.9 ± 12.9	59.0 ± 13.5	55.1 ± 13.1
CrC renal ($\mathrm{l\,wk^{-1}1.73\,m^{-2}}$)	69.7 ± 42.6	52.7 ± 35.1	50.7 ± 38.5
CrC total ($\mathrm{l\,wk^{-1}1.73\,m^{-2}}$)	121.6 ± 39.9	111.6 ± 33.8	105.8 ± 36.6
Kt/V pcycler	1.38 ± 0.27	1.54 ± 0.30	1.45 ± 0.30
Kt/V pday	0.79 ± 0.18	0.79 ± 0.17	0.77 ± 0.17
Kt/V ptotal	2.17 ± 0.42	2.33 ± 0.45	2.22 ± 0.45
Kt/V renal	1.08 ± 0.68	0.78 ± 0.52	0.79 ± 0.60
Kt/V total	3.25 ± 0.68	3.11 ± 0.61	3.01 ± 0.71

CrC, creatinine clearance; p, Peritoneal.