Computation of the Dose of Continuous Peritoneal Dialysis Required for Adequate Peritoneal Urea Clearance Without Taking into Account Peritoneal Transport Indices

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*To test the feasibility of calculating, in the absence of peritoneal transport studies, the dose (daily drain volume) of continuous peritoneal dialysis (CPD) that will produce a high probability of adequate fractional peritoneal urea clearance (K_pt/V_{urea}), we randomly separated 619 clearance studies in patients on continuous ambulatory peritoneal dialysis (CAPD) with 4 daily exchanges into a derivation (*n *= 322) and a validation (*n *= 297) group. In the derivation group, the dialysate-to-plasma urea concentration ratio (D/P_{urea}) was ≤0.799 within the lowest 5% of the studies. By the urea clearance formula, a D/P_{urea} value of 0.799 will produce weekly K_pt/V_{urea} values of 1.70 or better if the ratio of the daily drain volume to plasma water (Dv/V) is ≥0.304 L/L. Among the 56 studies in the validation group with Dv/V values of 0.304 L/L or more, 52 (92.9%) had weekly K_pt/V_{urea} values of 1.70 or better. Assuming a suitable (low) D/P_{urea} value for a given CPD treatment, it is possible to derive the dose of dialysis (the Dv/V ratio) that will provide adequate peritoneal urea clearance levels regardless of peritoneal transport characteristics. This method is applicable to the prescription of CPD for patients lacking studies of peritoneal transport. Anuric patients on CAPD with 4 daily exchanges require a Dv/V value of 0.304 L/L or better to have a ≥0.9 probability of achieving a weekly K_pt/V_{urea} of 1.70 or better.*

Key words
Peritoneal dialysis adequacy, urea clearance, drain volume, peritoneal transport

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Introduction

The prescription of continuous peritoneal dialysis (CPD) must provide adequate urea clearance and adequate ultrafiltration (1). Computer programs for prescribing the schedule and dose of CPD require prior study of peritoneal transport (2–5). Prescription of the dose of CPD before a study of peritoneal transport is available is the subject of the present report.

Peritoneal ultrafiltration cannot be predicted with accuracy, even after peritoneal transport studies (6). However, several reports have suggested that body size and drain volume are the only major predictors of fractional peritoneal urea clearance (K_pt/V_{urea})—the effect of peritoneal transport being less critical (7–12). To test the hypothesis that the dose of CPD that will provide adequate K_pt/V_{urea} for a given CPD schedule can be computed with reasonable accuracy without taking peritoneal transport characteristics into account, we analyzed the effects of a size-adjusted dose of a given CPD schedule on adequacy of K_pt/V_{urea} without taking into account peritoneal transport.

Patients and methods

The formula for K_pt/V_{urea} can be expressed as the product of a volume ratio, Dv/V, where Dv is the daily drain volume and V is body water, and a concentration ratio that reflects both peritoneal transport and dwell time (D/P_{urea}, where D and P are respectively the dialysate and plasma urea concentrations), as follows (12):

$$K_pt/V_{urea} = (Dv/V) \times (D/P_{urea}). \quad [1]$$

The CPD prescription method explored here consists of finding the minimal Dv/V value that will ensure the target K_pt/V_{urea} for any given CPD schedule. This minimal Dv/V value corresponds to a specific D/P_{urea} value, because equation 1 allows for only a single Dv/V value for a fixed K_pt/V_{urea} and D/P_{urea} pair.

To test this prescription method, we used a large number of clearance studies in patients on continuous ambulatory peritoneal dialysis (CAPD). Using one group of clearance studies, we found a suitable specific D/P_{urea} value, and based on that value, we used equation 1 to calculate the minimal required Dv/V. In a second group of CAPD clearance studies, we tested whether the Dv/V value calculated based on the first group of clearance studies was associated with adequate values of K_pt/V_{urea}. The testing of the second group did not include D/P_{urea}.

Prescription of the CPD dose by this new method consists of calculating the required Dv value (the prescribed daily fill volume plus the expected ultrafiltration volume) by multiplying the chosen Dv/V value by a patient's individual V (12).

We analyzed 619 clearance studies in patients on CAPD with 4 daily exchanges. Clearance studies were performed using standard methods (13,14), and V was calculated by the Watson formula (15). Using a random number generator, we divided the 619 clearance studies into a derivation group ($n = 322$) and a validation group ($n = 297$). In the derivation group, the highest D/P_{urea} value from among the lowest 5% of those values was used in equation 1 to calculate the Dv/V value that would provide a weekly K_pt/V_{urea} of 1.7 (0.243 daily). This target K_pt/V_{urea} is for anuric patients (1). In the validation group, we determined the frequency with which clearance studies having Dv/V values equal to or higher than the cut-off value calculated in the derivation group had weekly K_pt/V_{urea} values of 1.70 or higher.

Continuous variables are presented as mean ± standard deviation. Statistical comparisons between groups and between studies with adequate (≥1.70) and with inadequate (<1.70) weekly K_pt/V_{urea} within each group were carried out by the two-tailed Student *t*-test for continuous variables and by the chi-square test for categorical variables. The performance in the validation group of the Dv/V value derived in the derivation group was tested by sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. The most important of these values for the purpose of avoiding underdialysis is the positive predictive value (the fraction of the studies with Dv/V at or above the cutoff value that have an adequate K_pt/V_{urea}). We here present calculations for a positive predictive value of 0.9 or better.

Logistic regression with weekly $K_pt/V_{urea} \geq 1.70$ as the dependent variable was carried out in the validation group twice, first with Dv/V as the sole predictor and then with D/P_{urea} as the sole predictor. In each regression, we calculated the area under the receiver operating characteristic (ROC) curve.

Results

Table I compares pertinent features between the derivation and validation subgroups with adequate and inadequate K_pt/V_{urea}. We observed no differences between the groups in regard to patient age, diabetic status, or duration of CAPD until the clearance study, but the percentage of men and all size and obesity indicators (height, weight, body mass index, body surface area, body water) were higher in the subgroups with inadequate K_pt/V_{urea}. Subgroups with adequate K_pt/V_{urea} had higher Dv and Dv/V values than did subgroups with inadequate K_pt/V_{urea}. Although plasma and dialysate urea concentrations did not differ between subgroups with adequate and inadequate K_pt/V_{urea}, the D/P_{urea} ratios were higher in the subgroups with adequate K_pt/V_{urea}. None of the variables in Table I differed between the derivation and validation groups.

In the derivation group, the D/P_{urea} value was 0.799 or less in 15 studies (4.6%). From equation 1, the Dv/V value that will produce a daily K_pt/V_{urea} of 0.243 at a D/P_{urea} of 0.799 is 0.304 L/L (0.243 / 0.799). In the validation group, among the 56 studies with a Dv/V of 0.304 L/L or better, 52 had an adequate (true positive) and 4 had an inadequate (false negative) K_pt/V_{urea}; among the 241 studies with a Dv/V of less than 0.304 L/L, 77 had an adequate (false positive) and

164 had an inadequate (true negative) K_pt/V_{urea}. The calculated accuracy indices for a Dv/V cutoff value of 0.304 L/L in achieving a weekly K_pt/V_{urea} value of 1.70 or better in the validation group were these:

- Sensitivity: 53 / (52 + 77) = 0.403
- Specificity: 164 / (4 + 164) = 0.976
- Positive predictive value: 52 / (52 + 4) = 0.929
- Negative predictive value: 164 / (164 + 77) = 0.680
- Accuracy: (52 + 164) / (52 + 164 + 4 + 77) = 0.727

The accuracy indices for the Dv/V cutoff value of 0.304 L/L in the validation group were recalculated using only the first study from each patient (*n* = 148). Time on CAPD was 4.9 ± 3.3 months for these studies. The results were almost identical with those obtained when all studies in this group were included in the analysis. Of the 30 studies with a Dv/V of 0.304 L/L or better, 27 had an adequate and 3, an inadequate K_pt/V_{urea}. Of the 118 studies with a Dv/V below 0.304 L/L, 41 had an adequate and 77, an inadequate K_pt/V_{urea}. The calculated accuracy indices for the Dv/V cutoff value of 0.304 L/L were these:

- Sensitivity: 0.397
- Specificity: 0.963
- Positive predictive value: 0.900
- Negative predictive value: 0.653
- Accuracy: 0.703

Logistic regression with weekly $K_pt/V_{urea} \geq 1.70$ as the dependent variable revealed an area under the ROC curve of 0.927 when Dv/V was tested as the sole predictor and 0.711 when D/P_{urea} was tested as the sole predictor.

Discussion

The findings of the present study suggest that using a predetermined value of D/P_{urea} with equation 1 to calculate a Dv/V value that will provide adequate K_pt/V_{urea} can lead to adequate levels of peritoneal urea clearance in CPD patients regardless of peritoneal transport characteristics. To achieve adequate clearances in most patients, the value of D/P_{urea} used in the

TABLE I Patient characteristics [a]

	Adequate K_pt/V_{urea}?			
	Derivation group		*Validation group*	
	Yes	*No*	*Yes*	*No*
Patients [*n* (%)]	109 (33.9)	213 (66.1)	129 (43.4)	168 (56.6)
Men/women (*n*)	22/87	166/47[b]	30/99	136/32[b]
Diabetes [*n* (%)]	45 (41.3)	94 (44.1)	50 (38.8)	79 (47.0)
Mean age (years)	51.9±15.5	54.8±14.9	54.4±15.9	55.1±14.3
Mean CAPD duration (mo.)	25.2±33.8	18.7±21.2	19.5±22.2	20.1±22.9
Height (cm)	158.1±9.8	169.8±8.9[b]	160±8.5	168.9±9.6[b]
Weight (kg)	59.4±11.7	76.3±14.6[b]	61.7±11.1	75.1±13.9[b]
BMI (kg/m^2)	23.9±4.8	26.6±5.4[b]	24.2±4.6	26.3±4.5[b]
BSA (m^2)	1.60±0.17	1.87±0.18[b]	1.64±0.15	1.85±0.19[b]
V_{Watson} (L)	30.4±4.4	39.6±5.6[b]	31.2±3.8	39.3±5.9[b]
Dv (L/24 h)	9.3±0.7	9.0±0.3[b]	9.1±0.6	8.9±0.7[c]
Dv/V_{Watson} (L/L)	0.310±0.043	0.230±0.035[b]	0.296±0.033	0.231±0.040[b]
P_{urea} (mmol/L)	18.9±5.6	19.8±6.2	18.6±4.7	19.6±6.2
D_{urea} (mmol/L)	18.1±5.6	17.3±6.0	17.8±4.8	17.0±5.8
D/P_{urea}	0.956±0.090	0.871±0.122[b]	0.958±0.102	0.870±0.118[b]
Weekly K_pt/V_{urea}	2.07±0.29	1.39±0.20[b]	1.98±0.23	1.39±0.21[b]

[a] Comparisons within each group found nonsignificant differences for variables without a superscript in the columns of inadequate clearance.
[b] $p < 0.001$.
[c] $p = 0.03$.
CAPD = continuous ambulatory peritoneal dialysis; BMI = body mass index; BSA = body surface area; V_{Watson} = plasma water by the Watson method; Dv = drain volume; P = plasma; D = dialysate.

calculation of Dv/V for any given CPD schedule should be within the lowest 5% of expected values. In CAPD with 4 daily exchanges, Dv/V values of 0.304 L/L or better, corresponding to a D/P_{urea} of 0.799, provide weekly K_pt/V_{urea} values of 1.70 or better in ≥90% of patients. The Dv/V cutoff value of 0.304 L/L is close to the 0.301 L/L value calculated by a different statistical method in a smaller number of studies (16).

Although D/P_{urea} is a mathematical determinant of K_pt/V_{urea}, it is substantially less important than is Dv/V in determining adequacy of K_pt/V_{urea}—probably because, in any given CPD schedule, the range of potential D/P_{urea} values is substantially narrower than is the range of potential Dv/V values, the latter range being greatly affected by the size of the patients (17). In two studies, Dv/V but not D/P_{urea} was found to predict adequate levels of Kt/V_{urea} in CAPD (8,16). In the present study, the area under the ROC curve was substantially greater when Dv/V was tested as the sole predictor of weekly $K_pt/V_{urea} \geq 1.70$, than when D/P_{urea} was so tested.

Although most patients in this study had weekly K_pt/V_{urea} values below 1.70 (Table I), 81% had adequate total (peritoneal plus renal) Kt/V_{urea} values because of substantial residual renal function. The presence of substantial residual renal function changes the target K_pt/V_{urea}. In the calculation of the desired Dv/V for CAPD with 4 daily exchanges in patients with residual renal function, the same D/P_{urea} (0.799) should be used; however, the target (minimal) weekly K_pt/V_{urea} should be calculated as 1.70 – renal Kt/V_{urea}.

The present study has two weaknesses.

First, calculation of the required daily drain volume for anuric CAPD patients as 0.304 times each patient's body water will lead to the use of excessive amounts of PD fluid in a substantial fraction of these patients. Many anuric patients can achieve adequate K_pt/V_{urea} values with Dv/V values below 0.304 L/L. Indeed, 77 of the 129 clearance studies (59.7%) in the validation group with a Dv/V below 0.304 L/L had weekly K_pt/V_{urea} values of 1.70 or better—hence the low sensitivity of the Dv/V cutoff value of 0.304 L/L. This low sensitivity is needed to produce a high percentage of adequate urea clearance values when peritoneal transport is unknown.

The second weakness of the study is the unavailability of large numbers of clearance studies that can provide data for calculating the desired Dv/V value for automated peritoneal dialysis (APD) schedules with short dwell times. Validation in APD of the method presented here will require further studies. In the present report, we can give only an example of the application of this method in APD.

A 76-year-old man with negligible residual renal function decided to change from hemodialysis to CPD. His weight was 101 kg, his height was 172.7 cm, and his V by the Watson formula was 45.7 L. The required drain volume for CAPD with 4 daily exchanges and a weekly K_pt/V_{urea} of 1.70 would be 13.9 L/24 h (0.304 × 45.7 L)—a volume at the margins of the drain volume that CAPD with 4 daily exchanges and a 3-L fill volume can be expected to produce. He elected APD.

A 9-hour nocturnal APD session with four 3-L exchanges would allow an approximate dwell time of 2 hours. From the relevant nomogram of the original Twardowski report on the peritoneal equilibration test (18), we selected a (low) D/P_{urea} of 0.50 for a 2-hour dwell. Assuming a drain volume of 13.5 L (ultrafiltration of 1.5 L per APD session) and a D/P_{urea} of 0.5, the delivered weekly K_pt/V_{urea} by APD alone would be 1.03. Two added daily CAPD exchanges with a 3-L fill volume, assuming a D/P_{urea} of 0.80 and no ultrafiltration, would produce a weekly CAPD K_pt/V_{urea} of 0.74, for a total weekly K_pt/V_{urea} of 1.77.

Actual measurements and calculations 1 month later on this CPD regime were these:

- Nighttime (APD): drain volume, 13.7 L; D/P_{urea}, 0.55; weekly K_pt/V_{urea}, 1.15
- Daytime (CAPD): drain volume, 6.2 L; D/P_{urea}, 0.91; weekly K_pt/V_{urea}, 0.86
- Total weekly K_pt/V_{urea}: 2.01

Conclusions

Without taking peritoneal transport into account, calculation of the dose of a given CPD schedule required for a target K_pt/V_{urea} can, in most instances, result in adequate peritoneal urea clearance values.

The method presented here is suitable for initial prescription of CPD. In addition, it permits prediction of whether a given CPD schedule can feasibly achieve the target K_pt/V_{urea} in patients for whom studies of peritoneal transport status are not available. To achieve a high probability (≥0.9) of a weekly K_pt/V_{urea} of 1.70 or better in anuric patients on CAPD with 4 daily exchanges, the daily delivered dose of CAPD should be ≥0.304 L per liter of body water.

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