Prediction of Dialysate Volume to Achieve the Adequacy Target of Small Solute Clearance in Chronic Peritoneal Dialysis Patients

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Abstract

Background: Adequacy of peritoneal dialysis (PD) depends partly on small solute clearance which is the product of daily total dialysate volume (dTV) and D/P of that solute. DTV depends largely on the body size. Studies on the prescription of PD to achieve adequacy in small solute clearance are limited. The present study aimed to find simplified equations that could predict individual dTV required to achieve the targets of small solute clearance in patients receiving continuous ambulatory PD (CAPD) and nocturnal intermittent PD (NIPD).

Methods: We retrospectively analyzed 246 CAPD patients and 100 NIPD patients using the results of peritoneal equilibration test (PET), and residual renal function. The average dialysate/plasma urea (D/P urea), dialysate/plasma creatinine (D/Pcr) and urine/plasma urea (U/P urea) were used to calculate dTV to achieve small solute clearance target of weekly total KT/V urea ≥1.7 and normalized creatinine clearance (nCCr) ≥45 L/week/body surface area (BSA) of 1.73 m^2.

Results: The average D/P urea and D/Pcr in CAPD patients were 0.94 ± 0.10 and 0.73±0.10, respectively. The median U/P urea among non-users of furosemide was 4.2. The median U/P urea for users of <250 mg of furosemide daily and ≥250 mg daily were 3.76 and 2.93, respectively. To achieve the target KT/V, the predicted dTV was 0.26 x total body water (TBW) – 3 x urine volume (UV) for those using furosemide ≥250 mg daily and 0.26 x TBW – 4 x UV for those using furosemide <250 mg daily. To achieve the nCCr target, the predicted dTV was 5 x BSA – 2 x GFR (ml/min). In NIPD, the average D/P urea was 0.68 ± 0.12 and the median U/P urea for furosemide users and non-users were 3.35 and 4.2, respectively. To achieve the target KT/V ≥1.7, the predicted dTV was 0.36 x TBW – 5 x UV and 0.36 x TBW – 6 x UV for furosemide users and non-users, respectively. The predicted dTV to achieve the nCCr goal depended on the category of PET and residual renal function.

Conclusions: The adequate dTV in CAPD patients was one-fourth of TBW. APD patients required 40% higher dTV than CAPD patients. Residual renal function significantly reduced dTV.

Keywords: PD; adequacy; small solute clearance

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การทำนายปริมาตรน้ำยาล้างไตที่สามารถขจัดของเสียโมเลกุลเล็กได้อย่างพอเพียงในผู้ป่วยล้างไตทางช่องท้อง

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บทคัดย่อ

บทนำ: การขจัดของเสียโมเลกุลเล็กได้อย่างเพียงพอเป็นตัวชี้วัดหนึ่งที่แสดงถึงความเพียงพอของการล้างไต ซึ่งขึ้นกับปริมาตรน้ำยาล้างไตที่ใช้ต่อวันและค่าสัดส่วนความเข้มข้นของสารนั้นในน้ำยาล้างไตที่ถูกปล่อยออกจากช่องท้องและในเลือด ปริมาตรของน้ำยาล้างไตที่ใช้ต่อวันขึ้นกับขนาดร่างกายของผู้ป่วย ปัจจุบันยังไม่มีแนวทางการหาปริมาตรของน้ำยาล้างไตเพื่อให้ได้การขจัดของเสียที่เพียงพอ การศึกษานี้มีวัตถุประสงค์เพื่อหาสูตรในการคำนวณปริมาตรน้ำยาล้างไตที่สามารถขจัดของเสียโมเลกุลเล็กได้อย่างเพียงพอในผู้ป่วยล้างไตทางช่องท้องอย่างต่อเนื่อง (CAPD) และการล้างไตทางช่องท้องด้วยเครื่องอัตโนมัติ nocturnal intermittent PD (NIPD)

วิธีการศึกษา: การวิเคราะห์ข้อมูลแบบย้อนหลังในผู้ป่วย CAPD จำนวน 246 ราย และ NIPD จำนวน 100 ราย ตามค่า peritoneal equilibration test (PET) และการทำงานของไตที่คงเหลือ โดยเก็บข้อมูล dialysate/plasma urea (D/P urea), D/Pcr และ daily renal urea and creatinine clearance เพื่อใช้ในการคำนวณหาปริมาตรน้ำยาล้างไตที่เหมาะสมของผู้ป่วย กำหนดความพอเพียงของการขจัดของเสียโมเลกุลเล็กในหนึ่งสัปดาห์ไว้ที่ KT/V urea เท่ากับ 1.7 และอัตราการขจัดครีเอตินิน (nCCr) เท่ากับ 45 ลิตร/สัปดาห์/1.73 ตารางเมตรของพื้นที่ผิวกายผู้ป่วย

ผลการศึกษา: ในผู้ป่วย CAPD ค่าเฉลี่ย D/P urea และ D/Pcr เท่ากับ 0.94±0.10 และ 0.73±0.10 ตามลำดับ ผู้ป่วยที่ไม่ได้รับยาขับปัสสาวะมีค่ามัธยฐาน U/P urea เท่ากับ 4.2 ในขณะที่ผู้ป่วยที่ได้รับยาขับปัสสาวะ <250 มิลลิกรัมต่อวัน และ ≥250 มิลลิกรัมต่อวันขึ้นไป อยู่ที่ 3.76 และ 2.93 ตามลำดับ คำนวณค่าปริมาตรน้ำยาล้างไตที่เหมาะสมอยู่ที่ 0.26 เท่าของปริมาตรน้ำในร่างกาย (total body water; TBW) – 3 เท่าของปริมาตรปัสสาวะ (ลิตร) เมื่อใช้ยาขับปัสสาวะ <250 มิลลิกรัมต่อวัน และ 0.26 เท่าของปริมาตรน้ำในร่างกาย – 4 เท่าของปริมาตรปัสสาวะ (ลิตร) เมื่อใช้ยาขับปัสสาวะ ≥250 มิลลิกรัมต่อวันขึ้นไป และเพื่อให้ได้ตามเป้าหมายของ nCCr สามารถคำนวณปริมาตรน้ำยาล้างไตที่ต้องใช้ต่อวันได้เท่ากับ 5 เท่าของพื้นที่ผิวกาย (ตรม.) - 3 เท่าของอัตราการกรองผ่านของไต ในผู้ป่วย NIPD ค่าเฉลี่ย D/P urea เท่ากับ 0.68±0.12 และค่ามัธยฐานของ U/P urea เท่ากับ 3.35 และ 4.2 ในผู้ป่วยที่ได้รับและไม่ได้รับยาขับปัสสาวะตามลำดับ ปริมาตรน้ำยาล้างไตที่ต้องใช้เท่ากับ 0.36 เท่าของ TBW – 5 เท่าของปริมาตรปัสสาวะ (ลิตร) และ 0.36 เท่าของ TBW – 6 เท่าของปริมาณปัสสาวะ (ลิตร) ในผู้ป่วยที่ได้รับและไม่ได้รับยาขับปัสสาวะตามลำดับ การคำนวณปริมาตรน้ำยาล้างไตเพื่อให้ได้ nCCr ตามเป้าหมายขึ้นกับค่าของ PET และ การทำงานของไตที่คงเหลือ

สรุป: ปริมาตรน้ำยาล้างไตที่เหมาะสมที่ใช้ในการขจัดของเสียโมเลกุลเล็กได้อย่างเพียงพอสำหรับ CAPD อยู่ที่หนึ่งในสี่ของ TBW และผู้ป่วย NIPD ต้องการปริมาตรน้ำยาล้างไตเพิ่มขึ้นประมาณร้อยละ 40 และการทำงานของไตที่เหลืออยู่สามารถลดปริมาตรของน้ำยาล้างไตได้

คำสำคัญ: การขจัดของเสียโมเลกุลเล็ก; การล้างไตทางช่องท้อง; การฟอกไต

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Introduction

Peritoneal and renal weekly total KT/V urea and normalized creatinine clearance (nCCr) are commonly used to determine adequacy of peritoneal dialysis (PD). However, these parameters do not always represent the clearance of all solutes.[1] Two large randomized controlled trials have shown the associations between KT/V and nCCr with clinical outcomes.[2,3] Peritoneal solute clearance depends on daily total dialysate volume (dTV) and dialysate to plasma ratio of solutes (D/P). DTV is associated with body size, whereas D/P ratio is affected by the type of membrane transport and peritoneal contact time (dwell time). Therefore, PD prescription should be individualized according to the body size, the characteristic of membrane transport and residual renal function.[4,5] Initial prescription of PD is mostly prescribed from the experience of the physician. Although the 2000 KDOQI guidelines suggested that the initial PD prescription should be based on the patient's residual renal function and body surface area (BSA). However, this suggestion is impractical in clinical setting.[6] The present study aimed to find simplified equations that could predict individual dTV required to achieve the targets of small solute clearance in patients receiving continuous PD.

Methods

Study Design and Population

This retrospective study included all adult (age ≥18 years) PD patients who were regularly followed at PD unit of Siriraj Hospital and had peritoneal adequacy test between January 2007 to December 2020. All continuous ambulatory PD (CAPD) patients that received the PD schedule of 2L/cycle with 2, 3, 4 and 5 exchanges per days and all nocturnal intermittent PD (NIPD) patients that received 9 to 10 liters of total dialysate volume in 10 hours with varying cycles per session. Data of PD adequacy and standard peritoneal equilibration test (PET) were collected. If there were several tests in the same patient, the most complete and the earliest test of each mode were selected for analysis. The mean of dialysate-to-plasma ratio of urea (D/P urea), creatinine (D/Pcr), urine-to-plasma ratio of urea (U/P urea), daily renal urea and creatinine clearance (rCurea and rCCr, L/day) were computed and used to calculate dTV to achieve adequate small solute clearance targets (weekly total KT/Vurea = 1.7 and nCCr = 45 L/week/1.73 m^2) according to the mode of dialysis, the number of exchanges per day and the results of PET. Exclusion criteria were patients who had adequacy and standard PET test within 1 month of the episode of peritonitis. The formula used for adequacy test in our study are as follows:

$$\text{Total weekly KT/V urea} = \{\{ [(D/P_{urea}) \times DV] + [(U/P_{urea}) \times UV] \} \times 7\} / V_{urea} \quad (1)$$

Equation (1) can be rearranged to predict the dialysate volume requiring for achieving the KT/Vurea = 1.7 as follows (V urea = TBW, total body water) :

$$DV = [(1.7 \times TBW/7) - (UV \times U/P_{urea})] / (D/P_{urea}) \quad (1.1)$$

$$dTV = [(1.7 \times TBW/7) - (UV \times U/P_{urea})] / (D/P_{urea}) \; ; \; DV \approx dTV \quad (1.2)$$

$$\text{Total weekly nCCr} = \{\{ [(D/Pcr) \times DV)] + \text{GFR (L/day)} \} \times 7 \times 1.73\} / \text{BSA.} \quad (2)$$

Equation (2) can be rearranged for predict dialysate volume requiring for achieve nCCr = 45 as follows:

$$DV = \{45 \text{ (BSA)}/(7 \times 1.73) - [(U/P_{Cr} + U/P_{urea}) \, UV/2]\} / [(D/P_{Cr}) \quad (2.1)$$

$$dTV = \{45 \text{ (BSA)}/(7 \times 1.73) - [(U/P_{Cr} + U/P_{urea}) \, UV/2]\} / [(D/P_{Cr}) \; ; \; DV \approx dTV \quad (2.2)$$

Adequacy tests were performed using standard method, where D/P urea and D/Pcr were the dialysate-to-plasma concentration ratio of urea and creatinine, respectively. U/P urea and U/Pcr were the urine-to-plasma concentration ratios of urea and creatinine, respectively. DV was total dialysate drain volume (L/day). UV was urine volume (L/day). dTV was total dialysate volume per day. TBW, total body water was calculated by using Watson formula,[7] as follow:

For Male: TBW = 2.447 - (0.09156 x age (yr.)) + (0.1074 x height(cm.)) + (0.3362 x weight(kg.))
For Female: TBW = -2.097 + (0.1069 x height (cm.)) + (0.2466 x weight(kg.))

BSA, body surface area was calculated by using Dubois & Dubois formula,[8] as follow:

$$BSA = 0.20247 \times \text{height (m.)}^{0.725} \times \text{body weight (kg.)}^{0.425}$$

The study was approved by the Ethics committee on Human studies at the Siriraj Institutional Review Board (SIRB). Informed consent was not required.

Sample size calculation

In CAPD group, the sample size was calculated based on the previous unpublished study of Siriraj Hospital by Kongtal N. et al in 2015. The estimating mean coefficient of BSA for nCCr = 45 was 4.9±0.8, 5.3±0.8 and 5.4±0.4, for CAPD 2L/cycle 3, 4, and 5 exchanges per day, respectively.[9] These are higher than the estimating mean coefficient of TBW for KT/V=1.7. The highest standard deviation variable was chosen to calculate for the largest sample size. In the 3 exchanges per day group, the sample size was 40 patients which was derived from the estimating mean of one group to achieve a 95% confidence interval and a margin of 5% error. For 4 groups of number exchanges per day (CAPD 2L/cycle 2, 3, 4, and 5 exchanges per day), the estimate of adequate sample size was 160 patients.

In NIPD group, the previous study showed that the estimating mean coefficient of BSA for nCCr = 45 L/week/1.73 m^2 was higher than the estimating mean coefficient of TBW for KT/V=1.7. The estimating mean coefficient of BSA of NIPD 10 L and 10 hr/day with 5 and 6 exchanges per day were 9.5±2.41 and 10.7± 2.19, respectively.[7] The highest standard deviation variable was chosen to calculate for the largest sample size. In the 5 exchanges per day group, the sample size was 25 patients which was derived from the estimating mean of one group to achieve a 95% confidence interval and a margin of 5% error. For 3 groups of number exchanges per day (NIPD 10 L, 10 hr/day 5, 6 and 10 exchanges per day), the estimate of adequate sample size was 75 patients.

Statistical methods

PASW Statistic (SPSS) 18.0 (SPSS, Inc., Chicago, IL, USA) program was used in statistical analysis. For continuous variables, the mean± SD were used for normally distributed variables and the median and interquartile range (IQR) were used for data with skewed distributions. We used the two- tailed Student t-test to compare the continuous data with normal distribution, and Mann-Whitney U test for the non-normal distribution data. Spearman rank correlation coefficient test (r) was used to quantify the degree of association between continuous variables with skewed distributions. Linear regression was used to study the relationship between different factors. P-value of <0.05 was considered to be statistically significant.

Results

Baseline demographic data are presented in **Table 1**. The average age was 65.35±13.15 years. Fifty percents were male. The average BSA was 1.61±0.19 m^2. The median GFR [IQR] was 3.25 [1.74, 4.79] ml/min. Twenty-four percent of the patients were anuric. The mean PET value was 0.69±0.12. Seventy-four percent of CAPD and seventy-one percent of NIPD patients took

furosemide during the adequacy test. Total body water (TBW) was calculated using Watson formula. To simplify the TBW calculation, the coefficient of true body weight was defined by the ratio of Watson formula TBW to the corresponding true body weight. The results of the coefficient value were 0.57 for male and 0.52 for female.

Table 1 Demographic data

Characteristics	Total (N 346)	CAPD (N 246)	NIPD (N 100)
Age (yrs.)	65.35±13.15	63.98±13.29	63.72±12.25
Sex; Male (%)	173 (50)	124 (50.4)	49 (49)
Body weight (kg.)	59.35±12.58	60.87±12.58	55.59±11.82
Height (m.)	159.7±9.13	160±9.43	159±8.37
Body surface area (m^2)	1.61±0.19	1.63±0.19	1.56±0.18
Body mass index (kg/m^2)	23.21±4.16	23.74±4.13	21.89±3.94
Urine volume (L; IQR) • Residual urine < 100 ml/day	0.65 [0.12,1.10] 84 (24.3)	0.60 [0.09,1.12] 65 (26.4)	0.66 [0.26,1.10] 19 (19.0)
Diuretics • Furosemide • Spironolactone	 252 (72.8) 25 (7.2)	 181 (73.6) 15 (6.1)	 71 (71.0) 10 (10.0)
Dose of diuretics • Furosemide • Spironolactone	 500 [250,1000] 25 [25,50]	 500 [250,1000] 50 [25,50]	 500 [125,750] 25 [25,50]
Residual kidney function (ml/min)	3.25 [1.74,4.79]	3.31 [1.61,4.98]	2.83 [1.82,4.48]
Ultrafiltration (L/day)	0.56 [0.09,0.92]	0.52 [0.04,0.92]	0.64 [0.20,0.94]
Peritoneal equilibration test	0.69±0.12	0.70±0.12	0.65±0.12
D/P urea D/P cr	0.85±0.17 0.64±0.21	0.94±0.10 0.76±0.12	0.66±0.10 0.40±0.13
U/P urea U/P cr	3.26 [2.53,4.68] 6.48 [4.23,10.55]	3.12 [2.32,4.31] 6.33 [3.95,9.88]	3.78 [2.77,5.24] 6.62 [4.33,12.6]
Total weekly KT/V	2.18±0.60	2.15±0.60	2.26±0.60

D/P urea, 24 hour-dialysate urea concentration and BUN ratio; D/Pcr; 24 hour-dialysate creatinine concentration and plasma creatinine ratio; U/P urea, 24 hour-urine urea concentration and BUN ratio; U/P creatinine, 24 hour-dialysate creatinine concentration to plasma creatinine ratio

The equations used for dTV calculation to achieve the adequacy targets in CAPD group are shown in **Tables 2 and 3.** The average D/P urea and D/Pcr in 2LX4 exchanges/day were 0.93±0.10 and 0.73±0.10, respectively. The average D/P urea and D/Pcr for other number of exchanges are shown in **Table 4**. Neither average D/P urea nor D/Pcr was significantly different between different category of PET. In anuric patients, dTV required for weekly total KT/V urea = 1.7 and nCCr = 45 L/week/1.73 m^2 were 0.26xTBW and 5xBSA. In patients with daily urine volume ≥100 ml, linear regression showed significant negative correlations between furosemide use and dosage with urine-to-plasma urea ratio (U/P urea). In contrast, urine volume did not show any correlation with U/P urea (**Table 5 and Figure 1**). Multivariate analysis confirmed the negative correlation between furosemide use and dosage with U/P urea after adjustment for urine volume (Coefficient-β = -1.24, p-value < 0.001 and Coefficient-β = -0.001, p-value = 0.008,

respectively). The equations of dTV required to achieve the targets of solute clearance according to the use and the dose of furosemide are shown in **Tables 2 and 3**. The median [IQR] of U/P urea in non-users and users of furosemide <250 mg/day, and ≥250mg/day were 4.2 [2.66,6.42], 3.76 [2.95,5.07] and 2.93 [2.20,3.86], respectively. To achieve nCCr target in patients with >100 ml of residual urine, the calculation of dTV followed the same aspect of KT/V urea. Thus, dTV used to achieve the adequacy targets had to be subtracted with urine volume or GFR as the equation shown in **Table 3**.

In NIPD, analysis was performed in patients who received 10 hours of 9-10 L of dialysate volume per session. The average D/P urea in patients who received 5, 6 and 10 cycles per day were 0.68±0.09, 0.67±0.10 and 0.62±0.10, respectively. The average D/Pcr was 0.40±0.14, 0.40±0.11 and 0.37±0.12, respectively. In anuric patients who received 5 or 6 cycles per day, dTV required to achieve the solute clearance targets were (0.36±0.10) x TBW or (9.3±0.14) x BSA. The average D/P urea was not different between the two categories of PET. However, D/Pcr was significantly higher in the faster transport type as shown in **Table 6**. This resulted in higher transportere requiring less dTV to achieve the creatinine clearance target (10 x BSA in PET<0.7 and 8.26 x BSA in PET> 0.7). In patients with residual kidney function, multivariate analysis showed a negative correlation between furosemide use and U/P urea. The coefficient-β value was -1.54; 95%CI [-2.56, -0.52]; p=0.004 (**Table 7**). The median U/P urea was 3.35; IQR [2.69,4.83], and 4.2; IQR [2.66,6.42] in furosemide users and non-users, respectively (Figure 2). Therefore, the predicteddTV was 0.36 x TBW – 5 x urine volume for furosemideusers and 0.36 x TBW – 6 x urine volume in non-users (**Table 2**). Total dialysate volume needed to achieve the creatinine clearance target in subjects that received 5 or 6 cycles, 10 L and 9 – 10 hours per session was 9.3BSA - 3.6GFR (ml/min). The slower transport group required higher dTV compared to the faster group (10.04±0.09 – 3.9GFR (ml/min) for PET <0.7 and 8.26±0.09 – 3.2GFR (ml/min) for PET ≥0.7).

Table 2 The daily dialysate volume for adequate small solute clearance, KT/V urea ≥1.7

	Number of cycles per day	Daily dialysate volume	
		Furosemide use less than 250 mg/day or not use	Furosemide use 250 mg/day or more
CAPD	2	0.24TBW - 4UV	0.24TBW - 3UV
	3	0.26TBW - 4UV	0.26TBW - 3UV
	4		
	5	0.28TBW - 4UV	0.28TBW - 3UV
NIPD	Number of cycles per day	Furosemide; not use	Furosemide use
	5	0.36TBW - 6UV	0.36TBW - 5UV
	6		
	10	0.39TBW - 6UV	0.39TBW - 5UV

TBW, total body water calculated by Watson formula or in our study formula, male = 0.57×actual BW(kg.) and female = 0.52×actual BW (kg.); UV, urine volume in liter.

Table 3 The daily dialysate volume for adequate small solute clearance, nCCr ≥45

	Number of cycles per day	Daily dialysate volume
CAPD	2	3.2BSA - 1.7GFR
	3	4.5BSA - 1.7GFR
	4	5.0BSA - 2.0GFR
	5	
NIPD	Number of cycles per day	Furosemide; not use
	5	9.3BSA - 3.6GFR
	6	
	10	10.0BSA - 3.9GFR

BSA, body surface area calculated by Dubois and Dubois formula; GFR, glomerular filtration rate calculated by the mean value of 24 hour - urine creatinine and urea clearance in ml/min.

Table 4 Mean D/P urea and mean D/Pcr categorized by membrane transport type in CAPD group

D/P urea (mean±SD)						
Cycle/day	CAPD (N = 131)					CAPD (N = 246)
	PET < 0.7	N	PET ≥ 0.7	N	p- value	Total
2	0.97±0.09	7	0.98±0.04	7	0.65	1.02±0.08
3	0.94±0.08	9	0.94±0.09	18	0.75	0.95±0.08
4	0.92±0.10	42	0.93±0.12	42	0.20	0.93±0.10
5	0.94±0.04	6	-	-	-	0.86±0.12
Total	0.94±0.10					
D/Pcr (mean ± SD)						
Cycle/day	CAPD (N = 131)					CAPD (N = 246)
	PET < 0.7	N	PET ≥ 0.7	N	p- value	Total
2	0.83±0.10	7	0.91±0.10	7	0.05	0.87±0.10
3	0.78±0.08	9	0.85±0.10	18	0.89	0.83±0.10
4	0.71±0.10	42	0.75±0.12	42	0.13	0.73±0.11
5	0.72±0.04	6	-	-	-	0.72±0.04
Total	0.76±0.12					

Abbreviations: PET, peritoneal equilibrated test

Table 5 Correlation among diuretics, urine volume and U/P urea in CAPD group

Variables	N	Univariate analysis		Multivariate analysis	
		Coefficient-β [95%CI]	p-value	Coefficient-β [95%CI]	p-value
Furosemide use	184	-1.30 [-1.93,-0.67]	<0.001	-	-
Furosemide dose	152	-0.001 [-0.001,-0.001]	0.01	-0.001 [-0.001,-0.001]	0.008
Spironolactone use	184	-1.60 [-1.13,0.81]	0.75	-	-
Urine volume (L)	152	-0.26 [-0.58,0.06]	0.11	-0.29 [-0.60,-0.02]	0.07

This table shows the multiple linear regression of furosemide dose, normalized by urine volume on U/P urea in CAPD group.

Table 6 Mean D/P urea and mean D/Pcr categorized by membrane transport types in NIPD group

D/P urea (mean±SD)						
Cycle/day	NIPD (N = 46)					NIPD (N = 100)
	PET < 0.7	N(32)	PET ≥ 0.7	N(14)	p- value	Total
5	0.67±0.09	13	0.70±0.06	8	0.32	0.68±0.09
6	0.70±0.14	12	0.71±0.03	3	0.86	0.67±0.10
10	0.66±0.12	7	0.71±0.10	3	0.56	0.62±0.10
Total	0.66±0.10					
D/Pcr (mean ± SD)						
Cycle/day	NIPD (N = 46)					NIPD (N = 100)
	PET < 0.7	N(32)	PET ≥ 0.7	N(14)	p- value	Total
5	0.34±0.05	13	0.43±0.09	8	0.01	0.40±0.14
6	0.40±0.11	12	0.48±0.11	3	0.30	0.40±0.11
10	0.38±0.08	7	0.53±0.10	3	0.04	0.37±0.12
Total	0.40±0.13					

Table 7 Correlation among diuretics, urine volume and U/P urea in NIPD group

Variables	N	Univariate analysis		Multivariate analysis	
		Coefficient-β [95%CI]	p-value	Coefficient-β [95%CI]	p-value
Furosemide use	81	-1.69 [-2.69,-0.69]	0.001	-1.54[-2.56,-0.52]	0.004
Furosemide dose	60	-0.001 [-0.002,<0.001]	0.11	-	-
Spironolactone use	81	-0.011[-0.064,0.043]	0.66	-	-
Urine volume (L)	60	-0.31 [-1.14,0.52]	0.46	-0.44[-1.27,0.39]	0.29

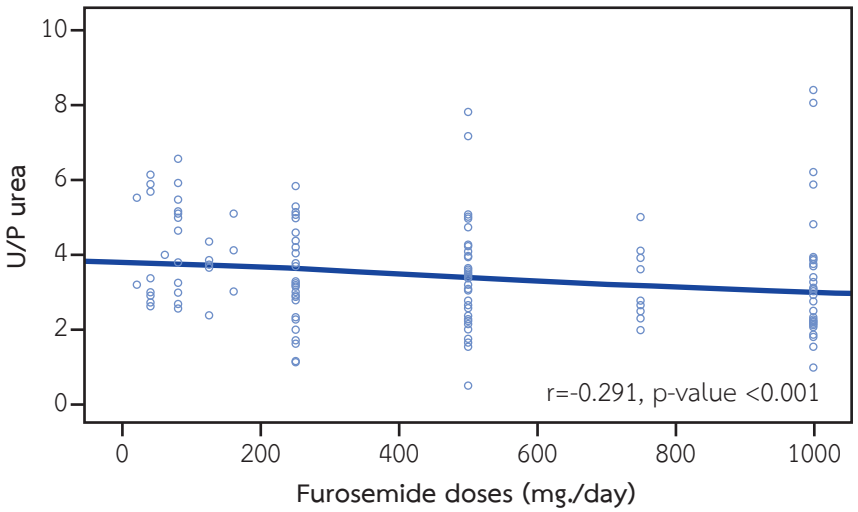

Figure 1 Correlations between furosemide doses and U/P urea in CAPD group

U/P urea, 24 hour-urine urea concentration and BUN ratio; CAPD, continuous ambulatory PD.

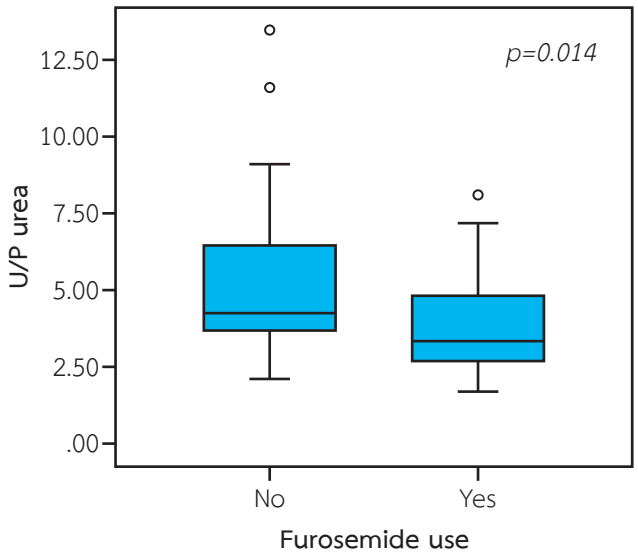

Figure 2 U/P urea between in furosemide users and non-users in NIPD group U/P urea, 24 hour-urine urea concentration and BUN ratio; NIPD, nocturnal intermittent PD.

Discussion

The current ISPD 2020 guideline recommends the assessments of patient report outcome measures, fluid status, nutritional status and toxin removal (urea and creatinine clearance) to provide the high quality PD care.[10] Although there are no specific small solute clearance targets, the data from two large RCTs showed that increasing KT/V urea to ≥1.7 could improve uremia related symptoms, hyperkalemic, metabolic acidosis and anemic status.[2,3] There is no high quality evidence regarding other measurements that can predict patient outcome and survival. This may justify using small solute clearance targets with clinical assessment to guide the treatment adequacy. Small solute clearance depends on dTV and D/P ratio of that solute. Our study attempted to simplify the estimation of dTV required to achieve the weekly total KT/V ≥1.7 and nCCr ≥45 L/week/1.73 m^2 in stable chronic PD patients. DTV depends on the body size (volume distribution of urea = total body water, body surface area) and D/P ratio of urea and creatinine. The D/P ratio is affected by dwell time and the type of peritoneal solute transport which can be tested by PET. Dwell time directly relates to total duration and the number of cycles per PD session, whereas transport depends on several individual factors. Residual kidney function also affects patient outcomes and is more efficient for solute clearance compared to peritoneal clearance. Residual kidney function also helps reduce dialysis dose and supports incremental PD prescription. Knowing the KT/V or nCCr targets, D/P urea, D/Pcr and residual renal function, we can estimate dTV according to TBW or BSA and their coefficient factors subtracted by the residual urine volume with its coefficient factors. To achieve the same KT/V target, dTV is approximately one-fourth of TBW in CAPD group which was less than dTV in NIPD (one-third of TBW) because of the longer dwell time in CAPD. The longest dwell time in NIPD is only 2 hours, whereas the dwell time in CAPD can be extended up to 6 hours.

In CAPD, the number of PD cycles per day affected dTV requirement due to decreased peritoneal contact time. Dialysate volume requirement needed to be decreased and increased about 8% to achieve adequate urea clearance when changing PD schedule from 3 or 4 cycles per day to 2 and 5 cycles per day, respectively. To achieve adequate creatinine clearance, dTV needs to be decreased by approximately 11% and 23% when changing PD schedule from 4 cycles per day to 2 and 3 cycles per day, respectively. These will have an effect only when the calculated dTV is suitable for 2 or 5 exchanges, for example, 4 L or 10 L. But it will have a small effect if the cycle of CAPD must be changed because increasing or decreasing 1 cycle of CAPD will change 20 – 30% of dTV which can overcome the changes in D/P ratio. The average D/P urea and D/Pcr in CAPD patients were similar in both groups of PET which could be explained by the long dwell contact time resulting in the equilibrium of both urea and creatinine in the blood and peritoneal fluid. Our study showed that the category of PET had less effect on D/P urea and D/Pcr in CAPD compared to the number of PD exchanges which was related to peritoneal contact time.

In NIPD, increasing the number of cycles per day from 5 or 6 to 10 reduced both D/P urea and D/Pcr by approximately 8%. The mean D/P urea was similar

between different peritoneal transport types (PET <0.7 and PET ≥0.7), which is in contrast to 24% higher D/Pcr in the faster group. Peritoneal transport type affected creatinine clearance but not urea clearance in NIPD patients. This is due to the lower molecular weight of urea compared to creatinine. The lower transport group needed 20% more dTV compared to the higher transport group. Due to the small number of enrolled patients, there were insufficient data to form the equation that would be able to predict dTV for each PET category. To achieve the same KT/V urea and nCCr targets, NIPD patients (10L/10hour 5 cycles/session) required 40% and 80% higher dTV.

In patients who had residual kidney function, dTV was significantly reduced especially in NIPD group. Every 250-350 ml of residual urine volume in CAPD and 150-200 ml in NIPD could reduce 1 liter of dTV requirement. Lower dTV can minimize metabolic complications of glucose such as hyperglycemia, peritoneal membrane dysfunction, peritonitis and can improve patient compliance. Our analysis showed that furosemide use was correlated with the decrease in U/P urea ratio which could be related to the effect of urinary dilution or increasing urea reabsorption in distal tubes. Rudolf et al demonstrated in 7 stable CAPD patients that furosemide increased urinary excretion of water without affecting the urea clearance.[11]

Limitations

The present study is a retrospective study and the association between furosemide and U/P urea could be affected by other confounders such as protein and water intake or volume status. CAPD patients in our study used only 2 liters of fill volume and NIPD patients used 9-10 liters of fill volume for 10 hours per session, therefore, the results may not be generalized to other types of prescription. Due to the small number of PD patients that received PET, the data might be insufficient for analysis among different types of peritoneal solute transport. These simplified formulae requires validation in other populations. Adequacy study should be performed again after changing the prescription.

Conclusions

This study demonstrated the possibility of calculating dTV to achieve the adequacy targets of small solute clearance in chronic PD patients.

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