ORIGINAL ARTICLE

Comparison of Efficacy between Conventional Method and Adapted Method of Automated Peritoneal Dialysis in End Stage Kidney Disease Patients

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Background: Conventional automated peritoneal dialysis (APD-C) is typically set cycles as the constant dwell time and fill volume while adapted APD (APD-A) is modified by prescribing mixed cycles of short dwell time with small fill volume and long dwell time with large fill volume. A few previous studies revealed that APD-A improved solute clearances and ultrafiltration (UF) compared with APD-C.

Objective: Because of the limited evidence, the authors compared the efficacy of both techniques.

Materials and Methods: A randomized crossover trial was conducted in patients on peritoneal dialysis between December 2018 and January 2020. The participants were randomized for the APD-A and APD-C groups in the first 6 weeks and then continued with the second 6-week period of crossover. The difference between APD-A and APD-C was time and fill volume for each cycle but total duration of APD and total inflow volume were equally set. Comparison of primary outcomes composed of weekly Kt/V_{urea}, creatinine clearance (CrCL), and normalized CrCL (nCrCL). Secondary outcomes included daily UF, sodium clearance (NaCL), phosphate clearance (PhCL) and blood pressure control.

Results: 23 patients with mean age of 61.1±11.8 years and median APD vintage of 23 months completed the two sequences of study. The APD-A group had significantly higher CrCL [48.47 (36.06 to 76.75) vs. 46.04 (32.23 to 61.71) L/week, p=0.022], nCrCl [53.24 (45.87 to 72.91) vs. 49.44 (37.94 to 58.15) L/week/1.73 m^2, p=0.02], serum bicarbonate level [25.5±2.8 vs. 24.1±2.4 mEq/L, p=0.01] and hemoglobin level [10.93±1.82 vs. 10.21±1.93 g/dL, p=0.04]. No significant difference of Kt/V_{urea}, NaCL, PhCL, UF and blood pressure.

Conclusion: APD-A group had higher efficacy in creatinine clearances compared with the APD-C group. However, there was no improvement in other clearances and UF which might be from too small sample size. Currently, APD-A is an optional practice for individualized and optimal treatment.

Keywords: Adapted automated peritoneal dialysis; Adequacy of peritoneal dialysis; Creatinine clearance; Sodium clearance; Phosphate clearance; Blood pressure

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In Thailand, the available renal replacement therapies for patients suffering end-stage kidney disease (ESKD) consist of peritoneal dialysis (PD), hemodialysis, and kidney transplant, with a portion of patients receiving palliative care. The PD first policy adopted in 2008 had a valuable impact on expanded care, wider access, and rising of PD cases especially in ESKD patients under the universal coverage scheme[1,2]. PD can be performed continuously or intermittently by manual technique or a dialysis machine as automated peritoneal dialysis (APD). APD is further separated into conventional APD (APD-C) and adapted APD (APD-A). With an APD-C treatment, a constant volume of peritoneal dialysate fluid (PDF) is kept in the abdominal cavity for the same dwell time in each cycle of PD. In contrast, the first few cycles of APD-A use a small volume of PDF during a short dwell time (30 to 60 minutes),

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before changing to a larger volume during a longer dwell time (90 to 240 minutes) in later cycles[3]. The volume of PDF used was derived from studies of Fischbach M, et al.[3-5], with 600 to 800 ml/m^2 of body surface area (BSA) for short cycles, and 1,300 to 1,500 ml/m^2 BSA for long cycles. The postulated concept of APD-A is to increase ultrafiltration (UF) during short cycles where PDF volume is low and increase efficacy of solute clearance during long cycles where PDF volume is high[4-9]. The enhanced benefit of APD-A compared with ADA-C, regarding to higher efficacy of solute clearances and ultrafiltration, were evidenced in few trials with small numbers of participants[3,5,9]. In disagreement, Oberg MC, et al. revealed that APD-A and APD-C had similar efficacy by the simulation assessment[10]. Because previous studies have been conducted in a limited population, and some results were relying on simulations which may not accurately represent the real outcomes occurring in patients, therefore, the conclusive evidence about the advantages of APD-A is still furtherly needed to explore especially in different population. The present study aimed to compare the effectiveness of applying APD-A and APD-C treatments in the Thai ESKD patients who differed from previous studies in terms of ethnicity, BSA, and volume of dwelled PDF. In addition, participants of all four types of peritoneal membrane transports assessed by peritoneal equilibrium tests (PET) were enrolled whereas in the previous study included only the ESKD patients with high-average and low-average membrane transports[3].

Materials and Methods

Study design and population

An open-label, crossover, randomized control study was conducted in ESKD patients currently on APD treatment at the peritoneal dialysis clinic, Srinagarind Hospital, Khon Kaen University from December 2018 to January 2020. The stable subjects who met the inclusion criteria: age >18 years; received CAPD treatment at least 3 months before or APD treatment at least one month before inclusion; had result of a PET within three months before inclusion; were free of infections in the abdominal cavity or other areas two months before inclusion; and agreed to participate in the present study, were recruited. Patients were excluded from the present study if they had at least one of the following conditions: pregnancy, abdominal wall defects, respiratory infections, cancer, or symptoms of an active heart disease.

The present study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki that was approved by the Ethics Committee for Human Research, Faculty of Medicine, Khon Kaen University, Thailand (project number HE 611436 and HE 671176). All patients were provided written informed consents.

Processes of randomization and intervention

The enrolled participants were randomly allocated into the APD-A group or APD-C group by a process of computer-generated block-of-four randomization. After the first 6 weeks of study (the first study period), the participants switched groups in week 7 until the end of the study in week 12 (the second study period).

Baseline characteristics and demographic data, e.g., age, sex, comorbid diseases, date of dialysis initiation, were reviewed and collected from interviews and medical records. Participants received a baseline evaluation of their APD efficacy based on weekly Kt/V_{urea}, creatinine clearance (CrCL), normalized creatinine clearance (nCrCL), phosphate clearance (PhCL), sodium clearance (NaCL), and ultrafiltration (UF). Their blood pressure (BP), body composition monitoring (BCM), and renal clearance were checked on their first week (week 0), and their PET was evaluated on week 0, or within three months before the study.

In the first study period, the participants followed their treatment as randomly allocated into APD-A and APD-C groups for weeks 1 to 6. After that, weekly Kt/V_{urea}, CrCL, nCrCL, PhCL, NaCL, UF, BP, BCM, and renal clearance were evaluated in week 6.

In the second study period at week 7, participants in the APD-A group switched treatment to APD-C and vice versa. At the end, weekly Kt/V_{urea}, CrCL, nCrCL, PhCL, NaCL, UF, BP, BCM, and renal clearance were checked in week 12. Then participants returned to their original APD prescription as before enrollment into the study.

During the 12 weeks of study period, besides the mentioned APD prescription, other related medications, e.g., phosphate binders, diuretics, antihypertensive and hypoglycemic drugs, and erythropoietic stimulating agents remained unchanged dosages which each group had two participants receiving diuretics.

Calculation of prescribed PDF volume and dwell time

Before allocation into groups, participants were treated with their usual APD schedules in which dialysis was performed in the nighttime and no retained PDF in abdomen during the day. During the study period, both APD-A and APD-C groups were set up the machine for receiving the same total PDF volume and dwell time per day by using solution of 1.5% dextrose PDF. The APD-C group continued the same prescription of APD, i.e., the same PDF volume and dwell time per cycle, and number of cycles per day as before the study, and on average, the PDF volume and dwell time given per cycle were equal.

In the APD-A group, the prescription of PDF volume and dwell time per cycle were calculated as the following steps. First, the BSA of each participant was calculated

using a computer program. Second, the D/P BUN (dialysate/plasma blood urea nitrogen) and D/D0 glucose values obtained from the PET were used to calculate the APEX time. Third, the administered PDF volume and dwell time were calculated as suggested by Fishback M, et al.[3,5] — for short cycles, a PDF volume of 600 to 800 ml/m^2 BSA and a dwell time per cycle of 1 APEX time (30 to 60 minutes); for long cycles, a PDF volume of 1,300 to 1,500 ml/m^2 BSA with a dwell time per cycle of 2 to 4 APEX time (90 to 240 minutes, or adjusted by basing on PET types as demonstrated in Figure 1). The total dwell time and PDF volume per day and number of cycles were prescribed consistently with the setting of before starting the present study.

As an example, here was the treatment prescribed to a patient with a BSA of 1.5 m^2, the PET showed an average transport, an APEX time of 45 to 60 minutes, and running of 5 cycles of APD during the nighttime:

APD-A: used a PDF volume of 1,200 ml with dwell time of 45 minutes per cycle for 2 short cycles, followed by a PDF volume of 2,200 ml with dwell time of 150 minutes per cycle for 3 long cycles.

APD-C: used a PDF volume of 1,800 ml with a dwell time of 108 minutes per cycle for 5 cycles.

The participants were continuously monitored by telephone and logbook checking for the compliance with protocols of APD-A and APD-C periods.

Study outcomes

Comparison of primary outcomes between the efficacy of APD-A and APD-C treatments included weekly clearances of urea (weekly KT/V_{urea}), and creatinine (CrCL, nCrCL). Secondary outcomes were differences of weekly PhCL, NaCL, UF volume, blood pressure control, and dry weight measured from a BCM using the bioimpedance technique.

Statistical analysis

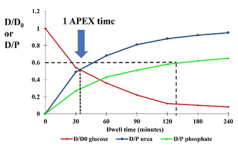
Sample size was calculated by using a 2×2 cross-over design in which the outcome is a continuous normal random variable referenced from Chow SC, et al.[11]. Reviewing of the previous study showed a difference in the mean nCrCL between the two groups of 2.3 L/week/1.73 m^2 (with a standard deviation of 13.59 L/week/1.73 m^2[3]. Using the minimum meaningful difference in nCrCL between the groups was 4 L/week/1.73 m^2, the sample size was 21 subjects recruited for the desired level of statistical significance at 0.05 and the 90% power. The estimated dropout rate was 20%, therefore, a total of at least 28 participants should be allocated to the study.

Descriptive analysis was used to demonstrate general characteristics of the participants, along with their basic demographic information, underlying conditions, comorbidities, and receiving treatment. Continuous data was presented as a mean ± standard deviation (SD), or a median (interquartile range; IQR). Weekly Kt/V_{urea}, CrCL, nCrCL, PhCL, NaCL, UF and BCM results between the two groups were compared using the crossover paired t-test and the Wilcoxon matched-pairs signed-rank test for normally and non-normally distributed data, respectively. An analysis is given for the carryover effects of alternating groups, periods effects from alternating time, and sequence effects.

Categorical data was expressed as percentages and compared between groups using the Chi-squared test or Fisher's exact test. A comparison of the drained peritoneal fluid volume recorded daily between the two groups was performed by using the generalized estimating equation (GEE). Statistical analysis was done by using STATA version 17 and p-value less than 0.05 was considered as statistical significance.

Results

During the study period, December 2018 to January 2020, 33 patients treated with APD were screened to enter the present study. Five cases were excluded because 4 of them declined to study and 1 case had peritoneal infection within 2 months before the enrollment. A total of 28 subjects were randomized into groups of 15 and 13, to be initially treated with APD-A and APD-C, respectively. Two patients in the APD-A group were withdrawn due to one of a peritoneal catheter malfunction and one peritonitis. In the APD-C group, three patients were withdrawn as one patient had volume overload, and two patients failed to set PDF volume per cycle as prescribed after switched to the APD-A. The study ended with a total of 23 participants (Figure 2).



Peritoneal transporter type	D/P Creatinine	aAPD Cycle time*** Short (minutes)	aAPD Cycle time*** Long (minutes)
High	1.03 - 0.88	40-44	89-104
High average	0.80 – 0.70	44-54	104-129
Low average	0.65 – 0.58	54-59	129-149
Low	0.5 – 0.42	59-64	149-154
Low	0.42 – 0.34	APD not recommended	APD not recommended

Figure 1. APEX time adjusted based on types of PET for the APD-A group.

APEX, accelerated peritoneal equilibration examination; PET, peritoneal equilibration test; APD-A, adapted- automated peritoneal dialysis

Baseline characteristics of participants

The study population had the following characteristics: most were elderly (mean age of 61.1±11.8 years), 52.2% were male, most had average transport type of PET. The median duration of APD treatment was 23 (12 to 44) months. The participants had systolic blood pressure of 139±19 mm Hg and diastolic blood pressure of 70±14 mm Hg. The common underlying conditions and co-morbidities were hypertension, hyperlipidemia, and diabetes. In

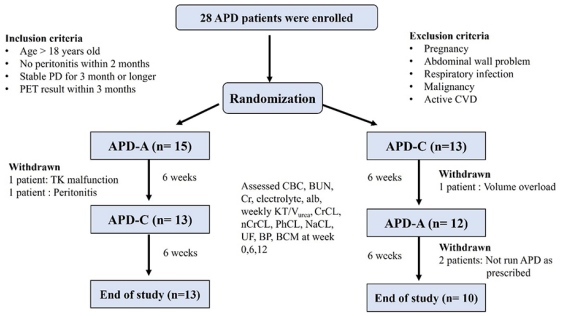


Figure 2. Illustration of study design and withdrawal of participants.

APD-C=conventional-automated peritoneal dialysis; APD-A=adapted-automated peritoneal dialysis; CVD=cardiovascular disease; TK=Tenckhoff catheter; CBC=complete blood count; BUN=blood urea nitrogen; Cr=creatinine; alb=albumin; CrCL=creatinine clearance; nCrCL=normalized creatine clearance; PhCL=phosphate clearance; NaCL=sodium clearance; UF=ultrafiltration; BP=blood pressure; BCM=body composition monitoring

Table 1. Baseline characteristics of the study population

Baseline characteristics	Participants (n=23)
Age (years), mean ± SD	61.1±11.8
Male (n, %)	12 (52.2)
Body weight (kg) mean ± SD	58.4±12.9
Height (cm) mean ± SD	159.3±7.4
Body surface area (kg/m^2), mean ± SD	1.6±0.2
PD treatment duration (months), median (IQR)	25 (14 to 60)
APD treatment duration (months), median (IQR)	23 (12 to 44)
Systolic blood pressure (mm Hg), mean ± SD	139±19
Diastolic blood pressure (mm Hg), mean ± SD	70±14
Types of peritoneal equilibrium test (PET)	
High (n, %)	4 (17.4)
High average (n, %)	7 (30.4)
Low average (n, %)	8 (34.8)
Low (n, %)	4 (17.4)
Underlying conditions and comorbidities	
Diabetes (n, %)	11 (47.8)
Hypertension (n, %)	22 (95.7)
Hyperlipidemia (n, %)	18 (78.3)
Hepatitis B/Hepatitis C (n, %)	7 (30.4)
HIV (n, %)	3 (13.0)
Cirrhosis (n, %)	6 (26.1)
Stroke (n, %)	6 (26.1)
Ischemic heart disease (n, %)	9 (39.1)
Hematologic disease (n, %)	8 (34.8)

APD=automated peritoneal dialysis; SD=standard deviation; IQR=interquartile range; HIV=human immunodeficiency virus

addition, about one in four patients had a history of stroke, and 40% of patients had ischemic heart disease (Table 1).

There were 14 subjects (60.9%) used the Baxter Homechoice APD system and the others used Fresenius Sleep●safe PD cycler. The mean and median daily volumes of urine and drained PDF were 517.4±610.5, 322 (0 to 973) ml and 662.3±287.4, 707 (440 to 883) ml, respectively. About 44% of participants had anuria. Results of BCM evaluation showed a mean dry weight of 55.1±12.4 kg and fluid excess (overhydration) of 3.3±1.8 kg. The mean solute clearances were 2.1±0.6 of Kt/V_{urea}, 45.2 (31.1 to 82.1) L/week of CrCL, 50.2 (37.1 to 84.6) L/week/1.73 m^2 of nCrCL, 60.4±14.5 L/week/1.73 m^2 of sodium, and 28.9 (21.7 to 38.9) L/week/1.73 m^2 of phosphate (Table 2).

Comparison between the APD-C and APD-A groups

There was no statistically significant difference in the total PDF volume and dwell time per day between the APD-C and APD-A groups. However, there was a statistically significant difference in the PDF volume and dwell time per cycle among the APD-C group, the short cycles of APD-A, and the long cycles of APD-A groups ($p<0.05$, shown in Table 3).

Primary outcomes

The mean weekly Kt/V_{urea} at week 12 of APD-A and APD-C groups were 2.23±0.82 and 2.03±0.54 with the mean difference of 0.20±0.50 (95% confidence interval (CI) -0.03 to 0.43, p=0.085, Figure 3). However, there was a significant difference in the creatinine clearances (CrCl and nCrCl) of both groups which presented as median difference due to a non-normal distribution. The CrCl of APD-A group was 48.47 (36.06 to 76.75) vs. of APD-C group 46.04 (32.23 to 61.71) L/week (median difference 2.43 L/week,

Table 2. Baseline laboratory and peritoneal dialysis data

Baseline laboratory and dialysis	Participants (n=23)
Hemoglobin (g/dL), mean ± SD	10.4±2.3
Hematocrit (%), mean ± SD	31.8±6.6
BUN (mg/dL), mean ± SD	52.1±17.4
Serum creatinine (mg/dL), mean ± SD	9.0±3.3
Serum sodium (mEq/L), mean ± SD	139.4±3.5
Serum potassium (mEq/L), mean ± SD	4.1±0.7
Serum chloride (mEq/L), mean ± SD	98.6±4.2
Serum bicarbonate (mEq/L), mean ± SD	24.7±2.8
Serum calcium (mg/dL), mean ± SD	8.7±0.9
Serum phosphate (mg/dL), mean ± SD	4.2±1.3
Serum albumin (g/dL), mean ± SD	3.6±0.6
Urea clearance, Kt/Vurea, mean ± SD	2.1±0.6
Creatinine clearance, Weekly CrCl (L/week), median (IQR)	45.2 (31.1 to 82.1)
Normalized weekly CrCl (L/week/1.73 m^2), median (IQR)	50.2 (37.1 to 84.6)
Sodium clearance (L/week/1.73 m^2), mean ± SD	60.4±14.5
Phosphate clearance (L/week/1.73 m^2), median (IQR)	28.9 (21.7 to 38.9)

SD=standard deviation, IQR=interquartile range, BUN=blood urea nitrogen, Kt/Vurea=weekly Kt/Vurea, CrCL=creatinine clearance

Table 3. PDF volume and dwell time per cycle, and per day, between the APD-C and APD-A

PDF volume and dwell time	Participants (n=23)
APD-C group	
• PDF volume per cycle (mL), mean ± SD, median (IQR)	1,709±217, 1,800 (1,500 to 1,900)
• Dwell time per cycle (minutes), mean ± SD, median (IQR)	128±16, 120 (120 to 150)
• Cycles per day (cycles) mean ± SD, median (IQR)	4.57±0.72, 5 (4 to 5)
• Total dwell time per day (minutes), mean ± SD, median (IQR)	576.5±64.5, 600 (600 to 600)
• Total PDF volume per day (mL), median ± SD, median (IQR)	7,848±1,746, 8,400 (6,400 to 9,500)
ADP-A group	
Short cycles	
• PDF volume per cycle (mL), mean ± SD, median (IQR)	1,215±254, 1,200 (1,000 to 1,500)
• Dwell time per cycle (minutes), mean ± SD, median (IQR)	53.7±7.1, 60 (45 to 60)
• Short cycles per day (cycles), mean ± SD, median (IQR)	1.74±0.45, 2 (1 to 2)
Long cycles	
• PDF volume per cycle (mL), mean ± SD, median (IQR)	1,961±237, 2,000 (1,800 to 2,100)
• Dwell time per cycle (minutes), mean ± SD, median (IQR)	167±18, 160 (160 to 170)
• Long cycles per day (cycles), mean ± SD, median (IQR)	2.87±0.34, 3 (3 to 3)
Total per day	
• Total cycles per day (cycles), mean ± SD, median (IQR)	4.61±0.66, 5 (4 to 5)
• Total dwell time per day (minutes), mean ± SD, median (IQR)	571.5±66.5, 600 (570 to 600)
• Total PDF volume per day (mL), median ± SD, median (IQR)	7,826±1,677, 8,200 (6,500 to 9,000)

SD=standard deviation; IQR=interquartile range

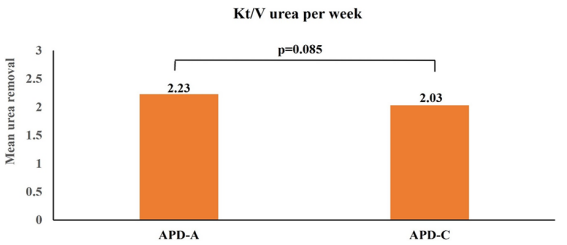


Figure 3. Difference in weekly Kt/V_{urea} between the two groups.

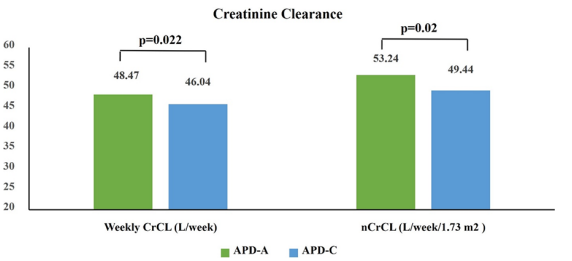


Figure 4. Weekly creatinine clearance and normalized weekly creatinine clearance of the APD-A and APD-C groups.

p=0.022), and nCrCl of APD-A was 53.24 (45.87 to 72.91) vs. of APD-C group 49.44 (37.94 to 58.15) L/week/1.73 m^2 (median difference 3.80 L/week/1.73 m^2, p=0.02, Figure 4).

The total clearances, peritoneal clearance and renal clearances of solutes are presented in Table 4 which demonstrate the peritoneal clearance of creatinine is the main part of higher median creatinine clearances of the APD-A group compared to the APD-C group [CrCl: 29.29 (22.51 to 37.61) vs. 27.26 (20.37 to 35.85) L/week, p=0.026, and nCrCl: 34.04 (24.57 to 43.40) vs. 29.71 (24.13 to 39.38) L/week/1.73 m^2, p=0.033)].

The other parameters which significantly differed between the groups were: serum creatinine levels [lower for group APD-A compared to APD-C (9.02±3.08 vs. 9.52±3.38, p=0.048)]; bicarbonate levels [higher for group APD-A compared to APD-C (25.48±2.74 vs. 24.13±2.35 mEq/L, p=0.012)]; hemoglobin and hematocrit levels [higher for group APD-A compared to APD-C (Hemoglobin, 10.93±1.82 vs. 10.21±1.93 g/dL, p=0.04, and hematocrit, 33.76±5.97 vs. 31.38±6.02%, p=0.035)]. Dosages of erythropoietin stimulating agent given to the participants of both groups were similar (APD-A group 116 (0 to 144) unit/kg vs. group APD-C 98 (0 to 147) unit/kg, p=0.40).

Analysis revealed no significance of carry-over, period, or sequence effects on primary outcomes.

Secondary outcomes

No significant difference was found in the remaining clinical outcomes between the two groups. These included systolic and diastolic blood pressure levels, UF volume, volume of fluid excess (via BCM), dry weight, and urine volume per day. No significant differences were found for serum chemistry levels: urea, sodium, potassium, chloride, calcium, phosphate (Table 5), sodium- and phosphate dialysis removals and clearances (Table 4, 5).

Table 4. Comparison of means and medians of total solute clearances, peritoneal clearances, and renal clearances between the two groups

Clearance	ADA-A group	ADA-C group	p -value
Kt/Vurea clearance			
• Peritoneal clearance	1.58±0.59	1.49±0.48	0.25
	1.58 (1.09 to 1.79)	1.36 (1.11 to 1.69)	0.20
• Renal clearance	0.65±0.99	0.54±0.74	0.18
	0.27 (0 to 0.93)	0.11 (0 to 1.03)	0.38
• Total clearance	2.23±0.82	2.03±0.54	0.09
	1.98 (1.78 to 2.22)	1.94 (1.67 to 2.40)	0.11
Weekly CrCl (L/week)			
• Peritoneal clearance	30.8±10.5	28.8±10.3	0.11
	29.3 (22.5 to 37.6)	27.3 (20.4 to 35.9)	0.026
• Renal clearance	30.5±41.6	25.4±33.3	0.15
	10.7 (0 to 50.6)	7.20 (0 to 42.8)	0.25
• Total clearance	61.3±36.8	54.2±29.5	0.07
	48.5 (36.1 to 76.8)	46.0 (32.3 to 61.7)	0.022
Normalized weekly CrCl (L/week/1.73 m^2)			
• Peritoneal clearance	34.0±11.3	31.7±11.3	0.11
	34.0 (24.6 to 43.4)	29.7 (24.1 to 39.4)	0.033
• Renal clearance	31.9±44.8	26.9±36.4	0.16
	12.8 (0 to 54.5)	8.49 (0 to 40.3)	0.25
• Total clearance	66.0±38.2	58.6±31.5	0.08
	53.2 (45.9 to 72.9)	49.4 (37.9 to 58.2)	0.02
Sodium clearance (L/week/1.73 m^2)			
• Peritoneal clearance	62.0±17.1	60.5±19.4	0.50
	67.6 (48.6 to 71.7)	62.8 (45.2 to 70.6)	0.96
• Renal clearance	2.08±2.81	1.43±1.80	0.042
	1.11 (0 to 3.60)	0.55 (0 to 2.57)	0.13
• Total clearance	64.1±15.0	61.9±18.2	0.34
	67.6 (52.2 to 71.9)	63.4 (50.6 to 70.6)	0.16
Phosphate clearance (L/week/1.73 m^2)			
• Peritoneal clearance	23.5±9.93	24.5±19.3	0.77
	20.1 (15.4 to 33.7)	17.6 (13.5 to 27.2)	0.16
• Renal clearance	16.7±29.7	13.4±20.2	0.29
	0 (0 to 29.8)	0 (0 to 22.3)	0.45
• Total clearance	40.2±25.8	37.9±23.3	0.63
	37.3 (24.0 to 43.7)	31.2 (20.9 to 48.9)	0.25

APD-A=adapted-automated peritoneal dialysis; APD-C=conventional-automated peritoneal dialysis

The UF volume was recorded every day during the 6 weeks of APD-A and APD-C periods. The daily UF volume between the treatment groups were compared using the GEE statistics which adjusted the baseline UF. No statistically significant difference of UF was found [mean difference ± standard error = 13.56±21.39, 95% CI: -28.38 to 55.49), p=0.53] (Figure 5).

Discussion

The effectiveness of PD depends on UF volume and clearance of solutes, e.g., urea (weekly Kt/V_{urea}), creatinine (CrCl, nCrCl) —where the efficacy of clearance depends on the PDF volume and dwell time both per cycle and in total[12]. The open-label, crossover, randomized control study of Fischbach M, et al.[3] in 19 participants noted an improved efficacy of solutes clearance and lower glucose absorption by using APD-A compared to APD-C during 45-day study periods. Specifically, there was a significant difference in weekly Kt/V_{urea} (1.53±0.37 vs. 1.44±0.32, $p<0.01$), and nCrCL (30.74±13.59 vs. 28.44±13.11 L/week/1.73 m^2, $p<0.05$). Additionally, APD-A had higher efficacy of phosphate, sodium and UF removals along with better blood pressure control. Another study conducted in 12 European patients also demonstrated improvement of Kt/V_{urea}, CrCL and UF with APD-A

Table 5. Comparison of clinical outcomes between the two groups after the 12 weeks of study

Clinical outcomes	APD-A group	APD-C group	Mean/median difference, (95% Confidence interval)	p-value
SBP (mm Hg)	135.7±20.9	130.7±15.9	5.00±22.3 (-4.90 to 14.9)	0.31
DBP (mm Hg)	69.3±15.4	70.2±14.3	-0.67±10.7 (-5.31 to 3.96)	0.69
Ultrafiltration volume (mL/day)	706.3±278.0	692.5±287.4	13.7±74.7 (-18.6 to 46.0)	0.39
	693 (466 to 1,000)	684 (483 to 984)	9 (-275.0 to 292.1)	0.42
Sodium dialysis removal (mEq/day)	1,114±272.9	1,082±294.8	32.1 (-50.1 to 114.3)	0.42
	1,130 (953 to 1,332)	1,048 (957 to 1,310)	82 (-171.8 to 311.3)	0.39
Phosphate dialysis removal (mg/day)	129.4±60.1	132.5±106.7	-3.11±102.1 (-50.9 to 44.7)	0.89
	125.7 (83.2 to 165.1)	112.6 (71.6 to 150.7)	13.1 (-38.8 to 66.0)	0.16
Urine volume (mL/day)	509.1±638.1	428.7±519.6	80.4±235 (-23.9 to 184.6)	0.12
	258 (0 to 762)	226 (0 to 788)	32 (-56.2 to 120.2)	0.34
Dry weight (kg)*	55.4±12.9	55.6±13.5	-0.15±2.48 (-1.25 to 0.94)	0.77
Fluid excess (overhydration, kg)*	3.20±1.98	2.91±1.95	0.29±1.18 (-0.22 to 0.80)	0.26
Hemoglobin (g/dL)	10.9±1.82	10.2±1.93	0.72±1.61 (0.02 to 1.42)	0.04
Hematocrit (%)	33.8±5.97	31.4±6.02	2.38±5.10 (0.18 to 4.59)	0.035
BUN (mg/dL)	48.1±15.8	50.3±17.7	-2.19±9.06 (-6.20 to 1.83)	0.27
Serum creatinine (mg/dL)	9.02±3.08	9.52±3.38	-0.50±1.11	0.048
			(-0.99 to - 0.005)	
Serum sodium (mEq/L)	139.0±3.69	139.0±3.70	-0.09±3.22 (-1.48 to 1.30)	0.90
Serum potassium (mEq/L)	4.15±0.80	4.17±0.59	-0.02±0.67 (-0.31 to 0.27)	0.88
Serum chloride (mEq/L)	98.1±4.68	98.3±4.42	-0.13±2.96 (-1.41 to 1.15)	0.83
Serum bicarbonate (mEq/L)	25.5±2.74	24.1±2.35	1.35±2.36 (0.33 to 2.37)	0.01
Serum calcium (mg/dL)	8.87±0.80	8.78±0.80	0.09±0.49 (-0.12 to 0.30)	0.40
Serum phosphate (mg/dL)	4.24±1.01	4.23±1.24	0.01±1.12 (-0.47 to 0.49)	0.97
Serum albumin (g/dL)	3.63±0.61	3.53±0.57	0.09±0.28 (-0.03 to 0.21)	0.14

Presented as mean ± standard deviation and median (interquartile range); BUN=blood urea nitrogen, *computed via BCM (body composition monitoring)

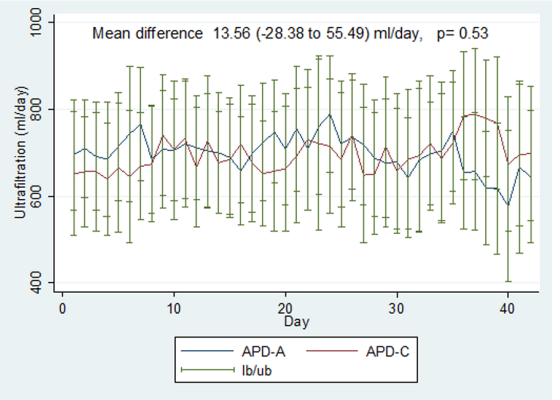


Figure 5. Ultrafiltration volume per day throughout the study, between the APD-A and APD-C groups.

treatment for 3 months[9]. In comparison, the present study had more participants (23 patients), was conducted in Thai patients with lower BSA and used less overall PDF volume and covered all four types of peritoneal transports assessed by PET as opposed to that of Fischbach M, et al.[3] where patients had only high average or low average transport (dialysate/plasmaCreatinine in range of 0.58 to 0.80). The present study noted a higher median nCrCl through APD-A as opposed to APD-C (34.04 vs. 29.71 L/week/1.73 m^2, a difference of 4.33 L/week/1.73 m^2, p=0.033) —a result was similar to that of Fischbach M, et al.[3]. Both studies also found a mean difference in weekly Kt/V_{urea} of 0.09. However, the present study did not find that difference to be significant, potentially because the present study had a higher standard deviation of weekly Kt/V_{urea}. A similar phenomenon appeared with sodium and phosphate clearances. A potential explanation is that the participants in the previous study[3] had only average peritoneal transport, thus might be the reason of smaller range for the standard deviation of various clearances.

The two prevailing theories for peritoneal transport are the three-pore model, and the distributed model. In the three-pore model, the transfer of water and substances depends on the number of pores with various sizes on peritoneal membrane[13,14]. Large pores allow substances comprised of large molecules to pass through, such as proteins. Small pores transport substances with smaller molecules, for example, urea, creatinine, sodium, and potassium. Finally,

the smallest pores, ultrapores, mainly drain out free water. In contrast, the distributed model focuses more on the importance of the distribution of peritoneal capillaries, and the distance between peritoneal fluid and capillaries where includes transport through capillary walls of the peritoneal membrane into the surrounding interstitium and reaching the mesothelium. Thus the transport of substances depends on the surface area of peritoneal capillaries, rather than the entire peritoneal surface area[13]. Therefore, two patients with the same peritoneal surface area, but dissimilar amounts of peritoneal capillaries, may have a different efficiency of substance transport[15]. This would explain the differing results between the present study and previous studies.

The concept of using a short dwell time and low PDF volume in short cycles of APD-A is to increase UF. PDF with high glucose concentration creates osmotic pressure pulling fluid through ultrapores into the abdominal cavity which this difference in osmotic pressure is prominent during the early dwell time of a cycle. Additionally, a low PDF volume leads to lower intraperitoneal and hydrostatic pressure, resulting in lower fluid absorption[3]. In contrast, a long dwell time and high PDF volume enhance the solute clearance of both urea and creatinine[16]. The larger volume increases diffusion and contact with peritoneal membrane and capillaries[17]. Too high amount of PDF, however, may lead to increased intraperitoneal pressure causing discomfort, abdominal wall hernia, inguinal hernia, diaphragmatic hernia, and enteric peritonitis[18]. Therefore, calculation of PDF volume and dwell time during short- and long cycles is crucial.

The present study revealed that participants in the APD-A group had significantly higher hemoglobin and hematocrit levels than those in APD-C group with similar doses of erythropoietin stimulating agent. Previous studies found improvement of anemia, less requiring of erythropoietin stimulating agent, and lower serum creatinine when enhanced adequacy of dialysis by increase of small solute clearance[19-21] corresponding with the present study that the APD-A group had a higher creatinine clearance, higher serum bicarbonate and lower serum creatinine.

In terms of UF volume, no significant difference was noted in both groups (706.27±278.04 ml in the APD-A group and 692.54±287.35 ml in the APD-C group). Previous studies performed by Fischbach M, et al.[3] and Oberg M, et al.[10] obtained contradictory results. UF volume was increased by about 90 ml by employing APD-A instead of APD-C (743±275 ml and 656±358 ml, $p<0.05$) in study of Fischbach M, et al.[3], while similar UF volumes (660 ml in APD-A vs. 656 ml in APD-C group) was shown in Oberg MC, et al. study[10]. Oberg MC, et al. postulated that the significant UF volume observed in the present study of Fischbach M, et al. may be due to the study design of crossover trial resulting in paired matches where participants were matched with themselves. Furthermore, measuring the PDF volume directly from the abdominal cavity is a difficult task and made an error in measurement, as there is usually PDF left over from previous cycles[10]. This error can be corrected by repeated measurements of UF volume which Oberg MC, et al.[10] performed a computer simulation of the same PD treatment allowing direct measurement of UF volume, therefore, resulted in different results of these two studies.

Phosphate clearance in peritoneal dialysis relies upon diffusion[22] and convection[23] processes which increasing of PDF volume and lengthening of dwell time magnify the phosphate clearance. However, the present study observed no significant difference in phosphate clearance between the APD-A and APD-C groups. Granja CA, et al.[23] demonstrated that higher UF volume led to higher phosphate clearance, thus no notable difference in phosphate clearance in our study might be explained by no significant difference in UF volume between the two groups.

There was no notable difference in sodium clearance, sodium dialysis removal, and blood pressure between the two groups disagreed with results observed in the previous study[3,5]. The PDF volume per cycle and PDF volume in total used in this current study was less than the volume used in that of Fischbach M, et al.[3], since the participants had a lower BSA (1.59 vs. 1.92 m^2) and some participants could not tolerate a high PDF volume due to abdominal pain. This may impact on solute clearance during the long cycles of the APD-A group.

Recently, Vera M et al. conducted the multi-national prospective cohort study in 160 patients and reported the current practice and outcomes of 1-year APD-A treatment. Volume status of patients was well controlled by the individualized and optimal APD-A treatment and without adverse events[24].

Limitation

The present study has some limitations. First, the study was conducted in a single center and a population group, thus less diversity of participants. Second, the sample size calculation referenced only the nCrCL value, so results of other substances may be inconclusive due to requiring of a larger number of participants. Finally, patients' compliance for following the APD-A prescription might affect the outcomes since some APD machines required manual adjustment of dwell time and PDF volume. In fact, two participants during the APD-A period were withdrawn from the study because of intolerance to high PDF volume and unable to adjust their treatments as prescribed. Nevertheless, all participants were asked to record their UF volume in a personal notebook and the investigators also checked the patients' PDF volume and dwell time adjustments,

referencing data in a card obtained from the companies which provided APD machines. Data in Table 3 displays the compliance of APD-A group, with values consistent with the treatment program set and no notable difference in total PDF volume or dwell time per day between APD-A and APD-C groups.

Conclusion

Adapted treatment of APD augmented more creatinine clearance, raised serum bicarbonate and hemoglobin levels, and also decreased serum creatinine level compared with the conventional APD. However, no statistical significances were observed for other solute clearances and UF volume. Further research in expanded number of participants and to ascertain long-term benefits of APD-A compared with APD-C is required.

What is already known about this topic?

A few studies conducted in small numbers of European patients (n=4 to 19), who had average-type of peritoneal transporter, revealed the benefit of APD-A on higher small-solute clearances and ultrafiltration compared with ADA-C.

What this study adds?

The present study performed in 23 Asian ESKD participants and covered all types of peritoneal transporters. The results insisted the enhanced efficacy of APD-A on creatinine clearance. In addition, higher hemoglobin and serum bicarbonate were noted in the APD-A group.

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Conflicts of interest

The authors declare no conflict of interest.

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Authors' contributions

AS, PW, and SA: setted up the research protocol. AS, WC, PW, TC, RT, CC and SA: collaboration in investigation, methodology and data curation. AS, WC, TC, RT, CC and SA: participated in data management and trial monitoring. AS, SA: analyzed the data. AS, WC and SA: writing the original draft. All authors were involved in refining study protocols, interpretation of data, critically revising the paper and approving the final version.

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