Original Article

An Initial Report on Operability and Safety of A Domestic Automated Peritoneal Dialysis Machine in Thailand

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Abstract

Background: Thailand had implemented the peritoneal dialysis first (PD first) policy which allowed access to peritoneal dialysis as a first-line treatment for end-stage renal disease (ESRD). However, all the patients under this policy are allowed to use only the self-operated Continuous Ambulatory Peritoneal Dialysis (CAPD) but not the Automated Peritoneal Dialysis (APD). While APD has a lot of advantages over CAPD, its cost is more than double in Thailand. Under these circumstances, it is crucial to produce APD equipment with a trade-off between good performance and affordable price.

Methods: This study is a pilot cross-sectional study to evaluate the operability and safety of the domestically developed APD machine. Three stable ESRD patients already treated with APD machines were recruited for the 7-day trial.

Results: There is a slight decrease in the dwell time due to the longer operational time of the developed machine; 11.26 ± 2.29%. Increases in serum creatinine and blood urea nitrogen were observed; 3.01 ± 1.83% and 22.92 ± 4.48%, respectively. No major adverse events were reported.

Conclusion: The developed machine used only gravity for the exchange, the dwell time was decreased as expected, resulting in a lower exchange of the waste products from the blood to the peritoneal cavity. Even though the results show a slightly lower treatment performance, no clinical significance during short-term follow-up was observed. To obtain similar performance for the domestically developed APD machine, total treatment time could be increased to maintain comparable dwell time overnight.

Keywords: Automated peritoneal dialysis machine, Peritoneal dialysis, End-stage renal disease, Universal health coverage scheme

Received: 29 December 2020 **Revised: 15 February 2021** **Accepted: 25 February 2021**

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Introduction

End-stage renal disease (ESRD) is a major medical problem for Thai population as the economic burden of the dialysis cost continues to increase.[1, 2] In 2008, Thailand had implemented the peritoneal dialysis first (PD first) policy which allowed people who were under the Thai Universal Health Coverage Scheme to have access to peritoneal dialysis as a first-line treatment for ESRD.[3, 4] As a result, the latest official report from the Thai Nephrology Society of Thailand in 2015 reported a yearly incidence of 317.71 patients per million population with the treatment options of hemodialysis, peritoneal dialysis, and kidney transplantation at 168.01, 140.56, and 9.14 patients per million population, respectively.[5] However, all the patients under this policy are allowed to use only the self-operated Continuous Ambulatory Peritoneal Dialysis (CAPD) but not the Automated Peritoneal Dialysis (APD). APD controls the exchange cycle and assists with the delivery and drainage of the peritoneal dialysis fluid to and from the patient's peritoneal cavity.[6] While APD has a lot of advantages over CAPD, the cost of automated peritoneal dialysis is more than double the cost of CAPD in Thailand. Under these circumstances, it is crucial to produce APD equipment with a trade-off between good performance and affordable price. With the advancement of microcontroller and electrical equipment, a gravity-based APD machine could be developed with only a fraction of the cost of an advanced machine without sacrificing safety. The Thailand National Science and Technology Development Agency (NSTDA) has cooperated with the National Health Security Office (NHSO) to allow funding the invention of the domestic APD machine to help reduce the economic burden and to help improve the quality of life of the patients under the Thai Universal Health Coverage Scheme. The machine must be able to perform the required functions and conforms to the safety standards for APD device. In this study, the aim is to observe the efficacy and safety of the domestically developed APD machine and to help the investigators fine-tune the machine operations for further improvement.

Material and methods

NSTDA Automated Peritoneal Dialysis (NAPD)

The NSTDA automated peritoneal dialysis (NAPD) project has initiated to develop a low-cost APD machine with acceptable performance. With the advancement of microcontroller and electrical equipment, a gravity-based APD machine could be developed with only a fraction of the cost of an advanced machine without sacrificing safety. Therefore, the first objective was to develop the prototype and performed the through tested in the laboratory to confirm that the essential functions worked as intended. Table 1 shows the samples of the accuracy test performed in the laboratory. The average volume errors for the fill and drain were less than 1%. An average fill and drain times in the laboratory simulation were 12.60 ± 0.55 minutes and 34.80 ± 5.07 minutes, for the bed height of 70 centimeters. Baxter Homechoice assumes a flow rate of 220 mL/minute for fill and 125 mL/minute drain.[7] Therefore, the fill and drain times for 2,000 mL will take approximately 9 minutes and 16 minutes, respectively. Figure 1 shows the pictures of the NAPD prototype.

Another crucial part of medical device development is standardized tests. To ensure the safety of the participants and conform to the Thai food and drug administration for the requirement of medical electrical equipment, the following internationally accepted general and particular standards were tested and passed:

1) IEC 60601-1: Medical Electrical Equipment - Part 1: General requirements for basic safety and essential performance

2) IEC 60601-1-2: Medical Electrical Equipment - Part 1-2: General Requirements for Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Disturbances - Requirements And Tests

3) IEC 60601-2-39: Medical Electrical Equipment - Part 2-39: Particular Requirements for Basic Safety And Essential Performance Of Peritoneal Dialysis Equipment

Table 1 Samples of NAPD accuracy test

	Setup Volume (mL)	Actual Volume (mL)	Difference (mL)	Percentage Difference	Time (minute)
Fill #1	2,000	2,020	0	1.00 %	12
Fill #2	2,000	2,005	5	0.25 %	12
Fill #3	2,000	2,003	3	0.15%	13
Fill #4	2,000	2,014	14	0.70 %	13
Fill #5	2,000	1,992	8	0.40 %	13
Average	2,000.00 ± 0.00	2,006.80 ± 10.76	10.00 ± 6.96	0.50 ± 0.35 %	12.60 ± 0.55
Drain #1	2,000	2,028	28	1.40 %	32
Drain #2	2,000	1,984	16	0.80 %	33
Drain #3	2,000	2,002	2	0.10 %	43
Drain #4	2,000	2,003	3	0.15 %	36
Drain #5	2,000	2,002	2	0.10 %	30
Average	2,000.00 ± 0.00	2,003.80 ± 15.69	10.20 ± 11.58	0.51 ± 0.58 %	34.80 ± 5.07

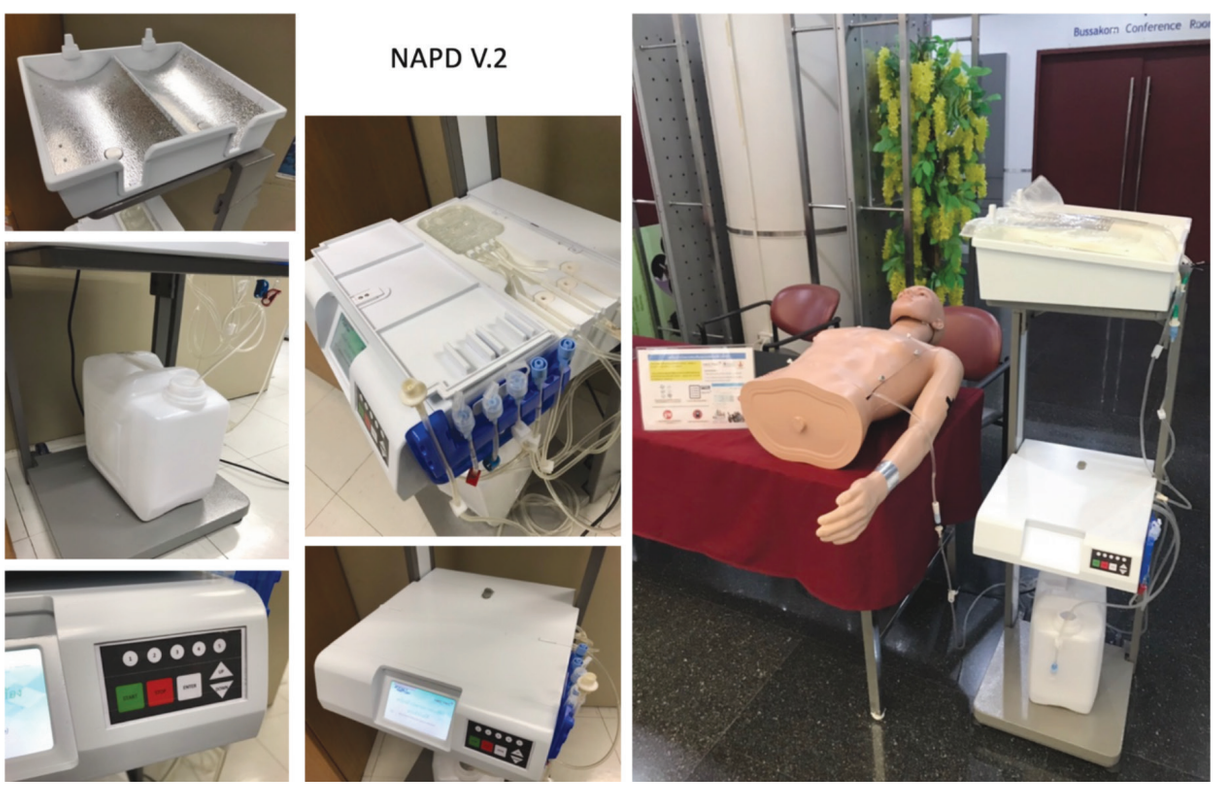

Figure 1 Prototype of the developed gravity-based APD machine.

Study design and population

This study is a pilot cross-sectional study to evaluate the operability and safety of the domestically developed automated peritoneal dialysis machine (NAPD). We selected three stable ESRD patients already treated with automated peritoneal dialysis machine at the peritoneal dialysis unit, Thammasat University Hospital, Pathum Thani, Thailand. The inclusion criteria were the patients' age 20 - 70 years with good consciousness and can do effective verbal communication with the investigators. We excluded patients with active major cardiovascular diseases or patients that were hospitalized with any medical conditions within

three months before the study. The experiment was conducted according to the principles expressed in the Declaration of Helsinki and it was reviewed and approved by the human research ethics committee No.1 Faculty of Medicine, Thammasat University. The patients provided their written informed consent to participate in this study. The clinical trial was registered in the public registry according to the criteria by the International Clinical Trials Registry Platform (ICTRP), study ID TCTR20200612003 in Thai Clinical Trials Registry (TCTR). All researchers had passed the good clinical practice (GCP) training evaluation.

Study procedure and outcome measurement

The operating characteristics of the currently used commercial automated peritoneal dialysis machine, such as the drain time, fill time, dwell time, and dialysate waste products, were recorded and tested before the start of the experiment. The patients were tested for baseline blood urea nitrogen (BUN), serum creatinine, and baseline serum electrolytes. After the initial testing, the patients were admitted to the hospital for overnight treatment with the NAPD for seven days. The patients were under the close observation of the investigators, dialysis nurses, and doctors all the time while treated with the new machine. The previous peritoneal dialysis prescription for each patient was unchanged and applied to the new peritoneal dialysis machine. The DIANEAL® Low Calcium Peritoneal Dialysis Solution 1.5% or 2.5% Dextrose, 5,000 mL were used in all the experiments. The total treatment time was also set according to the previous prescription. The dialysate waste products were collected and measured during the testing. The operating characteristics of the NAPD were recorded. The patients' vital signs and adverse events were also recorded and treated accordingly by the dialysis nurses and doctors. Following the seven-day experiment, the patients' blood urea nitrogen (BUN), serum creatinine, and serum electrolytes were retested. They were then discharged from the hospital and returned to their former commercial automated peritoneal dialysis system.

Table 2 Baseline characteristics of the three participants

	Participant #1	Participant #2	Participant #3
Age (years)	82	64	60
Gender	Male	Male	Male
Weight (kg)	51.3	63.4	65.8
Height (cm)	169	172	162
BMI	18.0	21.4	25.1
Systolic Blood Pressure	120 mmHg	150 mmHg	150 mmHg
Diastolic Blood Pressure	60 mmHg	80 mmHg	80 mmHg
Dialysis Duration (years)	1.8	1.6	2.1

Results

Baseline characteristics of participants

All three tested patients were elderly males. They could do normal daily life activities without the need for assistance and they could operate the automated peritoneal dialysis machine by themselves. All patients had started automated peritoneal dialysis for more than one year and they were clinically stable. No uremic complications, volume overload, or changes in physical status were detected in the past three months before the experiment. All patients had stable body weight, stable baseline urine output, and good dialysis adequacy for at least three months before the experiment. The additional baseline characteristics of the participants are listed in Table 2.

Operating performance of NAPD

The comparison between the treatment parameters before the research and the treatment parameters recorded during testing with NAPD are summarized in Table 3. Since the developed machine uses only gravity for the exchange and

the total treatment time was set according to the current APD setups of the patients, the time used for drain and fill periods were longer. Therefore, the dwell time overnight was decreased by an average of 11.26 ± 2.29%. Shorter dwell time lowers the exchange of the waste products from the blood to the peritoneal cavity. Surprisingly, participant #2 had an increase in ultrafiltration (UF) volume by 20.26%. Participant #1 and #3 had a decrease in UF volume by 15.68% and 195.75%, respectively. However, the result for participant #3 was skewed by an unexpected 677 mL decrease of the UF volume on one of the days during the research period. For all three participants, increases in serum creatinine and blood urea nitrogen were observed, with the averages of 3.01 ± 1.83% and 22.92 ± 4.48%, respectively. Dialysate urea concentration was decreased in all of the participants by an average of 11.86 ± 8.35%. However, the dialysate creatinine was decreased by 17.67% in participant #2, while participant #1 and #3 had an increase of 8.14% and 16.29%, respectively.

Adverse event

All participants had stable body weights and blood pressures at the end of the study. We found no major adverse events during the seven-day testing period. The only adverse event recorded was minor insomnia. All patients with adverse events were treated and they were able to continue the trial without interruption.

Table 3 Comparison of the treatment parameters before and after 7-day research

	Before the research	After 7-day research	Difference
Dwell time (minutes)			
Participant #1	93.00	83.41	-10.31%
Participant #2	90.00	81.85	-9.05%
Participant #3	85.00	72.73	-14.43%
Average	89.33 ± 3.29	79.33 ± 4.71	-11.26 ± 2.29%
Total UF Volume (mL)			
Participant #1	923.71	778.83	-15.68%
Participant #2	896.33	1078.00	+20.26%
Participant #3	184.50	-176.67	-195.75%
Average	668.18 ± 342.19	560.05 ± 535.06	-63.72 ± 94.50%
BUN (mg/dL)			
Participant #1	39.00	50.00	+28.20%
Participant #2	60.00	74.00	+23.33%
Participant #3	29.00	34.00	+17.24%
Average	42.66 ± 12.91	52.66 ± 16.43	+22.92 ± 4.48%
Creatinine (mg/dL)			
Participant #1	8.62	8.90	+3.24%
Participant #2	12.15	12.23	+0.65%
Participant #3	5.65	5.94	+5.13%
Average	8.80 ± 2.65	9.02 ± 2.56	+3.01 ± 1.83%
Dialysate urea (mg/dL)			
Participant #1	30.30	26.50	-12.51%
Participant #2	51.00	50.33	-1.31%
Participant #3	23.00	18.00	-21.73%
Average	34.76 ± 11.85	31.61 ± 13.68	-11.86 ± 8.35%
Dialysate creatinine (mg/dL)			
Participant #1	4.54	4.91	+8.14%
Participant #2	9.22	7.59	-17.67%
Participant #3	2.27	2.64	+16.29%
Average	5.34 ± 2.89	5.04 ± 2.02	+2.25 ± 14.48%

Notes: The result of the UF volume for Participant #3 after the research was skewed by an unexpected 677 mL decrease on one of the days during the research period.

Discussion

APD has a lot of advantages over the CAPD including the ease of use, nighttime only dialysis to allow better daytime activity, lower incidence of peritonitis, better small solute clearances and reduced incidences of hernias.[8, 9, 10, 11] However, with the cost of more than double the CAPD, the cost-utility analysis showed that the commercially available APD system in Thailand was not a cost-effective strategy as compared with CAPD at the current Thai budget threshold.[12] One of the major cost differences is the cost of an APD machine which is included in the cost of the APD fluid and disposable cassette. Therefore, the objective of this project is to develop an APD machine with a trade-off between good performance and affordable price.

In this experiment, the total treatment time was set according to the current APD setups of the patients. Since the developed machine used only the gravity for the exchange, the fill time and drain time were slightly longer than the commercially available machine with a mechanical pump. Longer fill and drain times resulted in shorter dwell time observed in the experiment. shorter dwell time could lead to a lower exchange of the waste products from the blood to the peritoneal cavity which could explain the higher BUN and serum creatinine observed at the end of the experiment. The slightly higher blood chemistry values had no clinical significance during short-term follow-up but the adequacy of the dialysis need to be further assessed in a larger prospective study. To obtain similar performance for the proposed gravity-based APD machine, total treatment time could be increased to maintain comparable dwell time overnight. This initial study shows that there could be an affordable alternative that could improve the quality of life for ESRD patients under the Thai Universal Health Coverage Scheme.

References

1. Li PK, Chow KM, Van de Luijtgaarden MW, et al. Changes in the worldwide epidemiology of peritoneal dialysis. *Nat Rev Nephrol.* 2017;13(2):90-103.
2. Navva PK, Venkata Sreepada S, Shivanand Nayak K. Present Status of Renal Replacement Therapy in Asian Countries. *Blood Purif.* 2015;40(4):280-287.
3. Chuengsaman P, Kasemsup V. PD First Policy: Thailand's Response to the Challenge of Meeting the Needs of Patients With End-Stage Renal Disease. *Semin Nephrol.* 2017;37(3):287-295.
4. Teerawattananon Y, Luz A, Pilasant S, et al. How to meet the demand for good quality renal dialysis as part of universal health coverage in resource-limited settings?. *Health Res Policy Syst.* 2016;14:21.
5. Chuasuwan A, Lumpaopong A. Thailand Renal Replacement Therapy: Year 2015. *The Nephrology Society of Thailand.* 2015.
6. Negoi D, Nolph KD. Automated peritoneal dialysis-indications and management. *Contrib Nephrol.* 2006;150:278-284.
7. Chaudhry RI, Golper TA. Automated cyclers used in peritoneal dialysis: technical aspects for the clinician. *Med Devices (Auckl).* 2015;8:95-102.
8. Yishak A, Bernardini J, Fried L, et al. The outcome of peritonitis in patients on automated peritoneal dialysis. *Adv Perit Dial.* 2001;17:205-208.
9. Piraino B, Sheth H. Peritonitis-does peritoneal dialysis modality make a difference?. *Blood Purif.* 2010;29(2):145-149.
10. Rodriguez AM, Diaz NV, Cubillo LP, et al. Automated peritoneal dialysis: a Spanish multicentre study. *Nephrol Dial Transplant.* 1998;13(9):2335-2340.
11. Dell'Aquila R, Berlingo G, Pellanda MV, et al. Continuous ambulatory peritoneal dialysis and automated peritoneal dialysis: are there differences in outcome?. *Contrib Nephrol.* 2009;163:292-299.
12. Thaweethamcharoen T, Sritippayawan S, Noparatayaporn P, et al. Cost-Utility Analysis of Continuous Ambulatory Peritoneal Dialysis and Automated Peritoneal Dialysis for Thai End-Stage Renal Disease Patients. *Value Health Reg Issues.* 2020;21:181-187.