Continuous Ambulatory Peritoneal Dialysis and Automated Peritoneal Dialysis: What, Who, Why, and How? Review and Case Study

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Peritoneal dialysis (PD) is an umbrella term that encompasses a variety of techniques such as continuous ambulatory PD, automated PD, tidal PD, and intermittent PD, among others. The various techniques exist to tailor the PD prescription to meet the goals of individual patients. Various clinical and nonclinical factors can change over time, requiring a change to the PD prescription. This article uses a practical case study to highlight the intricacies of the calculations behind PD prescription to achieve clearance goals. The objective is to demonstrate that all modalities of PD should be considered in the spectrum of clinical tools for achieving adequate dialysis.

Key words
Clearance calculations, PD prescription, CAPD, CCPD, APD, tidal PD

Introduction

In continuous ambulatory peritoneal dialysis (CAPD), peritoneal dialysis (PD) exchanges are performed manually. Manual CAPD is the traditional method of PD, and it requires no machine. Automated PD (APD) is all-encompassing term that is used to refer to all forms of PD in which a mechanical device assists in the delivery and drainage of dialysate. It includes continuous cycling PD (CCPD), intermittent PD, nightly intermittent PD, and tidal PD. Usually, CCPD consists of series of cycles delivered overnight using a cycler, with a last bag fill (LBF), or a midday exchange, or a "dry" day. Intermittent PD alternates dry and wet periods. In tidal PD (1), only a portion of the dialysate is drained and replaced by fresh dialysate with each cycle; thus, a variable amount of dialysate is left in constant contact with the peritoneal membrane until the end of the session, at which time the fluid is completely drained. The tidal technique was developed to improve clearance by ensuring minimal loss of exchange time between cycles. However, that time efficiency is offset by a reduction in the concentration gradient when the residual fluid mixes with fresh PD fluid. Although studies do not support enhanced clearances with the use of tidal PD, the technique can improve patient comfort by eliminating or reducing the pain associated with dialysate inflow or outflow, sometimes called "catheter kick" (1). Use of any of the foregoing modalities depends on which one best achieves the goals of the PD prescription.

The goals of PD prescription are to achieve

- adequate solute clearance,
- adequate volume removal,
- blood pressure control,
- the best possible glucose sparing strategy,
- residual renal function preservation, and
- assistance with meeting the patient's needs for work, travel, and so on.

History of APD

The first peritoneal cycler was described by Fred Boen in the early 1960s, when such machines were used for intermittent PD. The intermittent technique was popular in the early 1970s, but toward the end of that decade, it had fallen out of favor because of poor outcomes related to inadequate dialysis and consequent malnutrition (2,3).

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However, CAPD leads to patient fatigue and loss of motivation, especially after loss of residual renal function and for large patients. In the early 1980s, Jose Diaz-Buxo and C. Price, together with Wadi Suki, reintroduced APD in the form of CCPD by automated cycler at night. Since then, the use of cyclers has been increasing, mainly because it became easier to deliver more short dwells for patients with a high-transport membrane.

The CANUSA Peritoneal Dialysis Study (4), an observational prospective cohort study of PD adequacy, reported a strong positive correlation between total small-solute clearance and survival. That observation led to the implementation of guidelines from the Kidney Disease Outcomes Quality Initiative (KDOQI) stating that the weekly dose of CAPD should achieve at least a Kt/V urea of 2.0 for all patients, and that the weekly total creatinine clearance reach at least 60 L/1.73 m^2 for patients with high and high-average transport and at least 50 L/1.73 m^2 for patients with low and low-average transport (5). To achieve those goals, cycler use subsequently increased. However, a reanalysis of the study showed that the decline in solute clearance over time was caused by uncompensated loss of residual renal function.

The ADEMEX study, a prospective randomized clinical trial, evaluated the effect of an increase in peritoneal clearance on patient survival in patients doing CAPD (6). Results from that study and others supported the appropriateness of a total Kt/V urea of 1.7 or higher and a weekly peritoneal creatinine clearance of 45 L – 50 L or more. Subsequently, the Kt/V urea target was changed to 1.7 for PD (7). However, use of APD continued to increase significantly because of the positive changes in lifestyle it provides to dialysis patients.

Major trials comparing CAPD and APD

In 2007, the Cochrane renal group published a systematic review (8) of three randomized clinical trials comparing CAPD and APD. Those authors pooled data from 139 patients and found that mortality and hospitalization rates and the risks of peritonitis and fluid leaks were similar for both modalities. However, they also concluded that, because of its psychosocial advantages, APD might be considered advantageous in a select group of patients, such as the younger PD population and patients in employment or education (8).

Similarly, a multicenter prospective cohort study of 87 APD and 562 CAPD patients conducted by the NECOSAD group found no difference in overall mortality and technique failure for APD compared with CAPD in incident dialysis patients (9). An analysis by Mehrotra *et al.* (10) that used data from the U.S. Renal Data System for 66,381 incident patients on chronic PD in the years 1996 – 2004 (adjusted for demographic, clinical, laboratory, and dialysis facility characteristics) found that, in intention-to-treat, time-dependent, and as-treated analysis, little or no difference in risk for death or technique failure could be detected for patients using APD compared with CAPD.

All the evidence so far has been unable to demonstrate a consistent difference in the rates of residual kidney function loss or peritonitis and in maintenance of euvolemia, technique survival, mortality, or health-related quality of life in individuals undergoing CAPD compared with APD (11).

Water transport—"ultrafiltration" (UF)—occurs through AQP1 and the small pores (12). AQP1 accounts for 40% – 50% of solute-free water transport, driven by the osmotic gradient; the small pores account for 50% – 60% of solute and water transport, driven by a combination of the osmotic and hydrostatic pressure gradients (Table I).

Sodium transport depends on convective mass transport; diffusive mass transport determined by diffusion gradient, volume, and time; and peritoneal absorption of fluid and solutes that are absorbed into interstitial tissue and the lymphatic system (13).

The contribution of free water transport to total UF is highest during the early phase of an exchange. Beyond 60 – 90 minutes, UF driven by the small pores predominates, depending on the glucose concentration and the individual's small-solute transport status. Icodextrin-containing dialysate creates a colloid osmotic gradient that induces UF mainly through the small pores and not through AQP1. The process is slower, but provides more sustained UF, requiring longer dwell times. Although APD and CAPD both have a long dwell, the short dwells in APD tend to be shorter than those in CAPD. Therefore, in APD, if the number of cycles is increased, more sodium sieving can occur as a result.

With neovascularization or during peritonitis, the small-pore area is increased, leading to rapid glucose absorption and reduced UF. Such changes in the

TABLE 1 The three-pore model and dialysis modality (12)

Characteristic	*Ultrasmall pores*[a]	*Small pores*	*Large pores*
Abundance	Most abundant	Less abundant	Fewer than AQP1
Pore area (%)	2	95	3
Transport type	Sodium-free water transport (sodium sieving)	Allow for both diffusion and convection	Negligible ultrafiltration

[a] Also known as endothelial aquaporin-1 (AQP1) channels.

transport characteristic of the peritoneal membrane can require a change in prescription.

PD prescription

A patient starting dialysis will likely have residual renal function and can easily achieve adequate dialysis on either APD or CCPD. In choosing a PD modality for an individual, consideration of the patient's comfort, work schedule, and lifestyle is important, as is an understanding of the resources available to the individual and the costs that will be incurred for the modality.

The challenging patients are those who lack residual renal function, who have a high body surface area (BSA), and who show high or low small-solute transport status on a peritoneal equilibration test (PET). Patients with high transport achieve rapid equilibration of solutes between plasma and dialysate. Standard CAPD, with its prolonged dwell times, might not achieve sufficient fluid removal. Consequently, such patients will frequently have to use hypertonic solutions with shorter dwells or icodextrin solution, or both. Alternatively, such patients could be prescribed nightly intermittent PD or other forms of APD. If the patient is already on APD, then the option would be to increase the number of exchanges or the dwell volume, or both.

Case presentation

Consider the hypothetical case of a 58-year-old African American man with a history of end-stage renal disease secondary to hypertension. He has a BSA of 2.0 m^2 and no residual renal function. The PET at the end of training showed him to have an average-transport membrane. His dialysate-to-plasma (D/P) creatinine, estimated from the baseline PET curve, at various time intervals was 0.45 (2 h), 0.5 (2.5 h), 0.55 (3 h), 0.63 (4 h), 0.72 (6 h), and 0.78 (7 h). His UF was 450 mL at 4 hours and 475 mL at 6 hours.

The ISPD guidelines recommend a weekly creatinine clearance of 50 L for 1.73 m^2 BSA. For this patient with a BSA of 2.0 m^2, the target clearance to be achieved is 50 / 1.73 × 2, meaning 57.8 L. For small solutes, clearance is D/P × *V,* where *V* is the drain volume, inclusive of UF.

Option 1: Standard CAPD with 4 exchanges daily

Assuming a daily average of 4 exchanges of approximately 6 hours each, *V* must be calculated. The target creatinine clearance is 58 L weekly.

58 = D/P Cr (6 h) × *V*

58 = 0.72 × *V*

V = 58 / 0.72 = 80.5 L weekly = 11.5 L daily

That volume can be achieved using 4 daily exchanges of 2.5 L (10 L of dialysate in total) assuming 1.5 L of ultrafiltrate. However, if the patient fails to tolerate a 2.5 L fill volume, any lesser volume will fail to achieve the desired weekly target clearance of 58 L. For example, 4 exchanges of 2 L is only 8 L daily. To reach a *V* of 11.5, the UF has to be 11.5 L – 8 L (3.5 L), which would be impractical to achieve.

Other combinations, such as 5 exchanges daily, could be tried.

Option 2: APD with LBF

The APD part would use 4 exchanges of 2.5 L each delivered by a cycler over 10 hours at night. The LBF part would consist of 1 exchange of 2 L (7-hour dwell) during the daytime. The patient would drain that exchange after 7 hours and have no PD fluid in his abdomen until he reconnects to the cycler.

For the 4 cycler exchanges, 10 hours resolves to a 2.5-hour average dwell time. This patient's D/P creatinine at 2.5 hours is 0.5. For the 7-hour daytime dwell, his D/P creatinine would be 0.78.

Clearance = D/P Cr × *V*

Total clearance = cycler + LBF

Cycler = 0.5 × [(2.5 L × 4) + 1.5 L UF]

Cycler = 0.5 × (10.0 L + 1.5 L) = 5.75 L (40.25 L weekly)
LBF = 0.78 × (2.0 L + 0.5 L UF) = 1.95 L (13.65 L weekly)
Total clearance = 40.25 L + 13.65 L = 54 L weekly (below target)

The calculations imply that this APD prescription will not work.

Option 3: APD or CCPD with 2 daytime exchanges
The nighttime part would use 4 exchanges of 2.5 L each delivered by a cycler over 10 hours at night. The daytime part would consist of 2 exchanges of 2 L, each dwelling for 7 hours.

For the 4 cycler exchanges, 10 hours resolves to a 2.5-hour average dwell time. The patient's D/P creatinine for 2.5 hours is 0.5. His D/P creatinine for the 7-hour daytime dwells is 0.78.

Total clearance = cycler + LBF + manual exchange
Cycler = 0.5 × [(2.5 L × 4) + 1.5 L UF]
Cycler = 0.5 × (10.0 L + 1.5 L) = 5.75 L (40.25 L weekly)
LBF + manual exchange = 0.78 × 2 (2.0 L + 0.5 L UF) = 3.9 L (27.3 L weekly)
Total clearance = cycler (40.25 L) + LBF + manual exchange (27.3 L) = 67.55 L weekly

That prescription meets the clearance goal and appears practical.

Assume that the patient complains about abdominal fullness and wants to use only 2.0 L per exchange during cycler treatment. Maintaining the same prescription, the adequacy goal could be met as follows:

Total clearance = cycler + LBF + manual exchange
Cycler = 0.5 × [(2.0 L × 4) + 1.5 L UF]
Cycler = 0.5 × (8.0 L + 1.5 L) = 4.75 L (33.25 L weekly)
LBF + manual exchange = 0.78 ×2 (2.0 L + 0.5 L UF) = 3.9 L (27.3 L weekly)
Total clearance = cycler (33.25 L) + LBF + manual exchange (27.3 L) = 60.5 L weekly

Option 4: APD same as option 2, but with more cycles.
This option would apply, for example, to a patient wanting a dry period during the evening.

The nighttime part would use 5 exchanges of 2.5 L each delivered by a cycler over 10 hours at night. The daytime part would consist of 1 exchange of 2 L for a 7-hour dwell during the daytime. The patient would drain that exchange after 7 hours and have no PD fluid in his abdomen until he reconnects to the cycler.

For the 5 cycler exchanges, 10 hours resolves to a 2.0-hour average dwell time. The patient's D/P creatinine at 2.0 hours is 0.45. For the 7-hour daytime dwell, his D/P creatinine would be 0.78.

Clearance = D/P Cr × V
Total clearance = cycler + LBF
Cycler = 0.45 × [(2.5 L × 5) + 1.6 L UF]
Cycler = 0.45 × (12.5 L + 1.6 L) = 6.35 L (44.45 L weekly)
LBF = 0.78 × (2.0 L + 0.5 L UF) = 1.95 L (13.65 L weekly)
Total clearance = cycler (44.45 L) + LBF (13.65 L) = 58 L weekly

This prescription also meets the clearance goal.

Option 5: APD with 3 manual daytime exchanges
The nighttime part would use 3 exchanges of 2.5 L each delivered by a cycler over 9 hours at night. The daytime part would consist of 3 manual exchanges of 2.0 L for 5 hours each.

For the 3 cycler exchanges, 9 hours resolves to a 3-hour average dwell time. This patient's D/P creatinine at 3 hours is 0.55. For the 5-hour daytime dwells, his D/P creatinine would be 0.70.

Clearance = D/P Cr × V
Total clearance = cycler + LBF and 2 manual exchanges
Cycler = 0.55 × [(2.5 L × 3) + 1.5 L UF]
Cycler = 0.55 × (7.5 L + 1.5 L) = 4.95 L (34.65 L weekly)
LBF and 2 manual exchanges = 0.70 × [(2.0 L × 3) + 1 L UF) = 4.9 L (34.3 L weekly)
Total clearance = cycler (34.65 L) + LBF and 2 manual exchanges (34.3 L) = 68.95 L weekly

This prescription also meets the clearance goal.

Option 6: APD with icodextrin
A 14-hour exchange with 2 L icodextrin achieves near-complete saturation for small- and medium-size uremic toxins (14).

The nighttime part would use 4 exchanges of 2.5 L each delivered by a cycler over 10 hours at night. The daytime part would consist of 1 icodextrin exchange of 2 L for 14 hours. The patient

would drain that exchange before reconnecting to the cycler.

For the 4 cycler exchanges, 10 hours resolves to a 2.5-hour average dwell time. This patient's D/P creatinine for 2.5 hours is 0.5. For the 14-hour daytime dwell, his D/P creatinine is assumed to be 1.

Clearance = D/P Cr × *V*
Total clearance = cycler + LBF
Cycler = 0.5 × [(2.5 L × 4) + 1.5 L UF]
Cycler = 0.5 × (10.0 L + 1.5 L UF) = 5.75 L (40.25 L weekly)
LBF = 1 × (2.0 L + 1 L UF) = 3 L (21 L weekly)
Total clearance = cycler (40.25 L) + LBF (21 L) = 61.25 L weekly

This prescription also meets the clearance goal.

Adapted APD

One of the major drawbacks of sodium sieving is sodium retention, overhydration, and hypertension. Short-dwell exchanges with hypertonic dialysate can lead to hypernatremia (15). Fischbach *et al.* (13,16) proposed a new technique of APD called adapted APD to overcome this shortcoming and to optimize fluid and solute removal.

Adapted APD consists of two different sequences of exchanges during a single PD session. The first sequence is prescribed to promote UF; it uses a short dwell time and a small dwell volume. The subsequent sequence is prescribed to promote removal of solutes (sodium and uremic toxins); it uses a long dwell time and a large dwell volume. The dwell times and dwell volumes are both determined for each patient individually.

Dwell time is determined based on the patient's membrane transport characteristics (13). The APEX (accelerated peritoneal examination) is the point in time during a PET at which the dialysate urea saturation and glucose desaturation curves cross (17). The short dwell time is recommended to be the APEX time, and the long dwell time can be 3 – 4 times the APEX time. The large dwell volume is the highest volume that the patient can tolerate in the supine position, not to exceed an intraperitoneal pressure of 18 cm H_2O; and by convention, the small dwell volume for the short exchanges is one half the large volume.

The publications concerning this technique postulated that, because of the small dwell volume and low intraperitoneal pressure, the free water UF in the short cycle is only partially drained by gravity, which leads to a lower dialysate sodium concentration for the long dwells. That lower concentration, combined with hemoconcentration and increased plasma sodium, therefore increases the concentration gradient for sodium, leading to a greater diffuse reflux across the small pores during the long dwell.

A French national registry study [Suivi et Evaluation des Prescriptions Individualisées Adaptées (SEPIA)], an international registry study [PD—Improved Dialysis Efficiency with Adapted APD (PD-IDEA)], and a proof-of-concept study are ongoing to shed more light on this promising technique.

Summary

Continuous ambulatory PD and APD should be considered to be a spectrum of clinical tools for achieving adequate dialysis. As shown in the examples provided here, a patient can be treated with various combinations of dialysis exchanges to meet personal needs.

Disclosures

We understand that *Advances in Peritoneal Dialysis* requires disclosure of any conflicts of interest, and we declare that we have no interests to disclose.

References

1. Skorecki K, Chertow G, Marsden P, Taal M, Yu A. Brenner and Rector's the kidney. 10th ed. Philadelphia, PA: Elsevier; 2015.
2. Khanna R, Krediet RT, eds. Nolph and Gokal's textbook of peritoneal dialysis. 3rd ed. New York, NY: Springer; 2009.
3. Ing TS, Rahman M, Kjellstrand CM. Dialysis: history, development and promise. Hackensack, NJ: World Scientific Publishing; 2012.
4. Churchill DN, Taylor DW, Keshaviah PR, and the CANUSA Peritoneal Dialysis Study Group. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. J Am Soc Nephrol 1996;7:198–207.
5. II. NKF-K/DOQI clinical practice guidelines for peritoneal dialysis adequacy: update 2000. Am J Kidney Dis 2001;37(suppl 1):S65–136.
6. Paniagua R, Amato D, Vonesh E, *et al.* on behalf of the Mexican Nephrology Collaborative Study Group. Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol 2002;13:1307–20.

7. Clinical practice recommendations for peritoneal dialysis adequacy. Am J Kidney Dis 2006;48(suppl 1):S130–58.
8. Rabindranath KS, Adams J, Ali TZ, Daly C, Vale L, Macleod AM. Automated vs continuous ambulatory peritoneal dialysis: a systematic review of randomized controlled trials. Nephrol Dial Transplant 2007; 22:2991–8.
9. Michels WM, Verduijn M, Boeschoten EW, Dekker FW, Krediet RT on behalf of the NECOSAD Study Group. Similar survival on automated peritoneal dialysis and continuous ambulatory peritoneal dialysis in a large prospective cohort. Clin J Am Soc Nephrol 2009;4:943–9.
10. Mehrotra R, Chiu YW, Kalantar-Zadeh K, Vonesh E. The outcomes of continuous ambulatory and automated peritoneal dialysis are similar. Kidney Int 2009;76:97–107.
11. Bieber SD, Burkart J, Golper TA, Teitelbaum I, Mehrotra R. Comparative outcomes between continuous ambulatory and automated peritoneal dialysis: a narrative review. Am J Kidney Dis 2014;63:1027–37.
12. Rippe B, Venturoli D, Simonsen O, de Arteaga J. Fluid and electrolyte transport across the peritoneal membrane during CAPD according to the three-pore model. Perit Dial Int 2004;24:10–27.
13. Fischbach M, Schmitt CP, Shroff R, Zaloszyc A, Warady BA. Increasing sodium removal on peritoneal dialysis: applying dialysis mechanics to the peritoneal dialysis prescription. Kidney Int 2016;89:761–6.
14. Verrina E, Cappelli V, Perfumo F. Selection of modalities, prescription, and technical issues in children on peritoneal dialysis. Pediatr Nephrol 2009;24:1453–64.
15. Nolph KD, Hano JE, Teschan PE. Peritoneal sodium transport during hypertonic peritoneal dialysis. Physiologic mechanisms and clinical implications. Ann Intern Med 1969;70:931–41.
16. Fischbach M, Zaloszyc A, Schaefer B, Schmitt C. Adapted automated peritoneal dialysis. Adv Perit Dial 2014;30:94–7.
17. Fischbach M, Lahlou A, Eyer D, Desprez P, Geisert J. Determination of individual ultrafiltration time (APEX) and purification phosphate time by peritoneal equilibration test: application to individual peritoneal dialysis modality prescription in children. Perit Dial Int 1996;16(suppl 1):S557–60.

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