

Peritoneal Dialysis Prescription and Adequacy in Clinical Practice: Core Curriculum 2023

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As the global prevalence of peritoneal dialysis (PD) continues to grow, practitioners must be equipped with prescribing strategies that focus on the needs and preferences of patients. PD is an effective form of kidney replacement therapy that offers numerous benefits to patients, including more flexibility in schedules compared with in-center hemodialysis (HD). Additional benefits of PD include salt and water removal without significant changes in patient hemodynamics. This continuous yet gentle removal of solutes and fluid is associated with better-preserved residual kidney function. Unfortunately, sometimes these advantages are overlooked at the expense of an emphasis on achieving small solute clearance targets. A more patient-centered approach emphasizes the importance of individualized treatment, particularly when considering incremental PD and other prescriptions that align with lifestyle preferences. In shifting the focus from small solute clearance targets to patient needs and clinical goals, PD remains an attractive, patient-centered form of kidney replacement therapy.

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Introduction

Peritoneal dialysis (PD) is a type of kidney replacement therapy that is relatively simple and allows patients to receive treatment in the comfort of their home. Patients receiving PD also benefit from salt and water removal without the significant changes in blood pressure that may occur with hemodialysis (HD). Importantly, this continuous yet gentle solute and fluid removal may preserve remaining nephrons and in turn maintain the residual kidney function (RKF).

PD is less expensive than in-center HD in many jurisdictions and, given the rapidly rising cost of health care delivery, presents a viable alternative to HD. The lower cost associated with PD has led to an increase uptake in countries with a significant burden of poverty. Worldwide, approximately 11% of patients on dialysis receive treatment with PD. This prevalence is expected to increase in the coming years, given PD's benefits coupled with the emerging evidence of utility in managing heart failure patients with diuretic-refractory volume overload. In treating patients with PD, prescriptions have also evolved to adopt a more patient-centered approach using incremental PD. Incremental PD provides incident patients with sufficient dialysis to facilitate adequate solute clearance while reducing the burden of intrusiveness compared with "full-dose" PD. This approach allows patients to gradually become

accustomed to PD and may be associated with better quality of life and reduced cost.

As a result, practitioners must be familiar with various prescriptive strategies in caring for patients on PD. In this installment of AJKD's Core Curriculum in Nephrology, we will review the principles of incremental PD and other aspects of individualized prescriptions that align with the patients' day-to-day needs, moving away from solute kinetics and peritoneal membrane transport characteristics. We will also review the important concept of adequacy along with the pitfalls of Kt/V_{urea} measurements in PD.

How Do You Select an Initial PD Modality and Prescription?

Case 1: A 23-year-old woman with kidney failure secondary to lupus nephritis undergoes a laparoscopic PD catheter insertion. She comes to the dialysis unit 4 weeks later to begin training for PD at home. As part of the initial assessment, she completes a 24-hour urine collection and produces 1,860 mL of urine. She is completing her final year of undergraduate studies and wants to return to daily classes. She is curious about her initial PD prescription.

Question 1: What initial PD prescription would you recommend?

- Automated peritoneal dialysis (APD) at night without a daytime dwell.
- Two manual exchanges during the day only.
- APD at night with a daytime dwell.
- Continuous ambulatory PD (CAPD; including an overnight dwell).

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The Core Curriculum aims to give trainees in nephrology a strong knowledge base in core topics in the specialty by providing an overview of the topic and citing key references, including the foundational literature that led to current clinical approaches.

Case 2: A 73-year-old man with kidney failure secondary to diabetic nephropathy completed a peritoneal equilibration test (PET) 2 months after starting PD. The results show a ratio of dialysate to plasma concentrations of creatinine (D/P_{cr}) of 0.32, suggesting low, or slow, membrane transporter status. He has read information online suggesting that he may need to do manual daytime exchanges because of his “low transporter status.” He currently manages 3 small businesses that require frequent travel between sites, and he is nervous about the prospect of doing manual exchanges during his busy daily schedule.

Question 2: Given his transporter status, what is the most appropriate prescription for this patient?

- Change to CAPD.
- Continue nightly cyclor-based therapy.

Case 3: A 55-year-old woman with kidney failure secondary to IgA nephropathy has been on dialysis for 6 months with APD. She receives 3 exchanges per night in 7 hours on the cyclor with a fill volume of 1,500 mL for each exchange. Her morning routine includes short jogs around her neighborhood, and as such she has been resistant to adding fluid in the abdomen during the daytime. Recently, she described some nausea and itchiness. Her laboratory investigations suggest underdialysis, with concentrations for bicarbonate of 18 mEq/L; phosphate, 9.2 mg/dL; and urea, 86.8 mg/dL (31 mmol/L). She has not missed any treatments, and her weekly creatinine clearance (CL_{cr}) on PD is 31 L/1.73 m².

Question 3: What adjustment would you make to the PD prescription?

- Add a daytime dwell with 1,500 mL of icodextrin.
- Increase the number of exchanges to 4 and lengthen the treatment to 8 hours.
- Use 4.25% solutions with each exchange.
- Increase the fill volume from 1,500 mL to 2,000 mL.

For the answers to these questions, see the following text.

The Basics of Peritoneal Dialysis

The basic principle of PD involves instilling the peritoneal cavity with sterile solutions of different osmolality through a permanent indwelling silicone-based catheter in a process called an exchange. The exchange itself consists of 3 distinct phases: filling, dwelling, and draining. This allows for the solution within the peritoneal cavity to generate a chemical and osmotic gradient across the peritoneal membrane, facilitating the removal of toxins and water with PD fluid drainage. The overwhelming majority of solutions used in PD are glucose based, with higher concentrations exerting a greater osmotic gradient that leads to larger ultrafiltration (UF) volumes. PD solutions can be lactate or lactate/bicarbonate buffered, with the latter having a more neutral pH of 7.4 (Table 1). Clinical data have suggested that lactate/bicarbonate-buffered solutions reduce the generation of glucose degradation products (GDP) during the sterilization and storage of the dialysis

fluid, and in this way they may confer clinical benefit. Although studies have previously demonstrated conflicting results about the clinical benefits of pH neutral/low-GDP solutions, a recent meta-analysis showed that these solutions are associated with better preservation of RKF. Despite these emerging data on RKF benefits, neutral pH solutions are primarily used in clinical practice as an alternative to lactate-buffered solutions in patients who experience infusion pain.

Transport across the peritoneal membrane occurs through pores of 3 different sizes: ultrasmall or aquaporin 1 (AQP1) pores, small pores, and large pores. The principle of transport across the pore sizes is described as the 3-pore model. AQP1 allows for the exclusive transport of water across the peritoneal membrane. Small pores allow the transport of both water and small solutes, including most electrolytes. And large pores allow for the movement of macromolecules such as immunoglobulins and other proteins.

The exchange of solutes and water occurs at the areas of the peritoneal membrane that are surrounded by capillaries and in contact with dialysate. This is called the “effective peritoneal surface area” and can vary with changes in vascular resistance or increases in the dialysate fill volume. For example, PD peritonitis leads to inflammation and consequent vasodilation of the capillary bed, which in turn increases the effective peritoneal surface area (more open capillary beds able to take part in transperitoneal flux).

Table 1. Various Components in Peritoneal Dialysis Solutions for Lactate- and Bicarbonate- Buffered Solutions Highlighting the Different Osmolarity Depending on Dextrose Concentrations

Component	Lactate-Buffered Solution			Bicarbonate-Buffered Solution
	2.5%	4.25%	7.5%	2.5%
Sodium, mmol/L	132	132	132	132
Calcium, mmol/L	1.25/1.75	1.25/1.75	1.25/1.75	1.25
Magnesium, mmol/L	0.25	0.25	0.25	0.25
Chloride, mmol/L	96	96	96	96
Lactate, mmol/L	40	40	40	15
Bicarbonate, mmol/L	—	—	—	25
Dextrose, g/dL	2.5	4.25	—	2.5
Icodextrin, g/dL	—	—	7.5	—
Osmolarity, mOsm/L	396	484	282	396
pH	5.2	5.2	5.2	7.4

Higher dextrose concentration solutions have a higher osmolality and exert greater osmotic pressures across the peritoneal membrane, resulting in greater ultrafiltration volumes.

Peritoneal solute transfer rate can therefore increase in patients with PD peritonitis, leading to faster absorption of dextrose (glucose), early dissipation of the osmotic gradient, and transient loss of UF capacity.

Should Transporter Status Determine PD Prescriptions?

Using the PET, peritoneal membrane transport can be evaluated by assessing the transport of small solutes along with UF properties. For a given solute, equilibration ratios between the dialysate and plasma (D/P) are used to measure the diffusion that allows for quantification of small solute transfer rate across the peritoneal membrane, also referred to as the peritoneal solute transfer rate. The PET procedure involves filling the intraperitoneal cavity with 2,000 mL of a 2.5% or 4.25% dextrose solution. Once the abdomen is filled, up to 3 dialysate samples can be taken at separate time intervals. The mandatory dialysate samples should include the 4-hour sample and a sample from the stock solution used for the procedure. Dialysate samples drawn immediately after the fill and at the 2-hour interval are optional. In instances where sodium sieving is being assessed using a hypertonic dextrose-based solution, an additional dialysate sample should be drawn at the 1-hour interval. The sodium concentration in the dialysate sample after a 1-hour dwell allows for an indirect calculation of the free water transport across the peritoneal membrane. Blood samples need not be measured frequently, and a unique sample can be drawn at the 2-hour interval for plasma concentrations of sodium, urea, creatinine, and glucose to determine the D/P.

The ratio of the glucose concentration in dialysate at different time intervals after fill relative to the initial dialysate concentration is written as $D/D_{0(\text{glucose})}$. Historically, patients are then classified into 4 distinct categories (slow, slow average, fast average, and fast) based on the D/P_{cr} , D/P_{urea} , and D/P_{Na} (Fig 1). Patients classified as “fast transporters” have a rapid dissipation of the osmotic gradient in the dialysis fluid because the dextrose diffuses across the peritoneal membrane more quickly. This rapid dissipation leads to less UF and even reabsorption of fluid toward the end of a longer dwell. As result, cyler-based therapies had been historically favored in “fast transporters” due to the shorter dwells with each exchange, thus reducing the risk of fluid reabsorption.

By contrast, “slow transporters” have slower loss of dextrose from the PD fluid and maintain their osmotic gradient for longer periods of time. It followed from this observation that slow transporters would be better suited for longer dwells with manual exchanges. In theory, the longer dwells were aimed at maximizing diffusive transport with the maintenance of the osmotic gradient. Despite the aims of this theoretical approach to capitalize on peritoneal membrane transport properties, it is not ideal in routine clinical practice.

Categorizing patients based on peritoneal solute transfer rate has limitations in clinical practice because these values

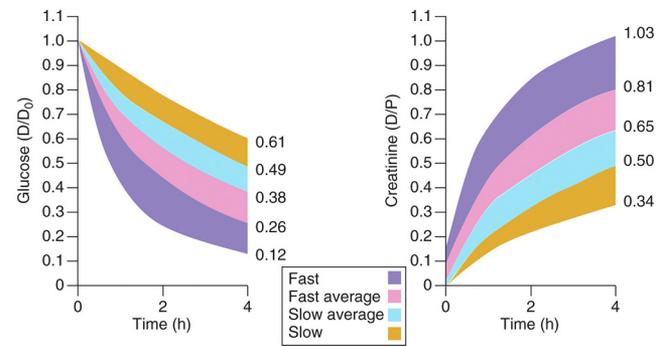


Figure 1. Peritoneal equilibration test (PET) showing the different types of membrane transporters. On the left, the glucose concentration of the dialysate at a given time is compared with the initial concentration of the solution. An individual with fast transport (purple) across the membrane loses the glucose osmotic gradient rapidly while a slow transporter (orange) has a longer maintenance of the osmotic gradient of glucose solution. Original graphic © 2019 Elsevier; reproduced with permission of the copyright holder from Johnson et al, 2019 (*Comprehensive Clinical Nephrology*, 6th ed.; ISBN: 9780323479097).

function more like continuous variables than clearly distinct groups. In addition, a strong center effect has been observed. Therefore, practitioners should consider a more practical approach to PD prescriptions that prioritizes the patient’s preferences and positive clinical outcomes over peritoneal membrane transport characteristics.

Prescribing Peritoneal Dialysis

PD exchanges can be provided to patients through manual exchanges or through APD using pneumatic/hydraulic cyclers. Automated cyclers are used while patients sleep, allowing for small solute exchange and effective UF with frequent exchanges. Beyond its efficiency in achieving effective solute clearance and fluid removal, cyler-based therapy is a favorable option among patients with busy daytime schedules. Modern day cyclers have evolved, and they offer greater precision and remote monitoring that allow for tailoring of the prescription based on patient needs.

Despite the benefits of cyclers, their utilization depends on availability, training capacity, and local resources. For example, in countries where government reimbursement policies are limited, overall PD prevalence and cyler use tends to be relatively low. Manual exchanges (ie, CAPD) are more cost-effective and have higher utilization in low-resource settings. With CAPD, patients typically undergo 3–4 exchanges per day depending on clinical status and patient preferences. CAPD is an excellent option for patients who do not wish to be connected to a cyler during sleep and have more flexibility in daytime schedules to perform exchanges. It also affords greater portability for patients who travel frequently without having to transport their cyclers. Although the terms “exchanges” and “cycles”

may be used interchangeably, practitioners should be aware that “cycles” usually refers to APD therapy and “exchanges” usually refers to CAPD.

Once a modality has been chosen, the prescription of the fill volume and number of exchanges must be finalized. Most patients can tolerate a maximum fill volume of 1,250-1,500 L/m² or about 2,000-2,500 mL per exchange. In the average adult patient, this will result in intraperitoneal hydrostatic pressures of less than 18 cm of H₂O. Although there are variations in intraperitoneal pressure (IPP) depending on patient positioning, an IPP of greater than 18 cm of H₂O is usually associated with discomfort. When patients are supine, the IPP is lowest; as a result, larger fill volumes are more tolerable at night compared with during the day when IPP is increased with either standing or sitting. Despite the opportunities for slightly higher volumes during sleep, fill volumes beyond 2,000-2,500 mL are not usually recommended given the increased risk of patient discomfort.

The principles of incremental PD can be used when starting patients on dialysis, allowing practitioners to tailor the PD prescription with a focus on laboratory investigations, clinical symptoms, and patient preferences. Incremental PD allows for patients who are new to the therapy to become comfortable with the treatment rather than beginning with a more demanding regimen. Initial large doses of PD can sometimes be an emotionally overwhelming experience for those who are new to treatment and carry significant burden of intrusiveness for many individuals in maintaining their regular routines.

There are also some important drawbacks that practitioners must consider with incremental PD. These drawbacks include more frequent monitoring of RKF, risk of underdialysis, and decreased patient acceptance to increasing the dose of dialysis if warranted (Fig 2).

Irrespective of a patient’s modality preference, the principles of incremental PD can be used for both CAPD and APD (Fig 3). For instance, patients who have expressed a preference for maintaining flexibility in their daytime

schedule can be placed initially on 2-3 cycles for 6-7 hours per night on the cycler using fill volumes of 1,200-1,500 mL with each exchange. The prescription can be “incrementally” adjusted based on laboratory investigations and clinical assessments. In cases where a patient requires more solute clearance, there can be an incremental increase in the volume by 20%-30% up to a maximum of 2,000-2,500 mL. Alternatively, the time on the cycler can be increased along with the number of exchanges.

Patients should not be routinely prescribed >8 hours on cycler therapy because most people do not sleep or remain in bed for that amount of time. Additionally, prolonged treatments on the cycler may be an added burden for patients because it may restrict activity and impair overall quality of life. Patients should not receive more than 5 exchanges per night on the cycler because this leads to wasted time and inefficient dialysis.

As highlighted earlier, every exchange has 3 distinct phases: filling, dwelling, and draining. It is during the dwelling phase that effective peritoneal surface area is maximized with dialysate fluid. The filling and draining phases account for a combined 20-30 minutes, and during this time there is very little to no effective dialysis. For example, if 6 cycles are prescribed for a patient in 8 hours, that effectively equates to 120-180 minutes of inflow and outflow time, or nearly 3 out of 8 hours where little effective dialysis occurs. Consequently, this regimen leads to significant wasted time and inefficient dialysis (Fig 4). Furthermore, rapid exchanges can also cause suboptimal clearance of sodium given that the electrolyte-free water movement across AQP1 tends to occur in the first hours of each dialysate dwell. As a result, if exchanges are rapid and short, sodium cannot diffuse down its concentration gradient from blood to dialysate across the small pores. This “sodium sieving” leads to more water than sodium removal, causing a transient increase in plasma sodium levels. This hyponatremia can increase thirst in patients, leading them to drink excessively which may exacerbate volume overload.

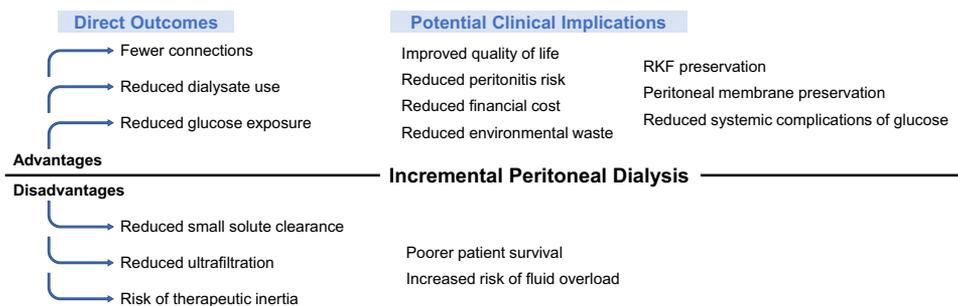


Figure 2. The benefits and advantages of incremental peritoneal dialysis must be considered for patients on an individual basis. Practitioners should consider these benefits and drawbacks along with potential downstream clinical implications when proposing incremental peritoneal dialysis. Abbreviation: RKF, residual kidney function. Original graphic © 2021 International Society of Nephrology; adapted with permission of the copyright holder from Cheetham et al 2021 (*Kidney Int Rep.* <https://doi.org/10.1016/j.ekir.2021.11.019>).

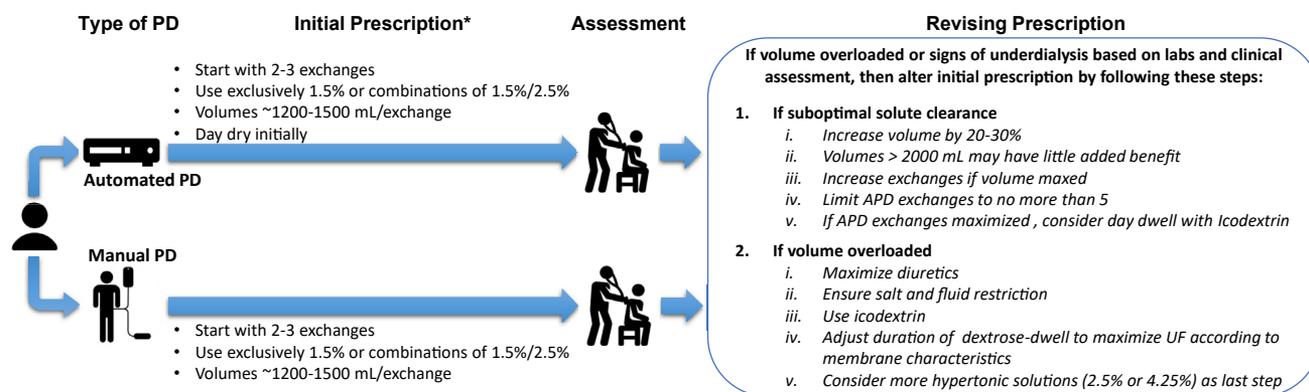


Figure 3. A simplified algorithm for initial PD prescriptions using an incremental approach. Patients can be started on 2-3 exchanges on the hydraulic cycler at night for a period of 5-7 hours initially with a fill volume of 1,200-1,500 mL per exchange. In case of manual PD, the patients can be started on 2-3 exchanges per day as well but will need to be monitored closely for signs of fluid reabsorption because the osmotic gradient for lower concentration solutions will dissipate, particularly with long dwells. The concentration of solution can be a combination of 1.5% or 2.5% solutions. We recommend that practitioners consider when to use (and if possible, to use exclusively) the lowest concentration solution that allows for maintaining fluid balance while reducing the risk of prolonged high-concentration dextrose exposure. Once starting patients on incremental PD, clinical assessment to identify early signs of volume overload or underdialysis is needed. The prescription can be adjusted based on the clinical assessment and having important discussions with the patient. *Not applicable to patients transferring from hemodialysis or those with no residual kidney function. Abbreviations: APD, automated peritoneal dialysis; PD, peritoneal dialysis; UF, ultrafiltration. Adapted from material distributed via Twitter by @bourneauguste; original graphics © 2022 B. Auguste.

Review of Cases 1 to 3

In the first case, the patient is relatively new to PD and has expressed an interest in continuing to attend university classes during the daytime. Although she does not yet have formal clearance studies available, her 24-hour urine output demonstrates good RKF, so she does not require a large initial PD prescription. As a result, APD at night with a daytime dwell (option (c) for question 1), also called continuous cyclic peritoneal dialysis (CCPD) is not the best option for this patient. Additionally, options (b) and (d) are not reasonable options because they require manual exchanges during the daytime. Therefore, the best answer

to question 1 is (a): APD during the night can allow her flexibility in maintaining her busy schedule during the day as she can get her dialysis treatment while she sleeps.

Similarly, in the second case the patient has a very busy schedule with frequent travel between different sites. Manual exchanges would present significant challenges to his daily routine, which would not be a patient-centered approach for this individual. The patient would have greater daytime flexibility in his schedule if he received PD treatments during the night. Therefore, the best answer to question 2 is (b), maintain current nightly cycler-based therapy. Although his membrane transport characteristics suggest that he is a slow-

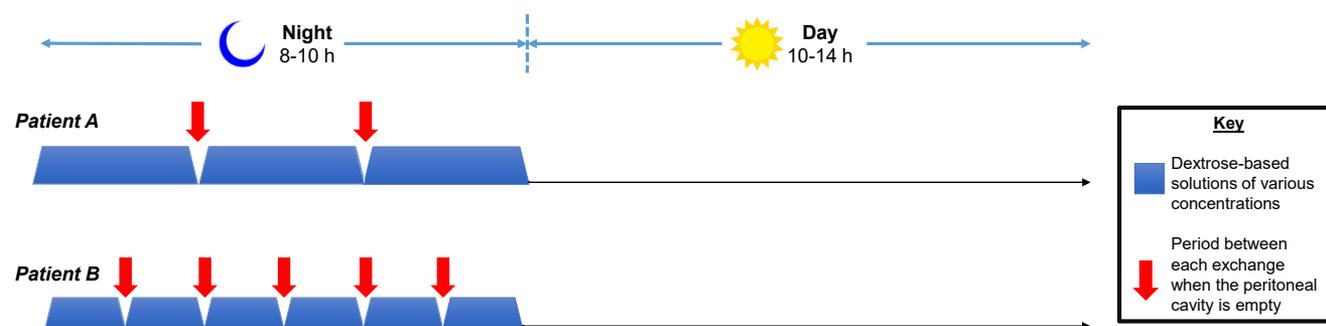


Figure 4. An illustration showing the differences in the effective dialysis treatment for patients on peritoneal dialysis. Patient A receives 3 exchanges over 8 hours on APD. Patient A only has minimal disruption in the time that dialysate fluid is in contact with the peritoneal membrane. This disruption or the interexchange period reduces effective peritoneal surface area. Patient B has 6 exchanges over 8 hours and has more disruptions in the treatment and reduced contact time with effective peritoneal surface area engagement. Each arrow represents about 20-30 minutes, and the more exchanges results in reduced effectiveness in treatment. Abbreviation: APD, automated peritoneal dialysis. Adapted from material distributed via Twitter by @bourneauguste; original graphics © 2022 B. Auguste.

average transporter, priority should be given to providing a prescription that is least disruptive to his lifestyle.

In the third case, the patient has been on PD for several months and is demonstrating clinical and biochemical signs of underdialysis probably because of declining RKF. In using an incremental PD approach, her fill volumes could be increased as an option but by 20%-30% as suggested with option (d) for question 3. In option (b), a fourth exchange is added, and the therapy time is extended by an additional hour for a total of 8 hours. In this case, options (b) and (d) are both reasonable to present to the patient. This allows the patient to be part of the decision-making process in choosing a suitable prescription that aligns with her personal preference. In most instances, patients are more likely to increase the fill volume rather than add an additional exchange or time on the cyclor. The patient has expressed a preference to not have a daytime dwell at this time, thus option (a) would be inappropriate. In keeping with the principle of incremental dialysis, if and when her RKF declines in the future, a daytime "last fill" can be added. Finally, the use of hypertonic solutions with each exchange would be inappropriate because the patient does not have any signs to suggest volume overload. While the consequent increase in UF will increase solute removal, it exposes the patient to unnecessarily high concentrations of dextrose, increasing the risk of hyperglycemia and other downstream effects of glucose loading. Therefore, option (c) is equally inappropriate in this case.

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How Is Adequacy Measured on PD?

Case 4: A 53-year-old woman has been on PD for 5 months and undergoes repeat adequacy testing. A few months earlier, her Kt/V_{urea} was 1.3, and her PD prescription was intensified to include a daytime dwell with icodextrin (1,000 mL) in addition to 5 exchanges on cyclor overnight with each fill volume of 2,000 mL. Her repeat Kt/V_{urea} is 1.4, and she reports feeling well with no concerns. Her body mass index (BMI) is 39 kg/m², and all her relevant laboratory values are within the desired target range.

Question 4: What are your next steps in the management of this patient?

- (a) No changes are required to her prescription.
- (b) She should be transitioned to HD.
- (c) Increase the time on the cyclor to 9 hours.
- (d) Repeat the Kt/V_{urea} .

For the answer to this question, see the following text.

Although dialysis adequacy remains a controversial topic in nephrology practice, it is commonly defined as providing sufficient dialysis to reduce the burden of uremic symptoms in patients. There are many other solutes that contribute to uremic symptoms, but clinical practice remains urea-centric, using it as a surrogate marker for small solute clearance. Adequacy in PD can be measured using either weekly Kt/V_{urea} or weekly creatinine clearance (CL_{cr}). Irrespective of whether CL_{cr} or Kt/V_{urea} is used, practitioners must remember to account for peritoneal and renal components in clearance calculations, as highlighted in the following equations:

$$\begin{aligned} \text{Total } Kt/V_{urea} &= \text{Peritoneal } Kt/V_{urea} + \text{Renal } Kt/V_{urea} \\ \text{Total } CL_{cr} &= \text{Peritoneal } CL_{cr} + \text{Renal } CL_{cr} \end{aligned}$$

Measures of Adequacy: Kt/V_{urea}

Historically, many programs have relied exclusively on Kt/V_{urea} as a marker of dialysis adequacy. The weekly Kt/V_{urea} targets are set by the weekly urea clearance (Kt) and normalized to the estimated volume of distribution

of urea (Kt/V_{urea}). The oversimplification of small solute clearance through weekly Kt/V_{urea} targets of 1.7-2.0 allows practitioners and administrators to perform rapid audits of large programs. This reliance on Kt/V_{urea} has minimized the importance of clinical assessments and developing individualized treatment plans. More contemporary data have shown that achieving prespecified Kt/V_{urea} targets may not confer clinical benefit as was previously thought; rather, the preservation of RKF is of greater importance. The reanalysis of the CANUSA study showed that better Kt/V_{urea} and CL_{cr} were more dependent on RKF, not on peritoneal clearance. Additionally, the randomized controlled ADEMEX trial of prevalent and incident CAPD patients showed that there was no significant clinical benefit in patients who had a higher Kt/V_{urea} compared with a lower value. Uremia is quite complicated, with numerous contributory molecules of various sizes and diffusive properties that cannot be simply measured by an equation that examines one small diffusible molecule.

Kt/V_{urea} is also affected by variations in total body water. There are notable differences in total body water between men and women and with extremes of weight irrespective of gender. Furthermore, calculation of V as a percentage of body weight does not take into account that the weight of adipose tissue will increase the size of this V, yet it is not part of the true volume of distribution of urea. For example, an overweight person with a larger BMI will have a larger calculated total body water compared with someone with a smaller BMI, which in turn leads to smaller Kt/V values. This erroneous “large V, small Kt/V ” idea may lead to the perception that patients are receiving suboptimal dialysis, often leading to premature and sometimes burdensome changes in PD prescription. The use of Kt/V_{urea} also does not address the importance of UF in patients on PD, many of whom are challenged with volume overload.

Measures of Adequacy: Creatinine Clearance

Given the drawbacks in assessing adequacy by relying solely on Kt/V_{urea} , weekly CL_{cr} has been adopted in conjunction with Kt/V_{urea} in many centers around the globe. Current European guidelines recommend a minimum weekly target for Kt/V_{urea} and CL_{cr} of 1.7 and 45 L normalized to 1.73 m² body surface area, respectively. The total CL_{cr} is the sum of peritoneal clearance and the RKF. In patients with RKF, the completion of 24-hour urine collections may be challenging. In circumstances where the serum creatinine is stable in the absence of changes in muscle mass or recent alterations in PD prescription, it can be assumed that the kidney CL_{cr} is preserved. The practice of using Kt/V_{urea} or CL_{cr} targets is not supported by evidence, and thus management of patients should focus on detailed clinical assessments coupled with discussions with patients to identify opportunities to adjust dialysis prescriptions when needed. In jurisdictions where weekly Kt/V_{urea} must be reported, the kidney contribution should be included and consideration be given to using fat-free body weight in the calculation of V for the

reasons previously discussed. In continuing to focus on these targets and without speaking to patients, we may do more harm than good by making unnecessary changes when they are not required or not making changes when they are needed. It is imperative that practitioners focus on the clinical responses of patients rather than fixate on equations that do not explain the entire clinical picture.

Review of Case 4

In this case, the patient has a larger BMI, which increases the estimation of overall total body water and in turn leads to a lower Kt/V_{urea} . Repeating the Kt/V_{urea} will give the same result, provided that the patient’s weight and current prescription have remained unchanged. The patient has reported a clinical improvement since starting dialysis and reports no concerns. She does not need an intensification of the PD prescription given her current clinical stability, so the best answer to question 4 is (a).

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How Should Low Ultrafiltration Capacity and Solute Clearance Be Addressed?

Case 5: A 58-year-old woman with kidney failure secondary to IgA nephropathy is on APD. The patient reports progressively worsening dyspnea, bilateral pedal edema, and a 5 kg weight gain over the last 3 weeks. You conduct a clinical examination and conclude that she has signs consistent with volume overload. Her residual urine output is approximately 250 mL/d, and she currently receives furosemide at 120 mg twice daily and metolazone at 5 mg once daily. In terms of APD, she receives four 2,000 mL exchanges overnight with all 2.5% dextrose solutions over 8 hours, and a 1,500 mL daytime dwell of icodextrin. Her daily average UF volume has been 1,250 mL.

Question 5: What would be your next steps in management?

- (a) Increase the dose of furosemide and metolazone.
- (b) Transition to HD.
- (c) Rule out catheter outflow obstruction.
- (d) Conduct a trial of 4.25% dextrose solutions.

Case 6: A 73-year-old man has been on PD for 5 years and is currently on APD with 5 exchanges of 2,100 mL with each exchange over 9 hours. He also has a daytime dwell with 2,000 mL of icodextrin followed by a mid-day exchange with 2,000 mL of 2.5% dextrose solution. He has no residual urine output. He describes progressive fatigue, anorexia, and pruritus, raising concern for worsening uremia. His urea over the last 2 months has increased from 60 mg/dL (21.4 mmol/L) to 98 mg/dL (35 mmol/L). He has not missed any therapy and continues to perform PD as has been prescribed. He indicates that he is not able to spend time with his family because he is too tired even after dialysis treatment.

Question 6: What would you offer the patient at this time?

- (a) Increase the time on the cycler to 11 hours.
- (b) Increase the volume with each exchange to 2,400 mL.
- (c) Transition to HD.
- (d) Repeat bloodwork and follow up in 2 months.

For the answers to these questions, see the following text.

Management of Volume Overload in PD

Volume overload is a common finding in patients on PD and is primarily driven by imbalances between dietary salt and water intake and its removal. The common causes for volume overload in this population can be grouped into 3 categories: excessive fluid and/or salt intake, reduced RKF, and low peritoneal UF (Box 1). Observational data from Europe using bioimpedance analyses demonstrated that about 25% of patients on PD over a 2-year period had severe volume overload. Additionally, volume overload is associated with an increased risk of technique failure and death among patients receiving PD.

In assessing patients for volume overload, practitioners may identify progressive weight gain, jugular venous distention, elevations in blood pressure, and peripheral edema as some of the more common features. However, the presence of peripheral edema in isolation should not always lead to the conclusion that a patient is volume overloaded. Edema, particularly in the lower extremities, can be caused by high doses of dihydropyridine calcium channel blockers.

Additionally, in patients with heart failure and liver disease the presence of edema can be misleading when in fact the intravascular compartment is contracted. As a result, the use of diuretics or higher concentration solutions to treat lower limb edema in such cases can cause hypotension and significant vascular collapse in patients.

Box 1. Common Causes of Volume Overload in PD

- Excessive fluid and/or salt intake
- Low residual kidney function
- Low peritoneal ultrafiltration
 - ◊ Mechanical problems (eg, catheter flow dysfunction, catheter malposition, and hernias)
 - ◊ Peritoneal membrane dysfunction/rapid peritoneal solute transport rates in which osmotic gradient dissipates rapidly (from either inherited or acquired injury)
- Suboptimal PD prescription

Abbreviation: PD, peritoneal dialysis.

This is of critical importance as overdiuresis or excessive UF will lead to hypotension, reducing kidney perfusion and in turn further diminishing RKF.

In managing volume overload, practitioners must consider pharmacological and nonpharmacological approaches in all patients. A nonpharmacological approach includes counseling patients about reducing their dietary intake of sodium (<2 g/d) and water. In recommending reductions in water intake, it is imperative that practitioners consider the impact of various PD prescriptions on thirst. For example, higher osmolarity solutions can increase blood glucose levels, which in turn may increase thirst and water intake. Additionally, frequent exchanges on the cycler can cause sodium sieving as described previously, leading to thirst and increased water intake. Suboptimal peritoneal UF must be considered as a potential cause for volume overload, particularly if patients miss treatments regularly.

In cases with refractory volume overload, icodextrin can be considered for the long dwell. Observational data have shown that patients with low daily UF volumes (<1,000 mL/d) may derive benefit from including icodextrin in their PD prescriptions to enhance fluid removal. Additionally, a recent systematic review comparing icodextrin-based to dextrose-based solutions used once daily in a long dwell demonstrated better UF, fewer episodes of volume overload, and reduced hyperglycemia. Icodextrin should never be used, however, for urgent or emergent volume overload because ultrafiltration occurs more slowly compared with that from a 4.25% dextrose solution.

In adopting pharmacological approaches, diuretic doses should be maximized in patients on PD with residual kidney function of >100 mL/d. Patients on maintenance dialysis have decreased diuretic responsiveness, and as such they require higher doses than usual compared with patients not on dialysis therapy. For example, furosemide can be prescribed in divided doses up to a maximum of 400 mg/d coupled with metolazone at 2.5-10 mg/d. (If using twice daily dosing of furosemide or other loop diuretics, the second dose should be given in the afternoon or at dinnertime, and not before bed.) If patients remain volume overloaded despite high doses of diuretics, then changes to the PD prescription with higher osmolarity

solutions must be considered. Higher concentration solutions exert greater osmotic pressure across AQP1, leading to enhanced peritoneal UF.

Suboptimal peritoneal UF can also be attributed to UF failure (UFF), which is uncommon. UFF is defined as the failure to attain at least 400 mL of net UF after a dwell period of 4 hours using 4.25% dextrose solution. There are 4 distinct categories of UFF, and there are important pathophysiological differences that must be highlighted. Type 1, the most common form of UFF, results from an increase in the effective peritoneal surface area. The presence of proinflammatory cytokines and neoangiogenesis can lead to the expansion of the effective peritoneal surface area, causing a rapid transport of solute and quick dissipation of the osmotic gradient that is needed for achieving effective UF.

By contrast, diminished hydraulic conductance across the aquaporins can lead to type 2 UFF. Although it remains unclear what factors may lead to aquaporin dysfunction, new research has suggested that differences in genetic expression may play a role. For instance, variations in AQP1 gene expression have been shown to have a strong association with peritoneal water transport. Patients with the TT genotype for the AQP1 single-nucleotide variant rs2075574 have significantly lower net UF than those with the CC genotype (506 ± 237 vs 626 ± 283 mL, $P = 0.007$). This highlights that patients may have a genetic predisposition to an increased risk of UFF.

Type 3 UFF is characterized by a reduction in the effective peritoneal surface area and is typically associated with peritoneal scarring as can be seen with encapsulating peritoneal sclerosis or recurrent episodes of peritonitis. In this subtype, patients have a combination of suboptimal peritoneal UF and solute removal due to the reduced effective peritoneal surface area.

The final form of UFF, type 4, is rare and is characterized by increased fluid reabsorption through the lymphatic system. Animal model studies have suggested that lymphangiogenesis in the presence of peritoneal fibrosis may play a role in its pathogenesis.

Despite the previous characterization of UFF, emerging expert opinions and data have suggested avoiding this term in favor of “low UF capacity.” First, the term “failure” can be discouraging to patients, so it should be avoided in clinical practice. In addition, a high degree of variability in UF volumes can occur with catheter flow dysfunction, which may lead to false-positive results. Also, the classification into 4 distinct categories of UFF has little clinical utility and is often challenging to diagnose in practice. Moreover, low UF capacity is a more fitting description given that membrane dysfunction may be related to genetic variation in AQP1 or due to acquired injury that leads to rapid solute transport rates.

Practitioners must identify and exclude other more common causes of low peritoneal UF volume before considering low UF capacity. These more common causes include PD fluid leaks and/or outflow obstruction. Pericatheter and genital leaks may present with localized edema in the abdominal wall or swelling in the perineum.

Swelling in the perineum is commonly seen in the presence of inguinal hernias due to a patent processus vaginalis. Therefore, patients must be examined closely for signs of edema localized to the abdomen or perineum.

Patients should also be assessed with a computed tomography (CT) peritoneogram to identify radio-opaque peritoneal fluid that tracks outside of the peritoneal cavity. This procedure is performed by having contrast material instilled in the peritoneal cavity with 2,000 mL of dialysate. The patients must be encouraged to ambulate for a period of at least 2 hours before the CT scan is done. If the CT scan is done too early after the administration of intraperitoneal contrast fluid, it may not allow enough time for the fluid to pass through small defects, potentially missing a leak.

The management of PD leaks is dependent on the type of leak. Most patients with genital edema will require surgical correction, particularly if ambulatory and larger volumes of PD are required to achieve effective UF and solute clearance.

When Should a Patient Transition to Hemodialysis?

Discussions about stopping PD and switching to HD can be extremely difficult for patients and practitioners. (The most common reason that patients change from PD to HD is infection; these and other infectious complications are beyond the scope of this review.) Despite this difficulty, a delay in the decision to switch modality can have a significant impact on quality of life and overall outcomes for patients. Whether to switch modality hinges on whether PD is achieving effective solute clearance and/or water removal. In instances where there is persistent volume overload despite interventions, patients should be advised to transition to HD. As highlighted earlier, volume overload is associated with poor outcomes in this population.

We believe that providing patients with a clear explanation about the reasons a prescription is being adjusted is a key step that allows for active patient engagement in formulating care plans. In patients with pleuroperitoneal leaks, a brief respite from PD is often required. This allows patients who have undergone a pleurodesis procedure enough time to heal, allowing blebs on the diaphragm to effectively seal and in turn reducing risk of recurrence. In cases where patients who are on large volume PD with a mid-day exchange continue to have signs of underdialysis, HD should be considered. However, the cumulative effects of comorbid disease such as diabetes, heart failure, and vasculopathy may at times be mistakenly attributed to underdialysis, leading to an inappropriate transition to HD. Patients on HD who have similar cumulative effects are often not considered to be underdialyzed, and their symptoms are appropriately attributed to the natural course of their comorbidities. Practitioners must therefore consider competing comorbidities in patients with clinical deterioration to avoid inappropriate transitions to HD.

Review of Cases 5 and 6

In case 5, the patient has ongoing volume overload and may benefit from further evaluation. An increase in the

dose of diuretics is unlikely to have additional benefit given that the residual urine output is about 250 mL. The patient has a UF of about 1,250 mL/d, and it is unlikely that there is a problem with catheter outflow. A transition to HD would be premature given that a higher concentration solution has not yet been trialed. Therefore, for question 5, the best answer is (d), a trial of 4.25% dextrose solutions. We would also like to highlight that in cases where practitioners want to limit chronic exposure to high-concentration dextrose, an off-label use of twice per day icodextrin can be considered. Icodextrin is currently licensed for once-a-day administration, but some observational data suggest that twice-daily use can be effective in patients. Practitioners should also be aware that it can lead to accumulation of maltose in the extracellular compartment, leading to movement of water from the intracellular compartment and causing mild hyponatremia.

In case 6, the patient has described symptoms that are consistent with uremia, highly suggestive of sub-optimal dialysis despite a large prescription. He describes factors that are affecting his quality of life and has not been able to spend time with his family; therefore, increasing the time spent on cycler is not appropriate. Additionally, increasing the fill volumes with each exchange to 2,400 mL may be uncomfortable for the patient and is unlikely to significantly improve solute clearance. Given the symptoms of uremia, delaying for an additional 2 months could result in worsening uremia and the need for urgent HD. Considering his worsening uremia and balancing the time attached to therapy, the best answer for question 6 is (c), transition to HD. Consideration should be given for a “home-to-home” transition—that is, from PD to home HD in order to preserve patient autonomy.

Additional Readings

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Conclusions

Historically, PD prescriptions have relied heavily on membrane transport characteristics and small solute kinetics, often ignoring patient preferences. Clinical practice has since evolved, incorporating shared decision-making processes that prioritize preferences of patients. As the worldwide adoption of PD continues to grow, practitioners must work closely with patients, families, and caregivers in developing prescriptions that prioritize individual needs over small solute clearance targets. An individualized care model allows for incremental PD to be seamlessly introduced into practice, addressing the unique needs of the patient while accomplishing agreed-upon clinical goals and objectives.

Article Information

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