Chapter 20
Peritoneal Dialysis in Special Situations

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Introduction

Peritoneal dialysis (PD) is used widely and successfully in treatment of end-stage kidney disease (ESKD) patients. The continuous nature of the therapy and its home-based, self-care character make it advantageous for certain subgroups of patients. This chapter focuses on the use of PD in subgroups of ESKD patients who require special considerations.

Autosomal Dominant Polycystic Kidney Disease

Autosomal dominant polycystic kidney disease (ADPKD) ranks as the most common hereditary kidney disease and the fourth leading cause of ESKD in the United States, with a prevalence rate of 4.7% [1]. Globally, polycystic kidney disease affects 4–6 million people and accounts for ESKD prevalence of up to 10% in certain countries. ADPKD patients present mainly with renal cysts, enlarged kidneys and intra-abdominal complications including cyst rupture, cyst infection, liver cysts, diverticulitis, and abdominal wall hernias. In the process of cyst growth,

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approximately 45% of patients progress to ESKD by the age of 60 and up to 75% by the age of 70 [2].

Previously, the presence of ADPKD was considered, by some, as a relative contraindication to peritoneal dialysis (PD) as a kidney replacement modality. The basis of this thinking was that the enlarged kidneys, which would, for various reasons, impair the patient's ability to tolerate the intraperitoneal volume of PD fluids and associated complications.

In recent years, several studies have analyzed clinical outcomes, patient and technique survival, and other complications regarding ADPKD undergoing PD, with different results.

One of the earliest studies of ADPKD patients undergoing PD, which was a small retrospective trial, paired 26 ADPKD patients with 26 non-ADPKD contemporary controls, in which no significant difference was found in patient or technique survival between the two groups. The transfer reasons from PD to hemodialysis (HD) were not different between ADPKD patients and controls [3].

Several subsequent studies [4–8] regarding PD technique survival have demonstrated similar findings. A retrospective study with longer follow-up involving 56 ADPKD cases compared with 56 age- and sex-matched nondiabetic patients on PD revealed no significant difference in mortality, PD technique survival, or the number of patients switching to HD [8].

In a multicenter historical prospective matched-cohort, involving 106 ADPKD and 212 non-ADPKD patients, all ADPKD patients initiated PD during the study window, simultaneously 2 consecutive non-ADPKD paired on PD (1:2 enrollment ratio). Peritoneal dialysis in ADPKD patients was associated with lower mortality rate and similar overall rate of technique failure, compared with non-ADPKD patients. Despite this, most technique failures were directly related to ADPKD itself (such as nephrectomy and leakage) [6].

A larger study from the French PD registry analyzing 4162 incident ESKD (nondiabetic) and 344 ADPKD cases between 2002 and 2008 demonstrated baseline lower comorbidity scores and younger age in the ADPKD group. Significantly, similar patient and technique survival in both groups were shown [7, 9].

A meta-analysis in 2018 featured a combination of 12 cohorts, including 14,673 patients on PD (931 ADPKD and 13,742 non-ADPKD). In this study, ADPKD, as the cause of ESKD, found to have a lower mortality risk, when compared with other etiologies. The risk of technique failure and peritonitis were not significantly different between the two groups, but abdominal hernia risk was significantly higher, and dialysate leakage also occurred in the ADPKD group compared with the non-ADPKD group.

The finding of lower mortality in ADPKD patients on PD was unexpected and challenged the traditional view that PD should be avoided. The underlying explanation for this is not known for certain, but a few points should be noted. First, it should be pointed out that a few studies [4, 10, 11] have also shown survival benefits in ADPKD patients on HD compared with those with other causes of ESKD, especially if diabetes is excluded [11] because it has been viewed as a poor prognostic factor in PD patients [12, 13]. Second, ADPKD progresses to ESKD at a younger

age and with fewer comorbidities and a better functional status than those with other etiologies of ESKD, which are good prognostic factors [14, 15].

In the meta-analysis, the higher risk of abdominal hernia and dialysate leak, both resulting from increased abdominal pressure, presumably due to enlarged polycystic kidneys within the abdominal cavity, was significantly demonstrated. Notably, this did not translate to higher technique failure, suggesting that abdominal hernia and dialysate leak are readily treatable without the need of transferring to HD.

The ADPKD patients should be considered at increased risk for abdominal hernia and leak. The prescription should be geared to limiting the intraperitoneal volume and thus the intraperitoneal pressure. Consideration should be given to night cycler PD wherein the patient dialyzes in the supine position, with lower consequent intraperitoneal pressure. If there is sufficient residual kidney function, the patient could be empty of dialysis fluid during the day. If the patient needs a long day dwell for sufficient solute removal, consideration should be given to using a lower fill volume for the day dwell than that used for the overnight exchanges.

Peritonitis risk also did not differ between the ADPKD and non-ADPKD group despite a higher risk of diverticulitis [16] and cyst infection [17, 32] in ADPKD group, both of which are usually caused by enteric Gram-negative bacteria.

It is possible that the microbiological profile of ADPKD-related peritonitis may be distinct from peritonitis in non-ADPKD, so the overall peritonitis rate did not differ in the two groups. However, a study regarding long term outcome of ADPKD patient on PD [8] reported the microbiological culture results did not show significant differences in the incidence of Gram-negative infection in ADPKD compared with controls.

In closing, the preponderance of data supports that ADPKD patients can safely perform PD with equivalent outcomes to other patients on PD and also compared with patients on HD. Personalization of PD prescriptions may allow effective methods to reduce complications and to expand the use of PD in ADPKD patients.

Chronic Heart Failure

Managing severe heart failure (HF) in patients refractory to diuretic therapy is a major challenge. While HD is conventionally reserved for patients with ESKD, PD has long been proposed for management of congestive HF [18]. PD offers potential advantages over extracorporeal therapy (EC), including less neurohumoral activation, better preservation of residual kidney function, the possibility of daily therapy in a home setting, and tighter control of sodium balance [19–21].

In chronic dialysis patients, PD was associated with better preservation of residual kidney function, which was considered a factor contributing to longer survival [22, 23]. A prior systematic review evaluating the before and after effects of PD in patients with HF found that hospitalization days declined significantly, with a lower class by the New York Heart Association (NYHA) criteria and better left ventricular ejection fraction (LVEF) [24].

A meta-analysis evaluated the clinical outcomes of PD compared to EC therapy in HF. Through a comprehensive search strategy, data was retrieved from 31 studies, including the largest study presently [25].

All the four observational, non-randomized studies [25–29] compared PD against EC therapy (HD or UF), and there was no significant difference in the mortality rates with either modality. Interestingly, application of PD in HF showed effective symptom relief. Almost all studies reported an improvement in the symptom score, when measured by the NYHA grade, and positive effects on LVEF with most studies reporting an increase in EF, typically ranging between 2% and 31%.

Moreover, the benefit of PD was a significant reduction in hospitalization rate and length of stay [30, 31].

The technique of PD in HF was variable. It appears that the most common technique employed was intermittent PD with manual exchanges using dextrose-based solutions. PD prescription in this highly variable cohort with different cardiac and renal status was largely focused on achieving adequate UF for the individual patients.

Peritonitis was reported as the commonest complication with the rate ranging from 0.02 to 0.46 episodes per patient-year. This rate is similar to other ESKD patients on PD, which, according to the ISPD guidelines, should be no more than 0.5 episodes per year at risk [32].

The option of a home-based therapy with family/community support may be an attractive option to patients especially if it results in lower hospitalization rates and duration of hospitalization. For the purpose of HF, PD can be performed intermittently based on weight gain or symptoms, empowering the patient to provide self-care and improve his/her quality of life.

However, the level of evidence is still weak as only observational data are available. There is inadequate evidence comparing PD to EC therapy, but limited data suggest similar mortality rates for either form of therapy.

Liver Cirrhosis

The exact prevalence of combined ESKD and cirrhosis is unknown, but few studies have shown 4–6% ESKD patients have the comorbidity of cirrhosis [33, 34]. The combination of ESKD and cirrhosis represents difficult management scenarios due to unstable hemodynamics and fluid balance compounded by coagulopathy, malnutrition, and encephalopathy.

PD can be considered as an alternative therapy in cirrhotic patients undergoing HD [35, 36].

In general, hemodialysis is the most prevalent RRT modality in cirrhosis with ESKD. The potential problems with HD in cirrhotic patients have been well described as hemodynamic instability, coagulopathy, and meeting dialysis adequacy goals. Intradialytic hypotension occurs frequently in cirrhotic patients undergoing HD.

Several observational studies supported PD as a substitute for RRT in those with complications associated with HD [37–39].

Three out of five patients transferred to PD due to hemodynamic instability during HD treatments. All patients were reported to have good hemodynamic tolerance, and similar to the prior study, mortality was not related to PD, but driven by cirrhosis complications [36].

A retrospective study compared 21 cirrhotic PD and 41 control PD to analyze survival outcomes of PD patients with liver cirrhosis. The survival of 5 years and hospitalization rates were similar in cirrhotic PD and non-cirrhotic PD patients.

More recently, several studies analyzed survival outcomes from cirrhotic patients undergoing PD and HD. Two different data sets from different centers, with 340 HD patients and 85 PD and 1116 HD patients and 279 PD, respectively, were studied retrospectively. Statistical data from both these cohorts demonstrated lower all-cause mortality in cirrhotic patients undergoing PD compared with HD.

Patients with cirrhosis are at increased risk of infections for several reasons, including reduction in leukocyte phagocytosis and recruitment, altered complement activity, and abnormal function of the reticuloendothelial system [23]. These abnormalities contributing to the development of spontaneous bacterial peritonitis (SBP) is suspected to be secondary to the hematogenous spread of enteric organisms to the peritoneum or transmural migration crossing the bowel mucosa. So, concern may arise that cirrhotic patients on PD are at increased risk of peritonitis, due to the inherent risk of SBP, and catheter- and technique-related peritonitis. Additionally, another risk factor for infections is thought to be the lactate-buffered PD solutions [40].

A retrospective review of 21 cirrhotic and 41 controls on PD showed a trend to a lower rate (statistically not significant) of peritonitis in the cirrhotic group. Interestingly, this study showed Gram-positive bacteria as the most common causative agent while excluding SBP as an inciting event. Additionally, while SBP is a strong risk factor for the development of hepatic encephalopathy, none of the patients in this cohort developed that complication following peritonitis episodes [37].

With the concerns of peritonitis, a retrospective analysis compared peritonitis rates between cirrhotic ($n = 25$) and non-cirrhotic ($n = 36$) PD patients with hepatitis B virus infection. There was no difference in the peritonitis rates or peritonitis-free survival in the two groups [38]. Time to first peritonitis was also similar in the groups, as were the rates of Gram-positive and Gram-negative infections. Treatment response rate and outcomes did not differ either [38]. Oral antibiotic prophylaxis has been recommended in cirrhotic patients with ascites, to prevent development of spontaneous bacterial peritonitis [41].

Common complications with PD are secondary to poor tunnel maturation (early) and increased intra-abdominal pressure (late) and include internal and external leaks, umbilical and inguinal hernias, and catheter malposition. Thirty-three cirrhotic on PD were compared with 33 controls on PD. Not only was there no difference in the early technical complications amid the two groups, but overall complications and surgical interventions were also similar [15, 21].

Abdominal Surgeries and Abdominal Complications

Patients with abdominal surgeries or other abdominal complications are not considered good candidates for PD and that prevalent PD patients needing abdominal surgery are commonly switched to hemodialysis. However, some data show that, when appropriately planned, PD can still be an acceptable option for ESKD with certain abdominal complications, undergoing abdominal surgery, or in pregnancy, etc [42].

Diverticular Disease of the Colon

Clinicians might be reluctant to offer PD to patients with colonic diverticulosis, because of the theoretical increase in the risk of peritonitis [43, 44].

In 1990, Tranæus et al. [45] used barium enema to assess 129 patients at start of PD and suggested that the risk factors significant for the development of peritonitis included more than 10 diverticula; diverticula size exceeding 10 mm; and diverticula found in the ascending, transverse, or descending colon (but not in the sigmoid colon).

Yip et al. [46] evaluated 604 PD patients for diverticulosis by colonoscopy or barium enema. Of those patients, 24% were found to have diverticulosis, with the most common site being the ascending colon and the organism most frequently associated with peritonitis being *Escherichia coli*. The investigators concluded that the presence of diverticulosis was an independent risk factor for the development of enteric peritonitis.

In general, PD is safe for patients who have diverticulosis. Episodes of diverticulitis that cause inflammation of the bowel wall theoretically lead to higher risk of translocation of organisms across the bowel wall into the peritoneal cavity. It is unclear whether holding PD during an attack of diverticulitis lessens the risk of bacterial translocation, but holding PD could be considered in patients who have sufficient residual kidney function. A history of recurrent diverticulitis is a concern when considering PD as a possible kidney replacement therapy.

Abdominal Hernia

Abdominal hernia affects 12–37% of PD patients [47, 48].

In 2003, Balda et al. [49] assessed the effect of hernias in patients on PD and demonstrated that hernia recurrence rates were low without negatively affecting PD technique survival.

In 2011, Wakasugi et al. [50] retrospectively analyzed nine patients on continuous ambulatory peritoneal dialysis (CAPD) with abdominal hernias. All these

patients undergoing hernia repair did not switch to HD, which suggested the possibility that perioperative HD can be skipped.

Moreover, from the 6-year experience of Sodo et al. with repair of abdominal hernias and simultaneous placement of a PD catheter, hernia recurrence and peritonitis were not reported during a mean follow-up of 551 days with continued PD [51].

Thereafter, based on the clinical experience and literature reviews, Khoury et al. [52] recommended the following:

- Careful initial examination before placement of the PD catheter to rule out any type of hernia
- Periodic abdominal examination after insertion of the PD catheter
- Elective hernia repair before initiation of PD
- Bilateral hernia repair for any young male patient with an inguinal hernia on one side

Abdominal Surgery in PD

Hsu et al. [53] described five patients undergoing radical nephrectomy by the retroperitoneal approach, preserving the peritoneal membrane, which helped in the immediate initiation of PD after the surgery. The authors preferred the retroperitoneal approach to the transperitoneal approach to preserve the peritoneal membrane due to no significant complications during the wound healing or peritoneal leakage over the postoperative period.

Malavade and Bargman's study [54] showed wound dehiscence or other surgical complication didn't present on the patients with nephrectomy and later started dialysis within 1 year. But, the risk for incisional hernia and retroperitoneal PD fluid leak were high, postoperatively.

Other surgeries, such as bariatric surgery in the form of sleeve gastrectomy, were also described in a PD patient by Imam et al. [55], which showed the patient did very well both in surgery and PD treatment.

Plus, laparoscopic cholecystectomy in 11 PD patients with the same procedure in 33 patients not on PD demonstrated none of PD-encountered peritonitis, leaks, or hernias, as Ekici et al. [56] reported.

Favorable outcomes in PD patients with stomas were described by Korzets et al. [57] in 1992. And in 1998, Twardowski et al. [58] demonstrated with 6-year data that PD can still be applied in PD patients with abdominal complications just using pre-sternal PD catheters, which was also successfully used in children by Chadha et al. [59].

As suggested by the reports described above, PD can be performed safely in such scenarios. An assessment of abdominal surgeries, and the possible complications, including abdominal surgeries, in this patient population, with appropriate tailoring of the PD prescription, can allow these patients to remain on PD without compromising their quality of life or increasing their healthcare expense.

Pregnancy

Although those receiving peritoneal dialysis are at a high risk of encountering maternal and fetal complications, the occurrence of successful pregnancies in women with end-stage kidney disease undergoing PD is becoming more common. With developed dialysis technology, women in this population should be monitored by a dedicated team of renal physicians and an obstetric team to ensure the best maternal and fetal outcomes.

The first successful full-term pregnancy in an ESKD patient on HD was first reported in 1971 by Confortini et al. [60]. Subsequently, in 1983, the first sustained pregnancy on PD was reported in a patient who had been receiving the treatment for 2.5 years. Despite the many challenges faced by pregnant ESKD women, the rate of successful pregnancy and live birth has increased to approximately 30% from the 1990s [61, 62]. From the 54 reported cases of pregnant women receiving PD available in the literature since 1983, 47 cases (87%) have resulted in a successful pregnancy, but only 6 cases were full-term deliveries [63, 64].

Preliminary data from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) showed that the live birth rate of HD patients on conception was approximately twice as likely as on PD patients [65].

In another large survey of pregnancy and ESKD from the United States, 1.1% of reproductive-aged women receiving PD conceived versus 2.4% on hemodialysis [66].

This lower conception rate in PD women has been postulated to be related to the presence of fluid in the abdominal cavity or inadequate dialysis intensity [65].

Interestingly, once conception was successful, infant survival was not significantly different between the hemodialysis and PD patients. It is also suggested that the outcome of pregnancy was better in women who conceived before starting dialysis than in women who conceived after starting dialysis [66].

The improved pregnancy outcomes are presumably related to amount of residual urine, conception during peri-initiation of the PD period, medication adjustment, tailoring PD prescription, blood pressure control, and correction of metabolic and nutrition profiles.

The goal of 2.2–2.6 for Kt/V in pregnant women on dialysis was suggested [66, 67]. But in the practical sense, most nephrologists would rather treat the patients clinically by monitoring blood parameters and adjusting the PD prescription as needed than following the Kt/V indicators. In the guideline published in 2015 [68], the authors do not recommend using Kt/V and/or peritoneal creatinine clearance as a measurement of dose of dialysis in pregnancy due to the lack of studies considering these markers in correlation to pregnancy outcomes.

Anemia should be managed with erythropoiesis-stimulating agents (ESAs) and vitamins [68]. The usual dose of ESA (Epogen) for a patient on PD is 50 U/kg twice weekly and should be frequently adjusted upward by 50–100% due to increasing body weight. Iron supplementation at a dose of 1–15 mg/day and folic acid 1 mg/day enhance the efficacy of ESA, and iron stores should be assessed before ESA is initiated. It is advisable that the hemoglobin levels be maintained at 10–11 g/dL, hematocrit at 30–35%, and serum ferritin of 200–300 μg/mL [68].

The patient's fluid status should be reviewed by the nephrologist and obstetrician closely. Ideally, a weekly or fortnightly ultrasound of the uterus should be carried out from the second trimester onward to assess the growth and weight of the fetus. Dry weight must be reviewed continuously because weight gain is expected to reach between 0.3 kg and 0.5 kg of weight per week during the second and third trimesters.

Blood pressure should be controlled with pregnancy-safe medications, such as long-acting nifedipine, labetalol, or methyldopa [69]. Management of hypertension in pregnancy to a tighter target is not associated with adverse neonatal effects or pregnancy outcomes, as the data from the Control of Hypertension in Pregnancy Study (CHIPS) has shown, which randomized women with diastolic blood pressure of 85 or 100 mmHg [70].

It should be pointed out that malnutrition is often caused by the lack of appetite experienced by pregnant women on PD due to the sugar load in dialysate and the delayed gastric emptying effect of dialysate inside the peritoneal cavity. It can also be caused by the hypercatabolic effect of pregnancy in ESKD and the decreased appetite induced by acidosis and urea levels. The recommendation for those PD patients who are at risk of protein depletion is 1.4–2.1 g per kg body weight/day of protein. In early pregnancy, water-soluble vitamins and minerals are essential, including folic acid. Other vitamins that should be supplemented are vitamin C, thiamine, riboflavin, niacin, and vitamin B6. And also the positive calcium balance should be retained with sufficient supplementation of calcium and vitamin D3 (Ref).

Several theoretical advantages are offered by PD to the pregnant patients: the continuous therapy avoids the fluid shifts and blood pressure variations, frequently seen in HD, and no heparin is required, which is thought to reduce bleeding complications. However, some complications specifically to PD have been reported in pregnancy including peritonitis and exit site infection. And also the complications, such as hemoperitoneum [71, 72], catheter malposition [73], catheter-related pain [74], and PD catheter-related uterine trauma, remain as concerns or challenges of PD therapy [72].

Conclusion

Peritoneal dialysis is a very effective, relatively inexpensive, and safe form of kidney replacement therapy. It is important to keep an open mind about the different subgroups of ESKD patients who can benefit from the therapy.

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