Peritoneal Dialysis: An Update for 2015

By John Burkart

In 2015, the overwhelming majority of patients with treated ESRD in the United States are treated with in-center hemodialysis (CHD), whereas peritoneal dialysis (PD) is the predominant modality used by home dialysis patients. Overall, this is not markedly different from the historical distribution of modality use: most patients use CHD. However, not only has the observed historical decline in percentage of patients using PD (1995–2009) stabilized, but the percentage of those using PD has actually been increasing since 2010 (1).

This trend is most likely a result of the new prospective payment system for Medicare patients, which has “bundled” the payment and treatment so that the overall payment amount per week of typical dialysis is the same for CHD and PD, effectively removing any unintended financial incentives that had favored the use of CHD. This trend may also be fueled by clinical observations over the past decade, such as those showing that in the United States, improvements in survival for patients using PD have outpaced those for patients using CHD, so that the differences in 5-year survival, if any, are probably not clinically meaningful (2–4). As a result, the PD population in the United States has almost doubled since 2008 (from about 23,000 in 2008 to about 46,000 in 2014 in the 10 largest providers) (1).

Some have been concerned that because of lack of infrastructure and of nurses’ and physicians’ experience, this new growth would be associated with a reported increase in mortality or a decrease in technique survival. To date there have been no published data to support that concern. One unexpected problem associated with this rapid growth in PD is the inability of the current manufacturers of peritoneal dialysate fluids to keep up with the demand for bags needed for cylinder therapy. This is being addressed by industry, national societies, and the US Food and Drug Administration. Most patients now use cylinder therapy (automated peritoneal dialysis [APD]), one of the submodalities of PD, because of issues related to their quality of life. Although there could be differences in selected patient outcomes between these two submodalities of PD, there are no consistently reported clinically relevant differences in clinical outcome between APD and manual exchanges (5). Transferring to hemodialysis for catheter-related problems and peritonitis continues to be a major concern, as is the realization that BP and volume may not be managed in PD as well as they potentially could be, given the daily nature of the therapy.

Peritoneal dialysis access–related issues

Catheter-related issues remain a reason for transfer to CHD. Most PD catheters are placed in the operating room by surgeons using open dissection. This requires general anesthesia, does not allow direct visualization of the peritoneal cavity and true pelvis, and may frequently result in primary catheter dysfunction because of the inability to identify anatomic arrangements that interfere with catheter function. In addition, because of difficulties in scheduling surgeons and operating rooms, delays in peritoneal catheter placement have often necessitated the initiation of dialysis with CHD by use of a temporary vascular access and delaying the start of PD.

The degree of success with the historical open dissection approach and other techniques (such as the percutaneous needle–guide wire approach, with or without imaging guidance, and the laparoscopic technique) is provider related and is associated with matching the appropriate placement technique with the appropriate patient. Ancillary procedures such as tacking of redundant omentum (omentumopexy) and lysis of adhesions that can potentially be performed by the advanced laparoscopic approach cannot be done with open dissection. In one report, when the advanced laparoscopic technique was used for catheter implantation, only 3 percent of patients transferred to hemodialysis as a result of catheter failure, compared with 17 percent nationally (6), and one center reported that 99 percent of catheters were problem free at 24 months (7). These ancillary procedures, however, are needed in only about one third of all patients, so it may be reasonable to avoid costs and minimize the risk of general anesthesia by using other implantation techniques.

Coincident with the recent growth in PD use are data such as the estimates from the 2013 Medicare Physician/Supplier Procedure use summary, which suggests that the use of open dissection for PD catheter placement is decreasing (now 22 percent of catheters placed) whereas the use of other techniques such as surgical laparoscopy (26 percent in 2007; 52 percent in 2013) is increasing. In addition, to facilitate the need for short-term and urgent PD catheter placement and avoidance of scheduling conflicts, general anesthesia, and overall costs, percutaneous needle–guide wire techniques (with imaging guidance, generally by interventional radiologists [22 percent], or without imaging guidance, generally by interventional nephrologists [4 percent]) have become more commonly used for placing PD catheters.

The important issue when other techniques are used is how the subcutaneous portion of the PD catheter is placed, because the ability to salvage a catheter is important, and efforts are being put in place to replace a PD catheter when there is a complication or nonfunction is related to the correctness of the original placement. Therefore, to improve overall outcomes and minimize costs, we should foster the use of a multidisciplinary approach to PD catheter implantation. This multidisciplinary approach does not necessarily involve all physicians at once but does imply that different physician specialists must work together to promote the delivery of seamless medical care. PD catheters are currently placed by surgeons, interventional radiologists, and interventional nephrologists.

Most practicing interventional radiologists and interventional nephrologists did not learn how to place PD catheters during training and are learning on the job. Moreover, surgery, radiology, and nephrology residency and fellowship programs continue to be poorly prepared and largely inadequate with respect to teaching PD catheter access procedures. In a survey of surgical residency programs in the United States, it was found that fellows typically place only two to five catheters during their training, and when asked, 38 percent of fellowship directors stated they could not provide more training. Unfortunately, 77 percent of PD programs start fewer than 10 patients with PD each year (8). As a result, catheter dysfunction remains a problem for PD patients and one of the major causes for morbidity and transfer to hemodialysis. Educating the physician who places the PD access is important, and efforts are being put in place by major national dialysis providers and the International...
Infectious complications

Infectious complications of PD, specifically peritonitis, remain a major cause of patient morbidity, hospitalization, technique failure with transfer to CHD, and occasionally death worldwide. Therefore, prevention of infections is of significant importance, and a multifaceted, multidisciplinary approach is needed to optimize patient outcomes. Dialysis unit home therapy infrastructure, nursing expertise, and patient training are keys to successful care of the catheter exit site is an important element of patient training. Part of the unit’s infection prevention protocol should include the use of daily topical prophylactic antibiotics such as mupirocin (12) or gentamicin cream (12) at the exit site. Mupirocin cream has been shown to result in a significant reduction in exit site infections compared with routine care in more than one study, and in another study gentamicin was found to be superior to mupirocin. Other antibiotics have been tried but have not been found to be superior to mupirocin or gentamicin and, in the case of Polysporin triple antibiotic use, may be associated with increased risk of fungal colonization (14). Other prophylactic measures should include use of appropriate antibiotic prophylaxis during procedures such as dental care, gastrointestinal procedures, and gynecologic procedures and after trauma to the exit site. Units should develop policies and procedures for timely diagnosis and treatment of peritonitis. It is important to state that many factors other than bacterial peritonitis may cause cloudy fluid. They include, but are not limited to, fungal peritonitis, chemical peritonitis, eosinophilic peritonitis, malignancy, and a specimen that is taken from a “dry” abdomen.

It is important not only to get a total white blood cell (WBC) count but also to obtain a differential count. If there is a significant number of neutrophils, or polymorphonuclear neutrophils (PMNs), is likely that the patient has bacterial peritonitis no matter what the total cell count may be. With these approaches, generally one should expect an overall infection rate of less than one episode of peritonitis every 3 years. With the use of exit-site antibiotic prophylaxis, the relative proportion of gram-positive episodes of peritonitis has markedly decreased, so when the patient presents with peritonitis, broad-spectrum antibiotic therapy should be initiated until the specific culture results are known.

The International Society for Peritoneal Dialysis has published guidelines for the diagnosis and treatment of myofibroblasts, which seem to play a critical role in the development of peritoneal fibrosis. It is typically characterized by mesothelial thickening, with an overabundance of the myofibroblasts, which, along with appropriate antifungal therapy, is the current treatment recommendation for fungal peritonitis. In many patients (almost one third), it is possible to replace the catheter and restart PD after the fungal peritonitis resolves (17). Prior antibiotic treatment is a predisposing factor for fungal peritonitis; therefore, antifungal prophylaxis during prolonged antibiotic use is recommended by many (18).

Cardiovascular issues and PD

Typically, PD patients receive therapy daily—most often 24 hours a day, in fact. As a result, one would think there would be an opportunity for much better BP and volume control than with CHD. Despite the continuous nature of the therapy, however, two studies showed that blood pressure was controlled in only about 50 percent of patients in one study (19,20). Another study showed that PD patients were more likely to have signs of volume overload compared with CHD patients (35.7 percent vs 12.4 percent) and evidence of hypertension (64.3 percent vs 51.2 percent) (21). Despite these observations, in one prospective study there was no association between quartiles of BP control and survival. However, observational studies have shown an association between ultrafiltration (UF) volume and presumably sodium removal and patient survival (22,23). Hence the recommendation in the latest Kidney Disease Outcome Quality Initiative guidelines for adequacy of PD to “normalize BP and volume” without mentioning a specific numeric BP goal. What is not a new observation, but is increasingly recognized as an important clinical caveat to address, is the dissociation between UF volume and the percentage of that UF volume that is sodium replete. Because of the presence of transcellular aquaporins, across which a high glucose gradient is maintained, a substantial portion (almost 50 percent) of the UF with a dextrose (glucose) dwell is sodium free. As a result of this “free water” UF volume, diuretic sodium drops. If the dwell is short (as it is with overnight cyclers), sodium cannot catch up with the free water by moving from blood to dialysate; therefore, any dilution of sodium in the UF volume can catch up with the free water. Generally, because one usually does only three or four overnight dwells, this is not of consequence, especially if a patient has any residual renal function. But if one were to do more than four dextrose exchanges over a 9-hour period, the patient could experience transient hypernatremia, with long UF glucose gradients, and thereby a large UF volume, about 50 percent of it would be sodium free.

One should also pay attention to the daytime dwell. If dextrose dwells are used, these long dwells are long enough for sodium to catch up with the UF volume that moved across the aquaporins. However, if the UF volume that moved across the glucose gradient will have dissipated as a result of glucose absorption, and UF would have ceased. In these cases, if the dwell time is long, UF volumes may be minimal, or in fact, as a result of continuous absorption of fluid from the PD cavity (almost 1 ml/min), drain volumes could be less than instilled volumes. If alternative osmotic agents such as polyglucose solutions (icodextrin) have been developed to correct some of these issues. Icodextrin has a slow but sustained UF profile, and over 95 percent of the UF volume is sodium replete. Many of the volume-overloaded PD patients who in the past transferred to CHD because of “membrane failure” are in fact currently well treated by individualization of the therapy and changes of the prescription as needed on the basis of transport types. One does this by changing dwell times, using midday medications, and considering the use of alternative osmotic agents such as icodextrin. Possibly in part as a result of these nuances in sodium and water removal, historical data suggest that the relative risk of death was related to transport type (higher relative risk of death in rapid transporters, who tend to have problems with UF volume during longer dwells) (24). However, in more contemporary cohorts, where prescriptions have been adjusted and various PD solutions and submodalities of PD have been used, that association has not been found (25,26).

In contrast to what has been observed in CHD patients, PD is likely associated with less rapid drops in BP and less transient cardiac wall motion abnormalities or cardiac stunning (27). Additionally, CHD patients are known to have transient cognitive deficits associated with their treatment and an increased incidence of abnormatilities in brain white matter than would otherwise be expected in age-matched control individuals. Presumably there would also be less transient brain ischemia in PD patients. Interest- ingly, data from the US Renal Data System suggest that there is a higher prevalence of dementia in CHD patients (28), and in a retrospective study evaluating the effect of dialysis modality on the development of dementia over time, PD patients were significantly less likely to experience dementia.

Finally, a very interesting but not unsuspected clinical observation that could result in low drain volumes has been formally described. This has to do with the fact that the concentration of dextrose or icodextrin in the dialysate fluid (say 4.25 percent dextrose or 7.5 percent icodextrin) may not be the concentration of that osmotic agent in the peritoneal cavity if a large residual volume is present when the fluid is instilled, effectively diluting the osmotic agent at instillation (29). As a result, if there was a 450-ml residual volume and 2 L of 7.5 percent icodextrin was infused, this would result in an immediate dilution of the icodextrin to about a 6.23 percent solution with resultant less UF—an important clinical caveat to add to our current diagnosis of a low UF volume in PD patients using icodextrin.

PD membrane "failure" and the long-term patient

A historical observation about PD was that it “worked” for a few years, but then patients experienced “membrane failure,” had problems with volume overload, and needed to transfer to CHD. As mentioned in the earlier discussion, this actually was often due to loss of residual kidney function and failure of the nephrology team to individualize and adjust the therapy in response, or to the patients’ unwillingness to change their dialysis prescriptions or inability to make needed dietary changes. Despite that recognition, one of the most important challenges to the PD community is preservation of PD membrane integrity or prevention of “peritoneal membrane failure” over time. Peritoneal membrane failure is functionally characterized by UF failure. This is reported to occur in up to 30 percent of patients receiving long-term PD. Some of the underlying factors include changes in the peritoneum that can be seen in diabetic microangiopathy. Deposition of advanced glycosylation end-products in peritoneal tissue has been described (30). It is well recognized that peritoneal fibrosis is typically characterized by mesothelial cell loss, angiogenesis, and progressive submesothelial thickening, with an overabundance of myofibroblasts in many patients (31). The origin of these myofibroblasts, which play a critical role in the development of peritoneal fibrosis, remains unknown. Some have suggested a role for interleukin-1, although the evidence is not unequivocal. A recent study demonstrated that IL-1β treatment of mesothelial cells results in an increase in the expression of aquaporin-1, a transcellular aquaporin that is present in the peritoneum (32). The exact role of this protein in peritoneal fibrosis is unknown, but it may contribute to the changes seen in this disease.
role in these changes in PD, is controversial. Some believe that myofibroblasts originate through epithelial–mesenchymal transition of mesothelial cells, and although in vivo and in vitro data suggest that observed morphologic changes in mesothelial cells are associated with the acquisition of mesenchymal markers, few of the cells in vivo and biomarkers specific enough to prove that mesothelial cell epithelial–mesenchymal transition is the true process driving peritoneal fibrosis (32). For now, though, this is the working hypothesis.

It is well demonstrated that over time during PD, increasing numbers of active myofibroblasts are stimulated by a variety of fibrogenic cytokines, such as TGF-β. In rodent models, PD has been associated with a local renin-angiotensin system, which over time during PD may be dysregulated (33). The question is: what causes this dysregulated, injured environment? Is it the result of repeated instillations of high-glucose–containing fluids or the presence of glucose degradation products (GDP) in dialysate? In vitro studies have suggested that when human peritoneal mesothelial cells are stimulated to produce vascular endothelial growth factor, incubation with an angiotensin converting enzyme or an angiotensin receptor blocker inhibits or reduces its production, suggesting a downregulation of the local renin-angiotensin system (34). Clinical outcomes in a prospective, observational cohort study, PD patients who were taking an angiotensin converting enzyme or an angiotensin receptor blocker for any reason were less likely to have their peritoneal membrane transport characteristics increase over time (35). It therefore seems reasonable to use one of these drugs for peritoneal, residual kidney, or intradialytic patients that have no glucose. The results of studies using biocompatible PD solutions or low-glucose (glucose-sparing) regimens have not confirmed an overwhelming clinical benefit in terms of membrane preservation over conventional PD solutions (36). These regimens seem to improve some aspects of PD health and viability but with no overall consistent clinical benefit in peritoneitis, peritonitis-free survival, or patient survival. Some low-GDP solutions may be associated with greater urine volume and “preservation” of renal function, but this effect may be compounded by the small increase in peritoneal transport with their use and less peritoneal UF volume, which may have an effect on residual kidney volume. A recent prospective randomized 12-month study using low glucose exposure (amino acids, icodextrin, and glucose), low-GDP fluids compared with conventional glucose fluids found increased urine volume, less biochemical evidence of membrane damage, lower inflammatory cytokines, and higher antifibrotic markers in patients using these fluids than in patients using conventional dialysate. Further studies are needed.

Conclusions

The use of PD in the United States is growing. This is likely driven by clinical outcome studies suggesting equal or better early survival in patients using PD than in those using CHD and by the financial realities of a bundled payment structure. It is recognized that the ability to individualize each patient’s PD prescription is helpful to optimize certain patient outcomes. To date there are no data to show that this recent acceleration in PD use has been associated with any overall detriment in patient outcomes.

References