REVIEW ARTICLE

The present and the future of Peritoneal Dialysis

Fourtounas C

Department of Internal Medicine- Nephrology, Patras University Hospital, Patras Greece.

Part of the present paper has been presented during the 1rst EKONY Congress in Patras 2011

Abstract

Peritoneal Dialysis (PD) has been established as an effective renal replacement therapy complementary to hemodialysis (HD) for End-Stage Renal Disease (ESRD) patients. However, its prevalence has been decreasing during the last decades in Western Europe and USA, whereas in some regions such as Hong Kong or Mexico its penetration remains higher than 70%. These dramatic differences around the world can not be explained only by medical reasons. There are also many "hidden" factors such as financial issues (for profit HD), completely unproven dogmatic beliefs about the superiority of HD over PD, or more recently a fear about "the epidemic" of encapsulating peritoneal sclerosis in long standing PD. During the last two decades, there has been a significant progress in many fields of PD, such as reduced PD related peritonitis rates by new connectology systems, prevention of exit site infections by mupirocin or gentamycin ointments, wide application of automated PD by reliable cyclers, use of icodextrin for the long exchanges, better preservation of residual renal function, newer and more biocompatible PD solutions and timely placement of PD catheters by nephrologists. In addition, basic and clinical research is focusing on future improvements such as the use of two icodextrin exchanges per day, the application of new PD solutions with low sodium concentration, the wider use of "assisted" PD, and a better understanding of the pathogenetic mechanisms that may lead to peritoneal sclerosis with new therapies that may prevent it. The dilemma regarding the best modality for ESRD (HD or PD?) should be abandoned and the modern nephrologist should be wise enough to recognize the possible advantages and contraindications of each modality and confident enough to offer both of them to the ESRD patients as appropriate. Hippokratia 2011; 15 (Suppl 2): 15-20

Key words: hemodialysis, icodextrin, peritoneal dialysis, peritonitis, exit site infection, review

Corresponding author: Costas Fourtounas, Department of Internal Medicine Nephrology, Patras University Hospital, Rio-Patras 26500, Greece. Tel: 00302610999724, Fax :00302610999724, e-mail:cfourt@usa.net

Currently about 200,000 patients are treated with Peritoneal Dialysis (PD) around the world, whereas more than 1.5 million patients are undergoing hemodialysis (HD) for End-Stage Renal Disease (ESRD)[1]. However there are countries such as Mexico or Hong Kong where PD dominates by far (70-80%). In Europe the prevalence of PD varies with Sweden, Norway, UK and the Netherlands to dialyze almost 20% of their ESRD patients with PD and Southern Europe countries to have a mean PD prevalence of about 8-10%. In Canada almost 18% of the ESRD patients are undergoing PD and in US the PD rates are about 7-8%. These dramatic differences around the world are not so easy to be explained [1-4]. It is well known that non medical reasons (financial) always drive heath-care practices but we should not neglect the medical reasons as well.

If we look carefully back to the past, the trend for the fall of PD penetration started in the late nineties. In 1995 Bloembergen et al reported dramatically higher mortality rates for patients who started PD in the late eighties compared with HD patients during the same time period [5]. In 1996 the CANUSA study reported that the targets for PD adequacy should include a Kt/V urea of > 2.1 and a weekly creatinine clearance of more than 70L[6]. Soon, these targets were adopted by the first KDOQI guidelines, although there were many voices against these recommendations. So then, the well informed nephrologist would be quite reluctant to offer to his patients a renal replacement modality with proven inferiority compared with the gold standard of HD and should strive to achieve these high targets of adequacy for the poor patients which would select to undergo this "second line" modality. Wise PD authorities argued these data and provided scientific evidence that the initial assumptions were completely false[7]. During the next years the ADEMEX study showed that the adequacy targets should be revised [8] and finally the new KDOQI guidelines adopted these results. Recently Mehrotra et al reported that PD and HD can achieve similar survival rates for the US patients which have started renal replacement therapy after 1996 [9]. During the last years, PD was accused once again as a fatal and short term only modality that eventually leads to encapsulating peritoneal sclerosis and death, even after successful renal transplantation[10].

All these data show that PD has not only dedicated "supporters" but also devoted "enemies". The open

Table 1: "Hot issues" for the present and the future of PD.

- Infectious Complications
- PD catheters
- Residual Renal Function
- Automated PD
- Assisted PD
- PD solutions
- Encapsulating Peritoneal Sclerosis

minded nephrologist should consider PD and HD not as competitors but collaborators in order to fight ESRD. If we omit the financial issues (that are the most important) we should try to examine the scientific evidence about PD. Is it a second line treatment for second line nephrologists, is it inferior to HD, patients like it or hate it, or has its own place in the treatment of ESRD? We strongly believe that any effort to speculate PD will impact the holistic approach regarding ESRD treatment.

Hard scientific data show that there are some barriers about PD, if we consider it as a self-therapy. However as we will see, there are also alternatives in order to overcome them if we wish to do so [2,11,12]. In the next lines we will try to provide data about the "hot issues" that may impact the present and the future of PD (Table 1).

Infectious Complications

PD related peritonitis rates have improved substantially during the last decades mainly due to the introduction of the double bag system and the improvements in the various connectologies with many PD units reporting peritonitis rates of one episode every more than 30 months [12-14]. However this progress is mainly due to the decrease of the milder forms of PD related peritonitis due to skin contamination by Staph. epidermitis strains, whereas the serious episodes due to organisms such as Pseudomonas, Staph aureus of fungi still remain a significant problem and a frequent cause of (temporary or even permanent) transfer to HD.

During the last years there were significant improvements regarding the prevention of the infectious complications of PD mainly by the daily application of mupirocin (for Staph aureus) or gentamycin ointment (for Staph aureus and Pseudomonas infections) to the exit-site of the PD catheter[12]. Two studies also provide evidence about the prophylactic use of antifungal agents (oral nystatin of fluconazole) for the prevention of fungal infections in PD patients receiving antibiotics for various reasons, especially in PD units with high rates of fungal peritonitis[15,16].

However, optimal and frequent training of the PD patient by the nursing staff with a detailed educational protocol, early identification of patients at risk and frequent data collection and evaluation remain the cornerstone of a successful PD program in order to prevent and minimize infectious complications.

PD catheter: The lifeline of the PD patient

Among the several reasons that may contribute to the decline of PD, a key factor remains the permanent access to the peritoneal cavity. The PD catheter has been characterized a0s the "lifeline" of the PD patient and catheter related problems remain a cause of permanent transfer to HD in up to 20% of patients needing a therapy change[17].

Although traditionally the vast majority of PD catheters has been inserted by surgeons under local or general anaesthesia with the open dissection or the laparoscopic technique, many nephrologists have started getting involved in catheter insertion, by percutaneous methods using the Seldinger technique[18,19] or more recently by the peritoneoscopic method [20,21].

PD catheter implantation by nephrologists has been reported to improve PD utilization and expansion of the PD programs in US[22], or Asia [23], mainly due to timely placement of the PD catheter, avoiding unnecessary delays that may drive patients to permanent HD.

As the European Best Practice Guidelines for Peritoneal Dialysis state, the most important element of success for PD catheter implantation does not rely on the technique used (surgical, percutaneous, or laparoscopic) but the experience of the people getting involved [24]. Li and Chow[25] also underline that "practice makes perfect", and all nephrologists dealing with PD and facing problems should be encouraged to start putting PD catheters by themselves regardless of the preferred technique.

The International Society of Peritoneal Dialysis[26] and the European Best Practice Guidelines for Peritoneal Dialysis[24] guidelines suggest that regardless of the technique used, one years' PD catheter survival should exceed 80% and all PD units should strive to increase their PD catheter survival rates.

Residual Renal Function

Preservation of Residual Renal Function (RRF) is one of the main clinical benefits of PD compared with HD. The initial hypotheses was that PD offers better stability of the volume status avoiding the excessive and rapid ultrafiltration of a HD session, where a large volume of ultrafiltrate is removed during a short time period (4 hours) with frequent hypotensive episodes[27] . This was also the explanation regarding a more rapid loss of RRF in patients undergoing APD compared with CAPD in some studies. However, some authorities claim that this happens just because PD patients tend to be more volume overloaded compared with HD patients[28].

The CANUSA study was the first which underlined the close association of RRF (and not peritoneal solute clearances) with better patient survival rates and this was also confirmed by others[6,29]. So, every PD program should strive to maintain RRF as long as possible by prescribing loop diuretics and angiotensin converting enzyme inhibitors or angiotensin receptor blockers and avoiding any nephrotoxic agents such as non-steroidal anti-inflammatory agents, unnecessary radio contrast media or aminoglycosides[28].

There is also growing experience from HD, that ultrapure HD dialysate preserves RRF compared with regular HD implying that biocompatibility may have a significant impact on RRF preservation[27]. The new more biocompatible PD solutions may also preserve RRF in PD patients as shown in small retrospective studies but further and better designed prospective studies are needed before definite conclusions. Fan et al in randomized prospective study with 93 PD patients failed to show any benefit of a more biocompatible bicarbonate/lactate PD solution regarding RRF[30].

Automated Peritoneal Dialysis

Automated PD is growing fast as a PD modality around the world. Although in USA the majority of the PD patients (almost 60%) are undergoing APD, its penetration is also increasing in Europe and Australia, expect Asia probably due to financial restrictions[31].

The European best practice guidelines for PD suggest that APD should be used according to patients' preference, problems with increased intraperitoneal pressure and problems with adequate ultrafiltration and solute removal[24]. However, there are multiple prescriptions of APD such as nocturnal APD with a dry daytime or with a wet abdomen during daytime with or without a daily exchange (CCPD). All these modifications of APD make comparisons with classical CAPD rather difficult[32]. Its main advantage is that the patient is undergoing his/her therapy during the night and remains free for his daily activities. So, it is preferable for the younger who want to work fulltime, the children and the students. It is also recommended for the elderly which are treated by "assisted" PD at home as the nurse has to visit them only twice per day in order to connect and disconnect them from the cycler.

Regarding medical issues it is definitely offering an advantage for the high/fast transporters as the short dwell time allows them to have increased ultrafiltrate per exchange. Although theoretically APD should be associated with lower peritonitis rates due to the positive effect of the dry abdomen on the immune function of the peritoneal cavity and the fewer connections per day, the clinical results are rather conflicting. Piraino and Sheth[33] have suggested that this may be due to the different connectologies used in these studies (luer-lock versus spiking) and the different prescriptions of APD (none versus one day time exchange). Regarding residual renal function (RRF), there are many studies reporting a more rapid loss with APD. Mehrotra[32] suggests that the effect of cycler use on native renal clearances, if any, is small and probably not clinically significant but a recent study[34] from the Netherlands is not in favour of his suggestions. Finally there are concerns about the nature of the modality as the main advantages of classic CAPD were its simplicity (no machines) and its continuous nature (24 hours per day). Although these concerns are of value (especially for the solute clearances) patients' preferences and quality of life issues are of paramount importance when we are dealing with a chronic and devastating disease [35].

"Assisted" Peritoneal Dialysis

The dialysis population is aging and carries a significant burden of co-morbidities. The number and extend of co-morbid illnesses in the average patient initiating dialysis have increased over the past two decades highlighting the need for more attention not only for prognostic reasons, but mainly for the day-to-day care of these patients. So, many patients are incapable for self therapies such as PD at home, or have no family members/partners to help[37].

The recently introduced concept of "assisted" PD, where patients can be assisted in performing their PD exchanges at home by private nurses is a real solution for these patients, provided that the local health systems are reimbursing this modality[38-41]. Most programs are choosing to offer "assisted" PD with cyclers (APD) than with CAPD due to fewer connections per day. The results regarding patient survival rates and infectious complications are improving but better results are reported when the "assistants" are well trained or registered PD nurses. Unfortunately, at the moment in Greece and many other European countries except Denmark, France, Belgium and one region in Spain, assisted PD is not reimbursed[41]. Intermittent PD (IPD) in the hospital three times per week with high dialysate volumes (15-20L) for 8-10 hours per session might be an option for this special ESRD population with acceptable survival rates [42].

Peritoneal Dialysis solutions

Icodextrin containing PD solutions

Icodextrin containing PD solutions have been introduced in PD for more than 10 years and have undergone extensive clinical studies[43]. Although icodextrin was firstly indicated only for PD patients with ultrafiltration failure and a high transport status, it has some extra advantages as it is not containing glucose and has been shown to result to higher ultrafiltration rates and sodium removal compared with hypertonic glucose containing solutions during the long exchange[44,45]. However there is an inter- and intra- variation of the amount of ultrafiltrate produced by icodextrin that has not been fully explained and diabetics and males seem to produce more ultrafiltrate[46]. There were some experimental studies about a possible detrimental effect of icodextrin in mesothelial cell cultures [45] questioning its biocompatibility mainly due to its acidic nature (pH 5.2), but its glucose-sparing effect with minimal concentrations of the harmful glucose degradation products (GDPs) and/or Advanced Glycosylation End-products (AGEs) is overcoming these experimental concerns. Gobin et al[48] were the first to explore the use of two daytime icodextrin exchanges for 6 months in 9 patients undergoing APD, as a glucose-sparing regimen, reporting also a slight increase of blood icodextrin levels at 3 months which remained stable at the 6 months of the study. Sav et al[39] have prospectively studied 40 CAPD patients with ultrafiltration failure with two icodextrin exchanges for 3 months and reported higher daily ultrafiltration rates and a decrease in left ventricular mass index (LVMI), with a mild but not statistically signifi-

cant increase of blood icodextrin and maltose levels at 3 months[49]. Dousdampanis et al[50] have recently reported reduced body weight in 6 out of 9 PD patients during a 6 months study with two icodextrin exchanges per day. Although hyponatremia remains a theoretical side effect of icodextrin therapy there were no reports of such side effects in these 3 studies. However, the possible accumulation of maltose in the blood during more extensive (> 6 months) therapy should be examined in future studies, whereas the application of 2 icodextrin exchanges will increase the daily cost of therapy[50].

New more biocompatible PD solutions

Long-term systemic exposure of the peritoneal cavity to glucose results into peritoneal membrane structural and functional alterations over time and eventually to technique failure expressed clinically as ultrafiltration failure and reduced solute clearance. In addition glucose and its degradation products have been implicated into various undesirable systemic metabolic and cardiovascular side effects. The new more biocompatible PD solutions have been designed in order to reduce the concentration of GDPs by separating the PD solution into two (Balance®, Fresenius) or three (Gambrosol Trio®, Gambro) chambers and by approaching to a more physiological pH (7.4), by a combination of bicarbonate/lactate (Physioneal®, Baxter) or pure bicarbonate (Bicavera®, Fresenius) as a buffer[12,13,51,52].

Most of the studies regarding these new PD solutions have shown reduced infusion pain and better correction of metabolic acidosis, although some times they may induce even alkalosis in patients with significant RRF[53]. The first reports with these new solutions have given rather enthusiastic results regarding better preservation of RRF, reduced rates of peritonitis and better preservation of the peritoneal membrane function,as expressed by several peritoneal biomarkers . Nevertheless, a randomized study from UK failed to maintain this enthusiasm[30]. In addition two studies from Korea have claimed a survival benefit for patients treated with these solutions [54,55]. Both studies were criticized for their design (retrospective and observational) and until now it is premature to conclude that the new PD solutions provide a clear survival benefit despite their significant cost. However, their theoretical superiority has created a great enthusiasm and in Europe there is trend to use them in the younger and healthier PD patients.

Low sodium PD solutions

Many patients undergoing PD are frequently overloaded. A low sodium diet and adequate sodium removal by PD are equally important in order to avoid overhydration. There are only a few studies examining sodium removal rates in PD patients and it has been argued that APD may be less effective than CAPD in sodium removal due its frequently lower capacity for ultrafiltration and also due to the short dwell schedule that may result in significant Na sieving and less efficient Na removal[56,57].

During the last years there was an attempt to develop new low sodium solutions in order to increase sodium removal by PD. Nakayama et al[58] from Japan have studied two different PD solutions with low sodium (126 and 118 mmol/L) in 41 CAPD patients. Although sodium removal was increased, there were concerns about hyponatremia and the need for increased concentrations of glucose in order to compensate the low osmolality of these solutions. Davies et al[59] in a short multicentre prospective study used two different low sodium PD solutions (115 mmol/l with 2.0% glucose and 102 mmol/L with 2.5% glucose) for one exchange per day in 25 patients for two months. He reported increased sodium removal but the ultrafiltrate was reduced in the 102 mmol/L solution. In patients with adequate ultrafiltrate, he reported improvement of blood pressure, thirst and fluid status but no hyponatremia during the study period. Both studies have shown a rather positive impact of the low sodium PD solutions on sodium removal, but the risk of hyponatremia and the need to use higher glucose concentrations should be further studied [59].

Encapsulating Peritoneal Sclerosis

The concerns regarding Encapsulating Peritoneal Sclerosis (EPS) have increased during the last years in the literature. There are many suggestions that PD duration should not exceed 5 years or it should be terminated when there are indications of ultrafiltration failure, as long-term PD is associated with increased rates of EPS[12,60]. Although EPS is a severe condition with significant mortality its pathogenesis remains rather obscure. The “two hit” hypothesis, where there is a first hit by the chronic exposure to PD that leads to simple sclerosis and in a few patients a second hit that eventually leads to EPS seems the most rationale according to the current knowledge[10]. In addition most cases of EPS in the literature are not associated with PD (spontaneous EPS) and there is indirect evidence that there is also a genetic background in patients with EPS. Epidemiological data from large centers have shown that the incidence of EPS is not so high (average 1.5%, range 0.5-2.8%), but is usually accompanied with a fatal outcome[61,62]. Treatment of EPS includes preventive measures, transfer to HD with prophylactic periodic peritoneal lavage and tamoxifen. For the most severe cases, patients should receive total parenteral nutrition and surgical exploration by experienced surgeons[61]. For the PD patients which are candidates for renal transplantation after a long period in the modality, it seems prudent to avoid steroid avoiding or sparing protocols and perhaps to aim towards mTOR inhibitors based immunosuppressive protocols and avoid calcineurin inhibitors which may induce or aggravate fibrosis[10].

Conclusions

Since its introduction by Moncrief and Popovich and its expansion after the application of the plastic bags by Oreopoulos, PD remains a field of continuous improvements and innovations. Although its prevalence and penetration decreased during the last years, this was mainly due to non medical reasons[1,2,4]. The new change of policy

regarding reimbursement of ESRD therapies (the "bundling") will overcome many of the financial issues that favored HD for a long time in USA[63]. All the unbiased scientific data provide evidence that PD is at least as effective as HD for the treatment of ESRD, if applied correctly. This is the main issue that should be our focus for the future. Local and international nephrology societies should strive to offer more education, training and exposure to PD, in order to equip the young nephologists with the appropriate knowledge, regarding the best therapeutic options for the individualized ESRD patient.

Conflict of Interest: None to declare

References:

1. Lameire N, Van Biesen W. Epidemiology of peritoneal dialysis: a story of believers and non believers. Nat Rev Nephrol. 2010; 6: 75-82.
2. Van Biesen W, Lamiere N, Vanholder R. Why less success of the peritoneal dialysis programs in Europe? Nephrol Dial Transplant. 2008; 23: 1478-1481.
3. Khawar O, Kalantar-Zadeh K, Lo WK, Johnson D, Mehrotra R. Is the declining use of long-term peritoneal dialysis justified by outcome data? Clin J Am Soc Nephrol. 2007; 2: 1317-1328.
4. Fourtounas C, Vlachojannis JG. PD underutilization in Europe: A call to action. Nephrol Dial Transplant. 2008; 23: 3365-3366.
5. Bloembergen WE, Port FK, Mauger EA, Wolfe RA. A comparison of cause of death between patients treated with hemodialysis and peritoneal dialysis. J Am Soc Nephrol. 1995; 6: 184-191.
6. The CANUSA study Group. Adequacy of dialysis and nutrition in continuous peritoneal dialysis: association with clinical outcomes. Canada-USA (CANUSA) Peritoneal Dialysis Study Group. J Am Soc Nephrol. 1996; 7: 198-207.
7. Vonesh EF, Moran J. Mortality in end-stage renal disease: a reassessment of differences between patients treated with hemodialysis and peritoneal dialysis. J Am Soc Nephrol. 1999; 10: 354-365.
8. Paniagua R, Amato D, Vonesh E, Correa-Rotter R, Ramos A, Moran J, et al. Mexican Nephrology Collaborative Study Group. Effects of increased peritoneal clearances on mortality rates in peritoneal dialysis: ADEMEX, a prospective, randomized, controlled trial. J Am Soc Nephrol. 2002; 13: 1307-1320.
9. Mehrotra R, Chiu YW, Kalantar-Zadeh K, Bargman J, Vonesh E. Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. Arch Intern Med. 2011; 171: 110-118.
10. Garosi G, Oreopoulos DG. No need for an "expiry date" in chronic peritoneal dialysis to prevent encapsulating peritoneal sclerosis. Int Urol Nephrol. 2009; 41: 903-907.
11. Oreopoulos DG, Coleman S, Doyle E. Reversing the decreasing peritoneal dialysis (PD) trend in Ontario: a government initiative to increase PD use in Ontario to 30% by 2010. Perit Dial Int. 2007; 27: 489-495.
12. Oreopoulos D, Thodis E, Paraskevas KI. The promising future of long-term peritoneal dialysis. Int Urol Nephrol. 2008; 40: 405-410.
13. Oreopoulos DG, Ossareh S, Thodis E. Peritoneal dialysis: past, present, and future. Iran J Kidney Dis. 2008; 2: 171-182.
14. Fourtounas C, Savidaki E, Dousdampanis P, Hardalias A, Kaliakmani P, Papachristou E, et al. Peritonitis during the first year after commencement of peritoneal dialysis has an impact on technique survival and patient morbidity. Adv Perit Dial. 2006; 22: 50-54.
15. Lo WK, Chan CY, Cheng SW, Poon JF, Chan DT, Cheng IK. A prospective randomized control study of oral nystatin prophylaxis for Candida peritonitis complicating continuous ambulatory peritoneal dialysis. Am J Kindey Dis. 1996; 28: 549–552.
16. Restrepo C, Chacon J, Manjarres G. Fungal peritonitis in peritoneal dialysis patients: successful prophylaxis with fluconazole, as demonstrated by prospective randomized control trial. Perit Dial Int. 2010; 30: 619-625.
17. Flanigan M, Gokal R. Peritoneal catheters and exit-site practice toward optimum peritoneal access: a review of current developments. Perit Dial Int. 2005; 25: 132-139.
18. Perakis K, Stylianou KG, Kyriazis JP, Mavroeidi VN, Katsipi IG, Vardaki EA, et al. Long-term complication rates and survival of peritoneal dialysis catheters: the role of percutaneous versus surgical placement. Sem Dial. 2009; 22: 569-575.
19. Henderson S, Brown E, Levy J. Safety and efficacy or percutaneous insertion of peritoneal dialysis catheters under sedation and local anesthesia. Nephrol Dial Transplant. 2009; 24: 3499-3504.
20. Asif A, Tawacol J, Khan T, Vieira CF, Byers P, Gadalean F, et al. Modification of the peritoneoscopic technique of peritoneal catheter insertion: experience of an interventional dialysis program. Semin Dial. 2004; 17: 171-173.
21. Zaman F. Peritoneal dialysis catheter placement by nephrologists. Perit Dial Int. 2008; 28: 138-141.
22. Asif A, Byers P, Gadalean F, Roth D. Peritoneal dialysis underutilization: the impact of n interventional nephrology peritoneal dialysis access program. Sem Dial. 2003; 16: 266-271.
23. Goh BL, Ganeshadeva YM, Chew SE, Dalimi MS. Does peritoneal dialysis catheter insertion by interventional nephrologists enhance peritoneal dialysis penetration? Sem Dial. 2008; 21: 561-566.
24. Dombros N, Dratwa M, Feriani M, Gokal R, Heimburger O, Krediet R, et al. European Best Practice Guidelines for peritoneal dialysis: Peritoneal Access. Nephrol Dial Transplant. 2005; 20(Suppl 9): S8-S12.
25. Li PK, Chow KM. Importance of peritoneal dialysis catheter insertion by nephrologists: practice makes perfect. Nephrol Dial Transplant. 2009; 24: 3274-3276.
26. Gokal R, Alexander S, Ash S, Chen DW, Danielson A, Holmes C, et al. Peritoneal catheters and exit site practice: toward optimum peritoneal access: 1998 update. Perit Dial Int. 1998; 18: 11-33.
27. Davies SJ. Preserving residual renal function in peritoneal dialysis: volume or biocompatibility? Nephrol Dial Transpl. 2009; 24: 2620-2622.
28. Perl J, Bargman JM. The importance of residual kidney function for patients on dialysis: a critical review. Am J Kidney Dis. 2009; 53: 1068-1081.
29. Bargman JM, Thorpe KE, Churchill DN. CANUSA Peritoneal Dialysis Study Group Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol. 2001; 12: 2158-2162.
30. Fan SL, Pile T, Punzalan S, Raftery MJ, Yaqoob MM. Randomized controlled study of biocompatible peritoneal dialysis solutions: effect on residual renal function. Kidney Int/ 2008; 73: 200-206.
31. Liakopoulos V, Dombros N. Patient selection for automated peritoneal dialysis: for whom, when? Perit Dial Int. 2009; 29(Suppl 2): S102-107.
32. Mehrotra R. Long-term outcomes in automated peritoneal dialysis: similar or better than in continuous ambulatory peritoneal dialysis? Perit Dial Int. 2009; 29(Suppl 2): S111-114.
33. Piraino B, Sheth H. Peritonitis - does peritoneal dialysis modality make a difference? Blood Purif. 2010; 29(2): 145-149.
34. Michels WM, Verduijn M, Grootendorst DC, le Cessie S, Boeschoten EW, Dekker FW, et al. Decline in Residual Renal Function in Automated Compared with Continuous Ambulatory Peritoneal Dialysis. Clin J Am Soc Nephrol. 2011; 6: 537-542.

35. Michels WM, van Dijk S, Verduijn M, le Cessie S, Boeschoten EW, Dekker FW, et al Quality of life in automated and continuous ambulatory peritoneal dialysis. Perit Dial Int. 2011; 31: 138-147.
36. Jager KJ, Korevaar JC, Dekker FW, et al. The effect of contraindications and patient preference on dialysis modality selection in ESRD patients in the Netherlands. Am J Kidney Dis. 2004; 43: 891-899.
37. Dimkovic N, Aggarwal V, Khan S, Chu M, Bargman J, Oreopoulos DG. Assisted peritoneal dialysis: what is it and who does it involve? Adv Perit Dial. 2009; 25: 165-70.
38. Povlsen JV, Ivarsen P. Assisted Automated Peritoneal Dialysis (AAPD) for the functionally dependent and elderly patient. Perit Dial Int. 2005; 25 (Suppl 3): S60-S63.
39. Lobbedez T, Moldovan R, Hurault de Ligny B, El Haggan W, Ryckelynck JP. Assisted peritoneal dialysis. Experience in a French renal department. Perit Dial Int. 2006; 26: 671-676.
40. Verger C, Duman M, Durand PY, Veniez G, Fabre E, Ryckelynck JP. Influence and type of home assistance on the prevention of peritonitis in assisted automated peritoneal dialysis patients. An analysis of data from the French Language Peritoneal Dialysis Registry. Nephrol Dial Transplant. 2007; 22: 1218-1223.
41. Brown EA, Dratwa M, Povlsen JV. Assisted peritoneal dialysis – an evolving dialysis modality. Nephrol Dial Transplant 2007; 22: 3091-3092.
42. Fourtounas C, Hardalias A, Dousdampanis P, Savidaki E, Vlachojannis JG. Intermittent Peritoneal Dialysis (IPD): An old but still effective modality for severely disabled ESRD patients. Nephrol Dial Transplant. 2009; 24: 3215-3218.
43. Davies SJ. Exploring new evidence of the clinical benefits of icodextrin solutions. Nephrol Dial Tranplant. 2006; 21(Suppl 2): 47-50.
44. Krediet RT. Effects of icodextrin on the peritoneal membrane. Nephrol Dial Transplant. 2010; 25: 1373-1375.
45. Finkelstein F, Healy H, Abu-Alfa A, Ahmad S, Brown F, Gehr T, et al. Superiority of icodextrin compared with 4.25% dextrose for peritoneal ultrafiltration. J Am Soc Nephrol. 2005; 16: 546-554.
46. Ventruroli D, Jeloka TK, Ersoy FF, Rippe B, Oreopoulos DG. The variability in ultrafiltration achieved with icodextrin, possibly explained. Perit Dial Int. 2009; 29: 415-421.
47. Chan TM, Yung S (2007) Studying the effects of new peritoneal dialysis solutions on the peritoneum. Perit Dial Int. 27(S2): S87-S93.
48. Gobin J, Fernando S, Santacroce S, Finkelstein FO. The utility of two daytime icodextrin exchanges to reduce dextrose exposure in automated peritoneal dialysis patients: a pilot study of nine patients. Blood Purif. 2008; 26: 279-283.
49. Sav T, Oymak O, Inanc MT, Dogan A, Tokgoz B, Utas C. Effects of twice-daily icodextrin administration on blood pressure and left ventricular mass in patients on continuous ambulatory peritoneal dialysis. Perit Dial Int. 2009; 29: 443-449.
50. Dousdampanis P, Trigka K, Chu M, Khan S, Venturoli D, Oreopoulos D, et al. Two icodextrin exchanges per day in peritoneal dialysis patients with ultrafiltration failure: one center's experience and review of the literature. Int Urol Nephrol. 2011; 43: 203-209.
51. Bargman JM. New technologies in peritoneal dialysis. Clin J Am Soc Nephrol. 2007; 2: 576-580.
52. McIntyre CW. Update on peritoneal dialysis solutions. Kidney Int. 2007; 71: 486-490.
53. Fourtounas C, Savidaki E, Dousdampanis P, Roumelioti M, Hardalias A, Kalliakmani P, et al. Acid-base profile and predictors of metabolic acidosis in patients undergoing peritoneal dialysis with lactate and bicarbonate buffered PD solutions. Adv Perit Dial. 2006; 22: 187-191.
54. Lee HY, Park HC, Seo BJ, Do JY, Yun SR, Song HY et al. Superior patient survival for CAPD patients treated with a peritoneal dialysis fluid with neutral pH and low glucose degradation product concentration (BALANCE). Perit Dial Int. 2005; 25: 248-255.
55. Lee HY, Choi HY, Park HC, Seo BJ, Do JY, Yun SR et al. Changing prescribing practice in CAPD patients in Korea: Increased utilization of low GDP solutions improves patient outcome. Nephrol Dial Transplant. 2006; 21: 2893-2899.
56. Rodríguez-Carmona A, Pérez Fontán M. Sodium removal in patients undergoing CAPD and automated peritoneal dialysis. Perit Dial Int. 2002; 22: 705-713.
57. Fourtounas C, Hardalias A, Dousdampanis P, Papachristopoulos V, Savidaki E, Vlachojannis JG. Sodium removal in Peritoneal Dialysis: The role of icodextrin and PD modalities. Adv Perit Dial. 2008; 24: 27-31.
58. Nakayama M, Kasai K, Imai H, TRM-280 Study Group. Novel low Na peritoneal dialysis solutions designed to optimize Na gap of effluent: kinetics of Na and water removal. Perit Dial Int. 2009; 29: 528-535.
59. Davies S, Carlsson O, Simonsen O, Johansson AC, Venturoli D, Ledebo I et al. The effects of low-sodium peritoneal dialysis fluids on blood pressure, thirst and volume status. Nephrol Dial Transplant. 2009; 24: 1609-1617.
60. Bargman JM, Krediet RT, Lo WK, Selgas R, del Peso G, Auxiliadora Bajo M, et al . What are the problems with using the peritoneal membrane for long-term dialysis? Semin Dial. 2008; 21: 11-23.
61. Trigka K, Dousdampanis P, Chu M, Khan S, Ahmad M, Bargman J, et al. Encapsulating peritoneal sclerosis: a single-center experience and review of the literature. Int Urol Nephrol. 201; 43: 519-529.
62. Balasubramaniam G, Brown EA, Davenport A, Cairns H, Cooper B, Fan SL, et al. The Pan-Thames EPS study: treatment and outcomes of encapsulating peritoneal sclerosis. Nephrol Dial Transplant. 2009; 24: 3209-3215.
63. Burkart J. The future of peritoneal dialysis: PD in 2010 and beyond Dial & Transplant. 2010; 41: 349-353.