

PERITONEAL DIALYSIS: HOW WE CAN ACHIEVE IMPROVEMENT OF PD PENETRATION

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Abstract: Peritoneal dialysis (PD) is a well established renal replacement therapy (RRT). It appears to have some excellent properties as a first line RRT, as it preserves residual renal function, improves clearance of middle and larger solutes and preserves vascular access.

To improve PD penetration, it is necessary to have a well established pre-dialysis programme, as information seems to be the clue in the choice and the success of PD.

Furthermore, it is important that patients and nurses are well educated in the practice of PD. This reduces the need for hypertonic bags by better compliance with the salt restrictive diet, reduces exposure to dialysate per se by adapting the number and length of the dwells to the needs of the patient, and increases peritonitis-free survival, thus prolonging the survival of the peritoneal membrane. In addition, it is clear that the use of new low glucose degradation products and normal pH solutions will also improve the technical success of PD. The collaboration of industry with local health care providers could be a necessity in overcoming the costs induced by the import of dialysate solutions paid for in foreign currency.

Key words: peritoneal dialysis, pre-dialysis programme, glucose degradation products.

Introduction

The use of dialysis and transplantation as complementary therapies in the provision of care for renal replacement therapy (RRT) is well established. Peritoneal dialysis (PD) and haemodialysis (HD) are most commonly seen as

competitive therapies. There are, however, many arguments for considering them as complementary, rather than competitive. These arguments not only include medical, but also logistical, financial and psycho-social aspects of RRT, as reviewed elsewhere by Van Biesen *et al.* [1].

The need for RRT has an enormous impact on the life-expectancy and the psycho-social life of the patient, and means a substantial cost to society in both money and manpower. In addition, the increasing number of patients in need of RRT, and the potential benefits of an earlier start of RRT, should urge the nephrological community to consider new patient-and-treatment flow charts to optimize the treatment of RRT in a cost-effective way [2]. The “integrated care concept” [3] advocates that RRT-providing centres should offer all three treatment modalities in an unbiased way to the patient. By this approach, the advantages of HD, PD and transplantation can be fully exploited, while the disadvantages can be avoided. In this way, every patient can be on the most optimal treatment for her/him at every particular stage of her/his disease.

Despite the first-proven benefits of PD, PD penetration throughout the world seems not to have increased to the same extent as HD penetration.

This paper will focus on 1) why having a PD programme is of importance; 2) how we can improve the number of patients starting on PD and 3) how we can extend the technique success of patients started on PD.

Benefits of integrated care/having a PD programme

The unbiased choice between the different RRT modalities is the first premise of the integrated care approach. This implies that all dialysis centres should at least offer the possibility of starting PD. This, in turn, implies education of patient and clinician regarding the advantages and disadvantages of the different RRT modalities, the potential benefits of PD-first, and the potential need to transfer between different modalities.

There is now accumulating evidence that educated “empowered” patients have better outcomes [4], and that patients who start on PD have more knowledge of their therapy than HD patients [5]. This results in a greater feeling of well-being, and probably also a better outcome. It is striking in this context that late-referred patients have a survival disadvantage in haemodialysis, but that this effect disappears in the peritoneal dialysis patients, probably because these patients receive highly intense education during their training [6].

The RRT-providing centre has to develop a well-structured assessment and education policy, including dedicated staff members conducting interviews in the home environment, with patient, family members and relatives.

The availability of both an established PD and HD programme increases the flexibility of the centre, as a PD programme can be expanded or shrunk according to the needs, which is far more difficult to achieve through a HD pro-

gramme. Eventual (short-term) emergency transfers, e.g. from PD to HD in case of severe peritonitis, or from HD to PD when vascular access fails, can also be managed more easily.

Although patients should have free choice between HD and PD, there are some advantages to start RRT with PD, and patients should be informed about these potential advantages.

The advantages of PD first have been well rehearsed elsewhere, and include (a) preservation of residual renal function, (b) improved early graft function after renal transplantation, (c) preservation of vascular access sites, (d) avoidance of blood-borne infection, e.g. hepatitis C, (e) financial and logistical advantages, and (f) improved quality of life and employment rates. There is also increasing evidence that the mortality risk is lower on PD as compared to HD during the first three to four years of RRT [7–10].

The preservation of the residual renal function on PD is probably not only related to the better haemodynamic stability of PD patients, but is probably also related to removal of middle molecules or biocompatibility issues since, as also in haemofiltration, residual renal function seems to be preserved [11].

Although the exact mechanism remains to be unravelled [12], there is evidence that the outcome after transplantation is superior [13] or at least equal [14] in patients initially treated with peritoneal dialysis.

As far as PD after a failed transplantation is concerned, there seems to be no evidence that this should be a contra-indication [15, 16].

There is accumulating evidence that peritoneal dialysis and the integrated care approach are, at least in the western world, more economic than haemodialysis, even when the costs related to eventual switches between modalities are taken into account [17]. It is, however, clear that the final cost of a modality will also strongly depend upon local circumstances. It is quite conceivable that in countries where the cost of labour is low, and where imported peritoneal dialysis solutions have to be paid for in cash in foreign currency, the picture might be the opposite. Therefore, most companies producing PD fluids are trying to set up joint ventures to produce the fluids locally, thus reducing the price of disposables.

There is evidence that when adequate education programmes are set in motion patients are more likely to opt for peritoneal dialysis as a first option [2, 18]. It has also been proven that the centre experience is enhanced if a sufficient critical mass is achieved to ensure expertise and quality of care.

Extending technique success in peritoneal dialysis

If we want to improve the penetration of PD, it is not only necessary to improve the inflow of patients starting on PD, we should also prolong the technique success of PD.

When looking at the reasons for transfer from PD to HD, it is clear that some reasons relate to the technique itself. On the other hand, it is also clear that the experience of the centre is of importance in the maintenance of a successful PD. Analysis of peritoneal dialysis services in the Netherlands (NECOSAD) has shown that in small peritoneal dialysis units there is a higher technical failure rate. These data have been confirmed in an analysis of USRDS data, which also showed worse survival in centres with a limited patient number on a certain modality.

There are various reasons why the initial benefits of PD disappear over time.

Both the progressive decrease of the residual renal function (RRF), and the deterioration of the peritoneal membrane function lead to an impaired clearance and ultrafiltration in long-term PD patients.

In a cohort of patients maintained on PD for more than 7 years, Faller *et al.* [19] have demonstrated that the decrease in adequacy was nearly totally attributable to a decline and finally a disappearance of RRF. While, in these patients, there was an initial improvement of blood pressure control after the start of PD, the beneficial evolution became totally inverse after the disappearance of RRF. It has long been neglected that residual renal function is important even in patients on RRT. The most important observation from the CANUSA study was the relation between RRF and outcome [20]. Studies such as that of Moist *et al.* [21] demonstrate that measures to preserve RRF also apply in patients on RRT.

In this regard, preservation of residual renal function by the avoidance of nephrotoxic medication, the use of Angiotensin Converting Enzyme-Inhibitors or Angiotensin Receptor Blockers is of importance [22], and should be advocated. The use of diuretics has in itself no impact on the preservation or deterioration of the residual renal function, but can be of great importance in the maintenance of fluid balance [23].

Davies *et al.* observed a steady decrease of ultrafiltration capacity in a cohort of patients with long-term PD [24]. This decrease of ultrafiltration was associated with an increase of MTAC for small solutes. This tendency became more expressed after 3 to 4 years of PD. It is striking that there is the impression that this creeping deterioration of peritoneal membrane function is only present in a certain subgroup of patients, and that other patients have a stable peritoneal membrane function even after years of PD treatment. The inter-patient variability in the evolution of RRF and peritoneal membrane function urge the clinician to test both on a regular basis. Methods to evaluate RRF and peritoneal membrane function are elegantly reviewed by Van Biesen *et al.* [25] and Davies *et al.* [26] respectively.

The progressive decline of RRF and the peritoneal membrane function urge the patient to use progressively more fluids, in a progressively more complex exchange regimen. This ultimately leads to a decreased quality of life, patient burn-out and finally technique failure.

In order to improve the survival of the peritoneal membrane, it is of importance to use biocompatible fluids, and avoid exposure to glucose.

There is compelling indirect, both in vivo and in vitro, evidence about the improved quality and biocompatibility of low-GDP PD solutions [27, 28]. There is also clinical evidence about the improved biocompatibility of low-GDP solutions as expressed by inflow pain reduction [29]. It has also been suggested in some trials that the use of low-GDP solutions leads to a reduction of peritonitis incidence (Montenegro *et al.*, abstract ASN 2003), which by itself is of course an important reason for patient drop-out from PD.

From the data of the Korean PD registry, it is apparent that survival in patients on low GDP solutions was superior. Although this was not a randomised trial, and some methodological problems thus remain, these are encouraging results that indeed the technique survival of patients on PD can be improved.

Besides the use of low-GDP solutions, it is also necessary to reduce glucose exposure as much as possible. This can be achieved by optimising the treatment of the patient to his/her needs and peritoneal membrane characteristics. It is important to understand that using more exchanges does not always result in better clearance, mostly to the contrary [30], but it does increase the glucose exposure tremendously, as glucose absorption is most enhanced in the beginning of the dwell.

Conclusion

There is now evidence that peritoneal dialysis has had advantages as a first-line renal replacement therapy. Therefore, PD should be offered as an option to all patients without clear medical contra indications.

To increase PD penetration, a good working pre-dialysis care and educational programme should be in place, as late referral is a major factor in low PD penetration. Some authors even believe that the good results of PD in the initial phase of renal replacement therapy are due to the better patient empowerment induced by PD educational programmes.

There is also evidence that the PD first strategy improves the long-term outcome of ESRD patients.

To improve the technique success of PD, it is important to use low-GDP solutions, and to adapt the prescribed regimen to the needs of the patient.

REFERENCES

1. Van Biesen W., Vanholder R., Lameire N. (2000): The role of peritoneal dialysis as the first-line renal replacement modality. *Perit Dial Int*; 20(4): 375–83.
2. Van Biesen W., Wiedemann M., Lameire N. (1998): End-stage renal disease treatment: a European perspective. *J Am Soc Nephrol*; 9(12 Suppl): S55–S62.
3. Van Biesen W., Davies S., Lameire N. (2001): An integrated approach to end-stage renal disease. *Nephrol Dial Transplant*; 16(Suppl 6): 7–9.
4. Curtis B.M., Ravani P., Malberti F. *et al.* (2005): The short- and long-term impact of multi-disciplinary clinics in addition to standard nephrology care on patient outcomes. *Nephrol Dial Transplant*; 20(1): 147–54.
5. Rubin H.R., Fink N.E., Plantinga L.C. *et al.* (2004): Patient ratings of dialysis care with peritoneal dialysis vs hemodialysis. *JAMA*; 291(6): 697–703.
6. Stack A.G. (2003): Impact of timing of nephrology referral and pre-ESRD care on mortality risk among new ESRD patients in the United States. *Am J Kidney Dis*; 41(2): 310–8.
7. Termorshuizen F., Korevaar J.C., Dekker F.W. *et al.* (2003): Hemodialysis and peritoneal dialysis: comparison of adjusted mortality rates according to the duration of dialysis: analysis of The Netherlands Cooperative Study on the Adequacy of Dialysis 2. *J Am Soc Nephrol*; 14(11): 2851–60.
8. Van Biesen W., Vanholder R.C., Veys N. *et al.* (2000): An evaluation of an integrative care approach for end-stage renal disease patients. *J Am Soc Nephrol*; 11(1): 116–125.
9. Fenton S.S., Schaubel D.E., Desmeules M. *et al.* (1997): Hemodialysis versus peritoneal dialysis: a comparison of adjusted mortality rates. *Am J Kidney Dis*; 30(3): 334–42.
10. Heaf J.G., Lokkegaard H., Madsen M (2002): Initial survival advantage of peritoneal dialysis relative to haemodialysis. *Nephrol Dial Transplant*; 17(1): 112–7.
11. McKane W., Chandna S.M., Tattersall J.E. *et al.* (2002): Identical decline of residual renal function in high-flux biocompatible hemodialysis and CAPD. *Kidney Int*; 61(1): 256–65.
12. Van Biesen W., Vanholder R., Van Loo A. *et al.* (2000): Peritoneal dialysis favorably influences early graft function after renal transplantation compared to hemodialysis. *Transplantation*; 69(4): 508–14.
13. Goldfarb-Rumyantzev A.S., Hurdle J.F., Scandling J.D. *et al.* (2005): The role of pretransplantation renal replacement therapy modality in kidney allograft and recipient survival. *Am J Kidney Dis*; 46(3): 537–49.
14. Chalem Y., Ryckelynck J.P., Tuppin P. *et al.* (2005): Access to, and outcome of, renal transplantation according to treatment modality of end-stage renal disease in France. *Kidney Int*; 67(6): 2448–53.
15. de Jonge H., Bammens B., Lemahieu W. *et al.* (2006): Comparison of peritoneal dialysis and haemodialysis after renal transplant failure. *Nephrol Dial Transplant*; 21(6): 1669–74.

16. Badve S.V., Hawley C.M., McDonald S.P. *et al.* (2006): Effect of previously failed kidney transplantation on peritoneal dialysis outcomes in the Australian and New Zealand patient populations. *Nephrol Dial Transplant*; 21(3): 776–83.
17. Shih Y.C., Guo A., Just P.M., Mujais S. (2005): Impact of initial dialysis modality and modality switches on Medicare expenditures of end-stage renal disease patients. *Kidney Int*; 68(1): 319–29.
18. Ravani P., Marinangeli G., Stacchiotti L., Malberti F. (2003): Structured pre-dialysis programs: more than just timely referral? *J Nephrol*; 16(6): 862–9.
19. Faller B., Lameire N. (1994): Evolution of clinical parameters and peritoneal function in a cohort of CAPD patients followed over 7 years. *Nephrol Dial Transplant*; 9(3): 280–6.
20. Bargman J.M., Thorpe K.E., Churchill D.N. (2005): Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol*; 12(10): 2158–62.
21. Moist L.M., Port F.K., Orzol S.M. *et al.* (2000): Predictors of loss of residual renal function among new dialysis patients. *J Am Soc Nephrol*; 11(3): 556–64.
22. Suzuki H., Kanno Y., Sugahara S. *et al.* (2004): Effects of an angiotensin II receptor blocker, valsartan, on residual renal function in patients on CAPD. *Am J Kidney Dis*; 43(6): 1056–64.
23. Medcalf J.F., Harris K.P., Walls J. (2001): Role of diuretics in the preservation of residual renal function in patients on continuous ambulatory peritoneal dialysis. *Kidney Int*; 59(3): 1128–33.
24. Davies S.J., Phillips L., Naish P.F., Russell G.I. (2001): Peritoneal glucose exposure and changes in membrane solute transport with time on peritoneal dialysis. *J Am Soc Nephrol*; 12(5): 1046–51.
25. Van Biesen W., Van Der T.A., Veys N. *et al.* (2006): Evaluation of the peritoneal membrane function by three letter word acronyms: PET, PDC, SPA, PD-Adequest, POL: what to do? *Contrib Nephrol*; 150: 37–41.
26. Davies S.J., Brown B., Bryan J., Russell G.I. (1993): Clinical evaluation of the peritoneal equilibration test: a population-based study. *Nephrol Dial Transplant*; 8(1): 64–70.
27. Wieslander A., Linden T. (1996): Glucose degradation and cytotoxicity in PD fluids. *Perit Dial Int*; 16 Suppl 1: S114–8.
28. Williams J.D., Topley N., Craig K.J. *et al.* (2004): The Euro-Balance Trial: the effect of a new biocompatible peritoneal dialysis fluid (balance) on the peritoneal membrane. *Kidney Int*; 66(1): 408–18.
29. Mactier R.A., Sprosen T.S., Gokal R. *et al.* (1998): Bicarbonate and bicarbonate/lactate peritoneal dialysis solutions for the treatment of infusion pain. *Kidney Int*; 53(4): 1061–7.
30. Demetriou D., Habicht A., Schillinger M. *et al.* (2006): Adequacy of automated peritoneal dialysis with and without manual daytime exchange: A randomized controlled trial. *Kidney Int*; 70(9): 1649–55.

Резиме

ПЕРИТОНЕАЛНА ДИЈАЛИЗА: КАКО МОЖЕ ДА СЕ ПОСТИГНЕ ПОДОБРУВАЊЕ ВО ПЕНЕТРАЦИЈАТА НА ПД**Van Biesen W.***Renal Division, University Hospital Ghent, Belgium*

Перитонеалната дијализа (ПД) е добро востановена ренална заместувачка терапија (РЗТ). Изгледа дека таа има одлично својства како РЗТ од прва рака, бидејќи ја зачувува резидуалната ренална функција, го подобрува клиренсот на средните и големи молекули и го заштедува васкуларниот пристап.

За да се подобри пенетрацијата на ПД, потребно е да се има добро востановена пре-дијализна програма, бидејќи информацијата изгледа дека е клучна во изборот и успехот на ПД.

Понатаму, е важно пациентите и сестрите да бидат добро едуцирани за практичните вредности на ПД. На тој начин се редуцира потребата за хипертонични кеси преку обезбедување на подобар коплајанс со рестрикција на сол во диететиката, се намалува излагањето на дијализатот пер се преку адаптирање на бројот и должината на траењето на промените според потребите на пациентот, и се зголемува времето поминато без перитонити, на тој начин пролонгирајќи го преживувањето на перитонеалната мембрана. Понатаму, јасно е дека употребата на новите раствори со нормален рН и ниска концентрација на гликозилациски деградациони продукти исто така ќе го подобрат успехот на третманот со ПД. Конечно, соработката на индустријата со локалните провајдери на здравствени услуги може да биде неопходна за надминување на скапата цена од увозните дијализатни раствори платени во странска валута.

Клучни зборови: перитонеална дијализа, пре-дијализна програма, гликоза деградациони продукти.

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