Adequacy of peritoneal dialysis and the importance of preserving residual renal function

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Abstract

The well-being and survival of dialysis patients not only depend on the removal of waste products and excess fluid, but also on the prevention of cardiovascular complications by maintaining normovolaemia and adequate blood pressure and avoidance of ectopic calcification. Also, the maintenance of nutritional status and adequate removal of middle molecules are amongst the most important issues in long-term renal replacement therapy. In this review, attention is given to optimal peritoneal small solute clearance and Kt/V and to the evidence concerning the role of residual renal function. In addition, factors that can influence this residual function are also discussed.

Keywords: adequacy; Kt/V; residual renal function; peritoneal dialysis

Introduction

Adequacy of treatment by peritoneal dialysis (PD), in fact, comprises much more than merely sufficient removal of small solutes by the dialysis regimen employed. Adequate treatment in addition demands strict attention to a host of other factors which endanger the well-being and survival of our patients on PD. Amongst these are the preservation of a normal volume-status and blood pressure, acceptable plasma levels of calcium, phosphate and parathyroid hormone, the aim towards prevention of renal osteodystrophy and ectopic calcification, and maintenance of a normal nutritional status with an adequate intake of protein and energy. In addition, the removal of middle molecules such as β2-microglobulin, which induce dialysis-associated amyloidosis when excessively accumulated, must be maintained at a certain level. Continuous attention is furthermore required in attempting to prevent the strikingly increased occurrence of cardiovascular disease in dialysis patients, which is at least partially the consequence of their abnormal lipid profile, hyperhomocysteinaemia, hypertension and anaemia. Finally, the health of these patients is frequently threatened by the infectious complications, which result from the presence of the peritoneal catheter and the daily exchange procedures.

Although the removal of small solutes is of unquestionable importance in providing adequate PD, recent studies have shown that it is equally relevant to focus attention on other factors as well, and that an increase in peritoneal Kt/V cannot compensate for other shortcomings in the management. Among the other determinants of survival, preservation of residual renal function has been shown to be of major importance.

In the present article, we review the recent literature with regard to optimal peritoneal small solute clearance and Kt/V, and the evidence for the cardinal role of residual renal function.

Peritoneal clearance

In 1997, the National Kidney Foundation Dialysis Outcomes Quality Initiative (NKF-DOQI) published clinical practice guidelines for the adequacy of PD, in an attempt to provide evidence-based guidelines for adequate PD [1]. At that time, many nephrologists believed that the guidelines provided a minimum of instruction for PD small solute clearance, and felt that more would probably be better in terms of well-being and survival for their patients. Uncertain, however, was to what degree further increases in Kt/V might contribute to better outcomes, and how this potential benefit should be weighed against the increased burden of spending more effort and time on the patient, as well as the burden to society due to increasing medical costs.
as a result. Based on the data of the CANUSA study, the NKF-DOQI Peritoneal Dialysis Adequacy Work Group advised that a target total solute clearance of Kt/V ≥ 2.0/week (APD ≥ 2.1/week) should be strived for. Implicit in this guideline, although as yet inadequately studied, was the assumption that one unit of small solute clearance (expressed as Kt/V) by residual renal function was equivalent to one unit of peritoneal clearance, and that the two might be interchanged and added at will, without consequences for the outcome of the patient.

In 2002, the ADEMEX study, which explored the benefits of higher levels of peritoneal solute clearance on the mortality of PD patients, was published [2]. The study enrolled 965 PD patients, randomly assigned to an intervention and a control group, in a 1:1 ratio. In the control group, patients were treated with a conventional PD prescription consisting of four daily exchanges with 2 l of standard PD solution. Patients in the intervention group were treated with a tailored PD prescription, to achieve a peritoneal creatinine clearance of 60 l/week/1.73 m². The two patient groups were similar with respect to other determinants of survival, including the level of residual renal function. After a minimum follow-up of 2 years, an intention to treat analysis revealed similar patient survival in the two groups. This study demonstrates that, within the range of small solute clearances studied (mean peritoneal creatinine clearance in the control group 46.1 vs 56.9 l/week/1.73 m² in the intervention group), increases in peritoneal small solute clearance failed to provide a survival benefit. These data gave rise to confusion in the nephrological community and have led to the assumption that, above a certain threshold, increasing small molecular clearance will not provide additional benefit to the patients. To put matters in perspective however, it may be useful to underscore that, expressed in another way, peritoneal creatinine clearance in the intervention group was 4.3 ml/min, whereas the difference in creatinine clearance between the control and intervention group amounted to only 1 ml/min. Thus, the question remains whether large benefits in clinical outcome might be expected from, in an absolute sense, minor changes in clearance.

Importance of residual renal function

Several recent publications underline the importance of residual renal function for the morbidity and survival of PD patients. In a logistic regression analysis of factors independently associated with death in a cohort study of 1446 PD patients, weekly urinary creatinine clearance proved to be a major determinant [3]. An increase of 101/week/1.73 m² resulted in a 40% reduction of mortality (P < 0.001), whereas a similar increase of peritoneal weekly creatinine clearance provided only 10% reduction (P = 0.41). In a re-analysis of the CANUSA study, each 51/week/1.73 m² increment in glomerular filtration rate (GFR) was associated with a 12% decrease in the relative risk of death, but no such association was found for peritoneal creatinine clearance [4]. This was in agreement with the results of the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD-2), which showed that for each millilitre per minute 1.73 m² of renal GFR, a 12% reduction in mortality was found. In contrast, no significant effect of peritoneal creatinine clearance on patient survival was observed. In addition, the different impacts of peritoneal and renal clearance were confirmed in an analysis of combined patient and technique survival and in an analysis of a number of quality-of-life variables [5]. Part of the relation between loss of residual renal function and mortality might be explained by the fact that comorbid factors, such as inflammation, may influence both mortality and residual renal function [6–8]. However, residual renal function also plays an important role in the removal of middle molecules, and the prevention of dialysis-associated amyloidosis caused by the tissue deposition of β 2-microglobulin [9–11], and perhaps most importantly, plays an important role in water and sodium removal. Total water and sodium removal in PD patients, as well as residual renal function, are independent parameters related to survival in PD patients [12].

Overhydration with resulting therapy-resistant hypertension and left ventricular hypertrophy is a frequent problem in PD patients [13]. Residual renal function proved to be an important determinant in the maintenance of a normal volume status in PD patients [14]. Moreover, an inverse relation was observed between residual renal function and the degree of left ventricular hypertrophy in dialysis patients [15]. Furthermore, fluid overload in these patients with lower residual renal function was associated with an increased plasma level of C-reactive protein (CRP), as a marker of inflammation and risk factor for increased cardiovascular disease. Another study also found an association between the loss of residual renal function and increased plasma levels of inflammatory mediators, such as IL-6, CRP, hyaluronan and neopterin [16] and increased levels of the advanced glycation end-product N-ε-carboxymethyllysine [17].

These data support the eminent importance of maintained residual renal function for the adequate treatment of PD patients, and their prognosis. In addition, higher levels of residual renal function may afford better endocrine function, reflected by endogenous production of erythropoietin and active vitamin D metabolites. Measures to protect residual renal function are clearly as important in PD patients, as they are in the pre-dialysis phase of their disease.

Protecting residual renal function

In order to preserve renal function as much as possible, we must avoid the factors that are known to be detrimental in this regard. Nephrotoxic drugs should only be used when no suitable alternative
is available. Attention must be focused on non-steroidal anti-inflammatory drugs, and aminoglycosides, although recently some conflicting results have been published on the use of intraperitoneally-administered aminoglycosides in peritonitis treatment [18]. Likewise, intravascular contrast agents constitute a threat to residual function, and should be avoided when possible. If their use is inevitable, the patient should be maintained in a well-hydrated state [19], and the concurrent use of N-acetylcysteine seems warranted [20]. Episodes of hypercalcemia, with its known negative effects on renal function, mediated through volume depletion and nephrocalcinosis, should be avoided through the cautious use of calcium-containing phosphate binders and vitamin D.

Close attention to fluid replacement during intercurrent disease, resulting in dehydration (gastroenteritis, vomiting, surgery, febrile states), is equally important. Also, dehydration due to excessive peritoneal ultrafiltration may result in a reduction in residual renal function [21]. The relative benefits of keeping the patient ‘as dry as possible’ vs preservation of renal function have not yet been settled [22]. In the opinion of the authors, it is best to attempt to achieve normovolemia while preventing both under- and over-hydration. Both judicious clinical assessment, (orthostatic hypotension) as well as objective techniques to assess fluid state, might be helpful in this respect [23].

The theoretical fear, with regard to ACE inhibitors and angiotensin II receptor blockers for the treatment of hypertension and cardiac failure, is not supported by the available data. To the contrary, ramipril resulted in a somewhat better preservation of residual renal function in PD patients [24]. Angiotensin II receptor blockers similarly had a protective effect when employed in PD patients [25].

Also, the choice of dialysis modality can influence the decline of residual renal function. Several studies have found that the residual renal function, as measured with GFR, urine production and creatinine clearance, declines faster in patients on haemodialysis (HD) than on PD. A retrospective study found that the monthly decline in RRF was 3% in PD and 6% in HD [26]. In a large cohort of prospectively studied patients in the NECOSAD study, the residual GFR, measured as the mean of the creatinine and urea clearance, was significantly higher at the start of PD when compared with HD, and this difference increased after 12 months of treatment. Potential explanations for the larger decline in residual renal function in HD patients might be the occurrence of hypotensive episodes during HD or bioincompatibility of the dialysis membrane [27]. However, the relative advantage of PD vs HD in the preservation of residual renal function has not yet been settled, given the lack of difference of decline in residual renal function between PD and high-flux biocompatible HD in a cohort of 475 patients [28].

**Conclusion**

Maintenance of residual renal function proves to be an important objective in the care of our PD patients, with benefits for their survival, quality of life (reduced severity of fluid restriction), and risk of complications. The loss of residual renal function cannot be fully compensated by increasing the small solute clearances by the peritoneal route.

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**References**


