

Clinical and practical aspects in peritoneal dialysis: Choosing the right modality for the right patient

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On the other side there is general opinion that patient's preference should be the first determinant of modality choice unless the patient has a strong contraindication against a certain modality.

Our "Dialysis Update" presents a study performed by Juergensen et al. that examined patients' satisfaction on HD and PD. Interestingly, PD patients believed that their treatment had less impact on their lives than did HD patients. To maintain satisfaction and to achieve optimal clinical outcomes in PD continuous quality improvement in therapy is mandatory. Recent examples of efforts to meet these high requirements are given in our two other abstracts. Szeto et al. found a lower degree of systemic inflammation in PD patients, as manifested by decreased serum C-reactive protein (CRP) levels, when using a novel PD solution with low levels of glucose degradation products and neutral pH compared to conventional PD solution. CRP was also the focus of interest in the study by Zalunardo et al. They identified it as a helpful marker for assessing the risk of short and long-term adverse outcomes of PD related peritonitis which still leads to frequent and serious complications in PD patients. *KB*

Preface

The use of peritoneal dialysis (PD) and haemodialysis (HD) in patients with end stage renal disease varies considerably. Medical, structural and social factors contribute to this discrepancy in modality allocation. However, the apparent initial survival advantage of PD during the first years of dialysis should support to see PD and HD rather as complementary than competitive treatments and advocate an integrated care concept starting dialysis with PD and later switching to HD.

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1. Haemodialysis and peritoneal dialysis: Patients' assessment of their satisfaction with therapy and the impact of the therapy on their lives

Several studies comparing haemodialysis (HD) and peritoneal dialysis (PD) have been performed so far, mainly focussing on morbidity and mortality. However, results of these studies have been inconsistent and divergent. This may make it difficult to select the right modality for the patient. Moreover, differences in comorbidities and problems with relative utilization of HD and PD in defined geographic areas have to be added on.

Since patients' quality of life and patients' satisfaction with HD and PD are important domains especially influencing clinical outcomes, such as compliance with care, morbidity and mortality, this study from **Juergensen et al.** was performed.

Patients were recruited from three US dialysis units affiliated with a hospital. They had to be at least 18

years old, on the same dialysis modality for a minimum of six months and clinically stable for a minimum of two months before study entry. Patients' basic demographic data were collected including the Charlson Comorbidity Index (CCI) score. In addition, patients completed a specially designed questionnaire. The first section asked patients about basic demographic information. The second section assessed patients' overall satisfaction with their dialysis therapy and the overall impact of the dialysis treatment on their life. The third section inquired about the impact that dialysis therapy had on specific aspects of patients' life, focussing attention on 15 specific domains (**Fig.1**). The fourth section was a free-text section for the patients to list the three most important positive and three most negative aspects of their dialysis therapy. The questionnaires generally took between 10 and 15 minutes to complete.

146 eligible patients, 84 patients on HD, and 62 on PD, participated in the study. Time on dialysis was not different between PD and HD patients. Regarding the basic demographic data there were no significant

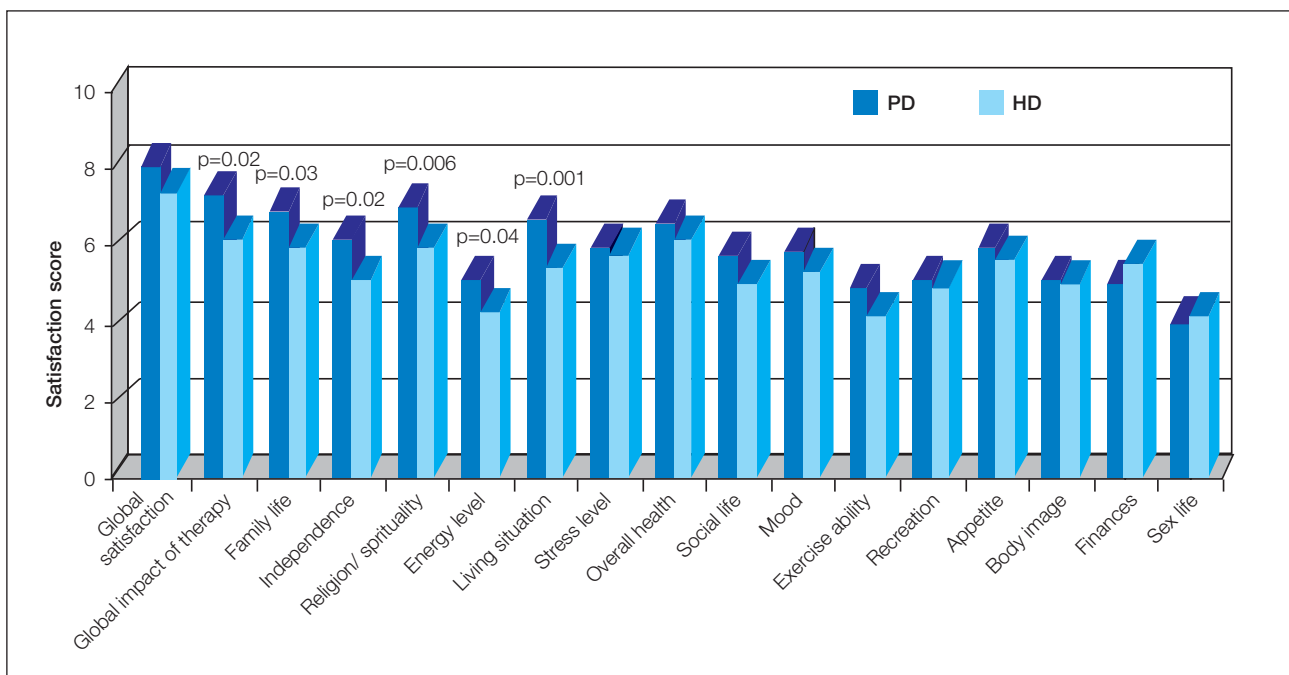


Fig. 1: Differences between PD and HD patients: Satisfaction with therapy and impact of therapy on their lives. (10 = the most satisfaction with or least impact of the therapy on their lives; 1 = the least satisfaction with and greatest impact of the therapy on their lives)

differences between the HD and PD patients in terms of educational backgrounds or home situations. However, there were significant differences concerning age (PD: 55 ± 14 vs HD: 69.6 ± 13.3 , $p < 0.0001$) and CCI score (PD: 5.80 ± 2.68 vs HD: 7.90 ± 1.87 , $p < 0.0001$; the higher the score of CCI, the more severe the burden of comorbidity). Nevertheless, no significant correlation was found between the CCI score and any of the patients' satisfaction or impact scores.

The mean overall satisfaction score of the PD patients (8.02 ± 1.41) was higher than that of the HD patients (7.4 ± 1.41), but the difference was not statistically significant ($p = 0.15$). PD patients indicated less impact of the dialysis therapy on their lives than HD patients ($p = 0.019$). Furthermore, significant differences between PD and HD patients were seen in favour of PD for the following parameters: family life, independence, religion/spirituality, energy level, living situation (**Fig. 1**).

The study confirms the results of a former study (CHOICE study), which revealed that PD patients in general reported a higher satisfaction with their therapy than HD patients. The results of the CHOICE study also showed that patients who received PD were 1.5 times more likely to rate their dialysis care as excellent compared with patients who received HD. In addition, another study confirmed that patients who are well informed about both dialysis modalities and choose PD are more likely to rate their care higher than patients who choose HD.

Among the various free comments on their dialysis therapy the most frequently cited positive aspect seen by HD patients was staff interaction, the most negative aspect length of treatment. In PD patients it was improved strength/energy on the positive side and on the negative side problems with supplies. The authors think that it is important to extend their observations to

a larger cohort of patients and eventually to incorporate the information into educational programs for patients with chronic kidney disease to assist with modality selection.

This study confirms the results of former studies with greater satisfaction of PD patients with their therapy than HD patients. Moreover this study shows that PD patients believe that their treatment has less impact on their lives than do HD patients. KB

Juergensen E, Wuerth D, Finkelstein SH, Juergensen PH, Bekui A, Finkelstein FO: Hemodialysis and peritoneal dialysis: patients' assessment of their satisfaction with therapy and the impact of the therapy on their lives; Clin J Am Soc Nephrol 1, 1191-1196, 2006

2. Clinical biocompatibility of a neutral peritoneal dialysis solution with minimal glucose-degradation products – A 1-year randomized control trial

Acidic pH and a high content of glucose degradation products (GDP), characteristic of standard peritoneal dialysis (PD) solutions, have been identified as contributing causes of progressive loss of peritoneal membrane function. Since recently the double-chamber bag system stay.safe® balance¹⁾ (Fresenius Medical Care (FMC), Germany) became available, **Szeto et al.** compared this newly formulated solution of neutral pH and low GDP levels to a standard PD solution (stay.safe®, FMC Germany) in long-term.

50 new continuous ambulatory peritoneal dialysis (CAPD) patients were enrolled from the hospital of the University of Hong Kong: 25 patients were randomized to the treatment with the PD solution *balance* (*balance* group) and 25 to the standard dialysis solution (control group). Patients were followed at 0, 4, 8, 16, 24, 32, 40 and 52 weeks. The primary outcome measures were the peritoneal transport, serum inflammatory markers and PD effluent (PDE) markers of biocompatibility. Secondary outcomes included nutritional and adequacy indices, residual renal function, peritonitis-free survival, hospitalization and technique survival.

Patients' demographic data were comparable although the patients treated with *balance* were marginally older and had a higher Charlson's comorbidity index. Of note was the difference in serum CRP – a prominent marker of systemic inflammation – (**Fig. 2**) between the two groups. In the *balance* group serum CRP declined from 3.09 ± 0.72 to 1.77 ± 0.42 mg/l over

52 weeks ($p = 0.05$), whereas that of the control group remained static (from 5.31 ± 2.01 to 7.73 ± 2.42 mg/l, $p = 0.3$). The control group had a higher serum CRP level than the *balance* group; at all time points the difference remained statistically significant.

Unfortunately, the CRP values before initiation of PD (i.e. week 0) were not available for comparison. However, it has to be pointed out that the *balance* group had lower serum CRP at four weeks, soon after treatment start.

After 52 weeks PDE CA125 (cancer antigen 125) rose from 2.45 ± 0.96 to 14.30 ± 2.17 U/ml in the *balance* group ($p < 0.001$) and from 0.89 ± 0.65 to 7.36 ± 2.23 U/ml in the control group ($p = 0.009$). The magnitude of increase was greater in the *balance* group, indicating a better recovery of the mesothelial cell mass. This result confirms the findings of former studies which revealed increased effluent CA125 levels in patients treated with more biocompatible PD solutions indicating a sign of better peritoneal mesothelium preservation. PDE hyaluronan (HA) declined from 2.26 ± 0.60 to 1.45 ± 0.32 μ g/ml in the *balance* group ($p = 0.07$),

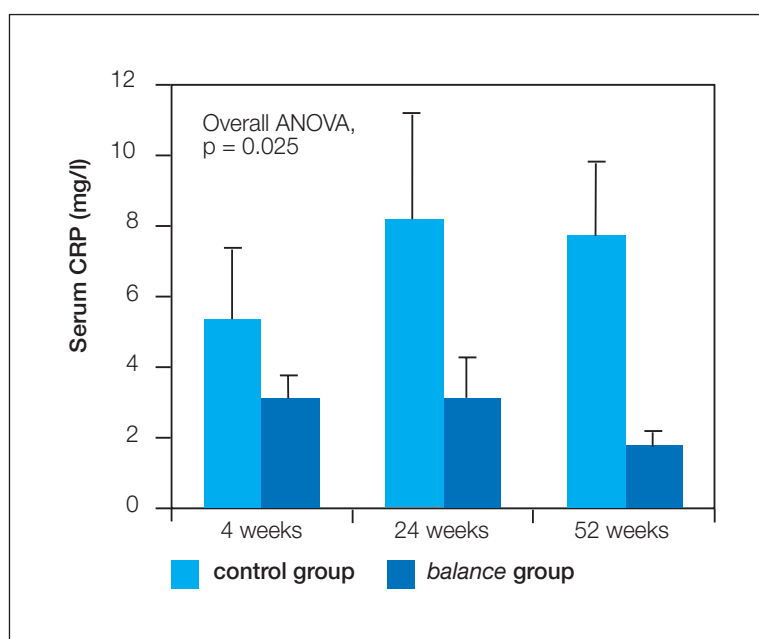


Fig. 2: Serum CRP (C-reactive protein) of the two groups during the study period (mean \pm SD)

but increased from 1.96 ± 0.33 to 2.55 ± 0.32 $\mu\text{g/ml}$ in the control group ($p = 0.12$). An increased level of HA may reflect ongoing tissue regeneration and remodelling after injury. In both groups TGF- β (transforming growth factor beta) concentration declined significantly in the PDE over 52 weeks, and there was no difference in PDE TGF- β level between the groups.

Total Kt/V, ultrafiltration, urine volume, residual glomerular filtration rate and the nutritional indices were similar between the groups. There was no difference in the peritonitis-free survival and no significant difference in any of the quality of life or patient satisfaction parameters between the groups throughout the study period.

The authors concluded that compared to conventional PD solution, the use of balance, a neutral pH, low GDP solution resulted in a lower degree of systemic inflammation, and a superior profile of PDE mesothelial cell marker. This difference was maintained for one year. KB

Szeto CC, Chow KM, Lam CWK, Leung CB, Kwan BCH, Chung KY, Law MC, Li PKT: Clinical biocompatibility of a neutral peritoneal dialysis solution with minimal glucose-degradation products – A 1-year randomized control trial; *Nephrol Dial Transplant* 22, 552-559, 2007

¹Editor's note: This system utilizes lactate-buffered PD solution in a two-chamber bag. The formation of GDP is greatly reduced by sterilizing the glucose, which is separated from the lactate, at a very low pH. Immediately before infusion, the seam between the two chambers is opened and the contents are mixed, resulting in a neutral pH of the PD solution.

3. Higher serum C-reactive protein predicts short and long-term outcomes in peritoneal dialysis-associated peritonitis

Since peritoneal dialysis (PD) patients are not generally hospitalized during the treatment of peritonitis the contact with medical personnel may be relatively infrequent. For this reason, easily obtainable predictors of outcomes would be clinically useful. **Zalunardo et al.** examined the association between serum C-reactive protein (CRP) levels and short-term and long-term outcomes after patients' first peritonitis since the initiation of their PD treatment.

This was a prospective cohort study with 209 PD patients of the Oxford Kidney Unit (United Kingdom) and its satellite facilities followed between 1 January 1999 and 31 March 2005. Empiric treatment consisted of intraperitoneal vancomycin and oral ciprofloxacin. Antibiotic treatment was subsequently tailored once antimicrobial sensitivities were available. The standard duration of antibiotic treatment was 2 weeks. Serum CRP levels were measured at baseline (within 48 h of diagnosis) and 3 weeks (range: 17 – 25 days) following initiation of antibiotic treatment. Short-term adverse outcomes included death, switch to haemodialysis (HD), persistent infection, and relapse (any PD fluid with white blood cell count >100 mm³ within 4 weeks of cessation of antibiotic therapy). Patients with resolved peritonitis at 3 weeks were followed for the development of a peritonitis occurring any time after cessation of antibiotic therapy and death from any cause. CRP values at baseline were divided into quartiles, from the lowest to the highest levels: ≤ 22.0, 22.1 – 56.0, 56.1 – 126.0 and

≥ 126.1 mg/l. Because patients in the lower three quartiles of CRP at week 3 had a similar time to event, they were grouped together (≤ 23.0 mg/l) and compared with those in the highest quartile (> 23.0 mg/l).

The mean age of the patients was 58.9 years, 58.9% were males, 31.1% diabetics, and mean duration of PD was 0.8 years. At baseline, the median CRP value was 56.0 mg/l (25–75th percentile: 22.0 – 126.0 mg/l).

Short-term adverse outcomes were observed in 72 (34.0%) patients. 33 patients were switched to HD, at least temporarily. Eleven patients died during the course of treatment; three of these had intra-abdominal pathology identified before death. Ten patients demonstrated evidence of persistent infection at week 3, resulting in an extension of antibiotic treatment. 18 patients experienced a relapse within 4 weeks of cessation of antibiotic treatment. After adjustment for age, gender, diabetes, duration of renal replacement therapy, and causative organism in the multivariable regression model, the upper two quartiles of CRP were statistically significantly associated with an increased risk of short-term adverse outcome com-

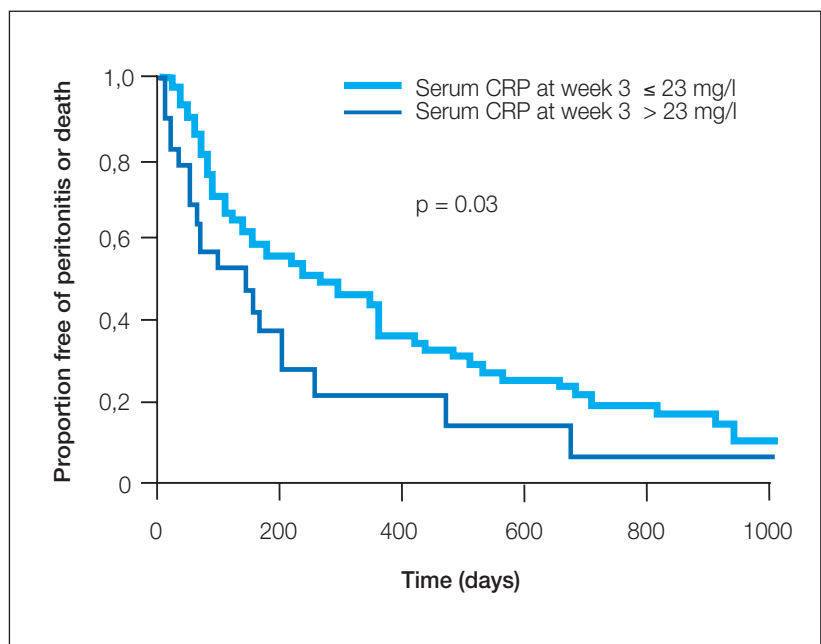


Fig. 3: Time to occurrence of a peritonitis event or death from any cause

pared to quartile 1 (quartile 3 odds ratio 2.73, $p = 0.03$; quartile 4 odds ratio 3.38, $p = 0.001$).

Three weeks following initiation of antibiotic treatment, 155 of 209 patients met the criteria for resolution of peritonitis. Of these patients, 122 had CRP measurements available at this time. The median CRP value reported at week 3 was 8.4 mg/l (25–75th percentile: 8.0 – 23.0 mg/l). 86 of the 122 (70.5%) patients experienced a long-term adverse outcome (11 deaths and 75 peritonitis episodes). The Kaplan–Meier survival curves for the development of a subsequent peritonitis event or death from any cause are shown in **Figure 3**. The time to occurrence of these long-term outcomes was statistically significantly shorter in the group with CRP values in the highest quartile (> 23.0 mg/l) compared to those with $CRP \leq 23.0$ mg/l ($p = 0.03$).

In the adjusted analysis, those patients with a serum $CRP > 23.0$ mg/l had a greater risk of a long-term adverse outcome compared to the patients with a serum $CRP \leq 23.0$ mg/l (hazard ratio 1.79, $p = 0.03$).

The authors point out that the potential association found between elevated CRP and increased risk of future peritonitis events is novel. Persistent elevations of CRP immediately following peritonitis treatment may indicate an ongoing subclinical infection at the PD catheter exit site or tunnel serving as the bacterial source for future infections.

In conclusion, in patients presented with an episode of PD-associated peritonitis, a higher level of serum CRP was independently associated with an increased risk of short- and long-term adverse outcomes. These results qualify CRP as a potential marker to identify patients at greater risk of treatment failure. CL



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