The First Weeks on Peritoneal Dialysis: Effects on Clinical Parameters

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Initiation of peritoneal dialysis (PD) induces several changes both locally in the peritoneum and systemically. We performed a pilot study to generate insights into the early clinical and systemic changes after catheter insertion and the first weeks of PD.

The study included 11 new PD patients (7 men, 4 women). The study period started just before implantation of the Tenckhoff catheter and finished 6 weeks after the start of PD. All patients were treated with lactate-buffered dialysis solutions. Clinical parameters, routine laboratory tests and markers of systemic inflammation were determined.

The mean (± standard deviation) age of the patients was 52.6 ± 12.1 years, mean weight was 81.3 ± 14.7 kg, and mean blood pressure was 143.3/87.8 ± 18.5/8.2 mmHg. Weight and blood pressure did not change significantly during the first weeks of PD. Throughout the study, 24-hour urine production declined by 6.9 mL/day ($p = 0.006$*). Daily residual creatinine clearance (CCr) decreased by 0.036 mL/min (*$p = 0.008$*). High-sensitivity C-reactive protein (hs-CRP) was significantly higher in patients who had undergone hemodialysis before the start of the study (*$p < 0.0001$*) and declined during the study in that group (*$p = 0.001$*). No significant change in hs-CRP was found in the group that started dialysis with PD.*

In this pilot study, we found no significant changes in the clinical parameters of weight and blood pressure during the first weeks of PD. However, urine production and residual CCr declined significantly during the study period, starting from the moment of catheter insertion. Levels of the systemic inflammatory marker hs-CRP were higher in patients who had previously undergone hemodialysis; its level in those patients decreased after hemodialysis ended.

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Introduction

Continuous ambulatory peritoneal dialysis, using the peritoneal membrane as a dialyzing organ, has become a well-established renal replacement modality for patients with end-stage renal disease. Initiation of peritoneal dialysis (PD) induces several changes both locally in the peritoneum and systemically (1). These changes can lead to progressive loss of peritoneal ultrafiltration.

Dialysis fluids are well-known to be bioincompatible because of their high glucose concentrations, glucose degradation products, and low pH (2,3). Chronic daily instillation of conventional peritoneal dialysis fluids leads to an angiogenic response in the omentum, mesentery, liver surface, and parietal peritoneal wall (4–7). Besides vascular changes, fibrotic alterations are an additional effect of exposure to these dialysis solutions (8,9).

Furthermore, PD is a state of chronic inflammation. The levels of inflammatory markers such as interleukin-6 and hyaluronic acid in the dialysis effluent increase with duration of therapy (10,11).

Whether the foregoing changes are the result of an inflammatory response following the catheter insertion or, later on, the installation of PD fluids is not known. Moreover, the exact time at which these changes actually occur is also unknown. Several earlier studies investigated the role of the composition of PD fluids on local and systemic inflammatory responses (12,13), but initial changes, immediately after implantation of the catheter, have not been investigated. We therefore studied clinical parameters and systemic effects during the first weeks of PD, starting at catheter insertion.

Patients and methods

From March 2005 until November 2006, we conducted a pilot study in patients with end-stage renal

disease without a history of PD. The study started just before surgical implantation of the Tenckhoff catheter. Patients were followed weekly during the 2-week fixation period for the Tenckhoff catheter. The day after implantation, and once weekly for the next 2 weeks, the Tenckhoff catheter was flushed with 50 mL dialysis solution. After those 2 weeks, the training period for PD exchanges started according to our clinical practice. The study finished 6 weeks after the start of PD.

Figure 1 shows the study timetable. Eligible patients had to be between 18 and 75 years of age and willing to participate in the study. Patients with signs of infection were excluded.

Baseline clinical data included age, sex, weight, and underlying renal disease. Blood pressure and weight were measured every week. Routine laboratory tests of plasma included levels of high-sensitivity C-reactive protein (hs-CRP), creatinine, urea, and glucose. Blood samples were drawn on day 0 (just before implantation of the Tenckhoff catheter) and on days 14, 21, 28, 35, 49, and 63. The level of hs-CRP was measured using a sensitive, enzyme-linked assay (DakoCytomation, Glostrup, Denmark) so as to detect values below the detection limit of standard assays. Urine volume and concentrations of urea and creatinine were measured. Urine samples were collected on the same day that blood samples were drawn. Residual creatinine clearance (CCr) was calculated. All patients were treated with lactate-buffered dialysis solutions (Dianeal: Baxter Healthcare BV, Utrecht, Netherlands). The dialysis prescription was adjusted using clinical judgment.

Statistical analysis

All data are shown as mean ± standard deviation unless otherwise specified. Endpoints were analyzed by the longitudinal data analysis technique called generalized estimating equations (GEE), using time as the independent variable. Differences in hs-CRP at $t = 0$ between patients new to dialysis and those who had previously undergone hemodialysis (HD) was calculated using a nonparametric two-sample Wilcoxon rank sum (Mann–Whitney) test. Course of hs-CRP level between the two groups was analyzed using GEE with time, previous HD (0 or 1), and product of time and previous HD as independent variables. A p value less than 0.05 was considered significant.

Results

Between March 2005 and November 2006, we enrolled 11 stable new PD patients into the study. Of these patients, 6 had undergone HD before the start of the study for at least 1 month, and up to 17 months. Table I summarizes the baseline clinical characteristics of the patients.

Three patients did not complete the study because of exit-site infection. They dropped out 3 weeks after study entrance. These patients were not included in the analysis of hs-CRP levels. After 7 weeks, 1 patient prematurely ended participation because of peritoneal fluid leakage into the thoracic space.

Among the study patients, weight and blood pressure did not change significantly during the first weeks of PD. Mean 24-hour urine production declined by 6.9 mL/day ($p = 0.006$, Figure 2). Daily residual CCr decreased by 0.036 mL/min ($p = 0.008$), reaching 2.26 mL/min at the end of the study period. Neither implantation of the Tenckhoff catheter nor PD start influenced this decline ($p = 0.664$ and $p = 0.965$ respectively). Levels of hs-CRP at $t = 0$ were significantly higher in the group of patients who had undergone HD before the start of the study as compared with those who started dialysis with PD ($p < 0.0001$;

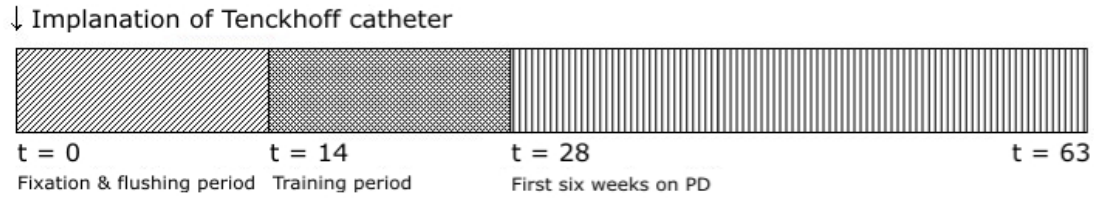

FIGURE 1 The study timetable. PD = peritoneal dialysis.

Figure 3). During the study, hs-CRP decreased significantly in the group that had previously undergone HD ($p = 0.001$; Figure 4). No significant change in hs-CRP level was seen throughout the study in the group that started dialysis with PD.

Discussion

This pilot study shows a rapid decline in residual CCr and urine production during the first 6 weeks on PD. Residual renal function is accepted as a significant factor influencing morbidity and mortality in chronic dialysis patients (14). It contributes to measures of dialysis adequacy, especially in PD patients (15).

Jansen *et al.* for the NECOSAD study group showed that the residual glomerular filtration rate (rGFR) is better maintained in PD patients than in HD patients (16). Those authors stated that the

TABLE I Baseline characteristics of the patients

Patients (*n*)	11
On HD before study start	6
Sex (M:F)	7:4
Age (years)[a]	52.6±12.1
Body weight (kg)[a]	81.3±14.7
Blood pressure (mmHg)[a]	
Systolic	143.3±18.5
Diastolic	87.8±8.2
Residual CCr (mL/min)[a]	9.61±4.7
Diagnosis (*n*)	
Diabetes mellitus type 2	4
Hypertensive nephropathy	2
Polycystic kidney disease	3
Secondary FSGS	1
Goodpasture disease	1

[a] Mean ± standard deviation.
HD = hemodialysis; M:F = male:female; CCr = creatinine clearance; FSGS = focal segmental glomerular sclerosis.

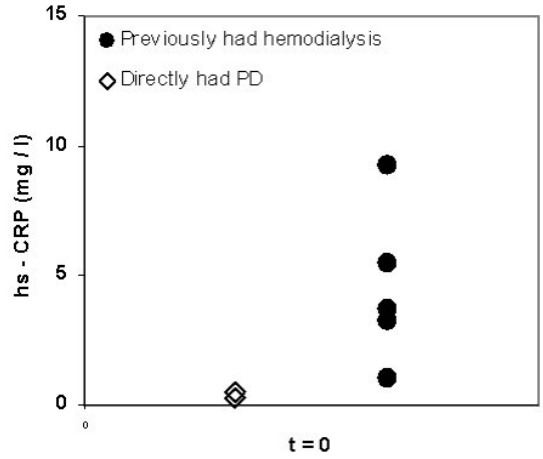

FIGURE 3 Serum levels of high-sensitivity C-reactive protein [hs-CRP (mg/L)] at t = 0 in patients on hemodialysis before the start of the study and in patients who started dialysis with peritoneal dialysis ($p < 0.0001$).

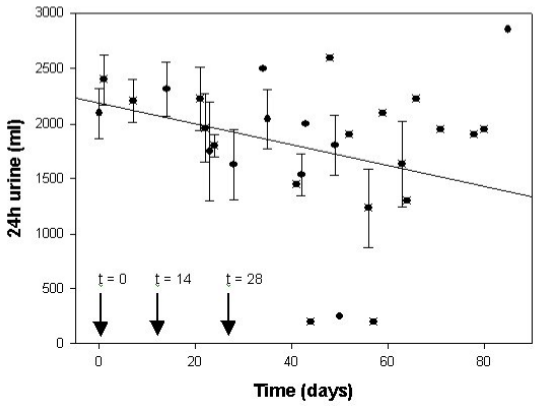

FIGURE 2 Decline in diuresis (milliliters in 24 hours) of 6.9 mL/day during the study period ($p = 0.006$). t = 0: implantation of the Tenckhoff catheter; t = 14: start training period; t = 28: start peritoneal dialysis.

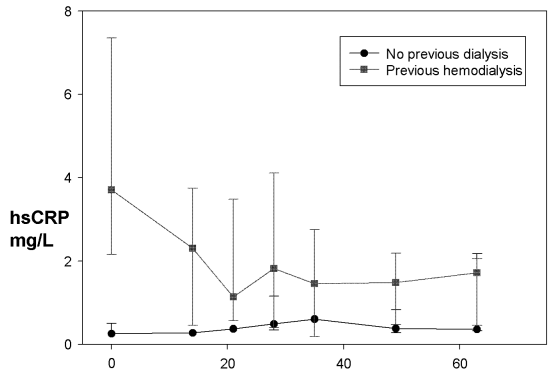

FIGURE 4 Serum levels of high-sensitivity C-reactive protein [hs-CRP (mg/L)] during the study period. During the study, levels of hs-CRP declined in patients who had previously undergone hemodialysis ($p = 0.001$). t = 0: implantation of Tenckhoff catheter; t = 14: start training period; t = 28: start peritoneal dialysis.

decline in rGFR was most pronounced in the first 3 months, with a reduction of 2.2 mL/min/1.73 m^2 during that time. The decline in rGFR was shown in our study to be even more pronounced, falling by 2.26 mL/min after 6 weeks of PD. That fall was not caused by implantation of the Tenckhoff catheter, nor by start of PD therapy. Thus, the most probable cause was progression of the underlying renal disease. Another explanation could be the presence of diastolic hypertension, which was identified as an independent risk factor for loss of rGFR in patients starting dialysis (16).

Furthermore, a remarkably and significantly higher serum level of hs-CRP was observed in patients who had undergone HD before implantation of the Tenckhoff catheter. That finding suggests that HD induces a systemic acute-phase inflammatory response that is higher than that seen in pre-dialysis chronic renal failure (CRF) patients, supporting the idea that dialysis induces a state of chronic inflammation (10,11). Recently, Wong *et al.* also found higher hs-CRP levels in patients on HD than in pre-dialysis CRF patients (17). Previous studies had already revealed CRP to be a predictor of death by all causes, including cardiovascular mortality, in CRF patients (18). We observed no significant change in the CRP levels measured during the study. Notably, CRP at a single point in time is predictive of outcome in PD patients (19), and the time course of serum CRP is even more predictive of mortality than is its baseline level in PD patients (20).

Conclusions

The clinical data presented in this study were obtained during the first weeks of PD, directly after implantation of the Tenckhoff catheter in patients with no history of PD. A reduction in residual CCr and diuresis was found during the first weeks of PD treatment. This decrease was not influenced by implantation of the Tenckhoff catheter nor by the start of PD fluid infusion. Levels of the systemic inflammatory marker hs-CRP were higher in patients who had previously undergone HD and declined in this group during the study. Future measurements of markers of peritoneal membrane function and systemic inflammation will possibly reveal the moment that PD-induced changes in peritoneal membrane function and local and systemic inflammatory response occur.

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References

1 Davies SJ, Bryan J, Phillips L, Russell GI. Longitudinal changes in peritoneal kinetics: the effect of peritoneal dialysis and peritonitis. Nephrol Dial Transplant 1996;11:498–506.
2 Wieslander AP. Cytotoxicity of peritoneal dialysis fluid—is it related to glucose breakdown products? Nephrol Dial Transplant 1996;11:958–9.
3 Nakayama M, Kawaguchi Y, Yamada K, *et al.* Immunohistochemical detection of advanced glycosylation end-products in the peritoneum and its possible pathophysiological role in CAPD. Kidney Int 1997;51:182–6.
4 Hekking LH, Zareie M, Driesprong BA, *et al.* Better preservation of peritoneal morphologic features and defense in rats after long-term exposure to a bicarbonate/lactate–buffered solution. J Am Soc Nephrol 2001;12:2775–86.
5 Mateijsen MA, van der Wal AC, Hendriks PM, *et al.* Vascular and interstitial changes in the peritoneum of CAPD patients with peritoneal sclerosis. Perit Dial Int 1999;19:517–25.
6 Krediet RT, Zweers MM, van der Wal AC, Struijk DG. Neoangiogenesis in the peritoneal membrane. Perit Dial Int 2000;20(Suppl 2):S19–25.
7 Margetts PJ, Kolb M, Yu L, *et al.* Inflammatory cytokines, angiogenesis, and fibrosis in the rat peritoneum. Am J Pathol 2002;160:2285–94.
8 Wieczorowska–Tobis K, Brelinska R, Breborowicz A, Oreopoulos DG. Morphologic aspects of chronic peritoneal dialysis in a rat model. Perit Dial Int 2001;21(Suppl 3):S342–4.
9 Margetts PJ, Gyorffy S, Kolb M, *et al.* Antiangiogenic and antifibrotic gene therapy in a chronic infusion model of peritoneal dialysis in rats. J Am Soc Nephrol 2002;13:721–8.
10 Pecoits–Filho R, Araujo MR, Lindholm B, *et al.* Plasma and dialysate IL-6 and VEGF concentrations are associated with high peritoneal solute transport rate. Nephrol Dial Transplant 2002;17:1480–6.
11 Yamagata K, Tomida C, Koyama A. Intraperitoneal hyaluronan production in stable continuous ambulatory peritoneal dialysis patients. Perit Dial Int 1999;19:131–7.
12 Krediet RT, Zweers MM, Ho-dac-Pannekeet MM, *et al.* The effect of various dialysis solutions on peritoneal membrane viability. Perit Dial Int 1999;19(Suppl 2):S257–66.

13 Fusshoeller A, Plail M, Grabensee B, Plum J. Biocompatibility pattern of a bicarbonate/lactate–buffered peritoneal dialysis fluid in APD: a prospective, randomized study. Nephrol Dial Transplant 2004;19:2101–6.
14 Merkus MP, Jager KJ, Dekker FW, de Haan RJ, Boeschoten EW, Krediet RT. Predictors of poor outcome in chronic dialysis patients: the Netherlands Cooperative Study on Adequacy of Dialysis. The NECOSAD Study Group. Am J Kidney Dis 2000;35:69–79.
15 Lameire NH. The impact of residual renal function on the adequacy of peritoneal dialysis. Contrib Nephrol 1998;124:76–93.
16 Jansen MA, Hart AAM, Korevaar JC, *et al.* Predictors of the rate of residual renal function in incident dialysis patients. Kidney Int 2002;62:1046–53.
17 Wong CK, Szeto CC, Chan MH, Leung CB, Li PK, Lam CW. Elevation of pro-inflammatory cytokines, C-reactive protein and cardiac troponin T in chronic renal failure patients on dialysis. Immunol Invest 2007;36:47–57.
18 Tripepi G, Mallamaci F, Zoccali C. Inflammation markers, adhesion molecules, and all-cause and cardiovascular mortality in patients with ESRD: searching for the best risk marker by multivariate modelling. J Am Soc Nephrol 2005;16(Suppl 1):S83–8.
19 Wang AY, Woo J, Lam CW, *et al.* Is a single time point C-reactive protein predictive of outcome in peritoneal dialysis patients? J Am Soc Nephrol 2003;14:1871–9.
20 Ates K, Ates A, Ekmekci Y, Nergizoglu G. The time course of C-reactive protein is more predictive of mortality than its baseline level in peritoneal dialysis patients. Perit Dial Int 2005;25:256–68.

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