AJKD
Original Investigation

A Combination of Biocompatible Peritoneal Dialysis Solutions and Residual Renal Function, Peritoneal Transport, and Inflammation Markers: A Randomized Clinical Trial

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Background: The benefits of biocompatible peritoneal dialysis (PD) fluids, particularly for residual renal function (RRF), are controversial. Moreover, the clinical effects of a PD regimen consisting of different biocompatible PD fluids have not been fully established.

Study Design: Prospective, randomized, controlled, open-label study.

Setting & Participants: Patients with end-stage kidney disease newly started on continuous ambulatory PD therapy (N = 150).

Intervention: A 12-month intervention with 3 biocompatible PD fluids (a neutral-pH, low glucose degradation product, 1.5% glucose solution; a solution with 1.1% amino acid; and a fluid with 7.5% icodextrin) or conventional PD fluid.

Outcomes: The primary outcome was change in RRF and daily urine volume. Secondary outcomes were peritoneal transport and inflammation markers.

Measurements: RRF, daily urine volume, serum and dialysate cytokine levels.

Results: RRF(3.24 ± 1.98 vs 2.88 ± 2.43 mL/min/1.73 m^2; $P = 0.9$) and rate of decline in RRF (−0.76 ± 1.77 vs −0.91 ± 1.92 mL/min/1.73 m^2 per year; $P = 0.6$) did not differ between the biocompatible- and conventional-PD-fluid groups. However, patients using the biocompatible PD fluids had better preservation of daily urine volume (959 ± 515 vs 798 ± 615 mL/d in the conventional group, $P = 0.02$ by comparison of difference in overall change by repeated-measures analysis of variance). Their dialysate-plasma creatinine ratio at 4 hours was higher at 12 months (0.78 ± 0.13 vs 0.68 ± 0.12; $P = 0.01$ for comparison of the difference in overall change by repeated-measures analysis of variance). They also had significantly higher serum levels of adiponectin and overnight spent dialysate levels of cancer antigen 125, adiponectin, and interleukin 6 (IL-6). No differences between the 2 groups were observed for serum C-reactive protein and IL-6 levels.

Limitations: Unblinded, relatively short follow-up; no formal sample-size calculations.

Conclusions: Use of a combination of 3 biocompatible PD fluids for 12 months compared with conventional PD fluid did not affect RRF, but was associated with better preservation of daily urine volume. The biocompatible PD fluids also lead to changes in small-solute transport and an increase in dialysate cancer antigen 125, IL-6, adiponectin, and systemic adiponectin levels, but have no effect on systemic inflammatory response. The clinical significance of these changes, while of great interest, remains to be determined by further studies.

Am J Kidney Dis. 60(6):966-975.

INDEX WORDS: Continuous ambulatory peritoneal dialysis; residual renal function; biocompatibility; peritoneal dialysis fluids; randomized controlled trial.

Conventional glucose-based peritoneal dialysis (PD) fluids are bioincompatible because of their high glucose and lactate concentrations, low pH, and the presence of glucose degradation products.[1] Long-term use of conventional PD fluids in patients undergoing continuous ambulatory PD (CAPD) could adversely affect residual renal function (RRF)[2] and lead to progressive damage of the peritoneal membrane,

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Received October 29, 2011. Accepted in revised form May 31, 2012. Originally published online July 27, 2012.

Trial registration: Hong Kong Clinical Trial Registry; study number: HKCTR-8.

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0272-6386/$36.00

http://dx.doi.org/10.1053/j.ajkd.2012.05.018

eventually resulting in PD failure.[3] Furthermore, it has been suggested that use of conventional PD fluids is associated with systemic and local inflammatory responses, which might increase the risk of cardiovascular diseases.[4,5]

In recent years, a number of more biocompatible PD fluids have been introduced into clinical use. These biocompatible PD fluids either use alternatives to glucose, such as amino acids or icodextrin, as the osmotic agent or adopt a multichamber design to maintain a more physiologic pH and reduce the formation of glucose degradation products.[6] The clinical benefits of these biocompatible PD fluids have not been fully established. Preservation of RRF is an important therapeutic target in PD.[7] Studies comparing the effect of biocompatible PD fluids with conventional PD fluids on the rate of decline in RRF have generated conflicting results.[8-12] Moreover, the effects of combining the use of different biocompatible PD fluids on RRF and daily urine volume hitherto have not been systematically studied. A CAPD regimen consisting of biocompatible PD fluids (a neutral pH and low–glucose degradation product PD fluid, an amino acid–based PD fluid, and a PD fluid based on the glucose polymer icodextrin) contains a substantially lower glucose load than conventional CAPD regimens and can significantly reduce glucose exposure to the peritoneum. However, the effect of such a combination of biocompatible PD fluids on peritoneal membrane integrity, as well as systemic and local inflammatory responses, remains to be determined.

The primary objectives of this study were to compare the effect of a combination of 3 biocompatible PD fluids with conventional PD fluid on RRF and daily urine volume in patients newly started on CAPD therapy. Secondary objectives included evaluation of the effects of the biocompatible PD fluids on peritoneal transport characteristics, peritoneal membrane integrity, systemic and local inflammatory responses, peritonitis-free survival, and serum biochemistry.

METHODS

Study Design

This study was a prospective, multicenter, randomized, controlled, open-label study comparing a CAPD regimen using a combination of 3 biocompatible PD fluids with one using conventional PD fluid in stable patients with end-stage kidney disease newly started on CAPD therapy. The biocompatible PD fluids comprised a neutral-pH low–glucose degradation product PD fluid (Physioneal [Baxter, www.baxter.com]), an amino acid–based PD fluid (Nutrineal [Baxter]), and a PD fluid based on the glucose polymer icodextrin (Extraneal [Baxter]), and the conventional PD fluid was Dianeal (Baxter). The study was undertaken from January 2006 to December 2009 in 8 renal centers in Hong Kong (Kwong Wah Hospital, Pamela Youde Nethersole Eastern Hospital, Princess Margaret Hospital, Queen Elizabeth Hospital, Queen Mary Hospital, Tuen Mun Hospital, Tung Wah Hospital, and United Christian Hospital). The study protocol was approved by the institutional review boards of all participating hospitals, with adherence to the Declaration of Helsinki. Written informed consent was obtained from all patients before enrollment.

Patients who had consented to join the study were randomly assigned to either the biocompatible- or conventional-PD-fluid group. Randomized assignment was obtained from sealed envelopes prepared and maintained by an independent third party not directly involved in the study.

Participants

Patients with end-stage kidney disease aged 18-75 years with body weight <75 kg who were newly started on CAPD therapy and had chosen to use the Baxter Ultrabag delivery system were eligible for the study. Patients who had a life expectancy of less than 6 months, had planned living-related kidney transplant within 12 months after the start of CAPD therapy, had childbearing potential (unless taking adequate contraceptive measures), or had chosen to use CAPD delivery products other than the Baxter Ultrabag system were excluded from the study. During the recruitment period between January 2006 and December 2008, 227 patients fulfilled the inclusion criteria; 150 patients consented to participate in the study. The flow of patients in the study is shown in Fig 1.

CAPD Regimens

The initial CAPD regimen of the biocompatible-PD-fluid group consisted of 1 exchange of Physioneal (1.5% glucose), 1 exchange of Nutrineal (1.1% amino acid), and 1 overnight exchange of Extraneal (7.5% icodextrin). The CAPD regimen of the conventional-PD-fluid group comprised 3 exchanges of Dianeal. The number of CAPD exchanges in the 2 study groups could be increased subsequently in case of inadequate clearance (total Kt/V <1.70) or ultrafiltration. The additional exchange in the biocompatible- and conventional-PD-fluid groups was Physioneal or Dianeal, respectively.

Clinical Follow-up

Baseline characteristics of the patients were recorded by chart review. These included age, sex, cause of kidney failure, use of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, or loop diuretics. The Davies score was used to compare comorbid conditions of the 2 study groups.[13] The treatment phase lasted for 12 months. During each clinic visit, clinical data, including body weight and blood pressure, were recorded. At 0, 3, 6, 9, and 12 months, hemoglobin level, serum biochemistry, serum high-sensitivity C-reactive protein (hs-CRP), interleukin 6 (IL-6), and adiponectin were measured. Overnight spent dialysate levels of IL-6 and adiponectin were measured at 1, 3, 6, 9, and 12 months. Cancer antigen 125 (CA-125) levels in the overnight spent dialysate were determined at 1, 3, 6, and 12 months. At 0, 6, and 12 months, lipid profiles, RRF, and daily urine volume were measured.

Adequacy of Dialysis and Peritoneal Transport Characteristics

Adequacy of dialysis and peritoneal membrane transport characteristics were determined by Kt/V urea and the modified peritoneal equilibration test, respectively, using standard methodology at 1, 6, and 12 months. Daily ultrafiltration volume was estimated by averaging the daily ultrafiltration volume from the patient's CAPD record over a 7-day period prior to a Kt/V assessment.