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Original Investigation

Three Versus 4 Daily Exchanges and Residual Kidney Function Decline in Incident CAPD Patients: A Randomized Controlled Trial

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Background: Incident patients treated with continuous ambulatory peritoneal dialysis (CAPD) are often prescribed either 3 or 4 exchanges per day. However, the effects on residual kidney function and clinical outcomes of 3 versus 4 exchanges are not known.

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

Setting & Participants: Incident CAPD patients aged 18 to 80 years with glomerular filtration rates (GFRs; mean of renal urea and creatinine clearance from a 24-hour urine collection) ≥ 2 mL/min and urine volume ≥ 500 mL/d. Exclusion criteria included refusal for informed consent, history of maintenance hemodialysis therapy or transplantation, or limited life expectancy.

Intervention: 24-month intervention with 3- or 4-exchange CAPD using glucose-based peritoneal dialysis fluids.

Outcomes: Primary outcomes were GFR, urine volume, and anuria-free survival. Secondary outcomes included peritonitis, patient survival, and technique survival.

Results: The study recruited 139 patients, 70 in the 3-exchange group and 69 in the 4-exchange group. Baseline body mass indexes were 21.4 ± 3.0 and 21.9 ± 3.2 kg/m^2 for the 3- and 4-exchange groups, respectively ($P = 0.4$). After 24 months, for 3 versus 4 exchanges, GFR (1.6 ± 2.0 vs 1.7 ± 1.9 mL/min; $P = 0.8$), urine volume (505 ± 522 vs 474 ± 442 mL/d; $P = 0.8$), and anuria-free survival (log-rank test statistic = 0.055; $P = 0.8$) did not differ between groups, but Kt/V (1.95 ± 0.39 vs 2.19 ± 0.48; $P = 0.03$) and ultrafiltration (404 ± 499 vs 742 ± 512 mL/d; $P = 0.004$) were lower in the 3-exchange group. The 3-exchange group had nominally longer peritonitis-free survival time (log-rank test statistic = 3.811; $P = 0.05$), and nominally fewer patients had peritonitis in this group, though this was not statistically significant (13% vs 26%; $P = 0.06$). Patient survival (log-rank test statistic = 0.978; $P = 0.3$) and technique survival (log-rank test statistic = 0.347; $P = 0.6$) were similar between groups.

Limitations: Single-center design; no formal sample-size calculations.

Conclusions: In this small trial, CAPD regimens with 3 and 4 exchanges had similar effects on residual GFR, urine volume, and time to anuria. Incremental peritoneal dialysis starts appear safe when patients are monitored.

INDEX WORDS: Continuous ambulatory peritoneal dialysis (CAPD); PD regimen; exchanges; residual kidney function (RKF); glomerular filtration rate (GFR); daily urine volume; diuresis; time to anuria; peritonitis; patient survival; technique survival; randomized controlled trial (RCT).

The importance of residual kidney function to survival and quality of life for dialysis patients has been well established.[1] Peritoneal dialysis (PD) is the preferred renal replacement modality for preservation of residual kidney function, and this advantage is considered to be a major factor accounting for the survival superiority of PD compared to hemodialysis (HD) patients during the first 1 to 2 years of renal replacement therapy.[2,3] Residual kidney function deterioration may be influenced by the primary cause of end-stage renal disease (ESRD),[4-6] comorbid conditions,[4,5,7,8] type of PD,[9-11] dialysate biocompatibility,[12-14] extracellular fluid status,[15,16] proteinuria,[17,18] and administration of renin-angiotensin-aldosterone system blockade[19,20] and other concomitant medications.[21-23] However, factors affecting residual kidney function in PD patients are still poorly understood.

Incident patients treated with continuous ambulatory PD (CAPD) are often prescribed either 3 or 4 exchanges per day. Studies from Hong Kong have reported comparable survival rates among patients undergoing 3- and 4-exchange CAPD.[24,25] However, larger PD fluid volume per day has been found to be a strong independent predictor of a steeper slope of residual kidney function decline,[22] and whether 3-

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and 4-exchange CAPD have different effects on residual kidney function deterioration is unknown. Therefore, we designed this study to compare the effect of 3-exchange CAPD with 4-exchange CAPD on residual kidney function.

METHODS

Study Design

This was a single-center, prospective, randomized, controlled, open-label study comparing the effects of different CAPD regimens using conventional PD fluid, 3 versus 4 exchanges, on residual kidney function in incident PD patients. The study was undertaken from June 2004 through December 2010, and all participants were followed up for 2 years. The study was approved by the Ethics Committee of Renji Hospital, School of Medicine, Shanghai Jiaotong University (approval number: 0016001) and was performed in adherence to the Declaration of Helsinki. Written informed consent was obtained from all patients before enrollment.

Outcomes

Primary outcomes were glomerular filtration rate (GFR; the mean of renal urea and creatinine clearance from a 24-hour urine collection), daily urine volume, and anuria-free survival (anuria was defined as consistent urine volume < 100 mL/d for >1 month). Secondary outcomes included peritonitis, technique survival, and patient survival. Peritonitis was diagnosed and managed in accordance with guidelines of the International Society for Peritoneal Dialysis,[26] and peritonitis rate was calculated as number of peritonitis episodes per patient-year at risk.

Participants

Inclusion criteria were: (1) patients with ESRD aged 18 to 80 years who had just initiated CAPD therapy, and (2) GFR ≥ 2 mL/min and urine volume ≥ 500 mL/d. Exclusion criteria included refusal to provide informed consent, history of maintenance HD or kidney transplantation, anticipated life expectancy less than 6 months, active malignancy, acute infection, significant heart failure, or other severe diseases at the time of enrollment. Enrolled patients were randomly assigned in a 1:1 ratio to the 3-exchange or 4-exchange group when they initiated PD therapy.

CAPD Regimens

CAPD regimens for the 3-exchange or 4-exchange group consisted of 3 or 4 exchanges of glucose-based PD fluid (Dianeal; Baxter) in 2-L bags provided by the same manufacturer. Dextrose and calcium concentrations in PD fluid were determined according to the patient's individual clinical condition. All patients dialyzed for a full 24 hours per day. Daily exchanges would be increased when at least one of the following indications was met: (1) onset of insufficient small-solute clearance (total Kt/V < 1.7) with significant clinical manifestations of uremia, and (2) fluid overload that could not be corrected by strict salt and water control, increasing dextrose concentration of PD fluid, and administration of diuretics.

Clinical Follow-up

Demographic characteristics of patients, including age, sex, cause of ESRD, and comorbid condition status, were collected at the time of enrollment. GFR and urine volume were determined within 1 week before initiation of PD therapy as the baseline and then at 1, 6, 12, 18, and 24 months after PD therapy initiation. Residual kidney function was no longer assessed when a patient became anuric. At all visits, clinical data, including blood pressure and body weight, were recorded, and laboratory parameters, including hemoglobin, serum albumin, glucose, calcium, phosphate, intact parathyroid hormone, and lipid profiles, were measured. At all visits except at baseline, adequacy of solute removal was determined by renal and peritoneal Kt/V using standard methodology, peritoneal membrane transport characteristics were evaluated by a standard peritoneal equilibration test, and daily ultrafiltration volume was calculated by averaging the daily ultrafiltration volume from the patient's CAPD record over a 7-day period prior to a Kt/V assessment.

Concomitant medications, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), loop diuretics, aminoglycosides, contrast, and nonsteroidal anti-inflammatory drugs, were recorded based on medical records. Glucose exposure from PD fluid during the period of every 2 consecutive visits was calculated as previously prescribed.[27]

Adverse Events

Adverse events included emerging complications and comorbid conditions, hospitalization, mortality, permanent switching to HD therapy, etc. Adverse events were ascertained based on medical records and self-report by participants or their family members.

Statistical Analyses

Results were expressed as mean $\pm$ standard deviation for continuous normally distributed variables, median and range for skewed variables, and frequency and percentage for categorical variables. Differences in patient demographic features; GFR, urine volume, and their decline rates; and clinical and laboratory parameters between groups were evaluated by t test for parametric data and Mann-Whitney test for nonparametric data. Comparisons of percentages between groups were made using χ^2 test. Anuria-free survival, technique survival, and patient survival curves were generated by the Kaplan-Meier method and compared on the basis of log-rank test. Pearson correlation analysis was used to investigate the correlation of daily ultrafiltration with daily urine volume. Comparisons between the 2 groups were done as intention-to-treat analyses. Data were censored at death, switch to maintenance HD therapy, kidney transplantation, or at 2 years after PD therapy initiation. Statistical analysis was performed using SPSS for Windows software, version 13.0 (SPSS Inc). $P < 0.05$ was considered statistically significant.

RESULTS

Study Participants, Patient Survival, and Technique Survival

From June 1, 2004, through December 31, 2008, a total of 285 patients initiated CAPD therapy in our center. Of these patients, 139 were recruited in the present study, 70 in the 3-exchange group and 69 in the 4-exchange group (Fig 1). Patients were comparable in terms of demographic characteristics, cause of ESRD, and comorbid conditions (Table 1).

None of the participants was lost to follow-up during the study. By the end of 2 years, deaths had occurred in 6 patients from the 3-exchange group (cerebral hemorrhage, 3; acute myocardial infarction, 1; sudden death, 1; gastrointestinal hemorrhage, 1) and 3 patients from the 4-exchange group (cerebral hemorrhage, 1; acute myocardial infarction, 2). Technique failure occurred in 1 patient from the 3-exchange group and 2 patients from the 4-exchange group; all 3 were switched to maintenance HD therapy due to refractory peritonitis. There was no