Peritoneal Dialysis International, Vol. 28, pp. 174–182
Printed in Canada.

0896-8608/08 $3.00 + .00

THE CLINICAL USEFULNESS OF PERITONEAL DIALYSIS FLUIDS WITH NEUTRAL pH AND LOW GLUCOSE DEGRADATION PRODUCT CONCENTRATION: AN OPEN RANDOMIZED PROSPECTIVE TRIAL

Hoon Young Choi, Dong Ki Kim, Tae Hee Lee, Sung Jin Moon, Seung Hyeok Han, Jung Eun Lee, Beom Seok Kim, Hyeong Cheon Park, Kyu Hun Choi, Sung Kyu Ha, Dae-Suk Han, and Ho Yung Lee

Division of Nephrology, Department of Internal Medicine, Institute of Kidney Disease, Yonsei University College of Medicine, Seoul, Korea

♦♦ ***Background:*** **Long-term peritoneal dialysis (PD) is associated with the development of various structural and functional changes to the peritoneal membrane when bioincompatible conventional peritoneal dialysis fluids (PDFs) are used. In this study, we looked at patients that were treated with conventional PDFs and then changed to novel biocompatible PDFs with a neutral pH and a low concentration of glucose degradation products (GDPs) to investigate whether this change could result in the arrest or reversal of peritoneal membrane deterioration.**

♦♦ ***Methods:*** **In an open label, randomized prospective trial, the clinical effects of conventional PDFs and biocompatible PDFs with neutral pH and very low concentration of GDPs were compared in 104 patients equally divided between both study PDFs. Blood and effluent dialysate samples, peritoneal equilibration tests, and adequacy evaluation were undertaken at baseline, 4, 8, and 12 months. The target variables were the ratio of dialysate-to-plasma (D/P) creatinine, peritoneal ultrafiltration, residual renal function, dialysis adequacy indices, and effluent cancer antigen 125 (CA125).**

♦♦ ***Results:*** **D/P creatinine values were not different in the two groups. Peritoneal ultrafiltration was significantly higher in the low-GDP PDF group than in the conventional PDF group at all follow-up times (4 months: 9.1 ± 4.3 vs 6.0 ± 3.0; 8 months: 8.3 ± 3.4 vs 6.0 ± 3.0; 12 months: 8.9 ± 3.3 vs 6.1 ± 3.3 mL/g dextrose/day; $p < 0.05$). Peritoneal Kt/V urea values and total weekly Kt/V urea values at 4 months were significantly higher in the low-GDP PDF group than in the conventional PDF group. Residual renal function was not statistically significant. Effluent CA125 levels were significantly higher in the low-GDP PDF group at all follow-up visits (4 months: 37.8 ± 20.8 vs 22.0 ± 9.5; 8 months: 41.2 ± 20.3 vs 25.9 ± 11.3; 12 months: 40.4 ± 21.4 vs 28.6 ± 13.0 U/mL; $p < 0.05$). Among anuric patients, peritoneal ultrafiltration at 4, 8, and 12 months, total weekly Kt/V at 4 and 8 months, and CA125 levels at all follow-up visits were significantly higher in patients treated with low-GDP PDF than those treated with conventional PDF. However, among anuric patients, D/P creatinine showed no significant differences between the low-GDP PDF group and the conventional PDF group.**

♦♦ ***Conclusion:*** **The use of biocompatible PDFs with neutral pH and low GDP concentration can contribute to improvement of peritoneal ultrafiltration and peritoneal effluent CA125 level, an indicator of peritoneal membrane integrity in PD patients.**

Perit Dial Int **2008; 28:174–182** **www.PDIConnect.com**

KEY WORDS: Glucose degradation products; neutral pH; biocompatibility; peritoneal function; CA125.

Peritoneal dialysis (PD) has been an important part of renal replacement therapy over the past 20 years. Although a number of studies have reported similar patient survival rates for PD and hemodialysis, all of those studies indicated lower technique survival rates for PD than for hemodialysis (1–5). Ultrafiltration (UF) failure remains a major cause of technique failure in patients treated with PD; the incidence of UF failure increases with PD duration because of acquired changes in peritoneal membrane function (6–13). The peritoneal membrane may be compromised by the development of various structural and functional alterations occurring during the course of long-term PD treatment. There is increasing evidence that repeated exposure to conventional peritoneal dialysis fluids (PDFs) plays a role in the development of peritoneal membrane changes (13,14). Conventional PDFs are bioincompatible because of their low pH, high glucose and lactate concentrations, hyperosmolality, and the presence of glucose degradation products (GDPs) formed during heat sterilization of the solutions. Recently, there has been increased interest

Correspondence to: H.Y. Lee, Department of Internal Medicine, Yonsei University College of Medicine, CPO Box 8044, Seoul, Korea.
hyl@yumc.yonsei.ac.kr
Received 18 December 2006; accepted 21 October 2007.

in the effect of glucose exposure on the peritoneal membrane's dialytic function. The alteration in dialytic function may be due to either the direct effects of glucose itself or to the GDPs formed during heat sterilization of the solutions. Absorption of GDPs from the peritoneal cavity may contribute to the generation of circulating carbonyl compounds, resulting in the acceleration of systemic advanced glycation end-product (AGE) formation and local AGE modification of peritoneal membrane structures, which is believed to be a major contributing factor to changes in membrane function (15–21). Therefore, low-GDP PDF may preserve peritoneal integrity and thus improve the longevity of the peritoneal membrane.

In a previous publication, we reported improved patient survival following the introduction of one such PDF (balance; Fresenius Medical Care, St. Wendel, Germany) in Korea (22). The aim of this current prospective study is to investigate the impact of novel PDFs with neutral pH and low GDP concentration on peritoneal solute and fluid transport characteristics, as well as on other biochemical and clinical parameters in PD patients.

METHODS

PATIENTS

A total of 126 PD patients in Yonsei University Severance Hospital were recruited. Each patient gave written informed consent before study entry; the local ethics committee gave approval for the study. Only patients that maintained continuous ambulatory PD (CAPD) with conventional PDFs for at least 6 months prior and were considered to be adequately dialyzed were enrolled. Patients used three or four 1.5- to 2.5-L exchanges per day, 7 days per week. Patients with dialysis-related complications (*e.g.*, CAPD peritonitis, exit-site infection, tunnel infection) within the previous 8 weeks or with more than 2 episodes of peritonitis within the previous 6 months were excluded. Twenty-two patients were excluded prior to the baseline study because of screening failure. The remaining 104 patients, after being assigned to a group, underwent a baseline study.

STUDY PROCEDURES AND MATERIALS

This was an open randomized prospective study with two parallel groups, comparing a conventional PD solution (C-PDF group) with a novel, neutral pH, low GDP concentration solution (balance; Fresenius Medical Care, Bad Homburg, Germany; L-GDP PDF group). The composition of each PDF is shown Table 1. After being randomly assigned to L-GDP PDF or C-PDF groups, all patients underwent an initial 4-week run-in phase. Subjects began the study phase, which provided for three additional assessment investigations at 4-month intervals, after the run-in phase (Figure 1).

A medical history was taken and a physical examination performed, which included mean arterial blood pressure, body mass index (BMI; kg/m^2), and nutritional status assessed by a Subjective Global Assessment (SGA) scale using a 7-point scoring system. This assessment was repeated at 4 months, 8 months, and 12 months. At

TABLE 1
The Composition of Each Study Solution

	Low-GDP PDF	Conventional PDF[a]
Sodium (mmol/L)	134	134
Calcium (mmol/L)	1.75	1.75
Magnesium (mmol/L)	0.5	0.5
Chloride (mmol/L)	101.5	103.5
Lactate (mmol/L)	35	35
Bicarbonate (mmol/L)	2	0
pH	7	5.5
Glucose (anhydrous; g/L)	15–42.5	15–42.5
3-deoxyglucosone (μmol/L)	42–60	172–324
Methylglyoxal (μmol/L)	<1	6–10
Acetaldehyde (μmol/L)	<2	152–182
Formaldehyde (μmol/L)	<3	7–13

GDP = glucose degradation product; PDF = peritoneal dialysis fluid.

[a] Conventional PDFs were made by Baxter Healthcare (Dianeal), Fresenius Medical Care (stay·safe), and Boryung Korea.

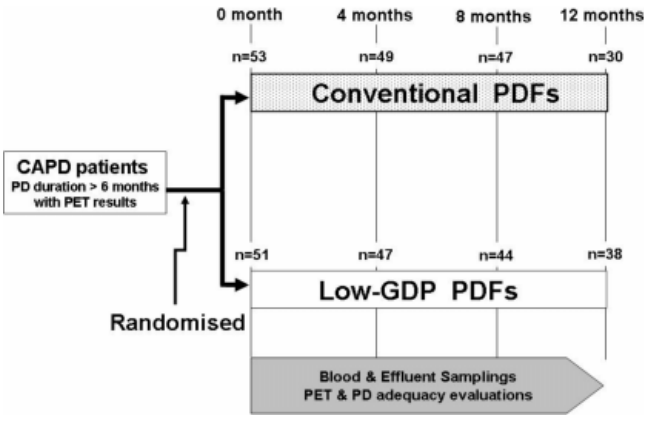

Figure 1 — The flow diagram of this study design and number of patients at each visit. PD = peritoneal dialysis; CAPD = continuous ambulatory PD; PET = peritoneal equilibration test; PDFs = peritoneal dialysis fluids; GDP = glucose degradation product.

the same times, blood and dialysate effluent samples were taken and the peritoneal equilibration test (PET) and adequacy evaluation were performed. Blood samples were analyzed for total venous CO_2, hemoglobin, albumin, calcium, phosphorus, total cholesterol, and C-reactive protein (CRP).

Peritoneal membrane function was evaluated by standard PET using a 2.5% glucose PD solution (23). Adequacy was calculated as Kt/V urea and creatinine clearance (L/week/1.73 m^2). These values were measured by collecting all of the dialytic effluent over a 24-hour period and taking a plasma sample during the PET. Residual renal function was evaluated by collecting all urine output over the same 24-hour period as the dialysate collection. Residual renal function (glomerular filtration rate; mL/minute) was calculated as the mean of renal urea and creatinine clearances.

Peritoneal UF, measured at each visit, was calculated as the difference in prescribed fill volume and measured drain volume over a 24-hour period. Ultrafiltration was adjusted for the prescribed dextrose load of PDF (UF as mL/g dextrose load per day). Creatinine clearance was standardized to a body surface area of 1.73 m^2, while urea clearance was expressed as Kt/V.

At the end of the 4-week run-in phase (0 months) and at the time points 4 months, 8 months, and 12 months, peritoneal effluent was collected from a timed overnight dwell (10 hours), using a 2.5% overnight drain. Approximately 50 mL of overnight drain fluids was collected and filtered, and 5-mL aliquots were stored at –70°C prior to assay in a single laboratory. Effluent CA125 was measured using an electrochemiluminescence immunoassay (Roche Diagnostics, GmbH, Mannheim, Germany) and CRP was measured by nephelometry (Dade Behring, Germany).

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, Illinois, USA). Simple comparisons between L-GDP PDF and C-PDF groups were made using an unpaired t-test. For a longitudinal view of the study, we analyzed the data by repeated-measures analysis of variance (ANOVA). This test was performed separately for each group. Change in D/P creatinine and change in peritoneal UF were calculated as percentage changes from the baseline values. Values are expressed as mean ± standard deviations. For display purposes, box and whisker plots were used. The median value is indicated within the box, each box including 50% of the values (the interquartile range), with the bars representing the highest and lowest values, excluding outliers and extreme values. A value of $p < 0.05$ was considered statistically significant.

RESULTS

BASELINE CLINICAL CHARACTERISTICS, PERITONEAL FUNCTION AND ADEQUACY, RESIDUAL RENAL FUNCTION

In the L-GDP PDF group, 13 patients exited the study due to peritonitis ($n = 3$), transplantation ($n = 1$), death due to causes unrelated to PD ($n = 3$), and withdrawal of informed consent for this study ($n = 6$) (L-GDP PDF group at 0 months: $n = 51$; 4 months $n = 47$; 8 months $n = 44$; 12 months $n = 38$). In the C-PDF group, 23 patients discontinued due to peritonitis ($n = 2$), death due to causes unrelated to PD ($n = 3$), and voluntary switch to the low-GDP PD solution ($n = 18$) (C-PDF group at 0 months: $n = 53$; 4 months: $n = 49$; 8 months: $n = 47$; 12 months: $n = 30$).

Baseline clinical characteristics of the two groups are shown in Table 2. Age, mean arterial pressure, proportion of diabetic patients, proportion of anuric patients, and PD duration were not significantly different between the two groups.

Actual D/P creatinine was not statistically different between the L-GDP PDF group and the C-PDF group (0 months: 0.67 ± 0.11 vs 0.67 ± 0.10; 4 months: 0.66 ± 0.10 vs 0.65 ± 0.10; 8 months: 0.67 ± 0.10 vs 0.66 ± 0.11; 12 months: 0.66 ± 0.10 vs 0.66 ± 0.11; p = NS). Change in D/P creatinine also showed no significant differences (Figure 2) between the two groups.

Dextrose loading of PDFs (g/day) was not different between the two groups. Peritoneal UF was significantly higher in the L-GDP PDF group than in the C-PDF group at all follow-up visits (Table 3). Peritoneal UF adjusted for dextrose load (UF as milliliters per gram dextrose load) was significantly higher in the L-GDP PDF group than in the C-PDF group at all follow-up visits (0 months: 7.5 ± 3.5 vs 6.3 ± 3.1, $p = 0.073$; 4 months: 9.1 ± 4.3 vs 6.0 ± 3.0; 8 months: 8.3 ± 3.4 vs 6.0 ± 3.0; 12 months: 8.9 ± 3.3 vs 6.1 ± 3.3 mL/g dextrose; $p < 0.05$). Change in peritoneal UF was significantly higher at 12 months in the L-GDP PDF group than in the C-PDF group (4 months: 33.1 ± 60.9 vs 21.8 ± 126.8, $p = 0.580$; 8 months: 19.5 ± 60.4 vs 15.0 ± 88.2, $p = 0.776$; 12 months: 25.8 ± 50.2 vs –12.6 ± 99.7, $p < 0.05$) (Figure 3).

Peritoneal Kt/V urea and total weekly Kt/V urea at 4 months were significantly higher in the L-GDP PDF group than in the C-PDF group (peritoneal Kt/V urea: 1.92 ± 0.37 vs 1.73 ± 0.30; total weekly Kt/V urea: 2.02 ± 0.39 vs 1.84 ± 0.33; $p < 0.05$), whereas renal Kt/V urea was not

TABLE 2
Baseline Clinical Characteristics and Biochemical Parameters in Low-GDP PDF Group and Conventional PDF Group

	Low-GDP PDF group (*n*=51)	Conventional PDF group (*n*=53)	*p* Value
Gender (male:female)	20:31	27:26	0.230
Age (years)	52.6±12.4	55.4±11.9	0.235
BMI (kg/m^2)	24.5±3.4	24.3±3.3	0.843
SGA	6.0±0.7	6.1±0.9	0.907
MAP (mmHg)	103.0±13.0	100.6±14.7	0.385
DM (yes:no)	9:42	10:43	0.872
PD duration (months)	67.0±46.7	70.4±45.8	0.709
Anuric patients (yes:no)	32:19	34:19	0.882
Hemoglobin (g/dL)	9.7±1.5	9.6±1.4	0.746
Calcium (mg/dL)	9.4±1.0	9.5±0.9	0.664
Phosphorus (mg/dL)	5.0±1.0	5.1±1.3	0.902
Fasting glucose (mg/dL)	100.1±23.7	107.2±37.4	0.254
Total protein (g/dL)	6.3±0.4	6.3±0.6	0.829
Albumin (g/dL)	3.6±0.3	3.5±0.4	0.356
Total cholesterol (mg/dL)	190.7±45.2	187.0±37.2	0.655
Total CO_2 (mmol/L)	24.7±3.6	25.1±3.3	0.602
CRP (mg/dL)	0.3±0.4	0.5±0.4	0.068

GDP = glucose degradation product; PDF = peritoneal dialysis fluid; BMI = body mass index; SGA = Subjective Global Assessment; MAP = mean arterial pressure; DM = diabetes mellitus; PD = peritoneal dialysis; CRP = C-reactive protein.
Data are expressed as number of patients and mean±SD. The number of patients was tested by chi-square and means by unpaired t-test. *p* Values compare Low-GDP PDF group to Conventional PDF group.

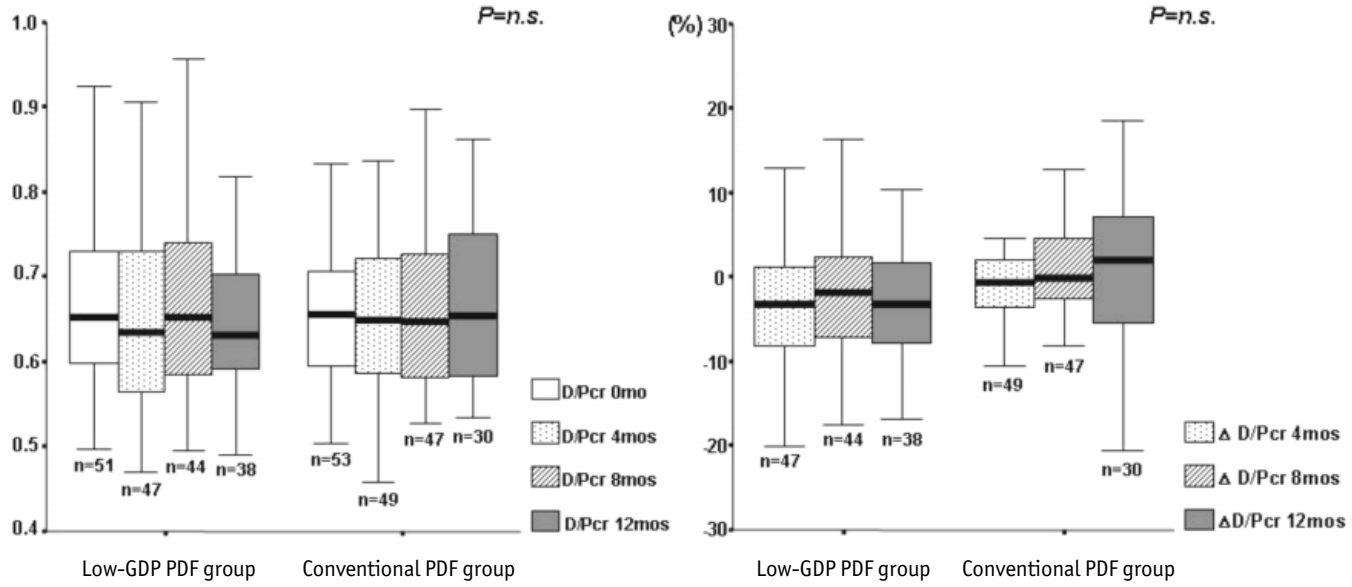

Figure 2 — Box plots of dialysis-to-plasma ratio of creatinine (D/Pcr; left panel) and change in D/P creatinine (ΔD/Pcr; right panel) for low-GDP PDF group and conventional PDF group. GDP = glucose degradation product; PDF = peritoneal dialysis fluid.

different between the two groups. Peritoneal, renal, and total weekly creatinine clearance values were not significantly different between the two groups (Table 3).

There were no significant differences in residual renal function, change in residual renal function (Figure 4), or urine volume between the two groups (Table 3).

EFFLUENT CA125 LEVELS

Effluent CA125 levels were significantly higher in the L-GDP PDF group at all follow-up visits during the 12 months (4 months: 37.8 ± 20.8 vs 22.0 ± 9.5; 8 months: 41.2 ± 20.3 vs 25.9 ± 11.3; 12 months: 40.4 ±

TABLE 3
Peritoneal Adequacy, Dextrose Loads of PDFs, Effluent CA125 Levels, and Urine Volume in Low-GDP PDF Group and Conventional PDF Group

	Low-GDP PDF group				Conventional PDF group			
	0 months	4 months	8 months	12 months	0 months	4 months	8 months	12 months
Peritoneal Kt/V urea	1.8±0.3	1.9±0.4[a]	1.8±0.3	1.8±0.3	1.70±0.3	1.7±0.3	1.7±0.39	1.7±0.3
Renal Kt/V urea	0.1±0.3	0.1±0.2	0.1±0.2	0.1±0.2	0.1±0.3	0.1±0.2	0.1±0.2	0.04±0.1
Total weekly Kt/V urea	1.9±0.4	2.0±0.4[a]	1.9±0.4	1.9±0.4	1.9±0.4	1.8±0.3	1.8±0.3	1.8±0.3
Peritoneal ClCr	49.2±7.0	51.3±9.0	49.3±7.4	48.7±6.0	48.3±6.3	49.8±8.8	48.0±6.2	48.3±6.2
Renal ClCr	7.9±17.7	5.7±11.0	4.9±10.9	4.7±10.7	8.9±22.9	5.7±11.0	5.2±9.5	1.86±6.44
Total ClCr	55.2±15.2	65.5±58.1	54.3±11.9	53.2±10.8	55.9±22.8	55.5±11.5	52.0±11.6	50.2±8.0
nPNA	0.9±0.2	0.9±0.2	1.0±0.2	0.9±0.2	0.9±0.2	0.9±0.2	0.9±0.2	0.9±0.2
Dextrose load (g/day)	145.1±38.3	146.1±31.4	145.0±29.2	151.4±54.5	155.7±44.3	160.6±43.0	159.8±43.7	167.3±38.8
UF (mL/day)	1110.8±555.2	1281.9±618.2[a]	1204.5±585.4[a]	1301.3±597.6[a]	921.2±498.0	954.1±542.7	922.3±496.7	981.7±538.8
Effluent CA125 (U/mL)	21.7±16.7	37.8±20.8[a,b]	41.2±20.3[a,b]	40.4±21.4[a,b]	21.2±10.5	22.0±9.5	25.9±11.3	28.6±13.0
Urine volume (mL/day)	385.5±330.7	272.6±217.8	215.3±222.5	280.0±236.6	447.1±278.4	383.7±272.0	362.5±332.1	143.0±172.9

PDF = peritoneal dialysis fluid; CA125 = cancer antigen 125; GDP = glucose degradation product; ClCr = creatinine clearance (L/week/1.73 m^2); nPNA = normalized protein equivalent of nitrogen appearance; UF = ultrafiltration.
[a] $p < 0.05$: Low-GDP PDF group versus Conventional PDF group.
[b] $p < 0.05$: baseline CA125 values versus those in other visit.
Data are expressed as mean±SD. The means at each visit were tested by unpaired t-test.

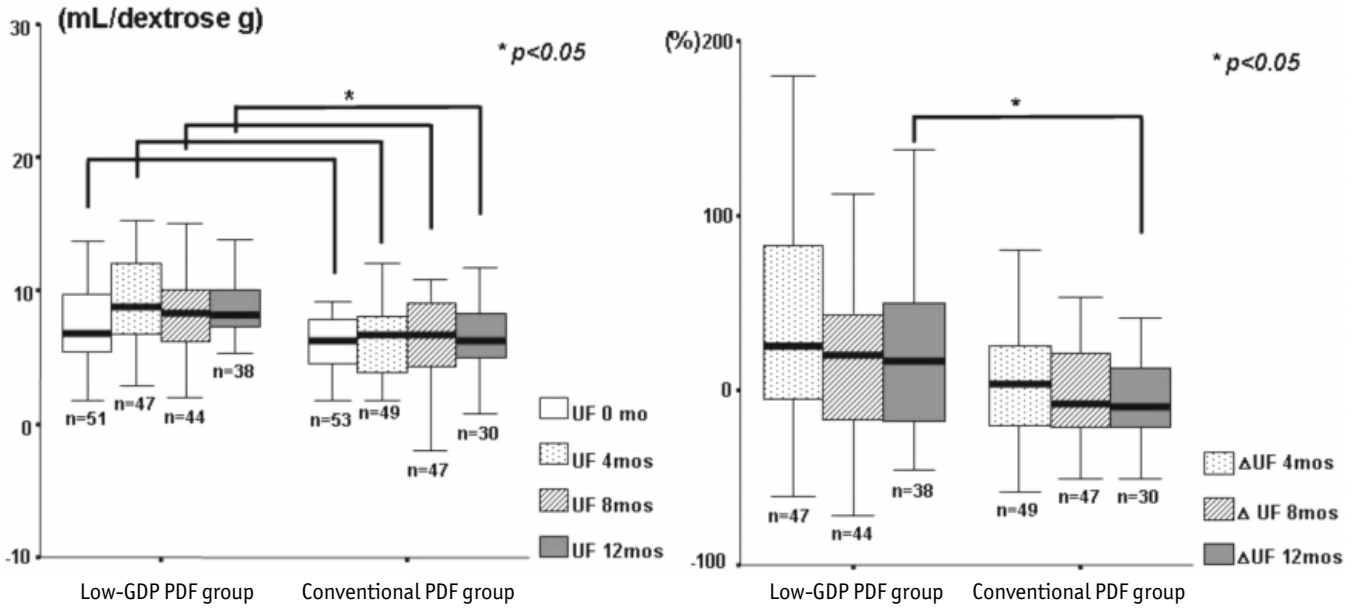

Figure 3 — Box plots of peritoneal ultrafiltration (UF; left panel) and change in peritoneal ultrafiltration (ΔUF; right panel) for low-GDP PDF group and conventional PDF group (mL/g dextrose load/day). GDP = glucose degradation product; PDF = peritoneal dialysis fluid.

21.4 vs 28.6 ± 13.0 U/mL; $p < 0.05$). Repeated-measures ANOVA comparing data from baseline (0 months) and other study visits revealed a significant increase in effluent CA125 levels within the L-GDP PDF group ($p < 0.05$). Mean effluent CA125 levels increased from 21.7 U/mL at 0 months to 37.8 U/mL at 4 months, 41.2 U/mL at 8 months, and 40.4 U/mL at 12 months. In the C-PDF group, there were no significant differences in effluent CA125 levels throughout the study (Table 3).

OTHER CLINICAL AND BIOCHEMICAL PARAMETERS

The CRP levels in the L-GDP PDF group were lower than those in the C-PDF group. The L-GDP PDF group main-

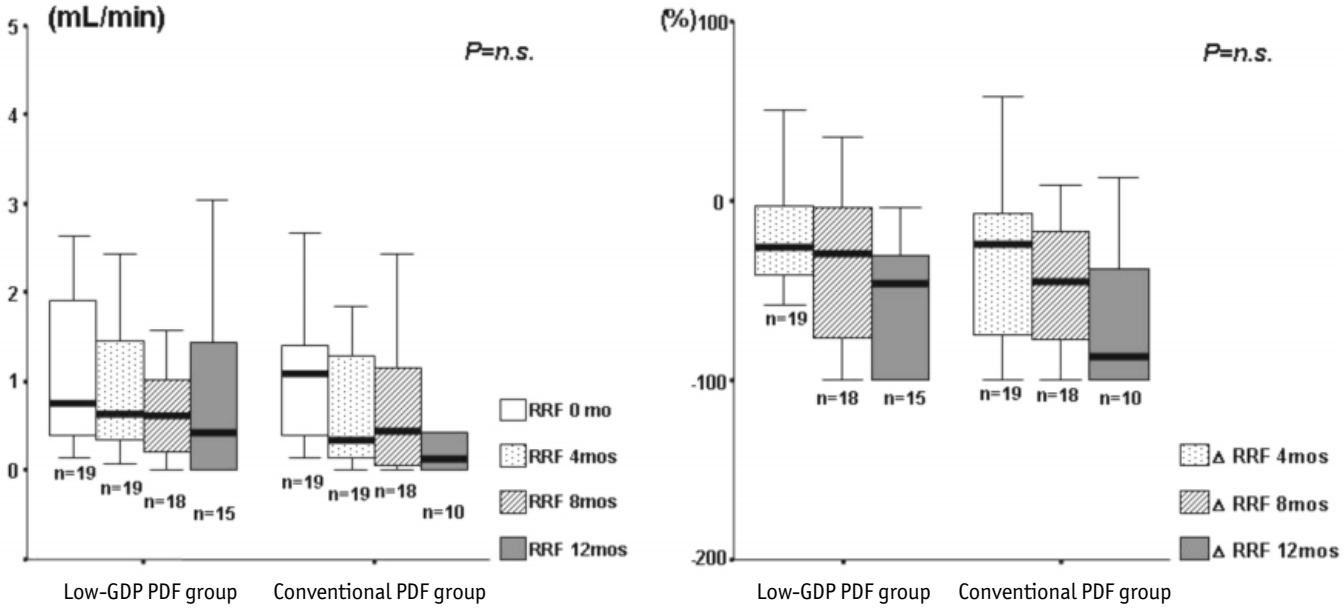

Figure 4 — Box plots of residual renal function (RRF; left panel) and change in residual renal function (ΔRRF; right panel) for low-GDP PDF group and conventional PDF group (mL/min). GDP = glucose degradation product; PDF = peritoneal dialysis fluid.

tained significantly lower CRP levels than the C-PDF group (Table 4). SGA was significantly higher in the L-GDP PDF group at 12 months than in the C-PDF group, while BMI was not different between the groups. Other biochemical parameters, such as total venous CO_2, hemoglobin, albumin, calcium, phosphorus, and total cholesterol, were not significantly different between the groups (Table 4).

ANURIC PATIENTS

The number of anuric patients (voided 0 mL of urine per day) was 32 in the L-GDP PDF group and 34 in the C-PDF group at 0 months. Peritoneal UF in anuric patients of the L-GDP PDF group was significantly higher than in anuric patients of the C-PDF group at 4, 8, and 12 months (0 months: 7.4 ± 3.1 vs 6.6 ± 3.9, $p = 0.34$; 4 months:

TABLE 4
Clinical and Biochemical Parameters in Low-GDP PDF Group and Conventional PDF Group

	Low-GDP PDF group				Conventional PDF group			
	0 months	4 months	8 months	12 months	0 months	4 months	8 months	12 months
BMI (kg/m^2)	24.5±3.4	24.3±3.4	25.0±3.5	25.3±3.3	24.3±3.3	24.6±3.3	24.6±3.4	25.5±3.7
SGA	6.0±0.7	5.9±0.8	6.1±0.8	6.4±0.7[a]	6.1±0.9	5.8±0.9	6.0±0.8	5.9±0.8
Hemoglobin (g/dL)	9.7±1.5	10.0±1.2	10.0±1.2	9.5±1.9	9.7±1.4	9.6±1.2	9.9±1.2	10.1±1.1
Calcium (mg/dL)	9.4±1.0	9.6±1.1	9.6±0.9	9.8±1.0	9.5±0.9	9.6±0.9	9.7±0.8	9.8±0.7
Phosphorus (mg/dL)	5.0±1.0	4.9±1.1	5.1±1.2	5.2±1.2	5.1±1.3	5.2±1.3	5.3±1.3	5.3±1.4
Fasting glucose (mg/dL)	100.1±23.7	100.7±26.6	102.0±32.1	100.1±24.1	107.2±37.4	101.4±29.3	101.0±26.5	102.4±25.1
Total protein (g/dL)	6.3±0.4	6.3±0.5	6.3±0.5	6.3±0.5	6.3±0.6	6.4±0.7	6.3±0.6	6.7±5.4
Albumin (g/dL)	3.6±0.3	3.5±0.3	3.5±0.3	3.5±0.3	3.5±0.4	3.6±0.4	3.5±0.4	3.7±0.4
Total cholesterol (mg/dL)	190.7±45.2	189.1±47.7	178.0±32.0	18.51±38.9	187.0±37.2	185.3±31.2	180.7±32.9	180.3±53.7
Total CO_2 (mmol/L)	24.7±3.6	24.4±2.8	25.0±2.4	23.8±4.0	25.1±3.3	25.5±3.1	25.6±2.5	23.8±4.2
CRP (mg/dL)	0.32±0.35	0.30±0.28[a]	0.28±0.48[a]	0.33±0.36[a]	0.46±0.41	0.74±1.15	0.59±0.79	0.59±0.67

GDP = glucose degradation product; PDF = peritoneal dialysis fluid; BMI = body mass index; SGA = Subjective Global Assessment; CRP = C-reactive protein.
[a] p Values < 0.05 compare Low-GDP PDF group versus Conventional PDF group.
Data are expressed as mean±SD. The means at each visit were tested by unpaired t-test.

8.7 ± 3.9 vs 6.5 ± 2.8; 8 months: 8.5 ± 3.5 vs 6.4 ± 2.9; 12 months: 8.9 ± 4.1 vs 6.5 ± 2.2 mL/g dextrose; $p < 0.05$). The L-GDP PDF group had significantly higher peritoneal Kt/V than the C-PDF group at 4 and 8 months (0 months: 1.8 ± 0.3 vs 1.7 ± 0.3, $p = 0.24$; 4 months: 2.0 ± 0.4 vs 1.7 ± 0.3; 8 months: 1.9 ± 0.3 vs 1.8 ± 0.3; $p < 0.05$). Effluent CA125 levels in the L-GDP PDF group were significantly higher at all follow-up visits than in the C-PDF group (0 months: 22.1 ± 14.6 vs 19.0 ± 8.9, $p = 0.31$; 4 months: 40.7 ± 24.6 vs 21.1 ± 9.1; 8 months: 42.3 ± 21.8 vs 26.1 ± 12.1; 12 months: 41.8 ± 20.3 vs 29.9 ± 14.7 U/mL; $p < 0.05$). Peritoneal creatinine clearance and D/P creatinine showed no differences between the groups.

DISCUSSION

We performed a randomized prospective study with parallel arms to demonstrate the clinical effects of a novel, neutral pH, low GDP concentration PDF on peritoneal membrane function and other biochemical parameters, compared to conventional lactate-buffered PDF.

We found no statistically significant differences in D/P creatinine or in change of D/P creatinine. Rippe *et al.* also demonstrated no significant differences in peritoneal transport characteristics by the assessment of unrestricted pore area over unit diffusion path length ("area parameter": for small solute transport; $A_0/\Delta x$) among patients treated with conventional PDFs and low-GDP PDFs (24,25). The Euro-Balance Trial group, however, reported D/P creatinine to be higher in patients treated with low-GDP PD solution (26).

Previous reports show varying results of peritoneal UF in PD patients treated with low-GDP PD solutions. In the Euro-Balance Trial, a decrease in peritoneal UF in was reported in their low-GDP PDF treatment group (26). However, the present study demonstrated that peritoneal UF was significantly higher in the L-GDP PDF group than in the C-PDF group at all follow-up visits. Net peritoneal UF was adjusted according to dextrose load, which was calculated from all four bags during 24 hours. The changes in peritoneal UF were more significant in the L-GDP PDF group than in the C-PDF group. The exact mechanisms for this difference are unclear. One hypothesis was postulated that, because subjects in this study had been maintained on CAPD for more than 6 years by the beginning of the study (L-GDP PDF group: 67.0 months; C-PDF group: 70.4 months), the characteristics of the peritoneal membrane could have changed during the long duration of treatment with CAPD. Therefore, the responses to the conversion from bioincompatible conventional PDFs to low-GDP PDFs may have been different from those in the Euro-Balance Trial. However, the Bicarbonate/Lactate Study Group demonstrated a statistically significant increase in mean net 24-hour peritoneal UF during the 6-month treatment period versus baseline in the bicarbonate/lactate PD solution treatment group (27). They also found that mean glucose concentration calculated from all four bags was relatively constant over the 6 months that UF measurements were made. In a subgroup analysis of anuric patients in the Euro-Balance Trial, membrane function, as assessed by D/P creatinine and peritoneal UF, showed no significant differences between the groups, although there was a tendency for UF to decrease over the course of the study in the Balance group (26). Our data demonstrated no significant difference in D/P creatinine among anuric patients treated with either PDF. However, the anuric patients in the L-GDP PDF group showed significantly higher peritoneal UF values than the C-PDF group.

Previous clinical trials of low-GDP PDFs showed no significant changes in Kt/V urea, as shown by urea clearance (27). The Euro-Balance Trial group revealed inconsistent results in changes in Kt/V in the group treated with Balance PDF (26). In our study, peritoneal Kt/V urea was significantly higher in the L-GDP PDF group at 4 months than in the C-PDF group. This difference was magnified among anuric patients and found to be present at 4 and 8 months. However, these effects of urea clearance were concealed at following visits. Contrary to urea clearance, creatinine clearance was not different between the two groups. This might imply that low-GDP PDF treatment could cause substantial enhancement of peritoneal UF along with removal of small molecules.

In the present study, residual renal function and urine volume showed no significant differences between the two groups. However, the number of patients that maintained urine volume during the 12-month study period was too small, raising the possibility of a type II error.

Cancer antigen 125 levels were consistently higher in the L-GDP PDF group at all follow-up visits during the 12-month period. First described by Visser *et al.*, CA125 has been well-established as a marker of mesothelial cell mass and turnover in *in vitro* and *in vivo* studies (28–33). In a previous study, longitudinal follow-up of CA125 levels in peritoneal effluent showed a negative trend over the course of PD. CA125 can be used to monitor the integrity of the mesothelium in PD patients (30). The mesothelium is thought to influence the kinetics of PD. After a few years on PD, the mesothelium is degraded due to repeated episodes of peritonitis and accumulating cytotoxicity driven by either glucose or GDPs in the PDF (34,35). All the PD patients in the present study had al-

ready been exposed to conventional PDFs, so their CA125 levels were similar upon beginning our study. Using ANOVA for repeated measures, CA125 levels within the L-GDP PDF group increased significantly from baseline values, while those in the C-PDF group remained stable. These higher effluent CA125 levels may imply that healthy mesothelial cell physiology could be restored with the use of novel, low GDP concentration PDFs.

Previous studies of biocompatible PDFs were associated with decreased interleukin-6 synthesis and vascular endothelial growth factor secretion. These data suggest that the biocompatible PDFs are associated with reduced intraperitoneal inflammation and reduced potential for angiogenesis (36,37). The higher levels of CRP in the C-PDF group at all follow-up visits may reflect an increase in chronic inflammation among PD patients treated with conventional PDFs compared to those treated with the novel PDFs in this study.

In conclusion, the present study compares the clinical impact of novel, low GDP concentration, biocompatible PDFs with conventional PDFs. We compared peritoneal function and other biochemical parameters such as effluent CA125 and CRP. The use of biocompatible PDFs with neutral pH and low GDP concentration may contribute to improvement of peritoneal ultrafiltration and increase peritoneal effluent CA125, a marker of peritoneal membrane integrity. This may preserve peritoneal solute transport in PD patients, including those with anuria.

ACKNOWLEDGMENTS

This study was supported by a faculty research grant of Yonsei University College of Medicine in 2005 (No. 6-2005-0045), by a research grant from the Korean Society of Nephrology in 2005, and by Fresenius Medical Care (FMC).

We thank Dr. Feidhlim Woods, Senior Vice President of FMC Asia Pacific (Hong Kong), for his advice on the statistical analysis and his help in preparing the manuscript. We also appreciate FMC for supporting this study.

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