

Original Article

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

Cheuk-Chun Szeto¹, Kai-Ming Chow¹, Christopher Wai-Kei Lam², Chi-Bon Leung¹, Bonnie Ching-Ha Kwan¹, Kwok-Yi Chung¹, Man-Ching Law¹ and Philip Kam-Tao Li¹

¹Department of Medicine & Therapeutics and ²Department of Chemical Pathology, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China

Abstract

Background. Chronic utilization of a bio-incompatible peritoneal dialysis (PD) solution with acidic pH and a high content of glucose degradation product (GDP) has been implicated as a contributing cause of peritoneal failure. We compared a newly formulated solution of neutral pH and low levels of GDP to a standard PD solution.

Methods. Fifty new PD patients were randomized to a conventional lactate-buffered fluid (control) and a pH neutral, lactate-buffered, low GDP solution (balance). Patients were followed for 12 months. Serum samples were assayed for C-reactive protein (CRP). PD effluent was collected and assayed for cancer antigen-125 (CA125) and hyaluronan (HA). Clinical end points were the residual renal function and dialysis adequacy indices.

Results. After 52 weeks of treatment, PD fluid CA125 rose from 2.45 ± 0.96 to 14.30 ± 2.17 U/ml ($P < 0.001$), and HA declined from 2.26 ± 0.60 to 1.45 ± 0.32 μ g/ml ($P = 0.07$) in the balance group. The balance group had a higher PD fluid CA-125 (14.30 ± 2.17 vs 7.36 ± 2.23 U/ml, $P = 0.007$), lower HA (1.45 ± 0.32 vs 2.55 ± 0.32 μ g/ml, $P = 0.007$), and lower serum CRP level (1.77 ± 0.42 vs 7.73 ± 2.42 mg/l, $P = 0.026$) than the control group at 52 weeks. There was no difference in dialysis adequacy indices, ultrafiltration volume, urine output, residual renal function, peritonitis rate or need of hospitalization in 1 year.

Conclusion. As compared to conventional PD solution, the use of balance, a neutral pH, low GDP solution resulted in a superior profile of PDE mesothelial cell marker and a lower degree of systemic inflammation, and the difference was maintained for 1 year.

It remains to be determined whether these effects could result in better long-term clinical outcome.

Keywords: biocompatibility; inflammation; nutrition; renal failure

Introduction

Chronic utilization of a bio-incompatible peritoneal dialysis (PD) solution has been implicated as a cause of progressive loss of peritoneal permeability [1,2]. Acidic pH and glucose degradation product (GDP) in the conventional PD solution are the major factors of bio-incompatibility [3,4]. Recently, a double-chamber bag Stay-Safe[®] Balance system (Fresenius Medical Care, Germany) became available. This system utilizes lactate-buffered PD solution in a two-compartment bag offered in the Stay-Safe[®] disconnect system. The formation of GDP is greatly reduced by separating the glucose component of the solution (kept at very low pH) from the lactate component of the solution (kept at alkaline pH) during sterilization and storage. Immediately before infusion, the seam between the two chambers is opened, and the contents are mixed. The ready-to-use solution has a physiological pH in the range 6.8–7.4, and a greatly reduced amount of GDP [5].

Previous studies show that PD solution with neutral pH and low GDP offers clinical benefit [6–10]. An observational study suggested that a short-term treatment of 8 weeks with the Stay-Safe Balance solution improved mesothelial cell mass as indicated by a rise in the dialysate level of cancer antigen-125 (CA-125) [6]. Both Jones *et al.* [7] and Rippe *et al.* [8] found that, as compared to the conventional PD solution, patients treated with a PD solution with neutral pH and low GDP content had a higher concentration of CA125 and lower hyaluronan (HA) in the overnight effluent,

Correspondence and offprint requests to: Dr C.-C. Szeto, Department of Medicine & Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China. Email: ccszeto@cuhk.edu.hk

indicating less mesothelial and interstitial damage. In a European multicentre prospective crossover trial that compared conventional solution with the new neutral solution [9], patients treated with the new solution had an improved profile of dialysate mesothelial markers. More importantly, residual renal function was better preserved with the new solution [9]. Nevertheless, because of the crossover design, a change in peritoneal transport and clinical outcome could not be determined with certainty. Another retrospective observational study that compared incident PD patients treated with conventional PD solution to those with the new solution found a significant survival advantage with the new solution [10]. Since there is no prospective randomized study on the long-term *in vivo* effect of this biocompatible solution, we performed a prospective randomized controlled study on the double-chamber bag Stay-Safe[®] Balance system to examine its *in vivo* effects on peritoneal transport, serum inflammatory marker and PD effluent (PDE) markers of biocompatibility.

Patients and methods

Patient selection

The study was approved by the Clinical Research Ethical Committee of the Chinese University of Hong Kong. Fifty new continuous ambulatory peritoneal dialysis (CAPD) patients were enrolled: 25 with the Balance system (balance group) and 25 with the disconnect system with glucose-based dialysis solution (Stay-Safe[®], Fresenius Medical Care, Germany) (control group). We excluded patients who were unlikely to survive, planned to have elective living-related kidney transplant or transfer to other renal center within 6 months. Informed consent was obtained at the time of Tenckhoff insertion. Individuals were randomized by drawing sealed envelopes, which were prepared and then maintained by a third party not involved in the conduction of the study. Training for CAPD exchange was performed according to our routine clinical practice.

Clinical follow up

Baseline clinical data were recorded by chart review. These included age, sex, underlying renal disease and CAPD regimen. A panel of comorbid conditions, including coronary artery disease, heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disorder, peptic ulcer disease, liver disease, diabetes with and without complications, hemiplegia, malignancy and acquired immunodeficiency syndrome (AIDS), were also recorded. The modified Charlson's Comorbidity Index, which was validated in CAPD patients [11], was used to calculate a comorbidity score.

Patients were followed at 0, 4, 8, 16, 24, 32, 40 and 52 weeks. Except for the dialysis solution preparation, the clinical management was identical for the two groups. No patient received an amino acid or glucose polymer-based PD solution. Dialysis prescription was changed only

when there was clinical evidence of under-dialysis [12]. We documented the following during each follow-up visit: body weight, blood pressure, presence of oedema (semi-quantitative score from 0 to 3+), and compliance to dialysis exchange by direct questioning. Haemoglobin level, serum electrolytes, urea and creatinine were checked upon each clinic visit. Peritoneal glucose exposure over 1 year was expressed as the total annual exposure to glucose calculated from the dialysis regimen reported every 6 months as described by Davies *et al.* [13].

Biocompatibility marker levels in PDE

We have previously described our methods for estimation of peritoneal biocompatibility markers [14]. Briefly, PDE samples (glucose 1.56% for 4h) were collected and the volume measured. Well-mixed PDE samples were centrifuged at 1600 rpm for 10 min at room temperature. Cell-free PDE samples were collected and stored at -70°C until analysis. HA was measured by an ELISA assay (Corgenix Inc., Westminster, CO) with a detection limit of 10 ng/ml. CA125 level was measured by ELISA assay (Alpha Diagnostic International, San Antonio, TX) with a detection limit of 5 U/ml. Sandwich ELISA were used to measure TGF- β 1 in PDE (Biosource International Inc., Camarillo, CA). The detection limit of the assay was 15.6 pg/ml. All assays were performed according to the manufacturer's instructions. All samples were assayed at the same time to avoid inter-batch variation. Intra-assay coefficient of variation was less than 8%.

Nutritional, inflammation and dialysis adequacy assessment

Nutritional status was assessed by subjective global assessment (SGA), normalized protein nitrogen appearance (nPNA), serum albumin level and fat-free oedema-free body mass (FEBM). SGA was performed at 4, 24 and 52 weeks by trained observers who were blinded from the treatment group allocation and biochemical results of the patients. The four-item 7-point system was used [15]. As described in our previous study [16], the observers were trained to achieve a Cohen's kappa concordant coefficient for agreement of 0.84, which was an excellent level of agreement. At 4, 24 and 52 weeks, serum C-reactive protein (CRP) was measured by the Tina-quant CRP (Latex) ultra sensitive assay (Roche Diagnostics GmbH, Mannheim, Germany) as described in our previous studies [16,17].

At 4 and 52 weeks, 24h urine and dialysate collection was performed. Total ultrafiltration from CAPD was recorded. FEBM was calculated according to the formula described by Forbes and Brunining [18]. The nPNA was calculated by the modified Bergstrom's formula [19] and normalized to the ideal body weight (IBW), which was determined by the body height and sex according to a standard formula validated in Southern Chinese [20]. Kt/V and weekly creatinine clearance (CCr) were determined by standard methods [21]. Residual glomerular filtration rate (GFR) was calculated as the average of 24 h urinary urea and CCr, as described [22]. Serum albumin was measured by bromocresol purple method. All biochemical tests were performed in our hospital laboratory, which has meticulous quality control and is accredited as the Area of

Medical Testing by the National Association of Testing Authorities (NATA), Australia, in conjunction with the Royal College of Pathologists of Australasia.

Patient satisfaction and quality of life

Patient satisfaction and quality of life were assessed at 4 and 52 weeks by a questionnaire adapted from the Chinese version of World Health Organization Quality of Life—Brief version (WHOQOL-BREF) questionnaire [23,24] and validated by the Hong Kong Society of Nephrology.

Clinical outcome

The primary outcome measure was the peritoneal transport, serum inflammatory marker and PDE markers of biocompatibility. Secondary outcomes included nutritional and adequacy indices, residual renal function, peritonitis-free survival, hospitalization and actuarial and technique survival. Technique failure was defined as transfer to long-term haemodialysis.

Statistical analysis

The sample size was estimated by the Power Analysis and Sample Size for Windows software (PASS 2000, NCSS, Kaysville, Utah). Based on our preliminary data on PDE HA level [25], group sizes of 23 achieve 82% power to detect a difference of 100 µg/l between the study groups, with a significance level (alpha) of 0.05. Allowing for a 10% dropout rate, the study required 25 patients per arm.

Statistical analysis was performed by SPSS for Windows software version 11.0 (SPSS Inc., Chicago, IL). All data are expressed as mean ± SD unless otherwise specified. Parameters between groups are compared by Chi-square test, Student's *t*-test, or Mann–Whitney U-test as appropriate. Similar to our previous study [19], we analysed the effect of the dialysis system on longitudinal changes in biocompatibility marker levels in PDE and nutritional indices by the repeated measures analysis of variance (ANOVA), with the above-mentioned parameters as the repeated measure, treatment group as the between group factor and the age and Charlson's Comorbidity Index as covariate. The latter two factors were selected as covariates for the repeated measures ANOVA because baseline analysis showed substantial, though not statistically significant, differences in these two parameters between the treatment groups (see next). In this model, longitudinal change of a variable is represented by the interactions between follow-up time and the variable. A significant interaction between the treatment group and time indicates that the treatment group allocation has a significant effect on the parameter. *Post-hoc* analysis was performed by Student's *t*-test with Bonferroni's adjustment.

Results

The baseline clinical characteristics, major comorbid conditions are summarized in Table 1. There was no significant difference in any baseline parameter between the two groups. Although the balance group

Table 1. Baseline characteristics of the patients

	Control group	Balance group
No. of patient	25	25
Sex (M:F)	14:11	16:9
Age (years)	55.0 ± 13.7	60.9 ± 11.2
Body height (cm)	159.7 ± 7.2	160.7 ± 6.8
Body weight (kg)	59.4 ± 9.9	59.5 ± 8.7
Diagnosis (no. of cases)		
Glomerulonephritis	11	7
Diabetes	5	9
Hypertensive	4	3
Polycystic	1	0
Obstruction	1	1
Others/unknown	3	5
Major comorbidity (no. of cases)		
Coronary heart disease	4	5
Congestive heart failure	2	5
Peripheral vascular disease	0	3
Cerebrovascular disease	2	1
Dementia	0	1
Chronic pulmonary disease	1	1
Connective tissue disorder	0	0
Peptic ulcer disease	3	0
Mild liver disease	2	3
Diabetes	3	1
Hemiplegia	0	0
Diabetes with end-organ damage	5	9
Any tumour, leukaemia, lymphoma	1	0
Moderate or severe liver disease	1	1
Metastatic solid tumour	0	0
AIDS	0	0
Charlson's Index score	4.68 ± 2.19	5.40 ± 2.26

was marginally older and had a higher Charlson's comorbidity index score (Table 1), neither of the differences was statistically significant. One patient with hypertensive nephrosclerosis randomized to the balance group developed nosocomial pneumonia before CAPD training; another patient with underlying glomerulonephritis from the control group received a kidney transplant before completing the study. Both cases were excluded from further analysis.

Mesothelial and inflammatory markers

The change in PDE markers is summarized in Figure 1. After 52 weeks of CAPD, PDE CA125 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 ($P = 0.009$). PDE HA declined from 2.26 ± 0.60 to 1.45 ± 0.32 µg/ml in the balance group ($P = 0.07$), but increased from 1.96 ± 0.33 to 2.55 ± 0.32 µg/ml in the control group ($P = 0.12$). At 52 weeks, the balance group had a higher PDE CA125 (14.3 ± 2.2 vs 7.4 ± 2.3 U/ml, $P = 0.007$) and lower HA (1.45 ± 0.32 vs 2.55 ± 0.32 µg/ml, $P = 0.007$) than the control group. Repeated measures ANOVA confirmed a significant effect of treatment group on the change in PDE CA125 and HA levels after adjusting for patient age and Charlson's comorbidity score. On the other hand, the TGF-β concentration in the PDE in both groups declined significantly over 52 weeks

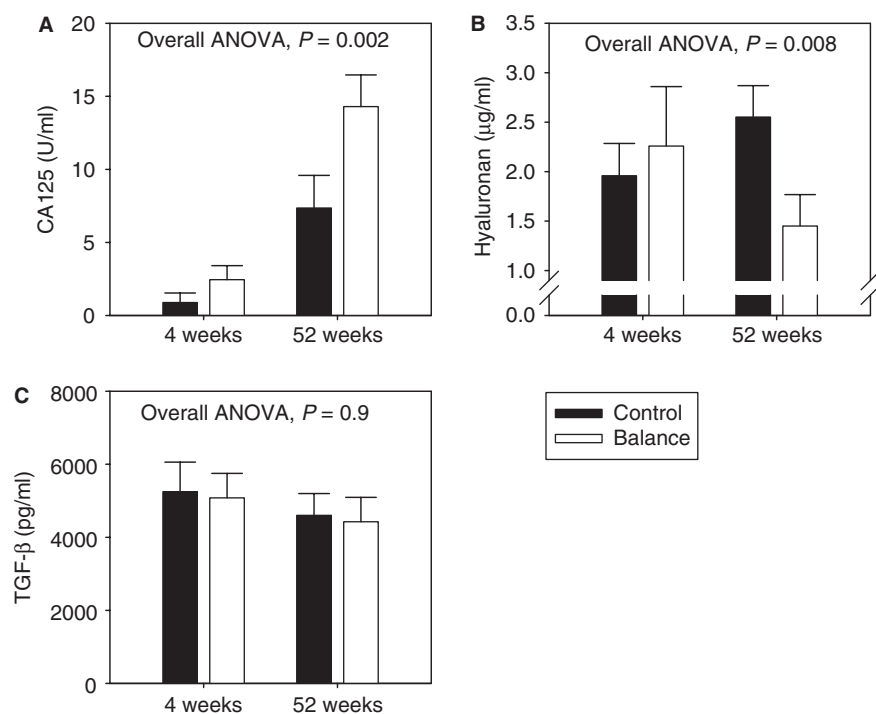


Fig. 1. Peritoneal dialysis effluent (PDE) markers of the two groups at 4 and 52 weeks: (A) cancer antigen-125 (CA-125); (B) hyaluronan; and (C) transforming growth factor beta (TGF- β). P values depicted are computed by repeated measures analysis of variance (ANOVA). Error bars denote SDs.

(5080 \pm 669 to 4424 \pm 669 pg/ml and 5249 \pm 809 to 4600 \pm 597 pg/ml for balance and control groups, respectively, $P < 0.01$ for both), but there was no difference in PDE TGF- β level between the groups at any time point.

The change in serum CRP is shown in Figure 2. Serum CRP declined from 3.09 \pm 0.72 to 1.77 \pm 0.42 mg/l in the balance group over 52 weeks ($P = 0.05$), while that of the control group remained static (from 5.31 \pm 2.01 to 7.73 \pm 2.42 mg/l, $P = 0.3$). The control group had a higher serum CRP levels than the balance group at all time points (for example, 1.77 \pm 0.42 vs 7.73 \pm 2.42 mg/l at 52 weeks, $P = 0.026$), and the difference remained statistically significant with repeated measures ANOVA after adjusting for patient age and Charlson's comorbidity score.

Nutrition, dialysis adequacy and residual renal function

The changes in dialysis adequacy, residual renal function and nutritional indices are summarized in Table 2. At 4 weeks, total Kt/V , ultrafiltration, urine volume, residual GFR and most of the nutritional indices were similar between the groups. The control group had a higher serum albumin and a better anorexia score in SGA than the balance group ($P = 0.004$ and $P = 0.023$, respectively), but the difference disappeared by 52 weeks. The balance group had a similar rate of decline in residual GFR similar to the control group (-1.19 ± 2.23 vs -1.02 ± 3.27 ml/min/ 1.73 m², $P = 0.8$). By the end of the study, 2 patients

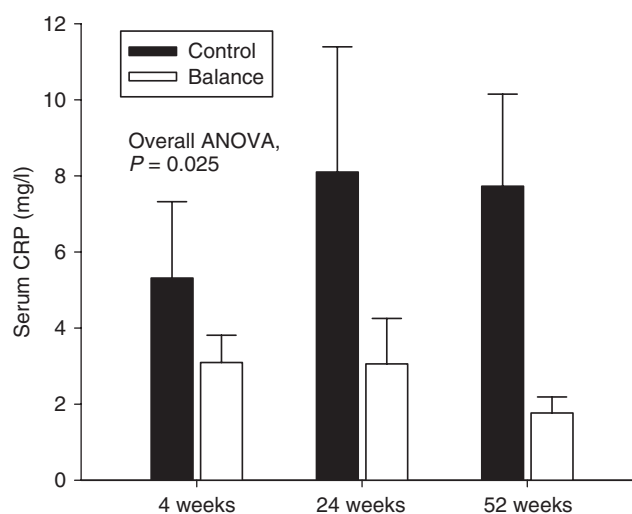


Fig. 2. Serum C-reactive protein (CRP) level of the two groups during the study period. P values depicted are computed by repeated measures analysis of variance (ANOVA). Error bars denote SDs.

(91.7%) in the balance group and 19 (79.2%) in the control group had a 6 l/day PD exchange ($P = 0.2$). The total glucose exposure during the 52 weeks of treatment was 34902 \pm 5808 and 37425 \pm 6045 gm for the balance and control groups, respectively ($P = 0.15$).

Peritonitis, hospitalization and survival

There was no difference in the peritonitis-free survival between the groups, as summarized in Figure 3.

Table 2. Dialysis adequacy, residual renal function and nutritional indices

	Control group		Balance group	
	4 weeks	52 weeks	4 weeks	52 weeks
PD exchange volume (l/day)	6.08 ± 0.40	6.42 ± 0.83	6.08 ± 0.41	6.17 ± 0.57
Glucose load (g/day)	100.9 ± 17.7	106.7 ± 24.9	100.7 ± 14.6	106.2 ± 23.7
Total <i>Kt/V</i>	2.23 ± 0.62	2.12 ± 0.32	2.28 ± 0.35	2.16 ± 0.56
Ultrafiltration (l/day)	0.56 ± 0.69	0.77 ± 0.59	0.56 ± 0.60	0.83 ± 0.56
Urine output (l/day)	0.90 ± 0.71	0.69 ± 0.52	0.87 ± 0.62	0.80 ± 0.60
Residual GFR (ml/min/1.73 m ²)	3.67 ± 2.27	2.81 ± 2.87	3.91 ± 2.09	2.72 ± 2.08
Serum albumin (g/l)	36.5 ± 4.1	35.7 ± 3.2	32.8 ± 4.4	34.3 ± 4.2
nPNA (g/kg/day)	1.18 ± 0.19	1.16 ± 0.17	1.07 ± 0.19	1.14 ± 0.21
FEBM (kg)	44.4 ± 7.8	51.5 ± 12.1	42.8 ± 9.3	51.7 ± 12.6
SGA score				
Overall	5.24 ± 0.78	5.30 ± 0.97	4.83 ± 0.87	5.26 ± 0.86
Anorexia	5.52 ± 0.77	5.39 ± 1.08	4.92 ± 1.02	5.35 ± 1.11
Weight loss	5.40 ± 0.91	5.30 ± 1.22	5.04 ± 1.23	5.39 ± 1.23
Subcutaneous fat	4.88 ± 1.01	5.26 ± 1.01	4.71 ± 0.86	5.17 ± 0.89
Muscle mass	4.92 ± 0.95	5.13 ± 1.10	4.46 ± 1.02	5.22 ± 0.74

PD, peritoneal dialysis; GFR, glomerular filtration rate; nPNA, normalized protein nitrogen appearance; FEBM, fat-free oedema-free body mass; SGA, subjective global assessment.

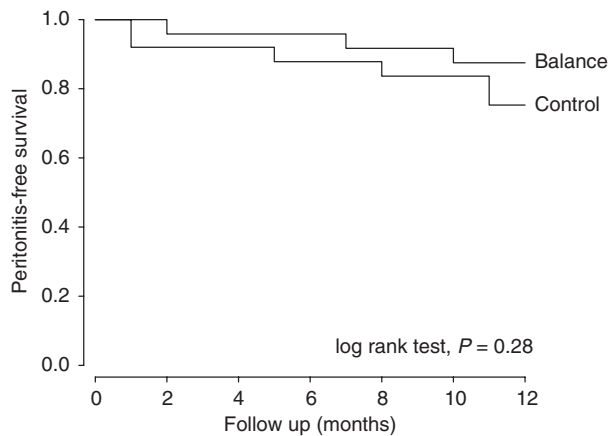


Fig. 3. Peritonitis-free survival. At 12 months, the peritonitis-free survival of the balance and control groups were 87.5% and 75.3%, respectively.

Over the 52 weeks of study period, the balance and control groups were hospitalized for 5.7 ± 11.4 vs 6.1 ± 10.9 days, respectively ($P=0.9$). As described earlier, one patient of the control group received a kidney transplant. No patient died or transferred to long-term haemodialysis during the study period.

Quality of life and patient satisfaction

The result of the modified WHOQOL-BREF questionnaire is summarized in Table 3. In short, there was no significant difference in any of the quality of life or patient satisfaction parameters between the groups throughout the study period.

Discussion

There is early experimental evidence suggesting beneficial effects of the lactate-based pH-neutral, low

GDP PD solution on the peritoneal membrane. Exposure of human peritoneal mesothelial cells (HPMC) *in vitro* to conventional PD solution resulted in a significant reduction in IL-6 release, which was fully restored following exposure to the Stay-Safe[®] Balance solution [6]. While exposure to conventional PD solution resulted in a significant reduction in HPMC viability after just 3–5 days, no significant cytotoxicity of the Stay-Safe[®] Balance solution was observed for up to 13 days [6]. Furthermore, there was a better preservation of *in vitro* phagocyte function with the new low GDP PD solution [26], and *in vitro* formation of advanced glycation end-product (AGE) was substantially reduced [27]. In a rat model of PD, chronic exposure to a PD solution with low GDP and a physiologic pH reduced the intraperitoneal inflammatory reaction, peritoneal fibrosis [28], and peritoneal vasodilatation [29].

In spite of our careful conduction of the randomization, there were important differences in the baseline characteristics between the groups. In short, the balance group was older, had a higher Charlson's comorbidity score and worse nutritional status than the control group. Our findings are, however, consistent with that observed in previous studies [7–9,30]. The double crossover Euro balance Trial demonstrated that dialysate CA125 rose with the introduction of the new PD solution and fell when patients were switched back to conventional solutions [9]. Our results suggest that the benefit could be maintained for at least a year of PD. It should be noted that the absolute level of CA125 differs substantially between the two studies, probably as a result of differences in the protocol of sample collection and activation before assay. It is interesting to note that in both groups of our study, the dialysate CA125 level increased after 1 year of PD, but the magnitude of increase was greater in the balance group (Figure 2), indicating better

Table 3. Quality of life and patient satisfaction^a

	Control group		Balance group	
	4 weeks	52 weeks	4 weeks	52 weeks
WHOQOL-BREF domains				
Physical	71.9 ± 12.6	68.7 ± 16.2	71.3 ± 11.6	66.9 ± 14.2
Psychological	60.5 ± 13.8	62.6 ± 14.0	60.8 ± 12.6	59.2 ± 14.8
Social	66.3 ± 9.8	69.2 ± 12.1	69.4 ± 10.9	66.9 ± 10.5
Environmental	69.6 ± 12.0	69.2 ± 9.8	67.7 ± 11.4	68.1 ± 13.1
Kidney disease specific items				
Burden of disease	39.7 ± 26.2	36.8 ± 29.3	33.7 ± 18.8	32.3 ± 27.8
Symptom/problem of disease	69.7 ± 21.0	68.9 ± 22.3	59.2 ± 20.6	57.1 ± 19.6
Effect of disease	61.3 ± 21.3	60.4 ± 23.2	55.7 ± 21.6	51.4 ± 21.8

WHOQOL-BREF, The World Health Organization Quality of Life—Brief version.

^aAll scores range from 0 to 100; higher scores indicate better quality of life.

recovery of the mesothelial cell mass. Although increment in CA125 over time has not been observed in earlier reports of low GDP solutions, our result is similar to previous studies in other biocompatible PD solution, such as icodextrin [31] and amino acid/glycerol-based solutions [32]. Although the clinical significance of increased CA125 is not entirely clear; it is often suggested that dialysate CA125 levels reflect peritoneal mesothelial cell mass [33], and increased CA125 concentrations may be a sign of better preservation of the peritoneal mesothelium. To support this hypothesis, it has been reported that the effluent drained during dialysis with the new solutions supports the growth of human peritoneal mesothelial cells better than conventional solutions [34]. Furthermore, *in vitro* re-mesothelialization after mechanical scratch wounding was normal with the new solution but significantly retarded by conventional solution [35].

Similarly, the process of mesothelial wound healing is associated with the local synthesis of HA [36]. In other words, the increased level of dialysate HA may reflect ongoing tissue regeneration and remodelling after injury. Our result is consistent with previous studies [7–9,30], which showed that treatment with the new biocompatible solution resulted in lower dialysate levels of HA. Similar to another study on low GDP solution [37], our data showed that dialysate HA increased after 1 year of PD with conventional solution, indicating ongoing and progressive peritoneal injury. In contrast, dialysate HA *decreased* after 1 year of PD with the balance solution (Figure 1), indicating gradual recovery of the peritoneum. On the other hand, it is important to note that other previous studies found that PDE CA125 and HA levels fluctuated with time without a finite longitudinal trend [31,32,37]. Since we only measured those levels twice during the study, it remains probable that any change in CA125 or HA level represents a random fluctuation.

Neither the Euro balance trial [9] nor our present study found any difference in the dialysis adequacy index between patients treated with conventional and new biocompatible solution. The daily ultrafiltration

and urine volume were also similar between balance and control groups. We also did not find any difference in hospitalization for fluid overload or heart failure between the groups (details not shown).

We found that the new biocompatible solution did not only improve dialysate markers but also reduced the degree of systemic inflammation, as represented by serum CRP levels. Unfortunately, we did not have the data on serum CRP levels before initiation of PD (i.e. at 0 week) for comparison, while the balance group had lower serum CRP as soon as 4 weeks after treatment (Figure 2). Given the small sample size, it was possible that the difference might represent a type 1 error (i.e. false positive). On the other hand, the level of serum CRP between balance and control groups continued to diverge throughout the study period, suggesting a genuine difference that was already apparent early after treatment. Although rapid decline in serum CRP has not been reported in previous studies on PD solutions, other therapeutic measures, notably statins, have been found to reduce serum CRP after 1 month of treatment [38]. It is important to note that a single time-point CRP level is predictive of outcome in PD patients [39], and the time course of serum CRP is even more predictive of mortality than its baseline level in PD patients [40]. The effect of the new biocompatible PD solution on the systemic inflammatory state of PD patients has not been examined in previous studies [9,10], and our finding may have important implications for the long term benefit of the new biocompatible solution.

One major limitation of our study was the lack of data on peritoneal transport at the initiation of dialysis (because peritoneal transport characteristics change significantly within the first month of PD [41]), and determination of ‘baseline’ peritoneal transport status was not possible. Second, because of the small sample size and relatively short follow-up, we did not find any effect of the new biocompatible solution on residual renal function or patient survival. In contrast, the Euro balance study showed that patients treated with the new biocompatible solution had better preserved residual renal function [9], and Lee *et al.* [10] found

in a retrospective observational study that the new solution had a significant survival advantage over the conventional solution. In this study, we did not find any difference in the utilization of hypertonic exchange, total glucose exposure or dialysis adequacy indices between balance and control groups, indirectly suggesting that there was no clinically important difference in peritoneal transport.

In summary, we conclude 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, and the difference was maintained for 1 year. Further studies are needed to determine whether these beneficial effects could be translated into better long-term clinical outcome.

Acknowledgement. This study was supported in part by the Hong Kong Special Administrative Region Research Grants Council (RGC) Competitive Earmarked Research Grant 2002/03, project code 2140335 (reference number CUHK4122/02M), and in part by the Fresenius Medical Care (FMC), Hong Kong. FMC was not involved in the design of the study; the collection, analysis and interpretation of the data; or the decision to submit the manuscript for publication. We have had no involvements that might raise the question of bias in the work reported or in the conclusions, implications, or opinions stated. We thank all medical and nursing staff from the Renal Unit, Prince of Wales Hospital, Shatin, Hong Kong, for their assistance.

Conflict of interest statement. This study was supported in part by the Fresenius Medical Care (FMC), Hong Kong.

References

- Davies SJ, Bryan J, Phillips L, Russell GI. Longitudinal changes in peritoneal kinetics: the effects of peritoneal dialysis and peritonitis. *Nephrol Dial Transplant* 1996; 11: 498–506
- Breborowicz A, Oreopoulos DG. Biocompatibility of peritoneal dialysis solutions. *Am J Kidney Dis* 1996; 27: 738–743
- Liberek T, Topley N, Jorres A *et al.* Peritoneal dialysis fluid inhibition of polymorphonuclear leucocyte respiratory burst activation is related to the lowering of intracellular pH. *Nephron* 1993; 65: 260–265
- Cappelli G, Bandiani G, Cancarini GC *et al.* Low concentrations of glucose degradation products in peritoneal dialysis fluids and their impact on biocompatibility parameters: prospective cross-over study with a three-compartment bag. *Adv Perit Dial* 1999; 15: 238–242
- van Biesen W, Kirchgessner J, Schilling H, Lage C, Lambert MC, Passlick-Deetjen J. Stay-Safe[®], a new PCV-free system for PD: results of the multicenter trial [abstract]. *Perit Dial Int* 1999; 19 [Suppl 1]: S43
- Lage C, Pischetsrieder M, Aufricht C, Jorres A, Schilling H, Passlick-Deetjen J. First in vitro and in vivo experiences with Stay-Safe Balance, a pH-neutral solution in a dual-chambered bag. *Perit Dial Int* 2000; 20 [Suppl 5]: S28–S32
- Jones S, Holmes CJ, Krediet RT *et al.* Bicarbonate/Lactate Study Group. Bicarbonate/lactate-based peritoneal dialysis solution increases cancer antigen 125 and decreases hyaluronic acid levels. *Kidney Int* 2001; 59: 1529–1538
- Rippe B, Simonsen O, Heimburger O *et al.* Long-term clinical effects of a peritoneal dialysis fluid with less glucose degradation products. *Kidney Int* 2001; 59: 348–357
- Williams JD, Topley N, Craig KJ *et al.* The Euro-balance Trial: the effect of a new biocompatible peritoneal dialysis fluid (balance) on the peritoneal membrane. *Kidney Int* 2004; 66: 408–418
- Lee HY, Park HC, Seo BJ *et al.* Superior patient survival for continuous ambulatory peritoneal dialysis patients treated with a peritoneal dialysis fluid with neutral pH and low glucose degradation product concentration (balance). *Perit Dial Int* 2005; 25: 248–255
- Beddhu S, Zeidel ML, Saul M *et al.* The effects of comorbid conditions on the outcomes of patients undergoing peritoneal dialysis. *Am J Med* 2002; 112: 696–701
- Szeto CC, Wong TY, Leung CB *et al.* Importance of dialysis adequacy in mortality and morbidity of Chinese CAPD patients. *Kidney Int* 2000; 58: 400–407
- Davies SJ, Phillips L, Naish PF, Russell GI. Peritoneal glucose exposure and changes in membrane solute transport with time on peritoneal dialysis. *J Am Soc Nephrol* 2001; 12: 1046–1051
- Lai KN, Szeto CC, Lai KB, Lam CWK, Chan DTM, Leung JCK. Increased production of hyaluronan by peritoneal cells and its significance in patients on CAPD. *Am J Kidney Dis* 1999; 33: 318–324
- NKF-K/DOQI Clinical practice guidelines for peritoneal dialysis adequacy: Update 2000. *Am J Kidney Dis* 2001; 37 [Suppl 1]: S65–S136
- Szeto CC, Wong TY, Chow KM, Leung CB, Li PK. Oral sodium bicarbonate for the treatment of metabolic acidosis in peritoneal dialysis patients – a randomized placebo-control trial. *J Am Soc Nephrol* 2003; 14: 2119–2126
- Wong TY, Szeto CC, Chow KM, Leung CB, Lam CW, Li PK. Rosiglitazone reduces insulin requirement and C-reactive protein levels in type 2 diabetic patients receiving peritoneal dialysis. *Am J Kidney Dis* 2005; 46: 713–719
- Forbes GB, Brunining GJ. Urinary creatinine excretion and lean body mass. *Am J Clin Nutr* 1976; 29: 1359–1366
- Bergstrom J, Heimburger O, Lindholm B. Calculation of the protein equivalent of total nitrogen appearance from urea appearance. Which formulas should be used? *Perit Dial Int* 1998; 18: 467–473
- Department of Health, Republic of China (Taiwan). *The ROC's Handbook of Diet*, 2nd edn, 20–21
- Nolph KD, Moore HL, Twardowski ZJ *et al.* Cross-sectional assessment of weekly urea and creatinine clearances in patients on continuous ambulatory peritoneal dialysis. *ASAIO J* 1992; 38: 142
- van Olden RW, Krediet RT, Struijk DG, Arisz L. Measurement of residual renal function in patients treated with continuous peritoneal dialysis. *J Am Soc Nephrol* 1996; 7: 745–748
- Niu SF, Li IC. Quality of life of patients having renal replacement therapy. *J Adv Nurs* 2005; 51: 15–21
- World Health Organization. WHOQOL-BREF Introduction, Administration, Scoring and Generic Version of the Assessment, field trial version, December 1996. www.who.int/entity/mental_health/media/en/76.pdf
- Szeto CC, Wong TY, Lai KB, Lam CW, Lai KN, Li PK. Dialysate hyaluronan concentration predicts survival but not peritoneal sclerosis in continuous ambulatory peritoneal dialysis (CAPD). *Am J Kidney Dis* 2000; 36: 609–614
- Alscher DM, Pauli-Magnus C, Kirchgessner J, Kuhlmann U, Mettang T. A new lactate-based, plasticizer-free, neutral peritoneal dialysis fluid provided in a two-compartment system: effect on peripheral leukocyte function. *Nephron* 2000; 86: 62–69
- Passlick-Deetjen J, Pischetsrieder M, Witowski J, Bender TO, Jorres A, Lage C. In vitro superiority of dual-chambered peritoneal dialysis solution with possible clinical benefits. *Perit Dial Int* 2001; 21 [Suppl 3]: S96–S101
- Wieczorowska-Tobis K, Polubinska A, Schaub TP *et al.* Influence of neutral-pH dialysis solutions on the peritoneal membrane: a long-term investigation in rats. *Perit Dial Int* 2001; 21 [Suppl 3]: S108–S113

29. Mortier S, de Vriese AS, van de Voorde J, Schaub TP, Passlick-Deetjen J, Lameire NH. Hemodynamic effects of peritoneal dialysis solutions on the rat peritoneal membrane: role of acidity, buffer choice, glucose concentration, and glucose degradation products. *J Am Soc Nephrol* 2002; 13: 480–489
30. Haas S, Schmitt CP, Arbeiter K *et al*. Improved acidosis correction and recovery of mesothelial cell mass with neutral-pH bicarbonate dialysis solution among children undergoing automated peritoneal dialysis. *J Am Soc Nephrol* 2003; 14: 2632–2638
31. Martikainen T, Ekstrand A, Honkanen E, Teppo AM, Gronhagen-Riska C. Do interleukin-6, hyaluronan, soluble intercellular adhesion molecule-1 and cancer antigen 125 in dialysate predict changes in peritoneal function? A 1-year follow-up study. *Scand J Urol Nephrol* 2005; 39: 410–416
32. van Biesen W, Boer W, De Greve B *et al*. A randomized clinical trial with a 0.6% amino acid/1.4% glycerol peritoneal dialysis solution. *Perit Dial Int* 2004; 24: 222–230
33. Krediet RT. Dialysate cancer antigen 125 concentration as marker of peritoneal membrane status in patients treated with chronic peritoneal dialysis. *Perit Dial Int* 2001; 21: 560–567
34. Witowski J, Korybalska K, Ksiazek K *et al*. Peritoneal dialysis with solutions low in glucose degradation products is associated with improved biocompatibility profile towards peritoneal mesothelial cells. *Nephrol Dial Transplant* 2004; 19: 917–924
35. Morgan LW, Wieslander A, Davies M *et al*. Glucose degradation products (GDP) retard remesothelialization independently of D-glucose concentration. *Kidney Int* 2003; 64: 1854–1866
36. Horiuchi T, Miyamoto K, Miyamoto S *et al*. Image analysis of remesothelialization following chemical wounding of cultured human peritoneal mesothelial cells: the role of hyaluronan synthesis. *Kidney Int* 2003; 64: 2280–2290
37. Kim YL, Do J, Park SH *et al*. Low glucose degradation products dialysis solution modulates the levels of surrogate markers of peritoneal inflammation, integrity, and angiogenesis: preliminary report. *Nephrology (Carlton)* 2003; 8 [Suppl]: S28–S32
38. Ridker PM, Cannon CP, Morrow D *et al*. C-reactive protein levels and outcomes after statin therapy. *N Engl J Med* 2005; 352: 20–28
39. 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: 1871–1879
40. Ates K, Ates A, Ekmekci Y, Nergizoglu G. The time course of serum C-reactive protein is more predictive of mortality than its baseline level in peritoneal dialysis patients. *Perit Dial Int* 2005; 25: 256–268
41. Johnson DW, Mudge DW, Blizzard S *et al*. A comparison of peritoneal equilibration tests performed 1 and 4 weeks after PD commencement. *Perit Dial Int* 2004; 24: 460–465

Received for publication: 22.5.06

Accepted in revised form: 18.8.06