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The effect of low glucose degradation product, neutral pH versus standard peritoneal dialysis solutions on peritoneal membrane function: the balANZ trial
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The effect of low glucose degradation product, neutral pH versus standard peritoneal dialysis solutions on peritoneal membrane function: the balANZ trial

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Abstract

Background. The balANZ trial recently reported that neutral pH, low glucose degradation product

(biocompatible) peritoneal dialysis (PD) solutions significantly delayed anuria and reduced peritonitis rates compared with conventional solutions. This article reports a

secondary outcome analysis of the balANZ trial with respect to peritoneal membrane function.

Methods. Adult, incident PD patients with residual renal function were randomized to receive either biocompatible or conventional (control) PD solutions for 2 years. Peritoneal equilibration tests were performed at 1, 6, 12, 18 and 24 months. Peritoneal small solute clearances and ultra-filtration (UF) were measured at 3, 6, 9, 12, 18 and 24 months.

Results. Of the 185 patients recruited into the trial, 85 patients in the Balance group and 82 patients in the control group had peritoneal membrane function evaluated. Mean 4-h dialysate:plasma creatinine ratios (D:P Cr 4h) at 1 month were significantly higher in the Balance group compared with controls (0.67 ± 0.10 versus 0.62 ± 0.10 , $P = 0.002$). Over the 2-year study period, mean D:P Cr 4 h measurements remained stable in the Balance group but increased significantly in controls [difference -0.004 per month, 95% confidence interval (95% CI) -0.005 to -0.002 , $P < 0.001$]. Similar results were obtained for dialysate glucose ratios (D/D0 glucose). Peritoneal UF was significantly lower in the Balance group than in controls at 3 and 6 months. Over the 2-year study period, peritoneal UF increased significantly in the Balance group but remained stable in controls (difference 24 mL/day/month, 95% CI 9–39, $P = 0.002$). No differences in peritoneal small solute clearances, prescribed dialysate fill volumes or peritoneal glucose exposure were observed between the two groups.

Conclusions. Biocompatible and conventional PD solutions exert differential effects on peritoneal small solute transport rate and UF over time. Adequately powered trials assessing the impact of these differential membrane effects on PD technique and patient survival rates are warranted.

Keywords: biocompatibility; glucose degradation products; outcomes; peritoneal dialysis; peritoneal equilibration test

Introduction

Approximately 200 000 end-stage renal failure patients worldwide (or 11% of the global dialysis population) utilize peritoneal dialysis (PD) for life-sustaining maintenance renal replacement therapy [1]. Most published observational cohort studies suggest that the medium-term survival (up to 3–4 years) of patients treated with PD is at least comparable, and possibly superior, to that of patients receiving haemodialysis (HD) [2–6]. However, PD is associated with a higher rate of technique failure than HD [7].

A large body of basic research in animal models and peritoneal cell culture systems has suggested that a major contributor to the high technique failure rate of PD is the bio-incompatible nature of conventional PD fluids, particularly as a result of their acidic pH (5.0–5.8) and high concentration of glucose degradation products (GDP) generated during the heat sterilization process [8]. Such ‘unphysiological’ characteristics may have both a negative impact on peritoneal cell populations and a pro-fibrotic effect on the peritoneal membrane [9–13]. In particular, experimental and clinical exposure of the peritoneal membrane to conventional PD solutions engenders significant

histopathological changes over time, including loss of the surface mesothelial cell layer, thickening of the sub-mesothelial compact zone and the development of a progressive vasculopathy [14, 15]. Most of these adverse effects have been largely abrogated by the use of neutral-buffered, low GDP fluids in *in vivo* studies [8, 11, 16, 17]. Subsequent short-term, small, clinical studies have demonstrated that the use of low GDP fluids in PD patients is accompanied by significant improvements in the effluent biomarkers of peritoneal membrane integrity, stable membrane function and reductions in peritoneal membrane inflammatory response [18–25]. However, evidence of a beneficial effect on the morphological and functional changes associated with long-term exposure to PD fluids is not yet available.

The recently published balANZ randomized controlled trial [26] found that the administration of a neutral pH, lactate-buffered, low GDP fluid (Balance[®]) to incident PD patients was associated with an appreciable reduction in peritonitis rates and a significant delay in the onset of anuria compared with conventional, standard, lactate-buffered PD solutions (stay.safe[®]). In order to further evaluate the impact of biocompatible fluid on PD outcomes, this secondary analysis aimed to determine whether neutral pH, low GDP (biocompatible) PD fluid exerted beneficial effects on peritoneal membrane permeability, small solute clearance and ultra-filtration (UF) over a 2-year period compared with conventional dialysate.

Materials and methods

The study design and methodology [27] and the main results of the balANZ trial [26] have been described previously. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki, the Good Clinical Practice guidelines of the International Conference of Harmonization, and local regulatory requirements. It was approved by ethics committees at all participating centres and all patients provided written informed consent prior to trial participation.

The study was an investigator-initiated, prospective, open-label, randomized controlled Phase 4 trial involving 16 centres across Australia, New Zealand and Singapore. It included incident, adult PD patients who had both a residual measured glomerular filtration rate ≥ 5 mL/min/1.73 m² and a measured urine volume ≥ 400 mL/day. Pregnant or breast-feeding patients, individuals expected to die within 12 months, patients participating in trials targeting residual renal function in PD or those with a significant cancer history in the past 5 years, acute infection at enrolment, contra-indications to PD, any physical or mental disorder that appreciably hampered study protocol compliance or known or suspected allergy to trial product or related products were excluded. Participants were randomized 1:1 to receive either neutral pH, lactate-buffered, low GDP solution (Balance[®]) or conventional, standard, lactate-buffered solution (stay.safe[®]). Randomization was performed centrally via a web-based system and was stratified for both centre and presence or absence of diabetic nephropathy. Patients in each trial arm were treated according to local PD unit management protocols. Icodextrin and automated PD were permitted in both groups. Each patient was followed for 24 months. The primary outcome measure of the study was residual renal function decline. This article focuses on the secondary outcome measures of peritoneal transport status, peritoneal small solute clearance and peritoneal UF.

Dialysate: plasma creatinine ratio at 4 h (D:P Cr 4 h) and the ratio of dialysate glucose concentrations at 4 and 0 h (D/D0 glucose) were determined by standard peritoneal equilibration test (PET) [28] at 1, 6, 12, 18 and 24 months. Weekly peritoneal creatinine clearance (CpCr) and urea clearance (CpUr) were calculated from 24-h dialysate collections at 3, 6, 9, 12, 18 and 24 months, normalized for body surface area (BSA) and expressed as L/week/1.73 m². BSA was calculated using the Du Bois

formula [29]. Peritoneal UF during the 24-h collection was also recorded and expressed as mL/day. Peritoneal glucose exposure was calculated according to the method described by Davies *et al.* [7]. Peritoneal UF was normalized for peritoneal glucose exposure on the day that the UF was measured.

Statistical analysis

Results were expressed as frequencies (percentages), mean \pm standard deviation or median [range], depending on data distribution. Group comparisons were performed by χ^2 -test, unpaired *t*-test or Mann–Whitney test, as appropriate. For the outcome measures of changes in peritoneal membrane permeability, small solute clearance and UF over time, a mixed effects General Linear Model was fitted for each outcome variable with treatment group, centre and presence or absence of diabetic nephropathy as fixed effects terms. Patient identification number was fitted as a ‘random’ term in the model, along with time and intercept. In this way, the model provided estimates of the rate of change (slope) in the outcome measure for each patient allowing them to also have a different intercept (starting level). From these data, an overall estimate of the rate of change in each treatment group was determined, corrected for the fixed-effects terms. The data were assumed to be normally distributed and to change in a linear fashion. Differences in the rate of change between the intervention and control groups were analysed on an intention-to-treat basis. Mixed models assume missing at random patterns to cater for missed visits or withdrawal for any reason other than those related to treatment. Data were analysed by Statistical Revelations Pty Ltd (<http://www.statisticalrevelations.com.au/>). P-values <0.05 were considered statistically significant.

Results

Patient characteristics

One hundred and eighty-five patients were randomized to receive either Balance ($n=92$) or control (stay.safe) fluid ($n=93$). Of these, 85 patients in the Balance group and 82 patients in the control group had peritoneal membrane function tests. As previously reported [26], the two groups were well matched for all baseline characteristics, including age, gender, end-stage renal failure cause, presence of cardiovascular disease, body mass index, initial dialysis modality, prescribed medications, blood pressure, prescribed dialysate volumes and glucose exposure, residual renal function and urine volume and laboratory parameters (serum albumin, calcium and haemoglobin). At baseline, the median [range] prescribed dialysate fill volumes were 8000 [2000–10 000] mL/day in the Balance group and 8000 [2000–8700] mL/day in the stay.safe group (P = not significant). The peritoneal glucose exposures were 121.5 ± 35.3 and 123.6 ± 36.3 g/day, respectively (P = not significant).

Peritoneal transport status

The results of PETs in each group at 1, 6, 12, 18 and 24 months are shown in Table 1. Mean D:P Cr 4 h values at 1 month were significantly higher in the Balance group compared with the control group (0.67 ± 0.10 versus 0.62 ± 0.10 , $P=0.002$). The respective proportions of high, high average, low average and low transporters were 8, 57, 29 and 6% in the Balance group and 5, 31, 58 and 7% in the stay.safe group ($P=0.001$), respectively. Over the duration of the study, mean D:P Cr 4 h measurements remained stable in the Balance group [0.001 per month, 95% confidence interval (95% CI) -0.001 to 0.002] but increased significantly in the stay.safe group (0.004 per

month, 95% CI 0.003 – 0.005) (Figure 1). The difference in D:P Cr 4 h gradients over time between the two groups was statistically significant (-0.004 per month, 95% CI -0.005 to -0.002 , $P<0.001$, Figure 1). At 6 months, the respective proportions of high, high average, low average and low transporters were 9, 53, 35 and 3% in the Balance group and 1, 49, 44 and 6% in the stay.safe group ($P=0.11$). No differences in peritoneal transport status were observed between the Balance and stay.safe groups at 12 months ($P=0.63$) or 24 months ($P=0.65$).

Similar results were observed for D/D0 glucose measurements. Mean values at 1 month were lower in the Balance group than in the stay.safe group (0.39 ± 0.08 versus 0.43 ± 0.08 , $P=0.003$). Over the duration of the study, mean D/D0 glucose measurements remained stable in the Balance group (0.001 per month, 95% CI -0.000 to 0.002) but decreased significantly in the stay.safe group (-0.002 per month, 95% CI -0.003 to -0.001) (Figure 2). The difference in D:P Cr 4 h gradients between the two groups was statistically significant (0.002 per month, 95% CI 0.001 – 0.004 , $P<0.01$).

Peritoneal small solute clearance

The results of peritoneal small solute clearance measurements in each group at 3, 6, 9, 12, 18 and 24 months are shown in Table 1. Peritoneal CpCr measurements were comparable between the two groups over time. CpCr values increased over time in both the Balance group (0.33 L/week/1.73 m²/month, 95% CI 0.21 – 0.46) and the control group (0.37 L/week/1.73 m²/month, 95% CI 0.25 – 0.49) (Figure 3). The difference between the groups was not statistically significant (0.04 L/week/1.73 m²/month, 95% CI -0.21 to 0.14 , $P=0.79$).

Similar results were observed for peritoneal CpUr measurements. CpUr values increased over time in both the Balance group (0.35 L/week/1.73 m²/month, 95% CI 0.19 – 0.50) and the control group (0.26 L/week/1.73 m²/month, 95% CI 0.11 – 0.41) (Figure 4). The difference between the groups was not statistically significant (0.08 L/week/1.73 m²/month, 95% CI -0.13 to 0.30 , $P=0.45$).

Peritoneal ultra-filtration

The results of peritoneal UF in each group at 3, 6, 9, 12, 18 and 24 months are shown in Table 1. Peritoneal UF was significantly lower in the Balance group than in controls at 3 and 6 months. These lower UF volumes in the biocompatible group coincided with higher urine volumes [26]. Over the course of the study, peritoneal UF increased significantly in the Balance group (16 mL/day/month, 95% CI 5 – 27) but remained stable in the stay.safe group (-8 mL/day/month, 95% CI -19 to 2) (Figure 5). The difference in gradients between the groups was statistically significant (24 mL/day/month, 95% CI 9 – 39 , $P=0.002$). This difference persisted after normalization of peritoneal UF for glucose exposure (0.08 mL/day/g/month, 95% CI 0.03 – 0.14 , $P=0.004$) (Figure 6).

Table 1. Measurements of peritoneal small solute clearance, UF and transport status over time in balANZ trial participants

| Parameter | 1 months | | 3 months | | 6 months | | 9 months | | 12 months | | 18 months | | 24 months | |
|--|---------------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|---------------------|-----------------------|
| | Balance (n = 85) | Stay.safe (n = 82) | Balance (n = 85) | Stay.safe (n = 80) | Balance (n = 76) | Stay.safe (n = 75) | Balance (n = 68) | Stay.safe (n = 68) | Balance (n = 62) | Stay.safe (n = 66) | Balance (n = 53) | Stay.safe (n = 59) | Balance (n = 42) | Stay.safe (n = 50) |
| Weekly CpUr (L/week/1.73 m ²) | N/A | N/A | | | | | | | | | | | | |
| n | | | 85 | 78 | 75 | 74 | 68 | 68 | 62 | 65 | 53 | 56 | 40 | 48 |
| Median | | | 52 | 56 | 54 | 56 | 55* | 58 | 56 | 59 | 56 | 58 | 59 | 61 |
| [min, max] | | | [19, 70] | [6, 86] | [23, 71] | [13, 92] | [35, 90] | [20, 106] | [1, 71] | [1, 93] | [30, 76] | [32, 99] | [39, 77] | [26, 93] |
| Weekly CpCr (L/week/1.73 m ²) | N/A | N/A | | | | | | | | | | | | |
| n | | | 84 | 78 | 75 | 74 | 68 | 70 | 62 | 66 | 53 | 56 | 40 | 48 |
| Median | | | 40 | 39 | 41 | 43 | 39 | 43 | 43 | 44 | 42 | 46 | 44 | 49 |
| [min, max] | | | [11, 54] | [2, 67] | [11, 58] | [12, 71] | [20, 74] | [17, 79] | [21, 63] | [20, 77] | [25, 69] | [21, 69] | [23, 62] | [19, 70] |
| UF (mL/day) | N/A | N/A | | | | | | | | | | | | |
| n | | | 85 | 79 | 75 | 74 | 68 | 70 | 62 | 66 | 53 | 56 | 40 | 48 |
| Median | | | 700* | 1090 | 850* | 1015 | 913* | 1233 | 955 | 1150 | 1100 | 951 | 900 | 993 |
| [min, max] | | | [-700, 3500] | [-400, 2800] | [-1040, 1966] | [-1716, 4040] | [-1082, 2300] | [-1000, 2900] | [-600, 2700] | [-400, 3000] | [-500, 2100] | [-1782, 3560] | [-100, 3340] | [-1338, 2568] |
| D:P Cr 4 h | | | N/A | N/A | | | N/A | N/A | | | | | | |
| n | 83 | 82 | | | 75 | 73 | | | 60 | 66 | 51 | 56 | 37 | 47 |
| Mean ± SD | 0.67 ± 0.10* | 0.62 ± 0.10 | | | 0.67 ± 0.10* | 0.64 ± 0.09 | | | 0.67 ± 0.10 | 0.67 ± 0.09 | 0.67 ± 0.09 | 0.68 ± 0.11 | 0.67 ± 0.09 | 0.70 ± 0.08 |
| D/D0 glucose 4 h | | | N/A | N/A | | | N/A | N/A | | | | | | |
| n | 83 | 82 | | | 75 | 73 | | | 59 | 66 | 50 | 56 | 37 | 47 |
| Mean ± SD | 0.39 ± 0.08* | 0.43 ± 0.08 | | | 0.40 ± 0.08* | 0.43 ± 0.07 | | | 0.40 ± 0.08 | 0.40 ± 0.08 | 0.98 ± 0.15 | 0.42 ± 0.15 | 0.41 ± 0.07 | 0.39 ± 0.08 |
| 4 h UF during PET (mL) | | | N/A | N/A | | | N/A | N/A | | | | | | |
| n | 83 | 82 | | | 75 | 73 | | | 60 | 66 | 51 | 56 | 37 | 47 |
| Median | 300* | 354 | | | 300* | 400 | | | 260* | 400 | 300 | 345 | 300 | 350 |
| [min, max] | [-200, 900] | [-100, 1085] | | | [-110, 900] | [-100, 1010] | | | [-200, 750] | [-80, 650] | [-350, 900] | [-250, 988] | [-270, 900] | [10, 863] |
| 24 h dialysate fill volume (mL/day) | | | | | | | | | | | | | | |
| Median | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 8000 | 6000 | 8000 |
| [min, max] | [4000, 10 000] | [2000, 8700] | [4000, 10 500] | [2000, 13 500] | [3800, 12 300] | [2000, 14 995] | [6000, 12 000] | [4000, 14 500] | [5000, 12 300] | [4000, 15 194] | [4800, 12 300] | [4500, 14 685] | [8000, 14 500] | [4500, 15 000] |
| Peritoneal glucose exposure (g/day) | | | | | | | | | | | | | | |
| Mean ± SD | 139.1 ± 44.4 | 126.5 ± 35.5 | 142.1 ± 43.5 | 133.9 ± 36.9 | 143.7 ± 40.5 | 140.5 ± 43.5 | 149.2 ± 42.5 | 146.3 ± 46.2 | 150.0 ± 41.0 | 150.9 ± 48.5 | 158.4 ± 49.2 | 157.4 ± 52.3 | 161.7 ± 54.1 | 157.4 ± 52.3 |

Results are presented as mean ± SD or median [range], depending on data distribution.

*P < 0.05 versus Stay.safe (control).

CpCr, peritoneal creatinine clearance; CpUr, peritoneal urea clearance; D/D0 glucose, ratio of 4 h to initial dialysate glucose concentrations; D:P Cr 4 h, dialysate:plasma creatinine ratio at 4 h; N/A, not available; PET, peritoneal equilibration test; UF, ultrafiltration.

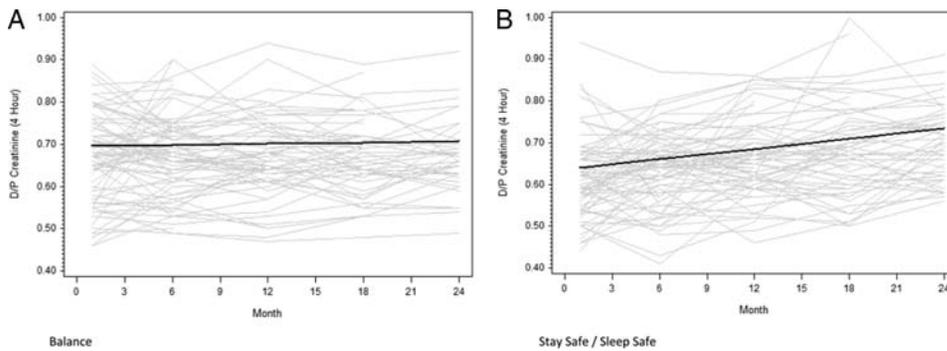


Fig. 1. Change in D:P Cr 4 h over time in the balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was statistically significant ($P < 0.001$).

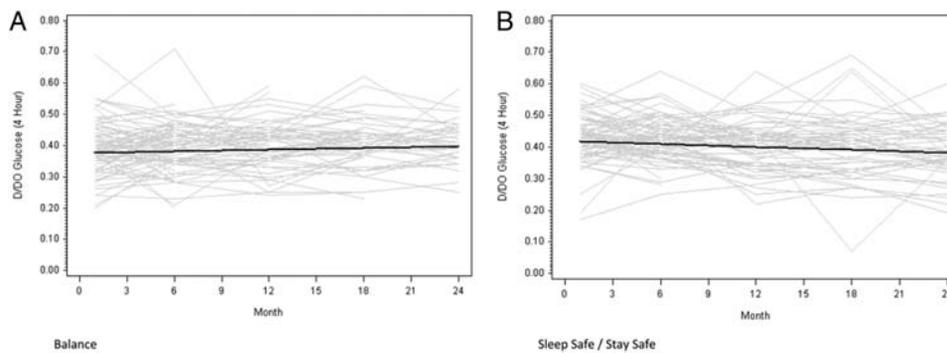


Fig. 2. Change in D/D0 glucose over time in the Balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was statistically significant ($P < 0.01$).

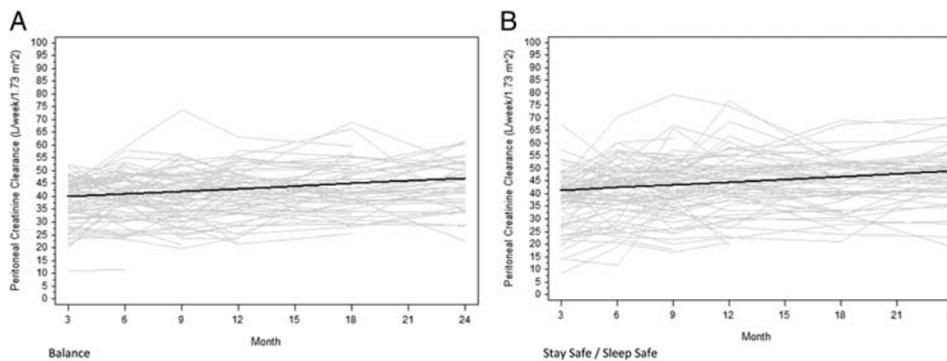


Fig. 3. Change in peritoneal CpCr over time in the Balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was not statistically significant ($P = 0.69$).

Discussion

This investigator-initiated, multi-centre, multi-country, prospective, open-label, randomized controlled Phase 4 trial involving 16 centres across Australia, New Zealand and Singapore demonstrated that prescription of neutral pH, lactate-buffered, low GDP (Balance) solution in PD patients was associated with an initially higher peritoneal membrane solute transport rate and lower peritoneal UF rate compared with controls. Moreover, whereas these parameters remained stable in the biocompatible group over

the 2-year follow-up period of the study, there was a progressive increase in peritoneal membrane permeability in controls. Peritoneal small solute clearance increased at comparable rates over time in both groups.

Serial elevations in peritoneal solute transport characteristics and deterioration in peritoneal UF over time have been reported in patients treated with conventional dialysis fluids and have been attributed to the bio-incompatible nature of these solutions [30, 31]. However, while *in vitro* studies have reported that biocompatible fluid administration was associated with significant improvements in

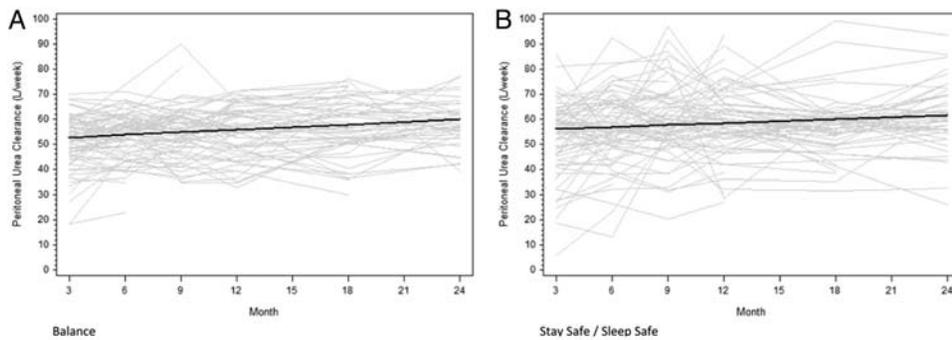


Fig. 4. Change in peritoneal CpUr over time in the Balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was not statistically significant ($P = 0.45$).

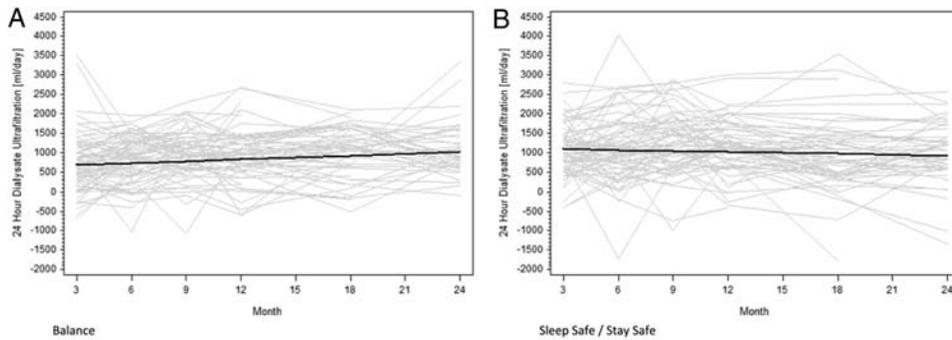


Fig. 5. Change in peritoneal UF over time in the Balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was statistically significant ($P = 0.002$).

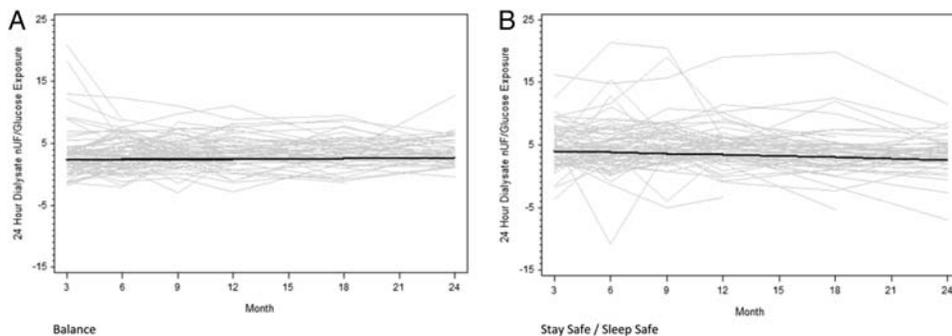


Fig. 6. Change in peritoneal UF, normalized for peritoneal glucose exposure, over time in the Balance (A) and control (B) groups over 2 years. Grey lines represent individual patient measurements while solid lines represent predicted gradients. The difference in gradients between the two groups was statistically significant ($P = 0.004$).

peritoneal cell viability, function and structure, clinical trials of biocompatible fluids on peritoneal membrane function have been both limited and conflicting. In keeping with the findings of the present investigation, the Euro Balance trial [19], a multi-centre, open-label, prospective randomized cross-over study of Balance versus standard PD fluid over two 12-week periods, observed significant increases in D:P Cr 4 h measurements in patients randomized to Balance. This rise in peritoneal permeability was associated with a significant fall in peritoneal UF. In a randomized controlled trial of a nutrineal,

extraneal and physioneal (NEPP) regimen versus conventional dialysis fluid in 63 incident PD patients, Le Poole found that the lower GDP NEPP regimen was associated with an increase in peritoneal solute transport rate. Similarly, Kim *et al.* [23] observed significantly higher D:P Cr 4 h values in 48 patients randomly allocated to Balance solution compared with 43 control patients receiving continuous ambulatory peritoneal dialysis / Dialyse Péritoneale Continue Ambulatoire fluid (Balnet study). Moreover, D:P Cr 4 h remained stable in the biocompatible group over a period of 12 months. However, in

contrast to the findings of the present study and those of other studies [32], Kim *et al.* reported a significant fall in D:P Cr 4 h over time in patients receiving conventional dialysis solutions. Peritoneal UF rates also tended to fall in the biocompatible group compared with controls, although this did not reach statistical significance ($P = 0.09$). Haag-Weber also observed a tendency to lower peritoneal UF in the biocompatible group ($P = 0.10$) without any significant changes in PET measurements, although these observations did not allow for the significant differences in overfill between biocompatible and standard PD solutions. On the other hand, two randomized controlled clinical trials [21, 33] have reported no changes in either PET measurements or peritoneal UF between biocompatible and conventional dialysates, while two other studies [34, 35] found no change in D:P Cr 4 h but a significant increase in peritoneal UF in association with biocompatible fluid use. The apparent disparities in findings between these studies and those of the present investigation may be explained by the fact that the other trials often suffered from a number of important limitations including insufficient statistical power due to small numbers, short-term follow-up, high drop-out rates, treatment-associated changes in fluid status, use of solutions with variable GDP content, sub-optimal methodological quality, lack of adjustment for peritoneal glucose exposure, enrolment of prevalent PD patients and single-centre designs. In contrast, our multi-centre study represents the largest and longest running randomized controlled trial to date evaluating the effects of biocompatible fluids on peritoneal membrane transport, small solute clearance and glucose-adjusted UF.

Similar to the results of the balANZ trial, the few previously published randomized controlled trials that have examined peritoneal small solute clearances have not observed a significant effect of biocompatible fluids [20, 23, 34]. However, Choi *et al.* [35] and Williams *et al.* [19] did report significant increases in peritoneal CpUr in patients receiving biocompatible fluids compared with controls, although peritoneal CpCrs were not different between the two groups. The similar overall findings between trials of comparable peritoneal small solute clearances in patients receiving biocompatible or conventional PD solutions in spite of variable observed differences in peritoneal solute transport rates may be potentially explained by the fact that PD patients' prescriptions were titrated to achieve common small solute clearance targets between the two groups.

The observed higher initial peritoneal solute transport rate in patients receiving biocompatible fluids in the balANZ trial, as evidenced by higher initial D:P Cr 4 h and lower initial D/D0 glucose values, may be potentially explained by alterations in peritoneal vascular surface area. Previous studies in animals have observed that conventional, acidic pH, lactate-buffered 4.25% glucose resulted in a doubling of arteriolar flow and a 20% increase of perfused capillary length per area, while administration of a pH-neutral, bicarbonate-buffered, low GDP solution did not affect haemodynamic parameters [36]. Alternatively, administration of biocompatible fluids may influence local peritoneal membrane production of vasoactive cytokines, such as vascular endothelial growth factor and

nitric oxide [19, 37]. The impact of these changes in peritoneal solute transport rate and UF on long-term patient-level outcomes remains uncertain. We have previously reported that technique and patient survival rates were comparable between the Balance and control groups in the balANZ trial [26], although the study had insufficient statistical power to exclude Type-2 statistical errors for these end-points.

The strengths of this study include its very large sample size, 2-year follow-up period, trial design and involvement of participants from a range of centres and countries with varying approaches to PD. This greatly enhanced the external validity of our findings. Randomization allocation was appropriately concealed and stratified for PD unit to mitigate against centre effects. The Balance and stay.safe groups were well balanced with respect to baseline demographic and clinical characteristics, thereby attesting to the success of the randomization process.

These strengths must be weighed up against the study's limitations, the principal one of which was that the relatively high drop-out rate (45% over 2 years) may have introduced informative censoring bias. However, the numbers of, and reasons for drop-out in each group were comparable. Moreover, missing peritoneal membrane tests due to withdrawal or non-treatment-related factors were catered for in the mixed effects general linear model analysis used in this study. The open-label design may have introduced the possibility of co-intervention bias. Observer bias could also not be excluded, although this was countered by the use of clearly defined, objective peritoneal membrane solute transport and UF measures. As with other studies in this area [19, 23, 30], a reciprocal relationship was observed in the balANZ trial between peritoneal UF and urine volume suggesting that some of the fall in peritoneal UF observed in the biocompatible group may have been explained by volume-driven changes. Overfill was not accounted for in the present study, although the difference in overfill between Balance and stay.safe is very small (~20 mL).

In conclusion, administration of a neutral pH, lactate-buffered, low GDP fluid (Balance) to incident PD patients was associated with higher peritoneal solute transport rates, which then remained stable over the 2-year follow-up period. Peritoneal UF was initially lower but increased significantly over time. In contrast, patients receiving conventional PD solutions experienced progressive increases in peritoneal solute transport rate and stable peritoneal UF over time. Future, adequately powered randomized controlled trials investigating the impact of biocompatible fluid-induced changes in peritoneal membrane function on PD technique survival are warranted.

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Comparison of the SF-36 Five-item Mental Health Inventory and Beck Depression Inventory for the screening of depressive symptoms in chronic dialysis patients

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Abstract

Background. The Beck Depression Inventory (BDI) is a standard and validated questionnaire to screen for depressive symptoms in chronic dialysis patients, but is relatively extensive to use repeatedly in clinical practice. We investigated whether the five-item Mental Health Inventory (MHI-5) of the 36-item Short-Form Health Survey Questionnaire (SF-36) could be applied to screen for depressive symptoms in dialysis patients. Moreover, we determined the optimal MHI-5 cut-off score to assess depressive symptoms.

Methods. Chronic dialysis patients from three centres filled out the SF-36 and the BDI. A receiver operating characteristic (ROC) curve was constructed for the MHI-5 score with BDI ≥ 16 as reference standard to (i) calculate the area under the curve to determine whether the MHI-5 could be considered as a useful screening instrument for depressive symptoms and (ii) proxy the optimal cut-off score of the MHI-5 to assess depressive symptoms. The optimal cut-off score was determined by the value for which the sum of sensitivity and specificity had an optimum.

Results. Of 133 included patients, 23% had depressive symptoms as determined with BDI ≥ 16 . The correlation of the BDI with MHI-5 was -0.64 . The area under the ROC curve was 0.82 (95% confidence interval 0.74–0.90). The optimal cut-off point of the MHI-5 was 70. MHI-5 ≤ 70 had 77 sensitivity, 72 specificity, 44 positive predicting value and 91% negative predicting value with the presence of depressive symptoms determined with BDI ≥ 16 .

Conclusions. The MHI-5 may help clinicians to screen for depressive symptoms in dialysis patients without using an additional depression screening questionnaire once the SF-36 is completed. A cut-off value of 70 can be used safely for the purposes of screening applications.

Keywords: depressive symptoms; dialysis patients; mental health inventory; screening; SF-36

Introduction

Depression is the most common psychiatric disorder among chronic dialysis patients [1]. It is of great importance that depressive symptoms are successfully recognized and treated. Depressive symptoms diminish patient's quality of life and are independently associated with an increased risk of hospitalization [2, 3]. In addition, depressive symptoms pose a risk factor for both cardiovascular and non-cardiovascular mortality [4–6]. Hence, the National Kidney Foundation, Disease Outcomes Quality Initiative (NKF KDOQI) guideline for cardiovascular disease in dialysis the patients recommends that the patient's psychological state should be assessed at least biannually with specific focus on the presence of depressive symptoms [7].

The assessment of depressive symptoms is frequently performed using self-reported depression screening tools, whereupon patients who are screened positive are