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ABSTRACT
Although twin-bag disconnect fluid-transfer systems for continuous ambulatory peritoneal dialysis (CAPD) have a lower rate of catheter-related infection than single-bag systems, their greater monetary purchase cost has prevented universal adoption. Therefore, a single-center randomized study was performed in 63 adult patients to compare the efficiency and total cost of Freeline Solo (FS, twin-bag) and Basic Y (BY, single-bag) systems. Patients were new to CAPD (N = 39), or had a new CAPD catheter, or had had no episodes of peritonitis or exit-site infection in the previous 12 months (N = 24). Total follow-up was 631 patient months (pt.mon), and 53 patients were still on the trial at its termination. Patients rated FS as easier to use than BY (P < 0.001). Peritonitis occurred on 23 occasions in 12 out of 30 patients using BY, and on seven occasions in five of 33 patients using FS. Time to first infection was less with BY than FS (hazard ratio, 2.4; 95% confidence interval (CI), 1.0 to 5.3; P < 0.04). Cumulative incidence of peritonitis was 1 per 14.0 pt.mon with BY and 1 per 46.5 pt.mon with FS (odds ratio, 3.6; 95% CI 1.5 to 8.5; P = 0.004). Length of hospitalization for peritonitis or exit-site infection was 98 days in six patients with BY, versus 17 days in two patients with FS. With BY, four catheters were removed because of infection, but none with FS (P < 0.05). With BY, the total cost of infection was $AUD127,079 ($5033 per pt.yr) versus $19,250 ($704 per pt.yr) with FS, which offset the higher purchase cost of FS. The total cost of CAPD was $AUD956 per pt.yr less with FS than BY. In conclusion, the higher purchase cost of the FS twin-bag system is more than offset by savings from its lower incidence of peritonitis.

Key Words: Peritonitis, exit-site infection, CAPD, disconnect system, hospitalization

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Peritonitis and exit-site infection cause considerable morbidity among patients on peritoneal dialysis, and together are the principle causes of technique failure with continuous ambulatory peritoneal dialysis (CAPD). For example, in Australia in 1994, the median survival period free of infection was 9 to 13 months, and 13% of patients on CAPD required permanent transfer to hemodialysis. An analysis of dialysis registries, showed that 27 to 52% of technique failure was the result of peritonitis.

Methods
Patients and Treatment
All patients either entering or established on the CAPD program in the Western Sydney Renal Service from May 1994 were eligible to be enrolled in the trial. Eligibility criteria were: age of 18 yr or older; ability to perform fluid-exchange procedures without nursing assistance; and provision of informed consent. Established patients were excluded from the trial if they had had more than three separate infective episodes related to CAPD in the previous year (unless the Tenckhoff catheter had been replaced subsequently) or until 2 months after resolution of an existing catheter-related infection. For the purposes of this study, the term "catheter-related infections" refers to peritonitis and exit-site and
tunnel infection. Patients were withdrawn from the trial for loss of self- or family-care, permanent removal of Tenckhoff catheter, or protocol violation.

Patients were stratified into three groups and randomized to use either Basic Y or Freeline Solo. The groups were: Group 1, new patients (N = 39); Group 2, established patients with no peritonitis or exit-site infections in the previous 12 months or with a new catheter (N = 24, six of whom had a new catheter); Group 3, established patients with one to three catheter-related infection in the past 12 months. Only nine patients were entered in Group 3 and there was a high early drop-out rate (primarily for reasons unrelated to the catheter); therefore, enrollment in this group stopped after 4 months. Of the six patients in group 2 with a new catheter prior (1 to 4 months) to the trial, five had the catheter removed because of exit-site infection and/or peritonitis.

Double-cuffed SILASTIC (Dow Corning, Corning, NY) Tenckhoff catheters (Quinton Instrument Co., Seattle, WA) were inserted by a single surgical team using a standardized method. Postoperative dressings were undisturbed for 48 hr and the catheter immobilized by adhesive tape. Catheters were used between 7 and 14 days after insertion with instillations of saline at 7-day intervals before use. All CAPD bag systems were manufactured by Baxter Healthcare (Sydney, Australia) and supplied to patients' homes. Identical fluid volumes and dialysate concentrations were available for the twin-bag Freeline Solo system and single-bag Basic Y system. Dialysis prescription and medical management of the patients was entirely independent of the bag system used. Among Group 2 patients, 11 each had used O-set or Basic Y before the trial, and one patient each Freeline Solo or Ultra-set.

Patients were trained in the use of either system as outpatients and the time to completion of attendance for training recorded. Standard training protocols utilizing the manufacturer's recommended methods were used by the training team.

Peritonitis and tunnel and exit-site infections were defined along standard lines (13). Treatment of infection was standardized by unit protocol, and included empiric use of vancomycin and ceftriaxone until the results of Gram stains and cultures were known. When patients were hospitalized for any reason, peritoneal dialysis for all patients was performed by nursing staff using the Freeline Solo system, and infections that occurred during hospitalization were excluded from analysis by study design. Peritonitis during hospitalization occurred in only one patient (who was using the Basic Y system outside hospital), arising from an infected leg wound while that patient was in a surgical ward. Exit-site infection arose during hospitalization in one patient who was using the Freeline Solo system outside hospital.

Costing

This study was designed to consider costs to the community rather than to individual patients or specific hospital, dialysis center, or pharmaceutical companies' budgets. A standard costing methodology based on economic principles of opportunity cost was thus used to estimate the cost of all treatment episodes (14). The total cost to the community per patient included that of the CAPD system, and the resource costs involved in the treatment of peritonitis, exit-site infections, and their complications. Resource costs of peritonitis and exit-site infections included those of outpatient treatment, hospitalization, drugs, pathology and radiological tests, surgical procedures, and dialysis (cost of hemodialysis, less the savings from suspending peritoneal dialysis), incurred as a result of infection. Hospitalization costs were calculated individually using bed-day costs for actual admission stratified by: district hospital (AUS$485); teaching-hospital standard bed (AUS$45); and teaching-hospital high-dependency bed (AUS$605). The costs to the community of procedures and tests were calculated using the Medicare Benefits Schedule Book (1st November, 1995), and that of drug treatment from the Schedule of Pharmaceutical Benefits (1st February, 1996), both published by the Commonwealth Department of Human Services & Health Canberra, ACT. All costs were direct except for bed-day costs for hospitalization. To increase the sensitivity of costing as determined by differences in bed-day costs, costing was repeated with the assumption that all bed-days had a similar cost.

At the completion of the trial, all patients were asked to rate the system used, and patients who had used both the Freeline Solo and Basic Y systems were asked to compare the two (using the Likert scale, 1 to 7, where 1 represented the least and 7 the greatest ease of use).

Data Evaluation

The primary outcome variable was the total cost per patient for use of each system. The secondary outcome variables were rates of infection and technique failure rate. The peritonitis rate was estimated by an independent statistical monitor, and the trial terminated when a significant difference in peritonitis rate was seen for 2 months. Covariates included demographic and clinical data, as described in Table 1. Data from both groups and combined data were analyzed on an intention to treat basis using the Statistical Package for Interactive Data Analysis (SPIDA, version 6, Macquarie University, Sydney, Australia). Chi-squared tests were used to analyze categorical data, Cox regression analysis to examine survival to first infection, logistic regression analysis to examine potential risk factors for infection, and one-way analysis of variance to assess continuous variables and patient preference. Data are presented as mean ± one standard deviation (SD).

RESULTS

There were no statistically significant differences in demographic data between patients randomized to use the Basic Y system versus the Freeline Solo, as shown in Table 1.

Mean time on the trial was 8.8 ± 3.5 (range, 3 to 15) months in Group 1, and 10.7 ± 3.5 (range, 4 to 16) months in Group 2. The total observation period was 303 pt.months with the Basic Y, and 328 pt.months with the Freeline Solo. Fifty-three of 63 enrolled patients were still on the trial at its termination, and three of these patients had new peritoneal dialysis catheters. Patients left the trial early because of transplantation (3), death from unrelated causes (2), return of renal function (1), blindness (1), and transfer to another renal unit (1); there were no differences in reasons for early termination between patients on the Basic Y or Freeline Solo systems. Two additional patients were transferred to hemodialysis, one on the Basic Y system, because of exit-site infection, and the other on Freeline Solo, for unrelated reasons.
TABLE 1. Demographic data of patients at the beginning and end of trial\(^a\)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
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<tbody>
<tr>
<td></td>
<td>FS</td>
<td>BY</td>
<td>FS</td>
<td>BY</td>
</tr>
<tr>
<td>At Beginning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>20</td>
<td>19</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>55 ± 17</td>
<td>51 ± 17</td>
<td>59 ± 11</td>
<td>60 ± 15</td>
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<tr>
<td>Sex (M)</td>
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<td>8</td>
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<td>3</td>
</tr>
<tr>
<td>English-speaking</td>
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<td>16</td>
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<td>9</td>
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<tr>
<td>Private health insurance</td>
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<td>1</td>
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<tr>
<td>Diabetes mellitus</td>
<td>5</td>
<td>3</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>New catheter before trial</td>
<td></td>
<td></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Time on CAPD(^b) (months)</td>
<td></td>
<td></td>
<td>28 ± 23</td>
<td>17 ± 10</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>36 ± 5</td>
<td>37 ± 6</td>
<td>36 ± 5</td>
<td>36 ± 5</td>
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<tr>
<td>Training time (days)</td>
<td>3.4 ± 1.9</td>
<td>3.4 ± 1.3</td>
<td>0.9 ± 0.2</td>
<td>0.8 ± 0.3</td>
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<tr>
<td>At End of Trial</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Time on trial (months)</td>
<td>9.1 ± 3.9</td>
<td>8.5 ± 3.2</td>
<td>9.9 ± 3.5</td>
<td>11.5 ± 3.6</td>
</tr>
<tr>
<td>Serum albumin (g/L)</td>
<td>35 ± 7</td>
<td>37 ± 5</td>
<td>34 ± 4</td>
<td>34 ± 4</td>
</tr>
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</table>

\(^a\) Data are presented as mean ± SD. There were no statistically significant differences between patients randomized to Freeline Solo (FS) or Basic Y (BY).

\(^b\) CAPD, continuous ambulatory peritoneal dialysis.

Overall, patients rated (on a scale of 1 to 7) the Freeline Solo system more easy to use than the Basic Y system (6.6 ± 0.9 versus 5.5 ± 1.6, \(P < 0.001\)), and among patients who had experience with both systems, the Freeline Solo was also rated as easier to use (difference, 1.8 ± 2.4; \(P < 0.02\)).

Peritonitis occurred on 23 occasions in 12 patients using the Basic Y versus seven occasions in five.

Figure 1. The number of episodes of peritonitis observed during successive months after entry into the trial for patients using Freeline Solo (light bar) versus Basic Y (dark bar) in Groups 1 and 2.
patients with the Freeline Solo. Among Group 2 patients, peritonitis occurred on 16 occasions in seven patients with the Basic Y, and four occasions in three patients with the Freeline Solo. Most of the peritonitis episodes with the Freeline Solo occurred within 3 months of entry into the trial, whereas those with the Basic Y continued throughout the trial (Figure 1). By Cox regression analysis, time to first infection was significantly shorter with the Basic Y than the Freeline Solo (hazard ratio, 2.4; 95% confidence interval, 1.0 to 5.3; $P = 0.04$); the median time was 7 versus more than 15 months. The cumulative incidence of peritonitis at the end of the trial was one every 14.0 pt-months with the Basic Y, versus one every 46.5 pt-months with the Freeline Solo (Figure 2; odds ratio, 3.6; 95% confidence interval, 1.5 to 8.5; $P < 0.004$).

Table 2 demonstrates that the difference in peritonitis rates could only be established clearly after more than 1 yr of the study.

Among Group 1 patients, the cumulative incidence of peritonitis for the Basic Y and the Freeline Solo was one every 24.1 and 63.1 pt-months respectively, and among Group 2 patients, one every 34.6 pt-months respectively (odds ratio, 4.2; 95% confidence interval, 1.3 to 13.0; $P = 0.013$). The probability of 1 yr infection-free survival was 41.1% with the Basic Y, and 77.0% with the Freeline Solo.

Among all patients, peritonitis was associated significantly with the use of the Basic Y (odds ratio, 3.6) and peritonitis during the 12 months before the trial (odds ratio, 4.0). In patients from Group 2, peritonitis was predicted significantly by the use of the Basic Y (odds ratio, 4.2), and the apparent associations with prior peritonitis, serum albumin concentration, and

<table>
<thead>
<tr>
<th>TABLE 2. Associations with peritonitis$^a$</th>
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<tr>
<td>Factor</td>
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<td>-------------------------</td>
</tr>
<tr>
<td>Basic Y</td>
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<tr>
<td>Prior Peritonitis</td>
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<tr>
<td>Serum Albumin</td>
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<td>Length of Training</td>
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$^a$ OR, odds ratio (95% confidence interval). Prior peritonitis refers to the 12-month period before the trial.
length of training did not reach statistical significance (Table 2). None of the other covariates was associated with peritonitis, including the fluid-transfer system used before the trial. Exit-site infections occurred on four occasions each with the Basic Y and the Freeline Solo in Group 1, and not in any of the patients who had peritonitis. Amongst Group 2 patients, exit-site infection did not occur with the Freeline Solo, and on four occasions occurred with the Basic Y, at the time of peritonitis on three occasions and once in a patient who had no peritonitis. A causative organism was identified in 34 of 39 infections, and was Gram-positive in 79% (Staphylococcus epidermidis, 47%; Staphylococcus aureus, 15%), Gram-negative in 15%, and fungal in 15%. There was no difference in the type of microorganism identified between patients using the Basic Y versus the Freeline Solo.

Six patients in Group 2 had a new catheter during the 12 months before the trial. During the trial, there were no episodes of peritonitis or exit-site infection among the three using the Freeline Solo, and six episodes of peritonitis (in three patients) and two of exit-site infection (in two) among those patients using the Basic Y.

Hospitalization for catheter-related infection was required for 98 days in six patients using the Basic Y, and 17 days in two patients using the Freeline Solo. Hospitalization was required in 36% of catheter-related infection with the Basic Y, and 17% with the Freeline Solo ($\chi^2 = 3.39; P = 0.05$). Among Group 2 patients, the total days of hospitalization for catheter-related infection (96 versus 3, $P < 0.03$) and the number of patients hospitalized (6 versus 1, $P < 0.01$) was significantly greater with the Basic Y than with the Freeline Solo (Table 3). Even after removing from Group 2 analysis the six patients who had had a new catheter before the trial, days of hospitalization (76 versus 3), number of patients (4 versus 1, $P < 0.001$), and number of catheters removed (3 versus 0, $P < 0.001$) were significantly greater among those using the Basic Y. Total days of hospitalization for reasons other than catheter-related infection was 173 with the Basic Y, and 349 with the Freeline Solo (P = not significant) (Table 4). The apparent difference in hospitalization for other reasons occurred only in Group 1 (78 versus 258 days), and was accounted for primarily by four patients with depression, cancer, and an aortic aneurysm.

In all of these cases, the reason for admission was clearly independent of the transfer system used.

The total cost of treatment of CAPD infection was more than 8AUD100,000 greater for the Basic Y than for the Freeline Solo (Table 5). Most of the difference related to the cost of hospitalization, in particular the actual bed-day costs. One patient each using the Basic Y was admitted to a high-dependency ward and a district hospital for treatment of peritonitis, where the bed-day costs were higher and lower respectively than for the other hospitalizations. When bed-day costs were standardized to the one rate, the cost difference between the Basic Y and the Freeline Solo was reduced to 8AUD80,309. When the six patients in Group 2 with a new catheter before the trial were excluded, the difference in cost was 8AUD89,630. As the extra consumables' cost for the Freeline Solo above that of the Basic Y was 8AUD3373 per annum at the time of the trial, the savings from reduced infection with the Freeline Solo were equivalent to 32 catheter-yr during this trial. If the bed-day costs were standardized, the consumable costs of the Freeline Solo were still covered by the savings from reduced infection.

**DISCUSSION**

The study presented here confirms the previous randomized controlled study (3) and a number of uncontrolled, nonrandomized studies (4–11) that have demonstrated the superiority of twin-bag disconnect fluid-transfer systems in reducing the incidence of peritonitis in patients treated with CAPD. The cumulative incidence of peritonitis was one every 46.5 pt.mon with the Freeline Solo, compared to one every 14.0 pt.mon with the Basic Y single-bag disconnect system, and the time to first infection significantly shorter with the Basic Y. Unlike the study of Kiernan...
et al. (3), in which the incidence of exit-site infection was also reduced, in this study, there was no significant difference in rate of exit-site infection. There was no overall relationship between exit-site infections and peritonitis, although on three occasions these infections occurred concurrently. Peritonitis was associated significantly only with the use of the Basic Y, and with peritonitis before the trial.

Despite consistent demonstration of the efficiency of twin-bag systems in reducing peritonitis, these systems have not been universally prescribed, primarily because of the increased purchase cost of the consumables. In an uncontrolled observation from Canada, it was suggested that reduced peritonitis might pay for the extra purchase cost of a twin-bag system, but in that study the peritonitis rate with the twin-bag system was 1 per 17 pt.yr, and the extra purchase cost above that of a single-bag system only $AUD244 per pt.yr (4). Until now, there has been no published controlled cost-effectiveness analysis comparing twin-bag and single-bag systems. In this study, hospitalization days for catheter-related infection were almost six times greater, and more patients were hospitalized and more catheters removed for infection with the Basic Y than the Freeline Solo. This suggests that peritonitis may have been more severe as well as more frequent with the Basic Y than the Freeline Solo. The savings accruing from the reduced cost of catheter-related infections more than covered the increased purchase cost of the Freeline Solo system.

The greater efficacy and the reduced total cost of the Freeline Solo demonstrated in this study must be extrapolated to other populations with some caution. Although the demographics of the patients were similar to those of many CAPD populations, it should be noted that approximately 20% each did not speak English or were diabetic and that all patients were either new to dialysis, had a new catheter, or had had no catheter-related infections in the 12 months before the present study. Moreover, more than 80% of the savings were realized because of reduced hospitalization for infection. Thus, the reduced total costs of twin-bag disconnect systems need to be analyzed in different centers and populations.

In summary, the Freeline Solo twin-bag disconnect system was associated with fewer cases of peritonitis and had a lower total cost than the Basic Y single-bag system. More expensive dialysis technologies should be subjected to rigorous costing before their use is excluded in the name of fiscal restraint.

ACKNOWLEDGMENTS

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REFERENCES