Superiority of Icodextrin Compared with 4.25% Dextrose for Peritoneal Ultrafiltration

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Several clinical observations suggest the superiority of icodextrin compared with 4.25% dextrose in optimizing peritoneal ultrafiltration (UF), but no rigorous controlled evaluation has hitherto been performed. For comparing icodextrin and 4.25% dextrose during the long dwell of automated peritoneal dialysis, a multicenter, randomized, double-blind trial was conducted in 92 patients (control, 45; icodextrin, 47) with 4-h dialysate to plasma ratio creatinine dextrose during the long dwell of automated peritoneal dialysis, a multicenter, randomized, double-blind trial was conducted

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The addition of icodextrin to the PD solution armamentarium is particularly relevant in light of the recent focus on fluid management as a key component of PD adequacy (2,4). Several observations (2) relate the level of fluid management with patient survival, incidence of morbidity, and preservation of residual renal function. Recently, the European Automated PD (APD) Outcome Study showed that greater UF at baseline was a predictor of improved patient survival (5). Current expert opinion (2,6) also reinforces the need to consider fluid management as a primordial focus of adequate dialytic therapy. Controlled clinical trials have demonstrated the superiority of icodextrin in effecting UF during the long dwells of both continuous ambulatory PD (CAPD) and APD compared with dextrose solutions of low (1.5%) and intermediate (2.5%) tonicity (1). Recent studies also provide evidence of icodextrin’s favorable effects on left ventricular hypertrophy (7), measures of fluid balance (8,9), and peritoneal membrane function (10).

Inadequate fluid removal during the long dwell with dextrose-based PD solutions is particularly common in patients with high-average or high peritoneal transport characteristics (11). Several clinical observations suggest that icodextrin is superior to 4.25% dextrose in these patients. Although no controlled comparative trials have been conducted to support this hypothesis, icodextrin has been shown to improve long-dwell UF in patients who have experienced UF failure and were
unable to achieve adequate fluid removal using 4.25% dextrose (12,13). It is widely recognized that patients with UF failure often have a high transport status (11). Furthermore, modeled UF profiles provide support for the hypothesis that icodextrin provides superior long-dwell net UF compared with 4.25% dextrose in high-average/high transport patients (14). These observations provided the basis for the recommendation of the International Society for Peritoneal Dialysis that icodextrin be the preferred therapy for UF failure (4). The purpose of the present study was to evaluate the response to icodextrin in comparison with 4.25% dextrose during the long dwell in patients with high-average or high peritoneal transport characteristics in a structured setting with a rigorous experimental design.

Materials and Methods

Study Design

Dialysis centers in the United States and Australia participated in this multicenter, prospective, randomized, double-blind, parallel-group comparison of icodextrin and 4.25% dextrose in patients who were on APD and had high-average to high peritoneal transport characteristics. The target for enrollment was 100 patients, which was required to establish a difference between treatments of at least 150 to 175 ml. The study was initiated on July 1, 2001, and completed on October 11, 2003.

The design of the study included a 6- to 14-d screening period, which was followed by a 2-wk treatment period (Figure 1). The screening period was used to determine eligibility for study participation, to obtain informed consent, and to perform the screening peritoneal equilibrium test (PET). All patients who met the entrance criteria used 4.25% dextrose for the long dwell at least 3 d before the baseline visit. At the baseline visit, patients were randomly assigned (1:1) to receive either 7.5% icodextrin (Extraneal; Baxter, McGaw Park, IL) or a control solution of 4.25% dextrose (Dianeal PD-2; Baxter) for the long dwell using a centrally maintained randomization list. Blinding of study group assignments was accomplished by use of identical solution bags. Fill volume (2.0 to 2.5 L) was based on the patient’s prestudy long-dwell prescription and was not varied during the study. Prescriptions for the short nighttime exchanges were identical to those used before the study. Although the duration of the long dwell could vary between 12 and 16 h to accommodate individual daily schedules, it was controlled to within 14 to 16 h on the baseline, week 1, and week 2 assessment days. The use of concurrent medications (including antihypertensive medications) was not restricted. Dose, frequency, and reason for use were recorded. After completion of the week 2 visit, patients resumed therapy with their prestudy prescription. The study protocol was approved by the institutional review board or ethics committee at each center.

Inclusion/Exclusion Criteria

The principal inclusion criterion was peritoneal membrane transport characteristics in the high-average or high category (4-h dialysate to plasma ratio [D/P] creatinine >0.70 and 4-h D/D0 glucose <0.34), based on the results of the screening PET. To be eligible for study participation, patients had to be at least 18 yr of age, receiving treatment with APD using the HomeChoice (Baxter) or HomeChoice PRO (Baxter) cycler for at least 30 d before the baseline visit, stable on their PD prescription before the screening visit, using an APD prescription for at least 3 d before the baseline visit that included a long-dwell exchange with duration of 12 to 16 h and fill volume of 2.0 to 2.5 L of a 4.25% dextrose solution (Dianeal PD-2 or PD-4; Baxter), in stable health and able to tolerate a 12- to 16-h long dwell, and free from peritonitis for at least 45 d before the use of study solution.

Clinical and Laboratory Evaluations

The primary measure of efficacy was net UF during the long dwell (drain volume minus last bag fill volume). Secondary measures of efficacy included the UF efficiency ratio (UFE), defined as net UF volume (mL) per gram of carbohydrate absorbed from the long-dwell dialysate; long-dwell peritoneal creatinine and urea clearances; drained body weight; and 24-h ambulatory BP measurements.

Assessments at baseline, week 1, and week 2 included drain volume and levels of icodextrin, glucose, creatinine, and urea in the dialysate drained from the long dwell; physical examination (baseline and week 2 only); vital signs; drained body weight; 24-h ambulatory BP measurements; laboratory analyses; and treatment compliance (week 1 and week 2 only). Twenty-four-hour ambulatory BP measurements were obtained using a noninvasive oscillometric ambulatory BP monitor (SpaceLabs Medical, model 90207; Issaquah, WA). Blood for chemistry and hematology evaluations was analyzed by Quintiles Laboratories (Atlanta, GA, for US sites or Singapore for Australian sites).

The PET was conducted by the procedure of Twardowski et al. (15). The D/P creatinine was calculated as the ratio of dialysis creatinine level at 4 h to plasma creatinine level at 2 h. The D/D0 glucose was calculated as the ratio of the dialysate glucose level at 4 h to the dialysate glucose level at time 0. The UFE was determined by dividing net UF volume (mL) by the number of grams of carbohydrate absorbed from the dialysate. The amount of carbohydrate absorbed was determined by the difference in glucose or icodextrin content between drained and infused dialysate. When net UF was negative (<0), UFE was entered in the database as 0.

Statistical Analyses

Analyses of primary and secondary efficacy variables and safety variables were conducted in the intention-to-treat population (all patients who were randomized to treatment and received at least one exchange of study solution). A repeated-measures analysis of covariance was used to evaluate differences between treatment groups for the primary and secondary efficacy variables. The model included the main effect of treatment, random subject (patient) effect within treatment, visit effect (repeated measures), and baseline as a covariate. A general linear model was used to analyze other continuous variables at each visit and included the main effect of treatment. Baseline values, when available, were used as a covariate. Correlation analysis and its test of significance were used to evaluate the relationship between net UF and baseline peritoneal transport status for each group. A Pearson $\chi^2$ test
was used to analyze differences in categorical variables between the two treatment groups at each time point. Fisher exact test was used when >20% of the cells had fewer than five expected counts.

The test of the difference between the two treatment groups (treatment effect) was conducted at \( \alpha = 5\% \). All analyses were performed using SAS software, version 8 (SAS Institute, Cary, NC). For each efficacy variable, values were reported as mean \pm \text{SEM}.

**Results**

**Baseline Characteristics and Disposition**

The baseline characteristics of the study population are shown in Tables 1 and 2. The two study groups were identical with regard to demographic variables, medical and renal disease history, peritoneal solute transport characteristics, and dialysis vintage.

Baseline PD prescriptions were not statistically different between the control and icodextrin groups, respectively, for total cycler therapy volume (11.67 \pm 0.45 \text{ ml} \text{ vs} 11.13 \pm 0.44 \text{ L}), total cycler therapy time (8.93 \pm 0.14 \text{ h} \text{ vs} 9.06 \pm 0.14 \text{ h}), fill volume per exchange (2.43 \pm 0.06 \text{ ml} \text{ vs} 2.35 \pm 0.05 \text{ L}), or average cycler dextrose concentration excluding the long dwell (2.38 \pm 0.11 \text{ ml} \text{ vs} 2.41 \pm 0.09\%). Chemistry and hematology measures, physical findings, vital signs, and incidence of pre-existing adverse events also were not statistically different between study groups.

A total of 92 patients (control, 45; icodextrin, 47) were enrolled in the study, and 85 (control, 42; icodextrin, 43) completed both the week 1 and the week 2 study visits. Seven patients (control, 3; icodextrin, 4) discontinued the study because of adverse events.

**UF Response**

The UF response during the long dwell was the primary outcome measure of this trial. The conditions under which the long-dwell UF response was measured were not different between groups or at different time points. Mean long-dwell duration in the control and icodextrin groups, respectively, was 855.2 \pm 6.47 \text{ min} (\text{P} = 0.647) at baseline, 853.9 \pm 6.05 \text{ min} versus 843.5 \pm 7.60 \text{ min} (\text{P} = 0.291) at week 1, and 843.7 \pm 11.80 \text{ min versus 850.9} \pm 7.34 \text{ min} (\text{P} = 0.605) at week 2. Mean long-dwell infusion volume was 2.18 \pm 0.04 \text{ ml} \text{ vs} 2.15 \pm 0.03 \text{ ml} (\text{P} = 0.603) at baseline, 2.19 \pm 0.04 \text{ ml} \text{ vs} 2.12 \pm 0.03 \text{ ml} (\text{P} = 0.173) at week 1, and 2.19 \pm 0.04 \text{ ml} \text{ vs} 2.12 \pm 0.03 \text{ ml} (\text{P} = 0.181) at week 2.

At baseline (when all patients used 4.25\% dextrose for the long dwell), long-dwell net UF was comparable between the control and icodextrin groups (201.7 \pm 103.1 \text{ ml} \text{ vs} 141.6 \pm 75.4 \text{ ml}, respectively; \text{P} = 0.637). The percentage of patients with negative net UF at baseline was also comparable between treatment groups (control, 37.8\%; icodextrin, 42.6\%; \text{P} = 0.641).

The long-dwell UF response was evaluated at week 1 and week 2 after randomization. During the treatment period, net UF was unchanged from baseline in the 4.25\% dextrose group, whereas icodextrin patients experienced statistically significant improvements in net UF at week 1 and week 2 (505.8 \pm 46.8 and 598.8 \pm 49.8 ml, respectively).

<table>
<thead>
<tr>
<th>Table 1. Patient characteristics at baseline$^a$</th>
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<tbody>
<tr>
<td>No. of patients</td>
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<tr>
<td>Age (yr)</td>
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<tr>
<td>Gender (% male)</td>
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<tr>
<td>Race (%)</td>
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<tr>
<td>white</td>
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<td>black</td>
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<td>Hispanic</td>
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<tr>
<td>Asian</td>
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<td>diabetic nephropathy</td>
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<tr>
<td>hypertensive nephropathy</td>
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<tr>
<td>glomerulonephritis</td>
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<tr>
<td>obstructive nephropathy</td>
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<tr>
<td>polycystic kidney disease</td>
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<tr>
<td>autoimmune disease</td>
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<tr>
<td>interstitial nephritis</td>
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<td>other</td>
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<tr>
<td>Height (cm)</td>
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<td>Weight (kg)</td>
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<tr>
<td>Diabetes (%)</td>
</tr>
<tr>
<td>Time since first dialysis started (mo)</td>
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<tr>
<td>Time since current PD started (mo)</td>
</tr>
</tbody>
</table>

$^a$Values are expressed as mean \pm \text{SEM}. \text{NS}, not significantly different between treatment groups; PD, peritoneal dialysis.
dextrose (4). Mean net UF during the PET was defined as 4-h net UF dextrin groups (not significantly different between the 4.25% dextrose and icodextrin groups) at week 1 and week 2 (37.2% versus 0% [P < 0.0001] at week 1 and 33.3% versus 0% [P < 0.0001] at week 2; Table 3). Similar long-dwell net UF of approximately 500 mL regardless of transport status (r = −0.124, P = 0.412; Figure 4). A similar analysis of the relationship between net UF change from baseline at weeks 1 and 2 combined and baseline peritoneal transport status (D/P creatinine) showed that in the control group, the change from baseline was similar regardless of transport rate (r = 0.038, P = 0.806). However, in the icodextrin group, the net UF change from baseline increased in magnitude as transport rate increased (r = 0.452, P = 0.002), indicating a greater improvement in net UF in patients with the higher transport profiles (data not shown).

Consistent with the known kinetic profiles of the osmotic agents, the proportion of infused carbohydrate absorbed into the circulation was significantly greater (P < 0.001) with 4.25% dextrose than with icodextrin (91.3 versus 35.3% at week 1 and 92.0 versus 35.6% at week 2; Table 3). Similarly, the total amount of carbohydrate absorbed was greater in the 4.25% dextrose group than in the icodextrin group (Table 3). The combination of less carbohydrate absorption and greater net UF with icodextrin resulted in a significant improvement in the UFE. In the control group, UFE at week 1 and week 2 were not significantly different from the baseline value (5.50 ± 1.02 mL/g at baseline, 5.12 ± 0.97 mL/g at week 1, and 4.71 ± 0.85 mL/g at week 2). However, in the icodextrin group, UFE increased significantly from 3.64 ± 0.82 mL/g at baseline to 10.51 ± 1.25 mL/g at week 1 (P < 0.001) and 10.90 ± 1.12 mL/g at week 2 (P < 0.001). The UFE with icodextrin was significantly greater compared with the control group at both week 1 and week 2 (P < 0.001).

Table 2. Peritoneal transport characteristics by PET at baselinea

<table>
<thead>
<tr>
<th></th>
<th>Control (4.25% Dextrose)</th>
<th>Intervention (Icodextrin)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>45</td>
<td>47</td>
<td>NS</td>
</tr>
<tr>
<td>Urea: D/P, 4 h</td>
<td>0.935 ± 0.006</td>
<td>0.949 ± 0.007</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine: D/P, 4 h</td>
<td>0.830 ± 0.013</td>
<td>0.851 ± 0.013</td>
<td>NS</td>
</tr>
<tr>
<td>Glucose: D/D0, 4 h</td>
<td>0.301 ± 0.006</td>
<td>0.295 ± 0.006</td>
<td>NS</td>
</tr>
<tr>
<td>Net UF during PET (mL)</td>
<td>235 ± 42</td>
<td>264 ± 30</td>
<td>NS</td>
</tr>
</tbody>
</table>

aPET performed with 2.5% dextrose; values are expressed as mean ± SEM. UF, ultrafiltration; PET, peritoneal equilibration test; NS, not significantly different between treatment groups; D/P, dialysate to plasma ratio.

Figure 2. Net ultrafiltration (UF) at baseline, week 1, and week 2. Values represent mean ± SEM for patients who were randomized to 4.25% dextrose (dashed line) or icodextrin (solid line). *P < 0.001 versus 4.25% dextrose (adjusted for baseline values).

Figure 3. Percentage of patients with negative net UF at baseline, week 1, and week 2 in patients who were randomized to 4.25% dextrose (□) or icodextrin (■). Between-group differences, *P < 0.0001.
Small Solute Clearances

Long-dwell peritoneal creatinine and urea clearances at baseline were not statistically different between study groups. During treatment, clearance of both small solutes was unchanged in the control group but significantly increased with icodextrin at week 1 and week 2 (\(P < 0.001\) for change from baseline and between-treatment comparisons of change from baseline; Table 4). The result was an additional 3.3 to 3.5 L of weekly creatinine clearance (21 to 23% increase in long-dwell clearance) and 2.7 to 2.9 L of weekly urea clearance (17 to 18% increase in long-dwell clearance).

Other Efficacy Measures

BP was relatively well controlled in both groups at baseline and throughout the study (Table 5). No statistically significant or clinically relevant differences from baseline or between treatment groups were found for 24-h ambulatory BP readings, sitting or standing BP measured during study visits, or drained body weight. The percentage of patients with more than a 10% drop in mean BP from wake to sleep readings (dippers) was low in both study groups; was not significantly different between groups at baseline, week 1, or week 2; and did not show any time trends during the study. Glucose concentrations in the
cycler-based part of the daily therapy did not vary from baseline in the course of the study.

Safety

No notable unexpected adverse events occurred during the study, and most reported events were related to medical conditions associated with ESRD. Only rash occurred significantly more often in the icodextrin group (eight patients, 17%) compared with the control group (zero patients; P = 0.006). Six of the eight patients with rash completed the study. Maculopapular rash was reported in three (6.4%) icodextrin patients and none of the control patients (P = 0.242). One of these patients completed the study. Cases of rash were similar to those reported previously in icodextrin-treated patients (1). No clinically or statistically significant differences between groups were found for the incidence of hypotension, hypertension, or hyperlipidemia reported as adverse events.

Seven patients (icodextrin, 4; control, 3) were discontinued from the study as a result of adverse events. The four patients in the icodextrin group were discontinued as a result of rash or macular rash. The reasons for discontinuation in the control group were fluid overload/diffuse body aches, peritonitis, and hypervolemia (one patient each).

Discussion

The results of the present study can be summarized as follows: (1) Patients with high-average or high peritoneal transport characteristics on APD have a high prevalence of negative net UF when 4.25% dextrose is used for the long-dwell exchange; (2) use of icodextrin for the long dwell abrogates the negative UF and results in a significant positive net UF (mean 500 ml per exchange); and (3) the enhanced UF achieved with icodextrin in comparison with 4.25% is paralleled by increased small solute clearances during the long dwell and a higher UF efficiency for the absorbed carbohydrate load.

Adequate fluid management is a major goal of PD and is necessary for achievement of good clinical outcomes (4). Clinical observations continue to document suboptimal fluid management in subsets of PD populations, particularly in patients who have high-average or high peritoneal solute transport patterns by the PET and are most likely to experience inadequate UF (2,11,16–18). Inadequate fluid removal is a common occurrence when dextrose-based solutions are used for the long dwell, particularly in high-average/high transporters (11,14).

Because of its small size, glucose is rapidly transported across the peritoneal membrane in these patients, leading to a progressive dissipation of the osmotic gradient as the dwell progresses and a corresponding reduction in net UF (14). Because the rate of glucose absorption is time dependent, its impact on net UF during the short dwells is generally limited. However, during the long dwell, the impact of glucose absorption can be considerable. In fact, toward the end of the long dwell, the osmotic gradient may be reduced to such an extent that more fluid is absorbed than ultrafiltered, resulting in a negative net UF volume (drained volume less than infused volume). Unlike glucose, icodextrin does not readily diffuse across the peritoneal membrane but instead is slowly removed from the peritoneal cavity primarily via convective pathways involving predominantly lymphatic absorption (19).

Because of the risk for low or negative net UF during the long dwell, dextrose solutions of higher tonicity (2.5 and 4.25% dextrose) are often used in an effort to compensate for the progressive decline in net UF. However, in addition to the fact that high tonicity dextrose solutions can contribute to a number of metabolic abnormalities such as obesity, hyperinsulinemia, and hyperlipidemia (20,21) and may well compromise peritoneal membrane function (22), they may still be unable to prevent negative net UF in high-average/high transporters. In the present study, 33 to 38% of high-average/high transporters who used 4.25% dextrose for the long dwell experienced negative net UF.

Previous studies have demonstrated that icodextrin provides significantly better net UF during the long dwell than either 1.5 or 2.5% dextrose (23,24). Evaluation of the comparative UF of icodextrin and 4.25% has hitherto been limited. The MIDAS study compared the two solutions in patients who were on CAPD using the typical dwell times of CAPD regimen (23). The study found comparable net UF between icodextrin and 4.25% dextrose, although a trend toward greater UF with icodextrin was observed particularly during the longer dwell exchanges (12 h). However, this study did not categorize patients by peritoneal transport characteristics or address the longer dwell times inherent to cycler-based therapy (3).

Before the present study, no controlled trials had compared icodextrin and 4.25% dextrose in high-average/high transporters, although evidence suggested the superiority of icodextrin in these patients. Several studies have demonstrated the success

| Table 4. Peritoneal creatinine and urea clearances during the long dwell
<table>
<thead>
<tr>
<th>Peritoneal Creatinine Clearance (ml/min)</th>
<th>Peritoneal Urea Clearance (ml/min)</th>
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<tbody>
<tr>
<td></td>
<td>4.25% Dextrose</td>
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<tr>
<td>Baseline</td>
<td>2.69 ± 0.11</td>
</tr>
<tr>
<td>Change from baseline</td>
<td></td>
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<tr>
<td>week 1</td>
<td>−0.07 ± 0.09</td>
</tr>
<tr>
<td>week 2</td>
<td>−0.08 ± 0.11</td>
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*aValues are expressed as mean ± SEM.
of icodextrin in patients who experienced UF failure and fluid overload despite the use of 4.25% dextrose for the long dwell. A retrospective review of one center’s long-term experience found that among 33 patients with UF failure (fluid retention despite two 4.25% dextrose exchanges per day), switching to icodextrin for the long dwell extended PD technique survival by a median of 22 mo (12). In a prospective, open-label study of 39 patients who were at the point of transfer to hemodialysis because of refractory fluid overload (13), substitution of icodextrin for 4.25% dextrose prolonged use of PD by a mean of 1.21 yr; among patients with daily net UF <1 L, time on PD was extended by a mean of 1.70 yr. Additional supportive evidence of the superiority of icodextrin compared with 4.25% dextrose comes from an open-label, single-dose, crossover study that was conducted to establish the relationship between peritoneal membrane transport pattern and UF volume (25). This study found that high-average and high transport patients achieved significantly greater net UF with icodextrin than with 4.25% dextrose. Furthermore, this study provides additional evidence of the superiority of icodextrin over 4.25% dextrose in patients with UF failure by International Society for Peritoneal Dialysis criteria.

The primary objective of the present study was to compare the fluid-removal capabilities of icodextrin and 4.25% dextrose in a population of APD patients who would most likely benefit from an improvement in UF, namely those with high-average/high peritoneal membrane transport characteristics. The study was limited to patients who were on APD for two reasons. First, APD is recommended when UF is inadequate in patients with high transport characteristics because the shorter dwell times of the nighttime exchanges will improve UF (4). Second, APD is becoming the dominant PD modality in modern practice (3). The long-dwell duration of 14 to 16 h in this study is typical for APD.

The results of this study demonstrated that use of icodextrin for the long dwell results in highly statistically significant and clinically meaningful improvements in net UF. Although our study was limited to a 2-wk observation period, our results are likely sustainable and reproducible over longer periods of observation on the basis of several considerations. Specifically, studies have shown that early increases in net UF with icodextrin are reproducible and sustainable for up to 21 wk of therapy, including in high-average/high transporters (23,24) (data on file, Baxter Healthcare Corporation).

In this study, icodextrin use was associated with a significantly greater UFE, indicating that more ultrafiltrate was produced for each gram of carbohydrate absorbed from the dialysate. Reduction of daily carbohydrate absorption through the use of icodextrin may help to reduce the risk of metabolic complications such as hyperinsulinemia, hyperlipidemia with elevated triglycerides and LDL cholesterol, appetite suppression, and obesity (20,21,26). Use of icodextrin in place of 4.25% dextrose would also reduce peritoneal glucose exposure, which may mitigate the detrimental effects of glucose on peritoneal membrane function (22) and extend the time that patients are able to use their PD modality of choice (8).

The BP profile of the study population displayed the com-
mon characteristics of predominance of nondippers that has been described in patients with chronic kidney disease and patients who are on dialysis (27–30). BP control was satisfactory at baseline, and the enhancement of UF with icodextrin did not result in any changes in BP control or in the circadian behavior of BP levels. This lack of change in BP control in a population that is known for its volume-dependent hypertension may seem disconcerting until we recognize that drained body weight also did not change. This suggests that this population likely compensated for the increased UF by a simultaneous increase in fluid intake, not an uncommon occurrence in PD patients. As the study protocol did not necessitate any constancy in dietary salt intake, patients may have viewed the increased UF as an opportunity to increase intake. In the settings in which investigators coupled enhanced peritoneal UF with dietary restrictions, improved BP control has been observed with the use of icodextrin (9,31).

The occurrence of maculopapular rash (6.4%) was expected, as the development of a new skin rash was the most common treatment-related side effect of icodextrin in previous clinical trials (1,24). Rashes that occur with icodextrin usually are mild or moderate, typically involve the palms and soles, and can be associated with peeling of the skin. When a rash occurs, it generally develops early in therapy, is self-limited, and resolves without sequelae after discontinuation of icodextrin.

In summary, this study demonstrated that in APD patients with high-average or high transport characteristics, icodextrin for the long-dwell exchange results in significantly greater net UF than 4.25% dextrose. The incidence of negative net UF during the long-dwell exchange was reduced from approximately 40 to 0% in this group of patients. Significant improvements in the amount of fluid removed per gram of carbohydrate absorbed from dialysate indicates that icodextrin is a more efficient osmotic agent.

Acknowledgments

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