Anemia is one of the most serious complications in patients on dialysis. Erythropoietin improves the anemia. However, erythropoietin resistance is sometimes encountered from causes such as functional iron deficiency, secondary hyperparathyroidism, blood loss, or interaction with other drugs.

To clarify the interaction between erythropoietin and the renin–angiotensin system, we studied the maintenance dose of recombinant human erythropoietin (rHuEPO) in patients on continuous ambulatory peritoneal dialysis (CAPD) with and without angiotensin converting enzyme inhibitor (ACEIs), angiotensin II type 1 receptor blockers (ARBs), and calcium channel blockers. We divided 36 hypertensive patients on CAPD into three groups—an ACEI group (n = 12), an ARB group (n = 12), and a Ca channel blocker group (n = 12)—and then we compared the doses of rHuEPO required to maintain the patients’ hematocrit (Hct) above 30%.

In the Ca channel blocker group, the weekly dose of erythropoietin had not changed significantly at the end of the study (74±7 U/kg at the end vs. 76±8 U/kg at the start). The (oral) ACEI group needed a significantly higher weekly dose of erythropoietin at the end of the study (89±9 U/kg at the end vs. 74±8 U/kg at the start, p < 0.01). The (oral) ARB group also needed a significantly higher weekly dose of erythropoietin at the end of the study (82±10 U/kg at the end vs. 76±8 U/kg at the start, p < 0.05). Furthermore, the weekly dose of erythropoietin required in the ACEI group was significantly larger than that required in the ARB group.

We conclude that treatment with ACEIs and ARBs induces erythropoietin resistance in patients on CAPD. The inhibitory effect of ARBs on erythropoiesis is less than that of ACEIs.

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Erythropoietin Resistance in Patients on Continuous Ambulatory Peritoneal Dialysis

Key words
Erythropoietin resistance, anemia, continuous ambulatory peritoneal dialysis

Introduction
Maintenance of red blood cell volume is fundamental to ensuring a supply of oxygen to tissues. Anemia is one of the most serious complications in patients on dialysis (1,2).

In 1990, recombinant human erythropoietin (rHuEPO) received marketing approved in Japan for treatment of anemia in patients on dialysis. With rHuEPO, a significant rise in the hemoglobin level of patients with end-stage renal disease (ESRD) can be obtained. However, not all patients have a good response to rHuEPO therapy. Failure of therapy can be caused by iron deficiency, infection, uremia, blood loss, and secondary hyperparathyroidism (3,4). Recently, interactions with certain drugs—for example, immunosuppressors, interferon, angiotensin converting enzyme inhibitors (ACEIs), and angiotensin II type 1 receptor blockers (ARBs)—have been reported as a cause of erythropoietin resistance (5,6), impairing the response to rHuEPO treatment.

Hypertension is the most common complication in patients on dialysis (7). In such patients, ACEIs have been widely prescribed for hypertension (8). The ACEIs are widely used in the treatment of hypertension, left ventricular dysfunction, and diabetic nephropathy, and in preventing the progression of established renal disease. However, side effects—including dry cough, hyperkalemia, angioedema, and anemia—have been reported in dialysis patients. Anemia has also been reported as a side effect of ACEIs in normal volunteers and in patients with essential hypertension (9), heart failure (10), chronic renal insufficiency (11), dialysis (12), and renal grafts (13).

In addition to ACEIs, the newly developed ARB antihypertensive agents have been used in patients on
dialysis and with predialysis end-stage renal disease. Anemia has been reported as a side effect of ARBs (6).

In the present study, we investigated the effects of ACEIs and ARBs on the response to rHuEPO in patients on continuous ambulatory peritoneal dialysis (CAPD). We also compared the dose of rHuEPO required to maintain our patients’ hematocrit levels above 30%.

Patients and methods
In this double-blind study, we randomized 36 hypertensive patients undergoing CAPD to 12 weeks’ administration of antihypertensive drugs as follows:

- ACEI-treated group: received benazepril 2.5 – 10 mg daily or enalapril 2.5 – 10 mg daily (n = 12)
- ARB-treated group: received valsartan 20 – 80 mg daily or candesartan 4 – 12 mg daily (n = 12)
- Calcium channel blocker–treated group: received amlodipine 2.5 – 10 mg daily (n = 12)

Previously administered antihypertensive drugs were withheld before the study. The target blood pressure (BP) was 140/90 mmHg or lower in all groups.

The causes of renal insufficiency were chronic glomerulonephritis in 28 patients, nephrosclerosis in 3 patients, and unknown in 5 patients. Patients with diabetic nephropathy were excluded. The most important exclusion criteria were presence of overt heart failure; history of heart failure, myocardial infarction, or cerebral accident in the preceding 6 months; pregnancy; illness requiring hospitalization; an episode of peritonitis within the preceding 6 months; possible existence of malignancy, active infection, or immunologic disease.

All the patients included in the study gave their informed consent to participation. The study was performed in accordance with the Second Helsinki Declaration and was approved by the local ethics committee. After a run-in period, the patients started to receive their assigned drug once daily. Patients were assessed at 4, 8, and 12 weeks.

During the study, all patients were asked to undergo the same dietary and dialysis regimen. The CAPD treatment consisted of 4 daily 2-L exchanges using dialysate containing lactate and 1.5 g/dL or 2.5 g/dL dextrose. Mean daily dietary intake was determined from individual 24-hour food records during a 3-day period. The dietary protein intake was at least 1 g/kg daily, and the energy intake was about 25 kcal/kg daily. Salt intake was restricted to about 7 g daily or less.

Correction of anemia with rHuEPO
Every week, or every other week, rHuEPO was administered by the subcutaneous route. Doses were adjusted monthly. Patients were given intravenous supplementation if they were diagnosed as iron deficient (serum ferritin < 100 ng/mL). Hematocrit (Hct) levels were maintained above 30% in each group.

Statistical analysis
All data are shown as mean ± standard error of the mean. Multiple comparisons were analyzed by analysis of variance (ANOVA) with the Kruskal–Wallis test and subsequent Dunn test. A simple regression analysis was performed for correlations among the variables. A p value < 0.05 was required for statistical significance.

Results
Baseline characteristics of the patients
Table I shows the baseline characteristics of the patients in each group. Patients in the three groups (Ca channel blocker, ACEI, and ARB) were well matched for age, duration of CAPD, total protein, albumin, total cholesterol, blood urea nitrogen, creatinine, serum iron, and serum ferritin. No significant differences

| TABLE I Baseline characteristics of the experimental groups |
|----------------|----------------|----------------|
|                | Ca group a      | ACEI group b    | ARB group c   |
| Age (years)    | 58±3            | 60±3            | 56±3          |
| CAPD duration (years) | 3.4±0.4       | 3.9±0.3        | 3.6±0.5       |
| Total protein (g/dL) | 6.8±0.2        | 6.6±0.2        | 6.8±0.2       |
| Albumin (g/dL)  | 3.8±0.1         | 3.7±0.2        | 3.8±0.1       |
| Total cholesterol (mg/dL) | 182±5         | 175±4          | 188±5         |
| BUN (mg/dL)     | 58±4            | 66±5            | 62±3          |
| Creatinine (mg/dL) | 8.4±0.4      | 8.9±0.5        | 7.9±0.7       |
| Serum iron (µg/dL) | 66±4          | 58±8           | 68±9          |
| Serum ferritin (ng/mL) | 168±21        | 196±26         | 172±24        |
| Serum EPO (mIU/mL) | 76±8           | 74±8           | 74±7          |

a Ca group (n = 12): received calcium channel blockers.
b ACEI group (n = 12): received angiotensin converting enzyme inhibitors.
c ARB group (n = 12): received angiotensin II type 1 receptor blockers.
were observed in the maintenance doses of erythropoietin among the three groups.

**Changes in blood pressure before and after treatment with antihypertensive drugs**

Figure 1 shows the changes in systolic and diastolic BP in the three groups. The baseline levels of systolic and diastolic BP were approximately the same in all three groups. Oral administration of Ca blockers, ACEIs, and ARBs significantly reduced both the systolic and diastolic BP by the end of the study. After treatment with antihypertensive drugs, no significant differences were observed in systolic and diastolic blood pressure between the groups.

**Maintenance dose of rHuEPO before and after treatment with antihypertensive drugs**

We compared the doses of rHuEPO required to maintain Hct above 30% in the three groups. Figure 2 shows the changes in the dose of rHuEPO before and after treatment with antihypertensive drugs in the groups. In the Ca channel blocker group, the weekly dose of erythropoietin was not significantly changed at the end of the study (74±7 U/kg at the end vs. 76±8 U/kg at the start). At the end of study, the weekly dose of rHuEPO was significantly increased in the group that received oral ACEIs (89±9 U/kg at the end vs. 74±8 U/kg at the start, p < 0.01). Similarly, at the end of study, the weekly dose of rHuEPO was significantly increased in the group that received oral ARBs (82±10 U/kg at the end vs. 76±8 U/kg at the start, p < 0.05). However, the required weekly dose of rHuEPO was significantly larger in the ACEI-treated group than in the ARB-treated group.

**Changes in plasma concentration of erythropoietin before and after treatment with antihypertensive drugs**

Figure 3 shows changes in the plasma concentration of erythropoietin before and after treatment with antihypertensive drugs in the three groups. We observed no changes in the plasma concentration of erythropoietin.
in the Ca channel blocker–treated group throughout the experiment. In the ACEI-treated group, the plasma concentration of erythropoietin showed a significant elevation to 22.8 ± 1.8 mIU/mL from 17.4 ± 2.2 mIU/mL (p < 0.05). In the ARB-treated group, the plasma concentration of erythropoietin increased to 19.9 ± 1.8 mIU/mL from 18.2 ± 2.4 mIU/mL (nonsignificant).

Discussion
In the present study, we evaluated the effect of renin–angiotensin system inhibitors on the progression of anemia in CAPD patients treated with rHuEPO. We compared the doses of rHuEPO required to maintain Hct above 30% in patients treated with Ca channel blockers or renin–angiotensin system inhibitors. Patients treated with ACEIs and ARBs required significantly higher dose of rHuEPO than did patients treated with Ca channel blockers.

We also compared the effects of ACEIs and ARBs on erythropoietin resistance. The effect of ARBs on erythropoietin resistance was smaller than that of ACEIs.

Our data lead us to conclude that treatment with ACEIs and ARBs induces erythropoietin resistance in patients on CAPD. Once other causes of erythropoietin resistance are ruled out, physicians must check the possibility of interaction with other drugs, including ACEIs and ARBs. In patients showing erythropoietin resistance and taking ACEIs, a switch to an ARB should be considered.

In Japan, the target hemoglobin level to avoid anemia in hemodialysis and CAPD patients is 10 g/dL (Hct: 30%). Our target hemoglobin level was 10–11 g/dL, which is the same as that for most European studies. In the United States, the upper target for hemoglobin has been extended to more than 12 g/dL.

Maintenance of the red blood cell volume is important for maintaining patients in good condition—especially patients on dialysis. Anemia is one of the most serious complications in dialysis patients (1,2). Erythropoietin improves anemia in patients on dialysis. However, rHuEPO resistance in hemodialysis patients is sometimes caused by functional iron deficiency, secondary hyperparathyroidism, aluminum overload, dialysis, blood loss, or drug interactions (3,4).

The renin–angiotensin system and erythropoietin secretion have been reported to be interrelated. Volume depletion during hemodialysis has been shown to increase plasma renin activity (PRA) and erythropoietin levels in patients without rHuEPO treatment who were maintaining a hematocrit of 30% (14). After captopril administration, the same volume depletion increased PRA; however, erythropoietin levels remained unchanged. Administration of ACEIs might diminish the secretion of erythropoietin, thereby increasing the required maintenance dose of rHuEPO in hemodialysis patients (14).

Fried et al. (15) reported that angiotensin II infusion increased erythropoietin secretion in experimental animals. Recently, an effect of angiotensin peptides on hematopoietic proliferation has been reported (16,17). Rodgers et al. (16) reported the effect of angiotensin II and angiotensin (1–7) on hematopoietic recovery after intravenous chemotherapy. Those authors concluded that angiotensin peptides accelerate hematopoietic recovery in multiple cell lineages after chemotherapy, perhaps through an increase in the number of early hematopoietic progenitors. In addition, Rodgers et al. (17) reported the effect of angiotensin peptides on hematopoietic recovery from irradiation injury. On the other hand, Chisi et al. (18) showed that the ACEI captopril affected the proliferation of primitive hematopoietic cells induced into cell cycle by irradiation or administration of cytotoxic drugs, but had no effect on cell proliferation in myeloid leukemia. They reported that angiotensin converting enzyme has been shown to be involved in the catabolism of the tetrapeptide N-acetyl-Ser-Asp-Lys-
Pro (AcSDKP). They concluded that AcSDKP might mediate the observed in vitro and in vivo inhibitory effects of captopril on primitive hematopoietic cell proliferation.

Another possible mechanism is a direct or indirect interrelationship between ACEIs and erythropoietin. Hirakata et al. (19) reported that captopril-induced worsening of anemia in hemodialysis patients was associated with reduced circulating angiotensin II concentrations; at the same time, plasma erythropoietin levels remained unchanged. From those data, it can be speculated that ACEIs might not inhibit secretion of erythropoietin from the native kidneys, but rather erythropoiesis in bone marrow.

In the present study, we measured the plasma concentrations of erythropoietin in patients before and after treatment with antihypertensive drugs. Calcium channel blockers induced no change in the plasma concentration of erythropoietin. In the ACEI-treated group, plasma concentrations of erythropoietin were significantly higher than those seen in the ARB-treated and Ca channel blocker–treated groups. In addition, plasma concentrations of erythropoietin in the ARB-treated group were higher than those seen in the Ca channel blocker–treated group. The plasma concentration of erythropoietin was correlated with the maintenance dose of rHuEPO. Those data support the speculation that ACEIs and ARBs affect erythropoiesis in the bone marrow of patients on CAPD receiving rHuEPO treatment.

Another important finding of the present study is that ACEIs and ARBs both have an inhibitory effect on erythropoiesis. However, the dose of rHuEPO required in our ACEI-treated group was higher than that required in our ARB-treated group. The ARBs and ACEIs all had the same renin–angiotensin inhibition effect. In the present study, BP levels in the ACEI and ARB groups were the same.

Our experiment does not clarify how the mechanisms differ. However, we can speculate on possible causes. Previously, we reported that the ACEI lisinopril induced an elevation in the plasma concentration of angiotensin (1–7), but that an ARB did not (20). On the other hand, the ARB losartan induced an elevation in the plasma concentration of angiotensin II, but an ACEI did not. The possibility exists that this difference in the metabolites of angiotensin peptide induce differences in erythropoietin sensitivity. Another possibility is the effect of other factors. Julian et al. (21) mentioned that enalapril did not inhibit erythropoiesis in cell culture. It remains to be clarified whether ACEIs stimulate erythropoietic inhibition factors such as cytokines (22). To clarify these points, further studies are needed.

Conclusion

Treatment with ACEIs and ARBs induces erythropoietin resistance in patients on CAPD. The inhibitory effect of ARBs on erythropoiesis by rHuEPO treatment was smaller than that of ACEIs. When, in CAPD patients, other causes of erythropoietin resistance have been ruled out, physicians should check the interaction of erythropoietin with other drugs, including ACEIs and ARBs. In patients with erythropoietin resistance linked to ACEIs, a change to an ARB should be considered.

References


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Hypertension is one of the main factors contributing to morbidity and mortality in dialysis patients. Peritoneal dialysis (PD) patients have been reported to have lower blood pressure (BP) in the first 6 months or so of treatment. After that, their BP can be the same or higher than that seen in hemodialysis (HD) patients.

We compared BP control between our PD patients and our HD patients. Systolic BP and pulse pressure were better controlled in PD patients; those PD patients required many fewer drugs. The difference was statistically significant. Anuric PD patients had a BP as good as that of the non anuric PD patients.

Because PD is a constant treatment, fluid removal is much easier than in HD. To achieve good BP control, nurses, dieticians, and physicians must all have the same approach: that is, always to be aggressive in volume control as a first measure for achieving an adequate BP. The team approach results in better BP control than that seen in HD.

Key words
Hypertension, hemodialysis, ultrafiltration

Introduction
The ADEMEX (1), revised CANUSA (2), and HEMO (3) studies have shown that increases in solute clearance beyond a certain point do not affect the morbidity and mortality of patients on dialysis. We should, therefore, turn our attention to other factors known to improve survival in the dialysis population.

Cardiovascular disease is the leading cause of death in dialysis patients (4). Urine output, residual renal function (2), ultrafiltration (5,6), and high blood pressure (7) have been recognized as independent predictors of survival in peritoneal dialysis (PD). A relationship has also been established between fluid overload, hypertension, and cardiac abnormalities (8). When patients are first initiated onto PD, a definite improvement in hypertension seems to occur; but, after 2 – 3 years of dialysis (at the same time that patients have lost residual renal function), hypertension and fluid overload become pronounced (9,10). A large survey of PD patients in Italy (11) showed a very high prevalence of hypertension—up to 88%.

In our PD unit, we practice an involved team approach to the treatment of hypertension and fluid overload. Our nursing staff and our dietitian are crucial in treating hypertension and fluid overload so that patients achieve adequate, successful dialysis. Because of the important involvement of the nursing staff and dietician, we decided to look at the success of the PD unit in controlling patients’ blood pressure (BP). We compared BP control in our PD unit with that in our hemodialysis (HD) unit.

Patients and methods
For the study, we evaluated 104 PD patients, comparing them to 104 randomly chosen HD patients. We recorded the following parameters in both groups: systolic and diastolic BP and pulse pressure; the number of patients needing no medication for hypertension; and the number of agents per patient for the treatment of hypertension.

We monitored BP in sitting HD patients before in-centre HD. In PD patients, the monitoring was done in sitting patients at the time of a clinic visit. We measured BP and pulse pressure, recorded the hypertensive drugs used by the patients, and the total daily fluid excretion in anuric and non anuric PD patients.
Results
The age and the number of patients with diabetes or heart disease were approximately the same in both the PD and the HD patients. Systolic blood pressure was much better controlled in the PD patients than in the HD patients ($p < 0.0001$). No significant difference in diastolic blood pressure was observed between the two groups. Pulse pressure was much lower in PD patients than in the HD patients ($p = 0.0132$).

The same pattern could be observed in the requirement for medication to control hypertension (Tables II and III). Approximately 40% of the PD patients required no hypotensive drugs, as compared with just 26% of the HD patients. Blood pressure was better controlled in the PD patients than in the HD patients ($p = 0.0001$; Table I).

Discussion
Because BP has been reported to be higher after 2–4 years on PD, mainly when patients have lost residual renal function (9–10), we were surprised by our results for anuric patients as compared with non anuric patients. Systolic BP and pulse pressure were well controlled in anuric patients even though they had been on PD for a longer period of time (mean PD duration: 49.3 months) than the non anuric patients (mean PD duration: 24.4 months). Unexpectedly, we observed no difference in total ultrafiltration between anuric and non anuric patients: both groups ranged near 1500 mL daily (Table IV). Those results are very good when compared with the results that have been reported in the literature (9,10).

Our approach to fluid overload and hypertension is multifaceted and uses a team approach that places responsibility on all team members (Table V).

The prevalence of hypertension in PD patients is much too high, given the knowledge that cardiovascular disease is the main factor affecting mortality (4). A multicenter analysis of hypertension in the Italian population (11) showed a prevalence of 88% for hypertension. Blood pressure has been reported to be better controlled at the beginning of PD; but, as residual renal function is gradually lost, more and more patients become hypertensive and have to use more medications to maintain BP at an adequate level (9,10). The prevalence of hypertension in our PD population was only 60% as compared with the 88% in the Italian study.

Velasquez et al. (12) showed that BP was better controlled in HD than in PD. In the present study, our team approach to the control of BP in PD yielded better results than those obtained in the HD unit.

Total daily fluid excretion (peritoneal ultrafiltration plus urine output) has been demonstrated to be a

<table>
<thead>
<tr>
<th>TABLE I</th>
<th>Blood pressure control by dialysis type</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PD</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>104</td>
</tr>
<tr>
<td>Patients taking no drugs [n (%)]</td>
<td>42 (40.4)</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>129.64</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>77.31</td>
</tr>
<tr>
<td>Drugs used (mean n)</td>
<td>0.92</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>51.0</td>
</tr>
</tbody>
</table>

PD = peritoneal dialysis; HD = hemodialysis; SBP = systolic blood pressure; DBP = diastolic blood pressure.

<table>
<thead>
<tr>
<th>TABLE II</th>
<th>Patients taking blood-pressure medications</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PD</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>62</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>134.9</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>79.50</td>
</tr>
<tr>
<td>Drugs used (mean n)</td>
<td>0.92</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>55.4</td>
</tr>
</tbody>
</table>

PD = peritoneal dialysis; HD = hemodialysis; SBP = systolic blood pressure; DBP = diastolic blood pressure.

<table>
<thead>
<tr>
<th>TABLE III</th>
<th>Patients using 3 or more blood-pressure medications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PD</td>
</tr>
<tr>
<td>Patients [n (%)]</td>
<td>6 (5.8)</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>129.67</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>81.00</td>
</tr>
<tr>
<td>Pulse pressure (mmHg)</td>
<td>48.67</td>
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</table>

PD = peritoneal dialysis; HD = hemodialysis; SBP = systolic blood pressure; DBP = diastolic blood pressure.

<table>
<thead>
<tr>
<th>TABLE IV</th>
<th>Comparison of anuric and non anuric peritoneal dialysis patients</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Anuric</td>
</tr>
<tr>
<td>Patients (n)</td>
<td>27</td>
</tr>
<tr>
<td>Patients taking no drugs [n (%)]</td>
<td>14 (51.9)</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>119.65</td>
</tr>
<tr>
<td>Mean DBP (mmHg)</td>
<td>78</td>
</tr>
<tr>
<td>Drugs used (mean n)</td>
<td>0.74</td>
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<tr>
<td>Pulse pressure (mmHg)</td>
<td>41.5</td>
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<tr>
<td>Mean daily ultrafiltration (mL)</td>
<td>1554</td>
</tr>
</tbody>
</table>

SBP = systolic blood pressure; DBP = diastolic blood pressure.
significant predictor of survival in PD patients (5). More recently, Brown et al. (6) reported that, in anuric patients, baseline ultrafiltration and not solute clearance is associated with patient survival. Patients achieving less than 750 mL ultrafiltration daily had a shorter survival than those who achieved more than 750 mL daily. By using automated PD plus icodextrin and, frequently, an extra peritoneal exchange around 1800 h, we were able to obtain, in our 27 anuric patients, a mean ultrafiltration of about 1500 mL daily. The age and incidence of diabetes mellitus and heart disease were not much different between our anuric and non anuric PD patients (Table VI).

Conclusions

In our cohort of PD patients, we were able to obtain much better control of systolic BP and pulse pressure than were achieved in our HD patients. Patients on PD used fewer hypotensive drugs to obtain better BP control. We were able to obtain very good BP control in our anuric patients even though they had been on PD for a long time. Good BP control in longstanding PD patients, as reported here, contradicts past reports in the PD literature. We also found, in our anuric patients, very good ultrafiltration that contributed significantly to BP control in those patients. The team approach (nurses, dietician, and physicians) is necessary to the successful control of BP and fluid overload.

References


7 Foley R, Parfrey PS, Harnett JD, Kent GM, Murray

### Table V

The team approach to blood pressure control and fluid overload in the peritoneal dialysis (PD) unit

<table>
<thead>
<tr>
<th></th>
<th>Anuric</th>
<th>Non anuric</th>
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<tbody>
<tr>
<td>Patients (n)</td>
<td>27</td>
<td>77</td>
</tr>
<tr>
<td>Age (years)</td>
<td>57.7</td>
<td>62.2</td>
</tr>
<tr>
<td>Heart disease [n (%)]</td>
<td>6 (22)</td>
<td>21 (27)</td>
</tr>
<tr>
<td>Diabetes mellitus [n (%)]</td>
<td>8 (30)</td>
<td>24 (31)</td>
</tr>
<tr>
<td>Time on dialysis (months)</td>
<td>49.3</td>
<td>24.4</td>
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</table>

### Table VI

Demographic data for anuric and non anuric peritoneal dialysis patients

<table>
<thead>
<tr>
<th></th>
<th>Anuric</th>
<th>Non anuric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>27</td>
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</tr>
<tr>
<td>Age (years)</td>
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<td>8 (30)</td>
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</tr>
<tr>
<td>Time on dialysis (months)</td>
<td>49.3</td>
<td>24.4</td>
</tr>
</tbody>
</table>


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A relative decline in the use of peritoneal dialysis (PD) as a treatment modality has led to much speculation regarding the reasons for the drop. One main concern focuses on the lack of education and training in dialysis options for nephrologists, nurses, and patients. To change the trend and improve clinical outcomes for dialysis patients, the industry is taking a leading role in educating health care professionals and patients about dialysis options. Fresenius Medical Care offers two complementary educational initiatives for physicians, nurses, and patients: PDServe and Kidney Options.

Key words
Education, pre–end-stage renal disease, chronic kidney disease

Introduction
Current utilization trends indicate a relative decline in the use of peritoneal dialysis (PD) as a treatment modality in recent years (1). Many theories have been postulated to explain the decline (2), including

• financial disincentives;
• proliferation of hemodialysis (HD) facilities, making it more convenient for patients who might have otherwise chosen a home therapy to access in-center care; and
• physician bias for one modality over another.

In addition, many health professionals feel that the decline is related to a lack of education and training in dialysis options for nephrologists, nurses, and patients.

Discussion
Educational deficits
In a recent survey, Mehrotra et al. (3) analyzed training in dialysis for nephrology fellows in the United States and Canada. The authors found that, in the U.S. training programs, 29% of fellows had fewer than 5 PD patients, and 14% spent less than 5% of their time in training for managing patients undergoing PD. Those findings raise the concern that many U.S. training programs either do not expose their fellows to an appropriate number of PD patients or that the programs do not spend sufficient time to be sure that fellows are prepared to adequately care for PD patients.

Similarly, nurse training in PD is either limited or nonexistent during actual nurse training or in dialysis facility training programs. In our (anecdotal) experience in interviewing PD nurses around the United States, the job responsibilities of PD nurses are generally shared between the in-center HD program and the PD program. The nurses are often asked to establish a PD program after reviewing a PD training manual, with very little other education or experience.

Not only do nurses and physicians often lack training in PD, many U.S. PD programs are so small (with fewer than 10 patients) that their experience with patient and program management is limited.

Educational deficits also extend to chronic kidney disease (CKD) patients themselves. Many patients are referred late to nephrologists from the primary-care physician. Those patients often end up in hospital being started on emergent HD. The patients therefore do not receive pre–end-stage renal disease (pre-ESRD) education and are not informed about their renal replacement treatment options.

Role for industry in education
Taken together, all of the preceding factors have created a “vicious circle” leading to the decline of PD (4). To reverse the trend and to improve clinical outcomes, industry is taking a leading role in educating physicians, nurses, and patients by providing seminars, workshops, and training tools.

Historically, industry has participated in the provision of PD training for nurses, both new and experienced, through one-on-one clinic visits, regional training seminars, and provision of training materials.
for staff and patients. More recently, such training has focused on universal best practices.

Dialysis facility personnel have limited knowledge, experience, resources, and time to engage in complex educational processes, but industry can fulfill that need as a value-added service to its customers. Fresenius Medical Care offers two key, complementary initiatives to meet the educational demands of physicians, nurses, and patients: PDServe and Kidney Options.

**PDServe from Fresenius Medical Care**

PDServe is a global service designed to satisfy the educational needs of renal professionals so that they can improve clinical outcomes in their patients. The knowledge acquired through better education should improve outcomes, increase patient retention, and increase experience—resulting in programs of excellence.

PDServe has four components:

- PDServe Information Centers
- The *PDServe Connection* newsletter
- Seminars and workshops (with associated training support tools)
- The PDServe.com Web site

PDServe Information Centers are toll-free “hotlines” that are available in several countries around the world. For health care professionals caring for PD patients, the centers provide direct consultation with nurses and nephrologists who have expertise in PD. Users can obtain clinical and operative support on all aspects of PD, including adequacy, modality selection, treatment of complications, and general troubleshooting, among other issues.

The *PDServe Connection* newsletter is published quarterly, with global distribution of more than 15,000 copies in 5 languages. *PDServe Connection* provides a taste of recent literature by publishing article reviews, editorials, practical clinical topics, and a “tips and timesavers” section called GEMS. New product information is also included, as is an international calendar of events.

Educational seminars and resources on PD are available as part of the Advanced Renal Education Program, which includes didactic courses for nurses and physicians. The courses contain the essentials for a proper understanding of renal medicine. Whenever possible, they are based on best practices, expert opinions, and evidence. The modules that make up the courses are developed by an international team of experts. Classes are offered as formal lectures and specialized workshops, allowing for hands-on experience. Class size is limited (often one-on-one in the facility for nursing personnel) so as to provide an intimate environment in which participants can feel comfortable to interact with speakers and ask questions.

Nursing courses are offered at a basic level for the new PD nurse. For nurses with more experience, classes on contemporary issues such as exit-site evaluation, care of pediatric PD patients, and evaluation of ultrafiltration failure are offered. Continuing education units are provided through the California Board of Nursing and are recognized by the American Nephrology Nurses’ Association for credit towards certification or renewal of the certified nephrology nurse credential.

Ancillary education courses are also available for the dialysis facility administrator or clinic manager. The courses focus on overall program management and include a section that introduces the administrator to PD and to the requirements for a successful program. Because the hospital nursing staff partners with the dialysis facility staff to care for PD patients, courses are also available on PD basics for the hospital setting, emphasizing hospital-specific procedures.

These numerous offerings make educational seminars available to most of the professionals responsible for the care and management of PD patients.

Training tools for PD staff and patients are necessary to supplement educational initiatives. In addition to the numerous classes and seminars described above, Fresenius Medical Care offers more than 55 different staff and patient training tools, including treatment algorithms, continuous quality improvement data collection tools, sample policy and procedure manuals, and reference tools in the form of posters, brochures, flip charts, videos, pocket guides, and more.

The PDServe.com Web site provides a vast array of PD information all in one location on the World Wide Web. On the PDServe.com site, users can find everything they need to know about PD or links to sites that contain the necessary information. Users can find whatever PD information they are looking for more easily, without spending hours searching the Web.
The All About PD section contains the most relevant PD information. Back issues of PDServe Connection can be downloaded there. Contact information for the PDServe Information Centers in various countries can also be found. In some countries—including the United States, Germany, the United Kingdom, Portugal, Turkey, Italy, and the Czech Republic—the site content has been translated or modified to meet specific needs of local customers. Approximately 15 other countries have committed to the same task for 2004.

The PDServe.com site is relatively new. It continues to be developed and modified to enhance its functionality and to make surfing it easier for the user. New content and additional links will continue to be added into the future. In the past year, the site received close to 4 million hits.

Kidney Options from Fresenius Medical Care
The mission of the Kidney Options program is to educate the pre-ESRD patient population in the benefits of early referral to nephrology services, and to partner with physicians and professional associations to encourage early referral of pre-ESRD patients for treatment options education. Early nephrology assistance and intervention can help to slow the progression of chronic renal insufficiency and to manage or reduce comorbid conditions.

The primary function of the Kidney Options program is to identify the target patient population, including those with a serum creatinine 3 mg/dL or greater, those with an anticipated dialysis start date within 1 year, and new dialysis patients who lack sufficient knowledge of available treatment options. Once patients are identified, education can be provided about renal replacement therapy options, including transplantation, PD, and HD.

The Kidney Options program comprises a Web site (www.kidneyoptions.com) and a number of promotional and training tools. The Web site was developed for patients, but has been visited and used by health care personnel as well. The site provides a simple overview of CKD and explains the renal replacement treatment options available to patients. In addition, users can find lifestyle and diet tips (including recipes of the month), a glossary of medical terms, a resource library, and a schedule of Kidney Options seminars. The Kidney Options Web site has received a Study Web Academic Excellence Award from Lightspan for its content, organization, and user-friendly functionality.

Kidney Options patient seminars are organized and hosted by a group of health care professionals and dialysis and transplant patients within a local community. The seminars provide information on treatment options, diet and nutrition, and living with dialysis from the patient perspective. They also provide support to the patient approaching CKD. Schedules for the seminars are advertised locally with patient flyers and posters that are displayed in dialysis clinics and doctors’ offices and on the Kidney Options Web site. To complement the seminars, Fresenius Medical Care offers a variety of patient education materials that patients can obtain by attending a seminar or by registering at the Kidney Options Web site. Additional tools are used by health care professionals to train the patients who attend the seminars or dialysis facilities.

A component of the Kidney Options program is dedicated to education and support of health care professionals by providing them with training tools for this cohort of patients. A “Grand Rounds” PowerPoint presentation on “Timely Referral for Treatment of Chronic Kidney Disease” can be presented to internal medicine and general practitioners. For professionals who are interested in starting their own Kidney Options program, a staff manual has been developed. That manual provides guidance on how to start the program and contains an implementation guide and checklist, seminar content guidelines, and a patient tracking program to monitor success.

To date, 13,000 patients have been educated with the Kidney Options program. Of those, more than 5,000 have initiated renal replacement therapy, with more than 2,000 (40%) having selected PD as their modality of choice.

Conclusion
In the future, additional patient and professional educational tools will be developed—including programs dedicated to HD education. Our industry has always assumed an important role in the process of educating dialysis professionals. As it continues to focus on universal best practices and improvements in the quality of care delivered to patients, it can meet the demand and grow centers of excellence that offer patients a choice of all renal replacement therapy options.
References

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