New Modality of Dialysis Therapy: Peritoneal Dialysis First and Transition to Home Hemodialysis

Hiromichi Suzuki, Hitosi Hoshi, Tsutomu Inoue, Tomohiro Kikuta, Masahiro Tsuda, Tsuneo Takenaka

From: Department of Nephrology, Saitama Medical University, Saitama, Japan.

Recent studies have clearly demonstrated that starting treatment with peritoneal dialysis (PD) is superior to starting with conventional hemodialysis (HD) because PD preserves residual renal function for a longer period. Similarly, because of the frequency of treatments, home HD (HHD) is also superior to conventional HD. The accumulated evidence suggests that a combination of PD and HHD might be a new and effective method for patients receiving dialysis therapy.

We analyzed 10 patients who, over the past 10 years, were started on PD and who were then transferred to HHD. Electronic databases were used to examine changes in their health status.

Mean age was 58 ± 8 years in these 2 female and 8 male patients. Mean duration of PD was 6.9 ± 2.4 years. The average total duration of dialysis therapy was 9.7 ± 1.9 years. The main reason for the transition from PD to HHD was loss of residual renal function. To the time of writing, no serious complications (including cardiovascular events and calcium homeostasis) had occurred. All patients continue to receive dialysis therapy and have been able to lead a nearly normal social life.

Major laboratory findings include serum albumin 4.2 ± 0.2 g/dL, hemoglobin 10.2 ± 1.4 g/dL (half the patients were not using erythropoiesis-stimulating agents), serum creatinine 7.5 ± 2.5 mg/dL, blood urea nitrogen 36 ± 17 mg/dL, serum phosphate 4.3 mg/dL. In two thirds of the patients, blood pressure was controlled without antihypertensive agents. No patient had left ventricular hypertrophy.

In this analysis, we found that relatively young subjects preferred PD first, with later transfer to HHD:

that PD is superior as an introduction to dialysis therapy; that patients starting with PD prefer self medical treatment; and that all patients were free from the various complications that are encountered during long-term dialysis therapy. We suggest that patients who need dialysis therapy consider this new dialysis approach of “PD first and transfer to HHD.”

Key words
Residual renal function, albumin, phosphate, blood pressure

Introduction
Selection of a dialysis modality is important for patients who start renal replacement therapy. However, more than 90% of patients begin in-center hemodialysis (HD) without receiving sufficient information. At least three modalities of renal replacement therapy are available to patients: transplantation, continuous ambulatory peritoneal dialysis (PD), and HD. These modalities differ clinically, and all offer advantages and disadvantages for the individual patient.

At present, of these three modalities, transplantation would be the ideal. However, in Japan, several factors such as a shortage of donors, the advanced age of patients, and an increase in patients with diabetes do not make transplantation a readily available option for most patients (1). Moreover, prospective randomized studies comparing outcomes between HD and PD are relatively rare in practice, because it is difficult to assign patients randomly to particular types of dialysis therapy (2,3).

Recently, residual renal function (RRF) has been recognized as an important marker of outcome in patients on both PD and HD (4–6). Residual renal function is an especially powerful indicator for better removal of middle- and larger-molecular-weight toxins and organic acids that accumulate...
during dialysis, supporting the use of PD as initial dialysis therapy. Then, as RRF decreases, a switch from PD to HD can be made.

There is concern that, in the absence of RRF, only a small proportion of PD patients are capable of clearing small molecules to acceptable levels without the use of automated PD (7). Combination therapy with HD and PD allows for the partial separation of the two essential components of effective renal replacement therapy—that is, fluid removal and solute clearance (8–13). Despite the use of PD and HD in combination, the peritoneal membrane gradually loses its ability to maintain adequate dialysis, and many patients switch to HD alone (14).

We have used the sequence of PD first, PD and HD in combination, and home HD (HHD) in 10 patients at the Kidney Disease Center, Saitama Medical University Hospital. The serial data obtained from these patients are expected to provide some clues about the selection and alternation of dialysis modalities.

Methods
Our single-center, retrospective cohort study included 10 patients (2 women, 8 men) who started PD as initial dialysis treatment during 1995–2010. All patients were regularly monitored at our center and had started their PD treatment at least 6 months before enrollment. We collected baseline data on each patient’s demographic characteristics, laboratory values, PD prescription, and duration on dialysis before enrollment.

Informed consent was obtained, and the study was performed in accordance with the principles of the World Medical Association Declaration of Helsinki. All work was conducted at the Kidney Disease Center in Saitama Medical University Hospital, Saitama, Japan.

Regular treatment modality
More than 60% of the patients were treated with a standard PD regimen that consisted of 4 daily exchanges of 1.5 L or 2 L dialysate; the other patients used 2–3 daily exchanges. The strength of the bags was individualized to maintain the desired weight. Dwell times were also individualized to maximize overall ultrafiltration volumes. Mean daily dietary intake was recorded from individual 24-hour food records during a 3-day period at the start of the study. All subjects consumed between 0.8 g and 1.0 g protein per kilogram body weight daily, and their daily energy intake exceeded 25 kcal per kilogram body weight. Salt intake was restricted to less than 9 g daily throughout the study.

Combination of PD and HD
Once weekly, a 4-hour HD session was added after 6 consecutive days of PD. The morning of the HD session, the PD dialysate was drained. With the abdomen empty, HD was performed using bicarbonate dialysate and a dialyzer with a polysulfone membrane.

Patient monitoring
Patients were followed every month during the study period. At each clinic visit, serum creatinine, electrolyte concentrations, complete blood count, and other serum chemistries (uric acid, glucose, liver enzymes) were measured. Indices of the adequacy of dialysis, including weekly creatinine clearance, were calculated using the PD Adequest computer program (version 2.0 for Windows: Baxter Healthcare, Tokyo, Japan). Chest radiographs were obtained regularly, and cardiothoracic index was calculated according to established methods.

During the study, target home blood pressure (BP) was 130/80 mmHg or lower, and home BP measurements were encouraged. The selection of antihypertensive agents depended on physician preference. Subjects were treated with recombinant human erythropoietin as necessary, and their hemoglobin levels were maintained between 10 g/dL and 11 g/dL. Subjects were given oral iron supplementation if they were diagnosed with iron deficiency.

Subjects with parathyroid hormone levels greater than 200 pg/mL were treated with 1,25(OH)2D3 and CaCO3 supplements. Patients with levels lower than 70 pg/mL were treated with CaCO3 to reduce the degree of hyperphosphatemia. Doses were adjusted based on serum levels of calcium and phosphate. Lipid-lowering drugs, primarily statin derivatives, were administered if serum cholesterol levels exceeded 240 mg/dL.

At home, HHD was administered using a Nikkiso DBB-27 (Nikkiso, Tokyo, Japan) with water treatment system MH-500CX (Japan Water System, Tokyo, Japan). Typical blood flows were 200 mL/min. Sessions varied in length from 3 to 5 hours and were performed an average of 6 times weekly. Each patient received training on the use of the home dialysis machine for at least 3 months.
Statistical analysis
Results are expressed as mean ± standard error of the mean. Statistical analyses used the Student t-test for unpaired samples and the Mann–Whitney test for comparison of means. Analyses of the effects of PD, PD and HD in combination, and HHD on longitudinal changes in serum albumin, hemoglobin, creatinine, calcium, phosphate, and intact parathyroid hormone were performed by repeated-measures analysis of covariance, followed by a Neuman–Keuls test for evaluation of significance. Statistical significance was set at $p < 0.05$. All calculations were performed using the StatView statistical software package (version 5.0: SAS Institute, Cary, NC, U.S.A.).

Results
Baseline characteristics
Table I shows the baseline demographics for the 10 patients in the study cohort. Mean age at onset of end-stage renal disease (ESRD) was 58 ± 8 years (range: 35 – 61 years). Before receiving combined therapy, the patients had been in ESRD for 3.9 ± 1.8 years. Mean age at the start of combined therapy was 62 ± 6 years. The underlying renal diseases in this group were chronic glomerulonephritis ($n = 4$), diabetes mellitus ($n = 2$), nephrosclerosis ($n = 2$), and others ($n = 2$).

Changes in urine volume
Daily urine volume—as a marker of RRF (15)—gradually declined from the start of PD to the start of combined therapy with PD and HD (to 300 ± 520 mL from 1030 ± 430 mL, $p < 0.05$). After the start of combination therapy, urine volume further declined and became less than 100 mL daily just before the start of HHD (Figure 1).

Changes in drain volume
At the start of combination therapy, the daily drain volume increased significantly to 960 ± 320 mL from 100 ± 60 mL ($p < 0.01$), a level that was maintained until the start of HHD (Figure 2).

Follow-up BP data
Systolic BP and diastolic BP both declined gradually throughout the study. After the introduction of HHD, they declined to less than 140 mmHg and 80 mmHg respectively ($p < 0.05$, data not shown).

<table>
<thead>
<tr>
<th>Table I</th>
<th>Basal characteristics of the patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pt</td>
<td>Age</td>
</tr>
<tr>
<td>ID</td>
<td>Sex</td>
</tr>
<tr>
<td>IG</td>
<td>Male</td>
</tr>
<tr>
<td>IT</td>
<td>Female</td>
</tr>
<tr>
<td>SY</td>
<td>Male</td>
</tr>
<tr>
<td>KT</td>
<td>Male</td>
</tr>
<tr>
<td>SK</td>
<td>Male</td>
</tr>
<tr>
<td>YT</td>
<td>Male</td>
</tr>
<tr>
<td>YM</td>
<td>Male</td>
</tr>
<tr>
<td>YM</td>
<td>Male</td>
</tr>
<tr>
<td>YN</td>
<td>Female</td>
</tr>
<tr>
<td>TN</td>
<td>Male</td>
</tr>
</tbody>
</table>

Pt = patient; IgA = immunoglobulin A.

Figure 1 Changes in urine volume. Urine volume gradually declined from the start of peritoneal dialysis (PD) to the start of combination therapy with PD and hemodialysis (HD), with significance (* $p < 0.05$, ** $p < 0.01$). After the start of combination therapy, urine volume continued to decline and became less than 100 mL daily just before the start of home HD (HHD).

Figure 2 Changes in drain volume. The daily peritoneal dialysis (PD) drain volume increased significantly from the start of combination therapy (*** $p < 0.01$) and maintained that increase until the start of home hemodialysis (HHD).
Changes in serum creatinine
After the start of PD therapy, serum creatinine gradually increased until the start of combination therapy. After the introduction of combination therapy, serum creatinine declined, and 1 year after HHD start, it continued to decline \([p < 0.05, \text{Figure 3(A)}]\).

Changes in serum albumin
Serum albumin declined after the introduction of PD, but after the start of combination therapy, it gradually increased. At 1 year after the start of HHD, serum albumin had increased significantly \([\text{start of PD: } 3.8 \pm 0.8 \text{ mg/dL; 1 year after HHD start: } 4.0 \pm 0.2 \text{ mg/dL; } p < 0.05; \text{Figure 3(B)}]\).

Increase in hemoglobin despite reduction in use of erythropoiesis-stimulating agents
Hemoglobin levels increased significantly from the start of PD therapy to the start of combination therapy \((\text{to } 10.0 \pm 1.6 \text{ g/dL at 1 year from } 8.5 \pm 1.5 \text{ g/dL})\) and continued to increase till the start of HHD. Thereafter, hemoglobin declined until HHD was started \([\text{Figure 3(C)}]\). Additionally, the need for erythropoiesis-stimulating agents declined significantly after the introduction of HHD \(\text{(data not shown)}\).

Changes in bone metabolism
Serum calcium gradually increased throughout the study, reaching \(9.1 \pm 1.0 \text{ mg/dL at 1 year after HHD start [Figure 3(D)}]\). Conversely, serum phosphate declined gradually to 1 year after HHD start, reaching \(4.3 \pm 1.5 \text{ mg/dL [Figure 3(E)]}\). Intact parathyroid hormone did not change significantly at any point during the study \(\text{(data not shown)}\).

Discussion
Our observations suggest that the sequence of starting with PD, then combining PD and HD, and finally starting HHD is a useful and successful way to treat a subset of patients with ESRD. This approach—starting PD in patients who choose that modality, adding HD if indicated, and eventually switching to HHD when combination therapy is no longer indicated—fits well with the concept of case integration. Previously, Van Biesen \textit{et al.} \(\text{(16)}\) showed that patients who start with PD and who are then transferred to HD in an integrated approach have better outcomes than do patients treated with HD alone. However, the literature on this approach is scant.

According to our data, mild undertreatment by PD can be salvaged by once-weekly HD, independent of when combination therapy is initiated \(\text{(10)}\). The long-term effects of combination therapy as studied at our hospital show that drain volume and weekly creatinine clearance increase significantly by year 1 and remained elevated over the subsequent 2 years. That finding clearly supports the hypothesis of Kawanishi and McIntyre \(\text{(12)}\) that combination therapy with HD and PD improves the clinical status of patients in whom adequate solute and fluid removal is difficult to achieve with PD alone. Moreover, despite a progressive loss of residual renal function observed as a result of an early start of combination therapy, weekly creatinine clearance in these patients is relatively well maintained.

Malnutrition and inflammation are well known to affect survival in HD patients. Many investigators have shown that serum albumin is depressed in patients on maintenance HD who show other signs of malnutrition \(\text{(17–19)}\). Moreover, serum albumin usually improves as nutrition is restored \(\text{(20)}\). Lower values for serum albumin that result from PD and HD may be the result of different mechanisms. For example, in addition to inadequate dialysis in HD patients, dietary restriction of vegetables and fruits in addition to salt might play a role; in PD patients, reduced protein intake might be the cause. In our study of the long-term effects of combination therapy, elevations in both weekly creatinine clearance and serum albumin might have been a result of the combination therapy. Subjects that received PD and HD in combination did not have to restrict their intake of vegetables and fruits and were adequately dialyzed.

In contrast to Rao \textit{et al.} \(\text{(21)}\), we observed no changes in hemoglobin with a reduction in the need for erythropoiesis-stimulating agents. In the study from London, Ontario, the changes were of only borderline significance, but in our study, hemoglobin levels had already increased before the start of HHD and the need for erythropoiesis-stimulating agents declined by 15% during 6 months of intensified HD.

Vascular calcification is a major contributor to the increased cardiovascular risk in dialysis patients. High calcium, phosphate, and Ca×P product are all well recognized to be independent risk factors for cardiovascular events in this patient population \(\text{(22–24)}\). In PD and HD patients alike, reduction of phosphate is not easily attained. However, from our observations, it is clear that phosphate removal is
adequately performed during HHD. Nevertheless, dietary protein and phosphorus intake are important considerations that cannot be neglected.

Most importantly, patients themselves should be intimately involved in the decision-making throughout their treatment period (25). Our goal as nephrologists is to prolong life while maintaining quality of that life. Patient preference is an important consideration in achieving that goal. As home treatments, PD and HHD spare the patient repeated visits to the dialysis unit.

All our study subjects acknowledged that their quality of life had improved after the start of combination therapy. Unfortunately, we did not evaluate their quality of life before and after they began the study. Their subjective assessment of improved quality of life induced increases in food intake and may have contributed to the observed increase in serum albumin.

Our study is limited by its observational nature. We are unable to determine if the patients had absolute contraindications to home dialysis that were otherwise unknown. We also did not study the perceptions and availability of caregivers. Furthermore, the study was performed in a center that favors a “home dialysis first” approach. Our home dialysis prevalence statistics—PD in 25%, HHD in 6%—are relatively higher than current Japanese statistics overall (1).

**Figure 3** (A) Changes in serum creatinine. After the start of peritoneal dialysis (PD) therapy, serum creatinine gradually increased until the start of combination therapy. After the introduction of combination therapy, serum creatinine declined, and 1 year after home hemodialysis (HHD), it declined significantly ($p < 0.05$). (B) Changes in serum albumin. Serum albumin declined after introduction of PD, but after the start of combination therapy it gradually increased. One year after the start of HHD, serum albumin increased significantly. (C) Changes in hemoglobin. Hemoglobin levels increased significantly with the start of PD therapy to the start of combination therapy. (D,E) Changes in bone metabolism. Serum calcium gradually increased throughout the study. Conversely, the serum phosphate declined gradually after the start of HHD.
Conclusions
Our observations suggest that PD first, followed by combination therapy with PD and HD, and then finally HHD is a useful and successful sequence for treating a subset of patients with ESRD. Our results will help to illuminate patient choice of a specific home dialysis modality and reinforce the complementary nature of the PD, HD, and HHD modalities.

Disclosures
The authors have no financial conflicts of interest to declare.

References

Corresponding author:
Hiromichi Suzuki, MD PhD, Department of Nephrology, Saitama Medical University, 38 Moroyama-machi, Iruma-gun, Saitama 350–0495 Japan.
E-mail: iromichi@saitama-med.ac.jp