Impact of Combination Therapy with Peritoneal Dialysis and Hemodialysis on Peritoneal Function

Misaki Moriishi, Hideki Kawanishi, Shinishiro Tsuchiya

Peritoneal dialysis (PD) is a continuous, slow dialysis method advantageous for retaining residual renal function; however, after renal function is lost, increasing the PD dose is difficult, resulting in insufficient dialysis. The addition of hemodialysis (HD) to PD [combination therapy with PD and HD (PD+HD)] increases the ultrafiltration volume and optimizes the dialysis dose. Based on this situation, we have applied concomitant HD after loss of residual renal function in PD patients. In the present study, we investigated peritoneal function in patients who underwent PD+HD therapy.

The subjects were 76 patients in whom PD+HD therapy continued for 6 months or longer. In PD+HD therapy, patients underwent PD 6 days each week and a 4-hour HD session once each week. The patients were divided into four groups based on their dialysate-to-plasma ratio of creatinine (D/P Cr) in a peritoneal equilibration test (PET) at the initiation of PD+HD therapy: high [H (n = 5)], high-average [HA (n = 29)], low-average [LA (n = 26)], and low [L (n = 16)].

Before and after initiation of PD+HD therapy, we measured PET D/P Cr values and effluent levels of fibrin degradation products (eFDPs) and cancer antigen 125 (eCA125) in the 4-hour PET effluent. In addition, we evaluated the ratio of overnight effluent to serum β₂-microglobulin (overnight D/P β₂MG) every year.

In the H group, D/P Cr remained high after initiation of PD+HD therapy, but it declined significantly in the HA group and tended to decline in the LA and L groups. Overnight D/P β₂MG remained high in the H group after PD+HD therapy, but significantly declined in the HA group and remained unchanged in the LA and L groups. After PD+HD therapy initiation in the H group, eFDPs declined markedly, although that change was not significant. No decrease was noted in any other group. Peritoneal dialysis was discontinued in 33 of the 76 patients (43.4%) who underwent PD+HD therapy: in 5 of the 5 patients in the H group (100%), in 16 of 29 in the HA group (55.2%), in 7 of 26 in the LA group (26.9%), and in 5 of 16 in the L group (31.3%). On long-term follow-up, the PET D/P Cr tended to decrease in the H and LA groups; it did not change in the LA and L groups. No significant changes were noted in any group for overnight D/P β₂MG, eFDPs, or eCA125.

We suggest that concomitant HD facilitates the continuation of PD treatment and the retention of peritoneal function in patients with uremic symptoms and excess body fluid associated with a loss of residual renal function. However, improvement in peritoneal function cannot be expected for patients in whom peritoneal function has already deteriorated. In those patients, a change of treatment method should be considered.

Key words
Combination therapy with peritoneal dialysis and hemodialysis, D/P Cr on PET, eFDP

Introduction
The advantages of peritoneal dialysis (PD) are retention of residual renal function (RRF) and continuous correction of acid–base equilibrium (1). However, after RRF is lost, increases in the PD dose are limited, resulting in insufficient solute clearance and possibly inducing a uremic state. For such cases, the addition of hemodialysis (HD) to PD may increase the dialysis dose and ultrafiltration volume, optimizing dialysis.

Agarwal et al. reported that the addition of HD to PD improved an insufficient dialysis dose and ultrafiltration failure (2). Our group also reported that switching from PD 7 days per week to PD 5 – 6 days per week combined with HD once weekly increased

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the dialysis dose and improved nutrition status (3). Those studies confirmed that a combination of PD and HD is a simple, reliable method for increasing the dialysis dose after loss of RRF.

In combination therapy with PD+HD, HD is performed 1–2 times per week, which means there is a period during which no dialysis solution is retained in the abdominal cavity. In addition, the ultrafiltration volume is controlled by HD, which reduces the need to use high-glucose dialysis solution, lowering the glucose load. These advantages have been suggested to favorably influence peritoneal function. We investigated the influence of PD+HD therapy on peritoneal function.

Patients and methods
The study subjects were 76 patients who started PD+HD therapy between January 1, 1998, and December 31, 2009, and who continued the therapy for 6 months or longer. Therapy with PD+HD was initiated with PD 6 days per week and a 4-hour HD session once weekly. The frequency of HD was increased to 2 times per week as needed. Based on the dialysate-to-plasma ratio of creatinine (D/P Cr) from a peritoneal equilibration test (PET) performed at the initiation of PD+HD therapy, the patients were divided into four groups: high [H (n = 5)], high-average [HA (n = 29)], low-average [LA (n = 26)], and low [L (n = 16)].

Before and after PD+HD therapy initiation, we measured the PET D/P Cr and levels of fibrin degradation products (eFDPs) and cancer antigen 125 (eCA125) in effluent of the 4-hour PET. In addition, we evaluated the ratio of overnight effluent to serum β2-microglobulin (overnight D/P =2MG) every year.

Results
Table I shows patient data at the initiation of PD+HD therapy. The durations of PD therapy in the transport groups before PD+HD initiation were 44.4 ± 18.7 months (H), 47.1 ± 45.7 months (HA), 50 ± 34.3 months (LA), and 52.6 ± 30.2 months (L). The duration was significantly shorter in the groups with higher peritoneal permeability. Overnight D/P β2MG was 0.3 ± 0.1, 0.28 ± 0.13, 0.18 ± 0.05, and 0.11 ± 0.05 in the respective groups, being significantly higher in the groups with higher peritoneal permeability. Measured eFDPs were higher in the groups showing marked peritoneal permeability, but eCA125 was lower in the L group than in the other groups.

Figure 1.1 shows the course of PET D/P Cr after initiation of PD+HD therapy. Values of D/P Cr remained at a high level in the H group, but declined significantly in the HA group and tended to decline in the LA and L groups. Overnight D/P β2MG remained high in the H group, but declined significantly in the HA group and remained unchanged in the LA and L groups. Values of eFDP decreased markedly after initiation of PD+HD therapy in the H group (Figure 1.2), although that change was nonsignificant; no change was noted in any other group. Values of eCA125 did not change after initiation of PD+HD therapy.

Peritoneal dialysis was discontinued in 33 of the 76 patients (43.4%) who started PD+HD therapy: in 5 of the 5 patients in the H group (100%), in 16 of 29 in the HA group (55.2%), in 7 of 26 in the LA group (26.9%), and in 5 of 16 in the L group (31.3%). The durations of PD+HD therapy in those groups were 33.4 ± 18.7 months, 46.8 ± 31.4 months, 50.3 ± 26.7 months, and 32.8 ± 24.9 months respectively. The PD discontinuation rate was greater in the groups with higher peritoneal permeability, and the duration of PD+HD therapy was significantly shorter in those groups. The most frequent reason for discontinuation of PD+HD therapy was reduction in peritoneal function in the H and HA groups, and peritonitis and catheter infection in the LA and L groups. The PET D/P Cr, the overnight D/P β2MG, and eFDPs tended to decline in the H and LA groups, but did not change in the LA and L groups. On long-term follow-up, no significant changes in eCA125 were noted in any group.

Discussion
In PD patients, RRF is an important prognostic factor (1). However, RRF is lost after several years, solute clearances become insufficient, and excess body fluid accumulates in such patients. The ADEMEX and Hong Kong studies (4,5) showed that increased clearances of low molecular weight solutes did not improve prognosis. Increases in the volume of dialysis solution and frequent use of hypertonic solution did not improve survival; rather, these techniques accelerated impairment of peritoneal function and increased the incidence of encapsulating peritoneal sclerosis (EPS). Thus, since 1996, we have chosen to apply PD+HD therapy in all PD patients with RRF loss, adding once-weekly HD to PD (6).

In the present study, we investigated whether PD+HD therapy improved peritoneal function.
the initiation of PD+HD therapy, PET D/P Cr significantly declined in the HA group and tended to decline in the LA and L groups. It remained high in the H group, however. These findings suggest that PD can be extended with PD+HD therapy. However, peritoneal function was not improved in the group that had a high PET D/P Cr at PD+HD initiation, suggesting that continuation of PD is difficult in these patients and that they should be switched to other treatments.

Therapy with PD+HD is applied in PD patients who have lost RRF and in those experiencing overhydration. Agarwal et al. observed an improvement of clinical

### TABLE 1  Patient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High</th>
<th>High-average</th>
<th>Low-average</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients [n (%)]</td>
<td>5 (6.5)</td>
<td>29 (35.2)</td>
<td>26 (34.2)</td>
<td>16 (21.1)</td>
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<tr>
<td>Age (years)</td>
<td>69.5±9.9</td>
<td>60.3±9.4</td>
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<td>Duration of PD (months)</td>
<td>44.4±18.7a</td>
<td>47.1±45.7a</td>
<td>50±34.3</td>
<td>52.6±30.2</td>
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<td>Reasons for PD+HD (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uremia</td>
<td>4</td>
<td>22</td>
<td>23</td>
<td>16</td>
</tr>
<tr>
<td>Hypervolemia</td>
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<td>7</td>
<td>3</td>
<td>3</td>
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<tr>
<td>Markers at start of PD+HD</td>
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<tr>
<td>Serum β2M (mg/L)</td>
<td>32.6±9.5</td>
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<td>33.4±9.9</td>
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<td>D/P β2M</td>
<td>0.85±0.03</td>
<td>0.74±0.04</td>
<td>0.58±0.04</td>
<td>0.46±0.06</td>
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<tr>
<td>Effluent FDPs (μg/mL)</td>
<td>0.3±0.14a</td>
<td>0.28±0.13a</td>
<td>0.18±0.05a</td>
<td>0.11±0.05</td>
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<tr>
<td>Effluent CA125 (U/L)</td>
<td>39.4±34.2a</td>
<td>21.4±21.9</td>
<td>10.2±10.1</td>
<td>4.6±4.6</td>
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<tr>
<td>Duration of PD+HD (months)</td>
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<td>23.9±9.8a</td>
<td>21.3±10.1a</td>
<td>14.5±7.1</td>
</tr>
</tbody>
</table>

* p < 0.01 vs. the value for the Low category.

PET = peritoneal equilibration test; PD = peritoneal dialysis; β2M = β2-microglobulin; PD+HD = combination therapy with PD and hemodialysis; D/P = dialysate-to-plasma ratio; Cr = creatinine; FDPs = fibrin degradation products; CA125 = cancer antigen 125.

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**FIGURE 1** Evaluation of peritoneal permeability [dialysate-to-plasma (D/P) ratio of creatinine (Cr)] and effluent fibrin degradation products (eFDP) during combination therapy with peritoneal dialysis (PD) and hemodialysis (HD): The D/P Cr remained high in the H (high transport) group, but declined significantly in the HA (high-average) group and tended to decline in the LA (low-average) and L (low) groups. The eFDP level decreased markedly after initiation of PD+HD therapy in the H group, although the change was nonsignificant.
several symptoms in 31 patients treated with PD+HD (2), and McIntyre et al. reported that PD+HD therapy led to a reduction in antihypertensive drug dose and left ventricular mass index in 8 patients (7). We previously reported that the addition of once weekly HD to PD 5–6 days per week increased the weekly Kt/V to 2.27 ± 0.43 from 1.55 ± 0.4 and the normalized protein catabolic rate to 0.93 ± 0.16 g/kg from 0.77 ± 0.16 g/kg daily. Combination therapy with PD+HD may be an effective therapeutic method that appropriately increases the dialysis dose and improves survival in PD patients who have lost RRF.

The once-weekly HD performed in combination therapy means that there is a period without retention of dialysis solution in the abdominal cavity. And because the ultrafiltration volume is controlled by HD, the use of high-glucose dialysis solution can be reduced, lowering the patient’s glucose load. Those factors are suggested to have a favorable influence on peritoneal function.

We investigated the influence of PD+HD therapy on peritoneal function. The patients were divided into four groups based on PET category at PD+HD therapy initiation, and we followed their course based on D/P Cr, overnight D/P β2MG, eFDPs, and eCA125. The D/P Cr declined or tended to decline in the HA, LA, and L groups after PD+HD initiation, but not in the H group. Eventually, PD was discontinued in all patients in the H group. Therapy with PD+HD induced a reduction in the volume of PD solution and the frequency with which high-glucose dialysis solution was used. Improvements in uremia and body water balance may have helped to retain peritoneal function, but peritoneal function did not improve in the H group, suggesting that PD+HD therapy does not repair advanced peritoneal deterioration.

In the H group, eFDPs [considered to be a factor predicting capsule formation in EPS (8)], were markedly high, but tended to decline after initiation of PD+HD therapy even though the PET D/P Cr and overnight D/P β2MG remained high. Hemodialysis may have inhibited the fibrinolysis system, suggesting the possibility that PD+HD therapy may delay EPS development.

Conclusions
Therapy with PD+HD led to retention of peritoneal function in PD patients who had lost RRF and facilitated continuation of PD. However, peritoneal function was not improved in patients in whom function had already deteriorated. A change in therapeutic method should be considered for such patients.

References

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