

Combination Therapy with Peritoneal Dialysis and Hemodialysis from the Initiation of Renal Replacement Therapy Preserves Residual Renal Function and Serum Albumin

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Peritoneal dialysis (PD) and hemodialysis (HD) combination therapy is considered for the improvement of ultrafiltration failure and uremic symptoms in PD patients with loss of residual renal function (RRF). However, a rapid decline in RRF is one of the critical drawbacks to such therapy. In contrast, we started patients on combination therapy as a proactive option at the initiation of dialysis.

In patients on HD (n = 52), PD (n = 21), and combination dialysis (n = 13), we studied changes in RRF, blood parameters, and peritoneal permeability for 30 months. Residual renal function was better preserved in patients who received PD and HD combination therapy from the start of the dialysis therapy than in patients who received HD alone, and serum albumin was better preserved in the combination-therapy patients than in the patients who received PD alone. No significant differences in peritoneal permeability were observed between the patients on PD and those on combination therapy. Blood parameters were not significantly different between the three groups.

Because our proactive combination therapy option has beneficial effects compared with HD or PD therapy alone, combination therapy should be considered a new modality of renal replacement therapy.

Key words

Residual renal function, renal replacement therapy, proactive option, albumin

Introduction

In peritoneal dialysis (PD) therapy, ultrafiltration failure and uremic symptoms caused by loss of residual renal function (RRF) can lead to withdrawal from PD. To avoid insufficient fluid removal and solute clearances, PD combined with hemodialysis (HD) is considered an alternative therapy that compensates for the limitations of PD therapy (1–8). Should solute removal or ultrafiltration become deficient, combination therapy supports PD continuation in the face of a need to achieve adequate dialysis in PD patients with loss of RRF (9–11). However, PD patients with well-preserved RRF are not usually started on combination therapy.

The rapid fluid removal in a short HD session accelerates loss of RRF, which is an important factor associated with mortality and quality of life in dialysis patients (12). Thus, to avoid loss of RRF, we designed a therapy to be used from the start of dialysis that combines PD with HD during which little or no fluid is removed. We call this therapy the proactive (Px) option, with conventional PD+HD therapy after RRF loss being the rescue option.

In the present study, we investigated the effect of Px PD+HD therapy on RRF, which is understood to be the most important factor in patient prognosis. We also investigated changes in blood parameters and peritoneal permeability. The investigation followed patients from the initiation of renal replacement therapy (RRT) to 30 months.

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Methods

The dialysis schedule consisted of PD for 5 days weekly, with 2 PD rest days, and HD once weekly. The PD modalities included both continuous ambulatory PD and automated PD, using only a 1.5% glucose dialysate concentration. The HD session, which used a high-flux membrane dialyzer, was performed for approximately 4–5 hours. The ultrafiltration volume at the HD session consisted of the increase in body weight during the week.

Our retrospective study looked at the cases of 86 patients with end-stage kidney disease. After receiving an adequate explanation of the three possible modalities (HD, PD, or Px PD+HD) from doctors and the medical staff, the patients made their own choice of modality: HD ($n = 52$), PD ($n = 21$), and Px PD+HD ($n = 13$).

In the study patients, we measured daily urine volume (as a marker of RRF), blood parameters (serum creatinine, albumin, hemoglobin, Na, K, Ca, P, low-density lipoprotein cholesterol, and β_2 -microglobulin), and the dialysate-to-plasma creatinine ratio by peritoneal equilibration test (as a marker peritoneal permeability). Measurements were taken every 6 months from the start of RRT to 30 months (0, 6, 12, 18, 24, and 30 months). Exclusion criteria were a change of modality or an interruption in follow-up during the observation period. The study was performed according to the Ethics of Clinical Research (Declaration of Helsinki). Written informed consent was obtained from each patient in the study.

Statistical analyses

The significance of any difference in median value between the groups was evaluated using the Mann–Whitney U-test or Kruskal–Wallis one-way analysis, with a *post hoc* Dunn test (Prism 6: GraphPad Software, La Jolla, CA, U.S.A.). A *p* value less than 0.05 was considered statistically significant.

Results

Table I shows the profiles of the three patient groups. No significant differences in age or blood parameters, except for serum albumin, were observed at RRT initiation. Serum albumin was significantly lower in the HD group than in the Px PD+HD or PD group.

Figure 1(A) shows the change in urine volume in the three groups. At the start of RRT, daily urine volume in the HD group was 991 ± 500 mL. That urine

TABLE I Characteristics of the study population

Variable	Modality group			p Value
	HD	PD	Px PD+HD	
Patients (<i>n</i>)	54	23	15	
Demographics				
Mean age (years)	66.6±14.9	69.6±11.9	65.3±8.0	NS
Sex (<i>n</i> men/women)	33/21	16/7	12/3	
Diabetes (yes/no)	26/28	13/10	7/8	
Mean laboratory values				
BUN (mg/dL)	96.5±40.0	95.0±36.1	94.3±22.4	NS
Creatinine (mg/dL)	10.4±4.2	9.3±2.5	10.0±2.0	NS
Albumin (g/dL)	3.0±0.64	3.2±0.60	3.4±0.56	<0.05
Calcium (mg/dL)	7.5±1.19	8.0±0.95	8.2±1.06	NS
Phosphate (mg/dL)	7.0±2.28	6.5±1.71	6.43±1.00	NS
LDL cholesterol (mg/dL)	89.8±29.2	91.2±30.4	97.7±19.0	NS
Hemoglobin (g/dL)	8.4±1.63	9.1±1.62	9.0±1.83	NS

HD = hemodialysis; PD = peritoneal dialysis; Px = proactive; NS = nonsignificant; BUN = blood urea nitrogen; LDL = low-density lipoprotein.

volume declined rapidly during the 6 to 30 months after initiation (to 136 ± 260 mL). Daily urine volume in the PD group declined slightly from dialysis initiation to 6 months and then stayed approximately constant up to 30 months (1077 ± 813 mL). Daily urine volume in the Px PD+HD group remained constant up to 30 months (1234 ± 684 mL).

Figure 1(B) shows the change in serum albumin in the three groups. Although serum albumin was lower in the HD group than in the other two groups at the start of RRT, it increased gradually and stayed within normal range. In contrast, serum albumin in the PD group declined from the start of RRT. From 6 to 30 months, serum albumin was lower in the PD group than in the other two groups. In the Px PD+HD group, serum albumin stayed constant.

The dialysate-to-plasma ratio of creatinine was not different between the PD and Px PD+HD groups at

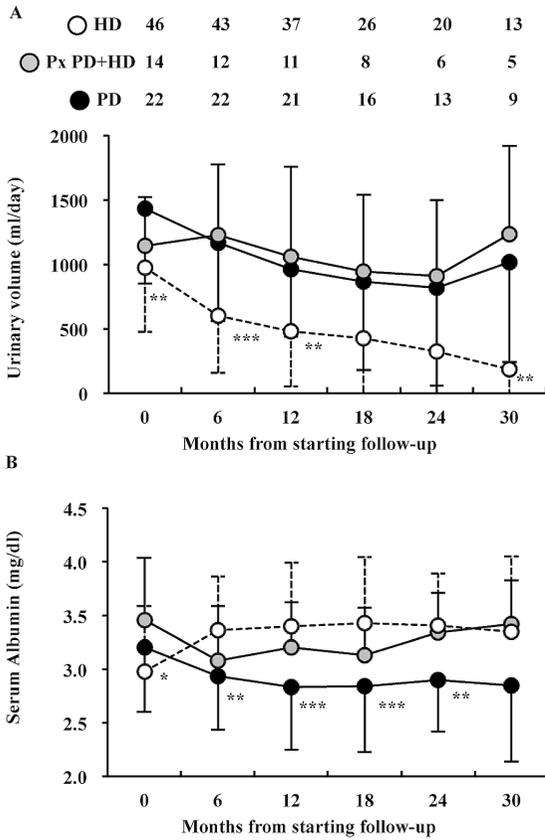


FIGURE 1 Changes in urinary volume and serum albumin for patients treated with proactive combined peritoneal dialysis (PD) and hemodialysis (HD), with PD, or with HD. (A) Urinary volume and (B) serum albumin by sequential measurement during follow-up in the study cohort. The numbers at the top indicate the population at risk at each time point. Median values at each time point were compared using the Mann-Whitney U-test. **p* < 0.05; ***p* < 0.01; ****p* < 0.001.

each observation point (Figure 2). The concentration of β_2 -microglobulin was lower at 0 and 6 months in the Px PD+HD group than in the other groups, but no significant differences between the three groups were observed at 12, 18, and 24 months (data not shown). Other laboratory data were not significantly different between the three groups at each observation point.

Discussion and conclusions

It has been reported that, compared with PD therapy alone, conventional PD+HD combination therapy improves not only overhydration and solute status, but also nutrition status and anemia (2,9–11,13).

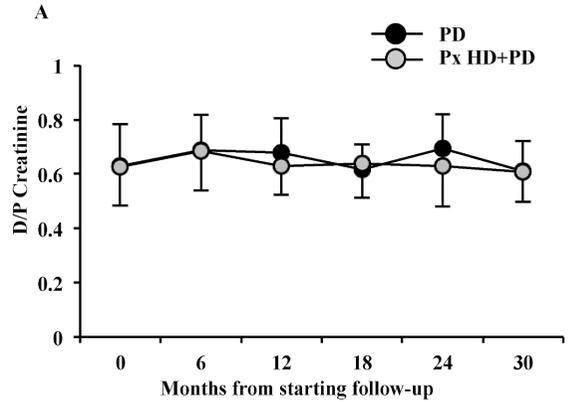


FIGURE 2 Changes in the dialysate-to-plasma (D/P) concentration ratio of creatinine for patients treated with proactive combined peritoneal dialysis (PD) and hemodialysis (HD) or with PD. The D/P creatinine was estimated by peritoneal equilibration test every 6 months. Median values at each time point were compared using the Mann-Whitney test.

Combination therapy as a rescue option was previously used only for patients with loss of RRF, because the needed removal of solutes and fluid is compensated by the HD session, and the rapid fluid removal in HD is known to cause a decline in RRF (12). Conventional PD+HD therapy has few adverse effects; however, previous reports showed that a decrease in urine volume, which is a factor critical for patient prognosis, is the one of the disadvantages of combination therapy (2,9,14). Although a decline in urine volume is one of the few adverse effects of combination therapy, it is a critical issue because of this direct effect on prognosis (13,15–17).

We thought that, in pre-dialysis patients with end-stage kidney disease, who usually have some urine volume, Px combination therapy should begin at the start of RRT to preserve RRF. We also paid attention to dietary intake for these patients, providing several diet counseling sessions by dietitians to control body-fluid balance. In our method, excess fluid volume could be removed constantly by both urine and PD ultrafiltration for 5 days each week. Thus, most patients could keep almost the same body weight throughout the week, meaning that there would be little need to remove an excessive amount of water at the HD session. In that way, Px PD+HD therapy was thought to overcome decline in RRF, which is a serious disadvantage in conventional PD+HD therapy.

Serum albumin concentration is also meaningful for prognosis in dialysis patients (18). When dialysis treatment is started, serum albumin in HD patients increases as RRF is lost and albumin excretion into the urine is suppressed. In contrast, serum albumin decreases in PD patients because albumin continuously leaks into the peritoneal dialysate and is excreted in urine. Interestingly, no decrease in serum albumin was observed in our Px PD+HD group. One limited explanation for those data might be the fact that peritoneal dialysate dwells were shorter by 2 days in the Px PD+HD group than in the PD group.

In the evaluation of peritoneal permeability by peritoneal equilibration test results, the PD and Px PD+HD groups showed no significant differences. The use of dialysate with a high concentration of glucose or of any glucose dialysate for a long time causes deterioration in the peritoneum, enhancing peritoneal permeability. Several publications reported that peritoneal rest decreases peritoneal hyperpermeability and the occurrence of ultrafiltration failure (19,20). Matsuo *et al.* (14) indicated similar and other beneficial effects in patients whose modality was changed from PD to conventional PD+HD therapy. In the present study, the fact that no significant differences in peritoneal permeability were observed between the PD and Px PD+HD groups could be attributed to the short period of observation.

Our study demonstrates that PD+HD therapy has advantages in preserving both RRF and serum albumin. Given that those beneficial effects might contribute to an excellent prognosis, Px PD+HD therapy should be considered a new modality of RRT.

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Disclosures

We understand that *Advances in Peritoneal Dialysis* requires disclosure of any conflicts of interest, and we declare that we have no conflicts to disclose.

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