

Evaluation of Dialysis Dose During Combination Therapy with Peritoneal Dialysis and Hemodialysis

Hideki Kawanishi, Misaki Moriishi, Shinichiro Tsuchiya

Peritoneal dialysis (PD) is effective way to preserve residual renal function (RRF) and should be the first-line dialysis option. However, after the loss of RRF, there are limitations to how well PD alone can control the uremic state. Combination therapy with PD and hemodialysis (PD+HD) is the simplest way to deal with these limitations. The general prescription for PD+HD should be 5 – 6 days of PD and 1 HD session weekly.

To determine the adequacy of PD+HD, we adopted the equivalent renal clearance (EKR), first transforming the weekly PD adequacy index (Kt/V), and then evaluating total clearance from both modalities. However, the EKR may overestimate the dialysis dose. To accurately track dialysis dose, we use the total effluent (PD, RRF, and HD) sampling method to yield Kt/V_{ef} and creatinine clearance (CCr_{ef}).

In comparing PD+HD with 7 days of PD alone, we found that weekly Kt/V_{ef} increased to 2.27 ± 0.43 from 1.55 ± 0.4 , and weekly CCr_{ef} increased to 60.3 ± 9.2 L/1.73 m² from 42.0 ± 7.7 L/1.73 m² ($p < 0.001$). In addition, the normalized protein equivalent of nitrogen appearance, percentage creatinine generation rate, and percentage lean body mass also increased (respectively) to 0.93 ± 0.16 g/kg from 0.77 ± 0.14 g/kg daily, to $126.5\% \pm 21.2\%$ from $82.6\% \pm 17.1\%$, and to $66.7\% \pm 10.9\%$ from $48.2\% \pm 8.9\%$ ($p < 0.001$). Protein losses in PD+HD were not different from those in PD alone, but serum albumin increased significantly to 3.6 ± 0.3 g/dL from 3.3 ± 0.3 g/dL, and serum β_2 -microglobulin decreased to 23.5 ± 11.1 mg/L from 33.3 ± 11.3 mg/L.

The total effluent sampling method can be used to evaluate the dialysis dose in PD+HD. The addition of once-weekly HD improved indices of nutrition, with increases in dialysis dose and serum albumin level.

In patients without RRF, PD+HD is recommended as a dialysis regimen to maintain the optimal dialysis dose and good nutrition status without peritoneal deterioration from an increase in the PD fluid volume.

Key words

Adequate dialysis, dialysis dose, nutrition status

Introduction

Successful outcomes of peritoneal dialysis (PD) in anuric patients have been reported (1), but as residual renal function (RRF) declines, standard PD may not be sufficient to avoid the risk of uremic complications. Increasing the dose of dialysis—which is currently the only measure available to diminish that risk—has the potential to augment the negative impact of dialysis solution on the peritoneal membrane. An alternative to increasing the dose of PD (2–6) is to combine PD with hemodialysis (PD+HD).

Although only limited outcomes data are currently available concerning combined therapy, PD+HD has rapidly gained popularity in Japan. Estimates suggest that, in 2005, approximately 10.5% of PD patients were prescribed PD+HD (7).

When PD is combined with HD, the dialysis dose by weekly HD must be converted to a continuous treatment value to obtain the total dialysis dose. The equivalent renal clearance (EKR) of urea (in milliliters per minute) proposed by Casino *et al.* (8) is used as the conversion method. The calculated HD dose is added to the dialysis dose achieved by 5 – 6 days of PD per week to obtain the total weekly dialysis dose for evaluation (3). Alternatively, Vonesh suggested the urea reduction rate to calculate a combined PD and HD dose (Vonesh EF. Combined hemodialysis and peritoneal dialysis. Presented at the American Society of Nephrology 37th Annual Renal Week Meeting; 27 October – 1 November 2004; St. Louis, MO, U.S.A.), and Hamada and colleagues showed the

usefulness of direct sampling of the total HD and PD effluent (9). In the present study, we used direct sampling of total effluent to evaluate PD+HD dialysis dose.

Patients and methods

Our study included 23 patients who had been on PD for a mean of 28.1 ± 20.3 months when they started combined therapy and who had thereafter been on PD+HD for a mean of 29.9 ± 23.1 months. The peritoneal equilibration test (PET) yielded these membrane transport classifications: high (1 patient), high-average (12 patients), low-average (5 patients), and low (5 patients).

The combination therapy regimen consisted of 5 or 6 days of PD and 1 weekly 4-hour session of HD with a high permeability membrane. The mean daily PD effluent volume before the start of PD+HD was 7.8 ± 2.0 L, and 6 months after the start of combination therapy, it was 8.1 ± 2.0 L. The patients were started on PD+HD because of inadequate dialysis in 16 patients (52.2%) and insufficient water removal in 7 patients (47.8%).

We used the total effluent (PD, RRF, and HD) sampling method to evaluate the dialysis dose before and 6 months after the start of PD+HD. The HD dose was defined as the effluent solute volume in HD divided by the pre-dialysis solute value. Total dialysis dose was then calculated:

$$\text{Total dialysis dose} = (\text{effluent volume per HD session} \times \text{effluent solute concentration} / \text{plasma solute concentration}) + (\text{dialysate-to-plasma concentration of the solute} \times \text{daily PD effluent volume} \times \text{days of PD per week}). \quad [1]$$

Urea and creatinine were corrected by total body water and body surface area (post-hemodialysis values) and expressed as weekly dialysis adequacy (Kt/V_{ef}) and weekly creatinine clearance (CCr_{ef}) respectively. For comparison, Kt/V was also calculated by the EKR method (3,8):

$$Kt/V_{EKR} = G / TAC, \quad [2]$$

$$G = V \times (C02 - Ct) \times 10 / \text{tid}, \text{ and} \quad [3]$$

$$TAC = [\text{td} \times (C01 + Ct)] + [\text{tid} \times (Ct + C02)] / 2 (\text{td} + \text{tid}) \quad [4]$$

where G is the urea generation rate, TAC is the time-averaged concentration of urea, V is total body water in liters, tid is the hemodialysis interval in minutes, and td is the hemodialysis session length in minutes. $C01$, $C02$, and Ct are blood urea values before the HD session, after the HD session, and before the subsequent week's HD session.

In addition, using the creatinine generation rate (CGR) in PD and HD, we calculated the normalized protein equivalent of total nitrogen appearance (nPNA) by the modified Bora method, the percentage CGR (%CGR) by the Shinzato method (10), and the percentage lean body mass (%LBM) by the Keshaviah method.

Data are expressed mean \pm standard deviation. Statistical analyses were conducted using the Pearson correlation test and the unpaired Student t -test. Values of $p < 0.05$ were accepted as statistically significant.

Results

We observed a significant positive correlation between Kt/V_{ef} and Kt/V_{EKR} , with the Kt/V_{EKR} tending to be somewhat higher (Figure 1). In comparing PD+HD with 7 days of PD alone, we found that weekly Kt/V_{ef} increased to 2.27 ± 0.43 (PD+RRF: 1.32 ± 0.4) from 1.55 ± 0.4 (Figure 2), and weekly CCr_{ef} increased to 60.3 ± 9.2 L/1.73 m² from 42.0 ± 7.7 L/1.73 m² ($p < 0.001$, Table I). The nPNA, %CGR, and %LBM also

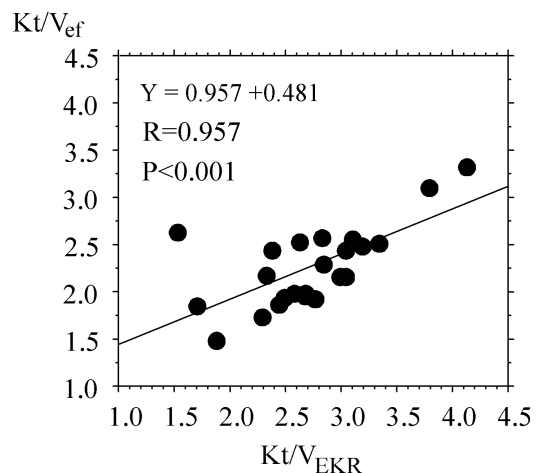


FIGURE 1 Correlation between dialysis adequacy (Kt/V) by the total effluent sampling (ef) method and the equivalent renal clearance (EKR) method.

increased, respectively, to 0.93 ± 0.16 g/kg from 0.77 ± 0.14 g/kg daily, to $126.5\% \pm 21.2\%$ from $82.6\% \pm 17.1\%$, and to $66.7\% \pm 10.9\%$ from $48.2\% \pm 8.9\%$ ($p < 0.001$, Table I).

In PD+HD, protein losses into the PD effluent decreased in association with the reduction in the number of PD days; however, when protein losses into the HD effluent were added, the total loss amounted to 5.0 ± 1.5 g weekly, which was not significantly different from the losses during PD alone (5.2 ± 2.5 g weekly, Table I). However, serum albumin levels increased significantly to 3.6 ± 0.3 g/dL after the start of PD+HD therapy from 3.3 ± 0.3 g/dL

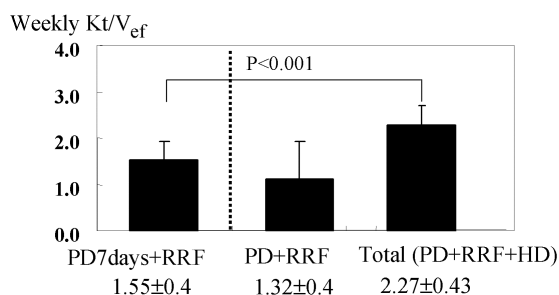


FIGURE 2 Comparison of weekly dialysis adequacy by the total effluent sampling method (Kt/V_{ef}) between peritoneal dialysis (PD) alone and combination therapy with PD and hemodialysis (HD). RRF = residual renal function.

TABLE I Dialysis dose and nutrition factors before and 6 months after combined peritoneal dialysis (PD) and hemodialysis (HD) therapy

	PD	PD+HD	p Value
Weekly Kt/V_{EKR}	1.53 ± 0.4	2.72 ± 0.30	<0.001
Weekly Kt/V_{ef}	1.55 ± 0.4	2.27 ± 0.30	<0.001
Weekly CCr_{ef} (L/1.73 m ²)	42.0 ± 7.7	60.3 ± 9.2	<0.001
Daily nPNA (g/kg)	0.77 ± 0.14	0.93 ± 0.16	<0.001
%CGR	82.6 ± 17.1	126.5 ± 21.2	<0.001
%LBM	48.2 ± 8.9	66.7 ± 10.9	<0.001
Weekly protein loss (g)	5.22 ± 2.46	4.97 ± 1.48	NS
Albumin (g/dL)	3.3 ± 0.3	3.6 ± 0.3	<0.001
β_2 -Microglobulin (mg/L)	33.3 ± 11.3	23.5 ± 11.1	<0.001

Kt/V_{EKR} = dialysis adequacy by the equivalent renal clearance method; Kt/V_{ef} = dialysis adequacy by the total effluent sampling method; CCr_{ef} = creatinine clearance by the total effluent sampling method; nPNA = normalized protein equivalent of total nitrogen appearance; %CGR = percentage creatinine generation rate; %LBM = percentage lean body mass.

with PD alone ($p < 0.001$), and serum β_2 -microglobulin decreased to 23.5 ± 11.1 mg/L from 33.3 ± 11.3 mg/L (Table I).

We used PET to evaluate changes of peritoneal permeability in terms of dialysate-to-plasma creatinine (D/P Cr) before and after the start of PD+HD, and we found that time-dependent D/P Cr values in most patients approximated straight lines (Figure 3). In 19 of the 23 study patients, D/P Cr values either remained unchanged or declined.

Discussion

In Japan, combination therapy with weekly HD started in 1995 (2,3). Later, limited experiences with combination therapy were also reported from the United States (4) and the United Kingdom (5). In Japan, the focus has been to use PD+HD in prevalent patients in whom RRF has declined to the extent that management with conventional PD prescriptions is difficult. Thus, the combination regimen is used as an alternative to increasing the dose of PD. Other considerations also underlie this approach:

- After loss of RRF, removal of large molecular solutes eventually becomes inadequate regardless of the volume of PD fluid used, with resulting increases in, for example, β_2 -microglobulin, leading to dialysis amyloidosis.
- An increase in the daily volume of PD fluid likely accelerates deterioration of the peritoneal membrane, thereby increasing the risk for developing encapsulating peritoneal sclerosis.

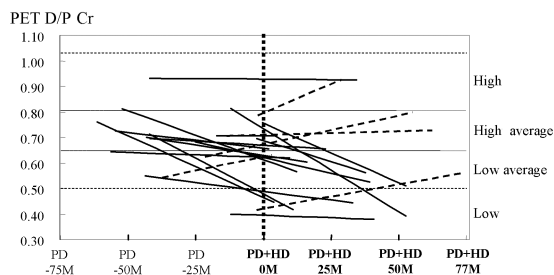


FIGURE 3 Changes of dialysate-to-plasma creatinine (D/P Cr) by peritoneal equilibration test (PET) before and after combination therapy with peritoneal dialysis (PD) and hemodialysis (HD). Broken lines indicate patients whose peritoneal permeability increased over time (4 of 23 patients). M = months.

The EKR (8) and standard Kt/V (11) are just two of the techniques used to evaluate dialysis dose with frequent or continuous modalities. However, because the EKR and standard Kt/V methods use TAC and peak value, respectively, they may respectively overestimate or underestimate the dialysis dose. Dialysis dose in PD, unlike the dose in HD, has generally been evaluated in terms of effluent concentration. In PD+HD, once-weekly HD is the standard regimen, and collection of the HD effluent to calculate the dialysis dose by the same formula as that used in PD therapy permits reliable evaluation.

In the present study, weekly dialysis dose was evaluated by totaling the dose achieved by PD, RRF, and HD. Weekly Kt/V urea was found to have increased to 2.27 ± 0.43 from 1.55 ± 0.4 —a significant dose increase despite the 1- or 2-day reduction in PD days. Similarly, weekly CCr rose to 60.3 ± 9.2 L/1.73 m² from 42.0 ± 7.7 L/1.73 m². The addition of 1 HD session increased the generation rates of urea and creatinine, resulting in elevations of nPNA, %CGR, and %LBM. Moreover, because of the increased dialysis dose and improved nutrition indices, a significant increase in serum albumin was also achieved, despite the lack of a reduction in total protein losses into the dialysate effluent.

Many factors—among them, dialysis dose, protein losses into the PD fluid, a reduced protein intake, chronic disease, and serum bicarbonate concentration—influence nutrition status in PD patients, but dialysis dose is one of the most significant. Mak *et al.* reported that an increase in PD fluid exchanges caused a rise in weekly Kt/V, but no change in serum albumin (12). In the ADEMEX study (13) and the Hong Kong study (14), increasing the weekly Kt/V by increasing the dialysis dose did not improve survival. Those observations indicated that increasing the PD fluid volume to increase the removal of small molecules does not improve nutrition status or survival in patients. However, in the present study, PD+HD increased the dialysis dose and the patients' protein intake, improving nutrition status as shown by the increase in serum albumin. This result presumably reflects the removal by HD of medium-to-large molecules and improvement in fluid status through more precise water removal. We further speculate that, in addition to permitting a reduction in the PD dose, combination therapy with added HD reduces the need to use high-concentration glucose solution,

and that the reduced glucose load favorably affects nutrition status.

Some investigators have suggested that HD 1 or 2 days per week with concomitant interruption of PD would allow for peritoneal rest and therefore prevent peritoneal deterioration. However, whether intermittent rest of this kind is indeed effective in postponing peritoneal impairment remains to be demonstrated. In the present study, 19 of the 23 patients showed a tendency toward a decrease in D/P Cr after the start of PD+HD therapy, suggesting that PD+HD reduced the PD fluid volume and glucose load, thereby slowing PD duration-related deterioration of the peritoneum.

Conclusions

In the presence of RRF, PD therapy with an optimal PD dose can maintain good nutrition status; however, as RRF declines, so does solute clearance, and nutrition status deteriorates. At this point, increasing the PD fluid volume results in increased removal of low-molecular-weight solutes only, and peritoneal deterioration may accelerate while nutrition status remains poor. In patients without RRF, a PD+HD regimen is recommended for maintaining an optimal dialysis dose and good nutrition status with less risk of peritoneal deterioration from an increase in PD fluid volume.

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- Corresponding author:*
Hideki Kawanishi, MD, Akane-Foundation, Tsuchiya General Hospital, 3-30 Nakajima-cho, Naka-ku, Hiroshima 730-8655 Japan.
E-mail:
h-kawanishi@tsuchiya-hp.jp