

# Peritoneal Dialysis Preserves Residual Renal Function and Reduces Oxidative Stress During the Initial Period of Dialysis Therapy

Atsushi Ueda,<sup>1</sup> Kei Nagai,<sup>2</sup> Aki Hirayama,<sup>3</sup> Chie Saito,<sup>2</sup> Kunihiro Yamagata<sup>2</sup>

*Patients with end-stage renal failure are believed to have an increase of oxidative stress. However, any variation in oxidative stress between patients receiving hemodialysis (HD) and those receiving peritoneal dialysis (PD) are still unclear. In the present study, we investigated variation in oxidative stress in 54 HD and 23 PD patients during their initial dialysis period.*

*We measured serum pentosidine and indoxylsulfuric acid as markers of oxidative stress every 6 months from the start of the dialysis therapy to 30 months of treatment. Serum pentosidine was significantly lower in the PD patients than in the HD patients. Serum indoxylsulfuric acid was also significantly lower in the PD group compared with the HD group at 6, 12, and 18 months. Compared with the HD patients, the PD patients maintained significantly higher urine volumes (a marker of residual renal function) throughout the study, except at 24 months.*

*Our findings demonstrate that, compared with HD patients, PD patients experience lower levels of oxidative stress because of higher preserved residual renal function during the initial dialysis period.*

## Key words

Residual renal function, oxidative stress, pentosidine, indoxylsulfuric acid

## Introduction

According to previous reports, patients with end-stage renal failure are known to experience an increase in oxidative stress (1–4). Excessive oxidative stress

causes inflammation and arteriosclerosis, resulting in cardiovascular complications (5–7). In hemodialysis (HD) patients, oxidative stress is known to increase with the mechanical stimulation that occurs during dialysis (8–10). In contrast, antioxidant activity is improved by dialysis treatment (2,3,8,10). However, the dynamics of those two phenomena are still unclear. Similarly, variations in oxidative stress in patients receiving peritoneal dialysis (PD) are not clear. In addition, the differences in oxidative stress between patients receiving HD and PD are also unknown.

In the present study, we investigated variation in oxidative stress, which is known to be an important factor in cardiovascular complications, in HD and PD patients during the initial dialysis period. We also investigated changes in serum parameters and urine volume as a marker of residual renal function (RRF). Our investigation followed patients from the initiation of dialysis therapy to 30 months after dialysis start.

## Methods

We retrospectively studied the cases of 54 HD and 23 PD patients who had no active infection. The HD patients were regularly treated 3 times weekly for 4–5 hours using a high-flux membrane dialyzer. The PD patients were treated with 4 bags daily or automated PD with low-glucose dialysate. Because the general condition of all patients was basically stable, the same dialysis method was continued.

We measured daily urine volume (as a marker of RRF) and blood parameters (serum creatinine, albumin, hemoglobin, Na, K, Ca, P, low-density lipoprotein, and  $\beta_2$ -microglobulin). We also measured serum pentosidine and indoxylsulfuric acid (IS) as a marker of oxidative stress. Measurements were taken every 6 months from the start of dialysis to 30 months of treatment (0, 6, 12, 18, 24, and 30 months).

From: <sup>1</sup>Department of Nephrology, Hitachi General Hospital, Hitachi, <sup>2</sup>Department of Internal Medicine, University of Tsukuba, Tsukuba, and <sup>3</sup>Center for Integrated Medicine, Tsukuba University of Technology, Tsukuba, Ibaraki, Japan.

Exclusion criteria were a change of dialysis 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**

Values are expressed as mean ± standard deviation or median ± standard error of the mean. The significance of differences in median values was evaluated using the 2-tailed Student t-test or the Mann–Whitney U-test, as appropriate (Prism 6: GraphPad Software, La Jolla, CA, U.S.A.). A *p* value less than 0.05 was considered statistically significant.

**Results**

Table I presents the profiles of the two patient groups. At the start of dialysis therapy, clinical profiles and blood parameters were not significantly different between the groups.

Figure 1(A) shows changes in urine volume. Urine volume in the HD patients declined rapidly and reached almost zero at 30 months. Compared with the HD patients, the PD patients maintained a significantly higher urine volume throughout the study, except

at 24 months. Urine volume in the PD patients stayed constant until 30 months.

No significant differences in serum β<sub>2</sub>-microglobulin were observed between the HD and PD groups from the start of dialysis therapy until month 30 [Figure 1(B)]. Serum albumin was significantly lower in the PD group than in the HD group from 6 months to 30 months (data not shown). No significant differences between the two groups in serum creatinine, hemoglobin, Na, K, Ca, P, and low-density lipoprotein were

TABLE I Profile of the hemodialysis (HD) and peritoneal dialysis (PD) patients

Variable	Modality group		p Value
	HD	PD	
<b>Cohort characteristics</b>			
Patients ( <i>n</i> )	54	23	—
Mean age (years)	66.6±14.9	69.6±11.9	NS
Men/women ( <i>n</i> )	33/21	7/16	
With/without diabetes ( <i>n</i> )	26/28	10/13	
<b>Blood chemistry</b>			
BUN (mg/dL)	96.5±40.0	95.0±36.1	NS
Creatinine (mg/dL)	10.4±4.2	9.3±2.5	NS
Albumin (g/dL)	3.0±0.64	3.2±0.60	NS
Calcium (mg/dL)	7.5±1.19	8.0±0.95	NS
Phosphate (mg/dL)	7.0±2.28	6.5±1.71	NS
LDL cholesterol (mg/dL)	89.8±29.2	91.2±30.4	NS
Hemoglobin (g/dL)	8.4±1.63	9.1±1.62	NS

NS = nonsignificant; BUN = blood urea nitrogen; LDL = low-density lipoprotein.

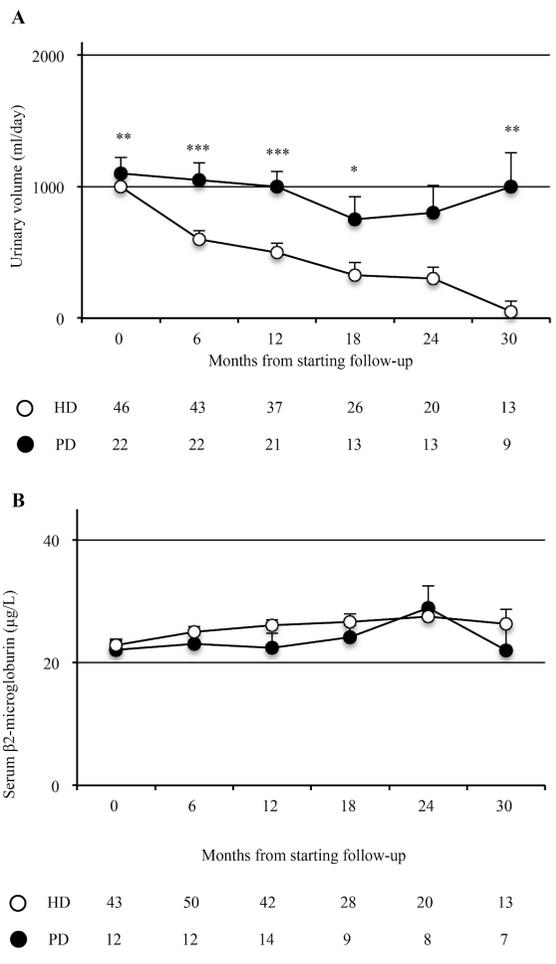


FIGURE 1 Changes in urinary volume and serum β<sub>2</sub>-microglobulin in hemodialysis (HD) and peritoneal dialysis (PD) patients. The numbers of patients at risk at each time point are shown below each graph. (A) Urinary volume by sequential measurement during follow-up. (B) Serum β<sub>2</sub>-microglobulin by sequential measurement during follow-up. Comparisons of the median values at each time point were performed using the Mann–Whitney test. \**p* < 0.05; \*\**p* < 0.01; \*\*\**p* < 0.001.

observed at any point. Serum pentosidine in the HD group increased gradually from the start of dialysis to 30 months. In contrast, serum pentosidine in the PD group stayed constant during the observation period. Comparing the two groups, we observed that serum pentosidine was significantly lower in the PD group than in the HD group at every observation point [Figure 2(A)]. Serum IS was significantly lower in the PD group than in the HD group at 6, 12, and 18 months. However, no difference in serum IS was observed at 24 and 30 months [Figure 2(B)].

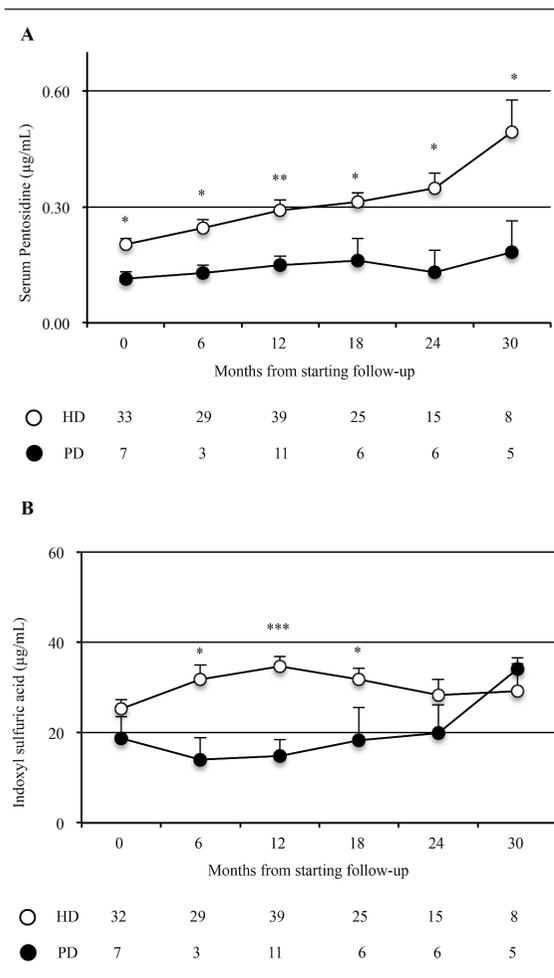


FIGURE 2 Changes in serum oxidative stress markers in hemodialysis (HD) and peritoneal dialysis (PD) patients. The numbers of patients at risk at each time point are shown below each graph. (A) Serum pentosidine and (B) indoxylsulfuric acid by sequential measurement during follow-up. Comparisons of the median values at each time point were performed using the Mann–Whitney test. \* $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ .

## Discussion

Patients with end-stage renal failure experience increased oxidative stress because of both the generation and the reduced removal of oxidative substances (1–4). The increase in oxidative stress experienced by those patients causes cardiovascular complications and a poor prognosis (11). Moreover, the increase in oxidative stress is considered to be caused not only by uremic status in itself, but also by the influence of the dialysis modality. Thus, dialysis therapy could improve the redox balance by removing oxidized substances (3,4).

For HD patients, the biocompatibility of the dialyzer membrane is involved in an augmentation of the production of reactive oxygen species (8,9). For PD patients, long-term exposure of the peritoneal membrane to glucose and high-osmolality dialysate might enhance oxidative stress (12,13). Several reports have compared the variation in oxidative stress between HD and PD patients. Capusa *et al.* (14) indicated that lipid peroxidation was significantly higher in HD patients than in PD patients. However, plasma antioxidant status did not differ between HD and PD patients. Those authors speculated that oxidative stress was enhanced by the characteristics of the HD procedure.

In the present study, we analyzed the variation in oxidative stress between HD and PD patients during the initial dialysis period. We measured serum pentosidine, a well-recognized surrogate marker of carbonyl stress (15), and IS, a well-known uremic toxin (16). Both are thought to strongly reflect oxidative stress in the body. Looking at the variations in serum pentosidine and IS, oxidative stress was observed to be significantly higher in HD patients than in PD patients. Given that we observed no differences in serum creatinine and  $\beta_2$ -microglobulin between the HD and the PD patients at every observation point, dialysis efficiency seems to have little involvement in the dynamics of oxidative stress.

Several reports have indicated that RRF is the main factor in reducing oxidative stress in dialysis patients. Measuring plasma advanced oxidation protein products and pentosidine in serum, Furuya and colleagues (15) showed a significant inverse relationship between RRF and oxidative substances in PD patients. By focusing on the start of dialysis therapy and using frequent observation points, our study confirmed the relationship between RRF and oxidative stress at the start of dialysis. Urine volume in HD patients is believed to decline dramatically from the

start of dialysis therapy. In contrast, urine volume is preserved for a time in PD patients (17). We were able to examine those factors in detail in the present study. Moreover, we were able to determine that oxidative stress is significantly lower in PD patients than in HD patients. Several reports have indicated that low RRF in dialysis patients causes complications and predicts a poor prognosis (17–20). Although we could not observe a beneficial effect on prognosis, we showed that, compared with HD patients, PD patients experience less oxidative stress because of higher RRF, which should result in a good prognosis.

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### Disclosures

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

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### Corresponding author:

Atsushi Ueda, MD PhD, 2-1-1 Johnan-cho, Hitachi, Ibaraki 317-0077 Japan.

### E-mail:

au-int@jcom.home.ne.jp