Renal Replacement Therapy

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Impact on change in serum beta 2 microglobulin by combination therapy of peritoneal dialysis and hemodialysis: a 12-month preliminary observational study

Shinobu Moriya[1], Shun Nishizawa[1], Yayoi Tsuchihashi[1], Yoshihiro Inoue[1], Kimio Watanabe[2*], Yugo Ito[2], Hassu Kin[1] and Masaaki Nakayama[2]

Abstract

Background: In the Japanese guidelines on combination peritoneal dialysis (PD) and hemodialysis (HD) therapy, patients with serum beta 2 microglobulin (β2MG) levels less than 30 mg/L are recommended. And PD patients with β2MG more than 30 mg/L are considered to transfer to the PD + HD combination therapy. However, the resultant changes in serum β2MG levels by the introduction of PD + HD combination therapy and the factors influencing the change have not clearly elucidated.

Methods: We retrospectively studied 11 PD patients (mean age 56.4 ± 12.9 years, 10 males) with baseline β2MG levels > 30 mg/L with respect to changes in β2MG and its related factors for 12 months after the introduction of combination therapy of PD plus once a week HD (4 h) using a high-performance dialyzer. Laboratory data including hemoglobin, albumin, C-reactive protein, blood urea nitrogen, creatinine, and the patients' demographic profiles, and HD-related factors, such as Kt/V and blood flow rate, were assessed.

Results: Serum β2MG levels decreased statistically significantly after the introduction of combination therapy: from 36.7 ± 6.7 mg/L at 0 months, to 33.4 ± 6.1 mg/L at 3 months ($p = 0.030$, compared to baseline), 32.9 ± 4.5 mg/L at 6 months ($p = 0.009$), and 33.3 ± 5.3 mg/L at 12 months ($p = 0.023$), respectively. However, only 27–36% patients achieved target β2MG levels of < 30 mg/L during the observation period. Regarding influencing factors, serum albumin levels, blood flow rates of HD, residual renal function and baseline β2MG were associated with a decrease in serum β2MG levels on univariate analysis. In multivariate analysis, serum albumin at 3 and 12 months correlated significantly with Δβ2MG ($\beta = -0.990$, $p = 0.032$ at 3 months, $\beta = -0.551$, $p = 0.033$ at 12 months). Urine volume at 12 months correlated significantly with Δβ2MG ($\beta = 0.507$, $p = 0.019$).

Conclusions: Combination therapy of PD and HD might reduce serum β2MG levels, but with marginal efficacy. Our preliminary data indicate that the combination therapy of PD and once weekly HD is not sufficient to significantly decrease serum β2MG levels. Additional HD prescriptions, such as increase in blood flow rate and hemodiafiltration, need to be tested in order to improve β2MG levels in these patients.

*Correspondence: spyh63x9@gmail.com

[2] Division of Kidney Center, St Luke's International Hospital, 9-1 Akashi-Cho, Chuo-Ku, Tokyo 104-8560, Japan
Full list of author information is available at the end of the article

Keywords: Serum beta2 microglobulin, Peritoneal dialysis, Hemodialysis, Combination therapy

Background

In Japan, combination therapy with peritoneal dialysis and hemodialysis (PD + HD) is widely used in PD patients as an alternative method for various reasons, such as to decrease serum beta 2 microglobulin (β2MG), improve fluid overload, and maintain residual kidney function [1]. Importantly, Murashima, et al. have reported using the Japanese Society for Dialysis Therapy registry data that combination of once-weekly HD with PD is associated with lower mortality compared with peritoneal dialysis alone [2]. At the end of 2014, 1913 PD patients were receiving PD + HD combination therapy in Japan, which is 20.7% of all PD patients [1]. Typically, combination therapy with 5 or 6 days of PD and once weekly HD is used to counteract the decline in total solute clearance caused by decreased residual kidney function and decline in ultrafiltration caused by increase in peritoneal permeability [3].

Serum β2MG has been widely accepted as a marker of overall middle molecular uremic toxins and is a key factor in the genesis of dialysis-associated amyloidosis [4]. Since β2MG is exclusively eliminated by the kidneys [5], its levels are particularly elevated in patients with HD or PD who have low residual kidney function [6–12]. Therefore, if the residual kidney function declines in patients receiving PD monotherapy, the removal of middle molecular weight substances, such as β2MG, is limited.

Managing serum β2MG at an appropriate level is one of the important reasons for initiation of PD + HD combination therapy. Recently, several studies have shown that higher serum β2MG is associated with poor prognosis, including worse survival in dialysis patients [13–16]. Okuno et al. demonstrated in hemodialysis patients that serum β2MG is a significant predictor of all-cause mortality [15] and the HEMO Study Group also showed that every 10 mg/L increase in serum β2MG in HD patients is a significant predictor of death due to infection, after adjustment for multiple confounding factors [13]. Koh et al. demonstrated that every 1 mg/L increase in serum β2MG is a significant predictor of all-cause mortality in PD patients [16]. Based on these findings, the new Japanese Society of Dialysis Therapy guidelines for Peritoneal Dialysis in 2019 recommended a target serum β2MG value of 30 mg/L or less [17].

However, it is unclear how much serum β2MG levels improve in PD patients who also undergo once-weekly HD. In addition, it is unclear which factors contribute to the improvement in β2MG levels. Here, we retrospectively investigated PD patients with baseline β2MG levels > 30 mg/L who started once-weekly HD combination therapy and analyzed the magnitude of the decrease in β2MG levels and its related factors for 12 months.

Methods

Study design and participants

This study was a 12-month, single-center, retrospective, observational study conducted at the Kidney Center of St. Luke's International Hospital (Tokyo, Japan) between June 2011 and August 2020. The study was approved by the research ethics committee of St Luke's International Hospital (approval number 21-R156) and adhered to the ethical principles set by the Declaration of Helsinki.

Patient selection in the present study is shown in Fig. 1. Nineteen patients were initially registered, from among whom 11 patients were finally included in this study. The inclusion criteria were as follows: (1) patients who started combination therapy of PD and HD at St. Luke's International Hospital, (2) those in whom the observation period was more than 12 months, and (3) patients with β2MG levels > 30 mg/L at the initiation of PD + HD combination therapy. Of the remaining eight patients, six patients were excluded due to a short observation period, and two cases were excluded since their β2MG levels were < 30 mg/L at the initiation of PD + HD combination therapy. The types of HD dialyzer used were I-a ($n = 10$) and II-a ($n = 1$) at 3 months, I-a ($n = 8$) and II-a ($n = 3$) at 6 months, and I-a ($n = 6$), II-a ($n = 4$), and S ($n = 1$) at 12 months. Clinical characteristics of the patients in this

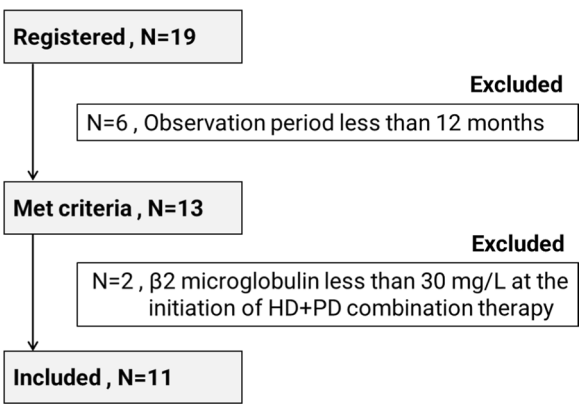

Fig. 1 Patient selection in the present study. *PD* peritoneal dialysis, *HD* hemodialysis

Table 1 Clinical characteristics of the patients in this study

Age (years)	**56.4 ± 12.9**	**Laboratory data**	
Male, n (%)	10/11 (90.9)	Hemoglobin (g/dL)	10.0 ± 1.5
Body mass index (kg/m^2)	25.3 ± 2.6	Serum albumin (g/dL)	3.1 ± 0.4
PD treatment period (year)	3.4 ± 1.3	Serum blood urea nitrogen (mg/dL)	58.0 ± 22.5
Etiology of renal insufficiency	Diabetes mellitus (7)	Serum creatinine (mg/dL)	15.1 ± 4.6
	Glomerulonephritis (2)	Serum sodium (mEq/L)	134.1 ± 2.6
	Polycystic kidney disease (1)	Serum potassium (mEq/L)	4.0 ± 0.5
	Renal sclerosis (1)	Serum calcium (mg/dL)	4.0 ± 0.6
Urine volume (mL/day)	100 (0–1050)	Serum phosphorus (mg/dL)	6.7 ± 2.3
Renal Kt/V urea	0.01 ± 0.01	Intact parathyroid hormone (pg/mL)	239.2 ± 99.5
Renal CCr (mL/min)	4.7 ± 5.5	C-reactive protein (mg/dL)	0.8 ± 1.5
Peritoneal dialysis treatment		Serum beta 2 microglobulin (mg/L)	32.7(30.7–51.2)
Total PD fluid volume (L/day)	9.5 ± 2.2		
Weekly Kt/V	1.6 ± 0.3		

Hemodialysis treatment conditions				
HD sessions per week	1	Dialyzer type (n)	Ia	10
Treatment time per HD session (hours)	4		IIa	1
Blood flow rate (mL/min)	200 (200–250)	Membrane area of the dialyzers (m^2)	2.4 ± 0.2	

Data are shown as the mean ± SD or median (min–max). *PD* peritoneal dialysis, *HD* hemodialysis

study in the present study is shown in Table 1. Timing of taking the blood sample for β2MG was before the HD session at 3, 6, 12 months in all patients.

Measurements and outcomes

The primary outcome was change in β2MG level at 12 months after the start of PD + HD combination therapy. The secondary outcome was the relationship between the decrease in β2MG levels and its related factors for 12 months. The related factors included age, sex, body mass index (BMI), β2MG level, blood urea nitrogen, creatinine, albumin, C-reactive protein, PD fluid volume, vintage of PD, weekly Kt/V of PD, dry weight, type of dialyzer, blood flow rate, HD treatment time per session, and Kt/V of HD at 0, 3, 6, and 12 months after the start of PD + HD combination therapy.

For analysis of the changes in β2MG after the initiation of PD + HD combination therapy over 12 months, the patients were divided into three groups according to the magnitude of the change in β2MG (Δβ2MG) in each patient as: increased: Δβ2MG of more than + 0.789 mg/L, no change: Δβ2MG between − 0.789 and + 0.789 mg/L, and decreased group: Δβ2MG of less than − 0.789 mg/L. This cut-off value was calculated using the data from 10 stable HD patients for 12 months. The average value of the 95% confidence interval of the coefficient of variation of the β2MG value of the 10 HD patient's over a 12-month period was determined as − 0.789 and + 0.789 mg/L.

Statistical analysis

Results are presented as the mean ± standard deviation for normally distributed data and the median (minimum–maximum) for data with non-normal distribution. Comparisons of β2MG values after the initiation of PD + HD treatment were performed with repeated-measures analysis of variance (ANOVA), followed by the Tukey test. Cochran's Q test was applied to compare the changes in β2MG between 0, 3, 6, and 12 months. Multiple regression analysis and Pearson's correlation coefficient were used to detect factors that affect Δβ2MG. All statistical analyses were performed using SPSS software (version 24) with p values < 0.05 considered to be significant.

Results

Effect of PD + HD combination therapy on β2 microglobulin reduction

The combination therapy of PD and once-weekly HD statistically significantly reduced β2MG levels, and the effect was maintained for 12 months. Mean values of β2MG at baseline, and 3, 6, and 12 months were 36.7 ± 6.7 mg/L, 33.4 ± 6.1 mg/L, 32.9 ± 4.5 mg/L, and 33.3 ± 5.3 mg/L, respectively. Mean values of β2MG at 3, 6, and 12 months were decreased significantly compared to baseline values, as seen by repeated-measures ANOVA with Tukey's correction (Fig. 2).

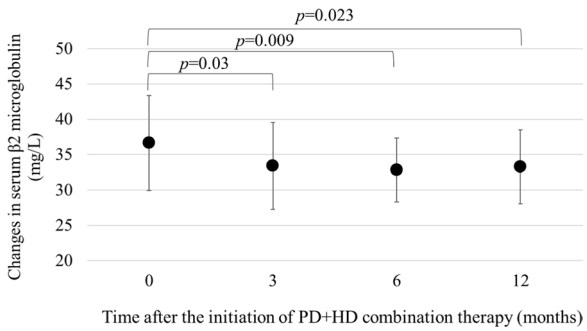

Fig. 2 Changes in serum β2 microglobulin by PD + HD combination therapy over 12 months. *PD* peritoneal dialysis, *HD* hemodialysis. Repeated-measures analysis of variance (ANOVA) with Tukey corrections revealed statistically significant decreases in serum β2 microglobulin over the 12-month follow-up ($p = 0.006$). Mean values of β2MG (mean ± standard deviation) at 0, 3, 6, and 12 months were 36.7 ± 6.7 mg/L, 33.4 ± 6.1 mg/L, 32.9 ± 4.5 mg/L and 33.3 ± 5.3 mg/L, respectively

Changes in Δβ2MG after the initiation of PD + HD combination therapy over 12 months are shown in Fig. 3. Mean values of Δβ2MG at 3, 6, and 12 months were − 3.3 ± 4.3 mg/L, − 3.8 ± 4.0 mg/L, and − 3.4 ± 4.6 mg/L, respectively. Nine patients (82%) experienced a decrease in β2MG throughout the 12-month observation period.

The percentage of patients with β2MG values less than 30 mg/L after the initiation of PD + HD combination therapy over the 12-month period is shown in Fig. 4. Only 27–36% of all patients achieved the target β2MG value of less than 30 mg/L at different points during the observation period: 4 cases (36%) at 3 months, 3 cases (27%) at 6 months, and 3 cases (27%) at 12 months. Cochran's Q test did not show significant differences in the percentages of such patients in each group for any period ($p = 0.717$).

No statistically significant difference was observed in the characteristics, including BMI, dialysis history, and urine volume, renal Kt/V and renal CCr between β2MG level of < 30 mg/L-achievement group and the non-achievement group. BMI, dialysis history, and urine volume, renal Kt/V, and renal CCr in the achievement group at 12 months were 26.9 ± 5.3 kg/m^2 (BMI), 3.5 ± 0.9 years (dialysis history), 0 mL/day (urine volume), 0.0 (renal Kt/V), and 0.0 (renal CCr), respectively.

In this study, we changed the dialyzer from I-a to II-a in three patients during the study period to increase the removal efficiency of β2MG. As the time of the dialyzer was changed, β2MG values of the three patients were 34.7, 44.4, and 29.2 mg/dL, respectively. None of these three patients achieved β2MG levels less than 30 mg/dL at 12 months (38.9, 39.5 and 32.9 md/dL). Also, no correlation was found between Δβ2MG and dialyzer type.

Factors that contribute to the decrease in β2 microglobulin

Next, we analyzed the correlation between Δβ2MG and related factors, including patient background (age, BMI, vintage of PD therapy), laboratory data (hemoglobin, albumin, blood urea nitrogen, creatinine, C reactive protein, baseline value of β2MG), dialysis-related factors (total PD fluid volume per day, weekly Kt/V of PD, blood

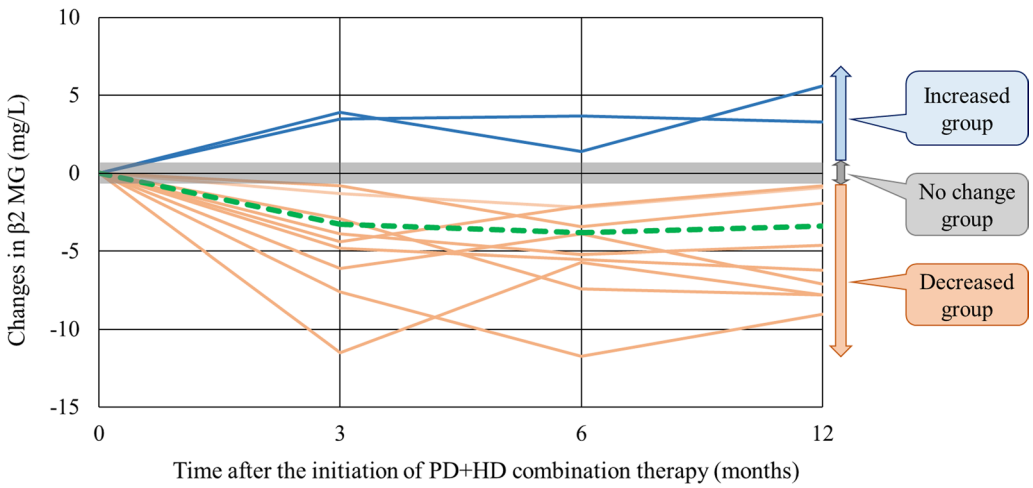

Fig. 3 Changes in β2 microglobulin (Δβ2MG) after the initiation of PD + HD combination therapy over 12 months. *PD* peritoneal dialysis, *HD* hemodialysis. We divided the patients into three groups based on changes in β2 microglobulin: increased group, no change group, decreased group. Δβ2MG ranged from − 0.789 mg/L to 0.789 mg/L in the no change group, defined based on the data from 10 stable HD patients. Mean values of Δβ2MG (mean ± standard deviation) at 3, 6, and 12 months were − 3.3 ± 4.3 mg/L, − 3.8 ± 4.0 mg/L, and − 3.4 ± 4.6 mg/L, respectively

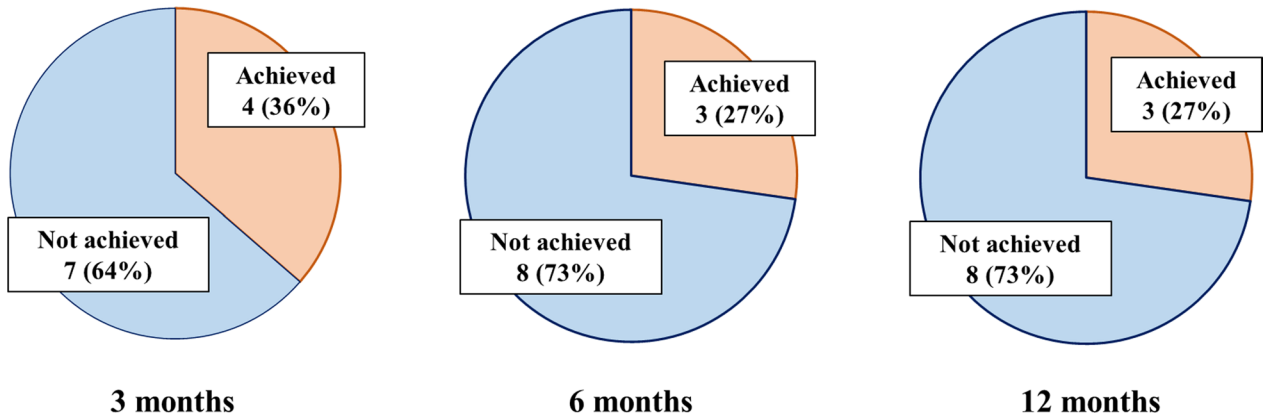

Fig. 4 Percentage of patients with β2 microglobulin values less than 30 mg/L after the initiation of PD + HD combination therapy over 12 months. The number of patients whose β2 microglobulin value was less than 30 was approximately 30% throughout the observation period. Cochran's Q test did not show significant differences in the percentages of patients in each group in all the study periods ($p = 0.717$)

flow rate of HD session, Kt/V of HD), and residual renal function (urine volume, renal creatinine clearance, renal Kt/V) (Table 2). On univariate analysis, serum albumin levels, blood flow rates of HD, residual renal function, and baseline β2MG were associated with a decrease in serum β2MG levels. Albumin and urine output were suggested to be independent influencing factors of Δβ2MG in multivariate analysis. Serum albumin at 3 and 12 months correlated significantly with Δβ2MG ($\beta = -0.990$, $p = 0.032$ at 3 months, $\beta = -0.551$, $p = 0.033$ at 12 months). Urine volume at 12 months correlated significantly with Δβ2MG ($\beta = 0.507$, $p = 0.019$). On the other hand, no significant difference was observed in multivariate analysis for baseline β2MG and blood flow rates, which showed significant difference in univariate analysis.

Discussion

Studies examining how much serum β2MG levels improve with combination PD + HD therapy, and which factors contribute to the improvement in β2MG levels, have been limited.

The present study revealed that the combination therapy of PD and once-weekly HD statistically significantly reduced serum β2MG levels, and the effect was maintained for 12 months. However, although statistically significant, the effect is clinically limited (Δβ2MG = −3.4 mg/L/12 months), with only 27–36% of patients showing β2MG values less than 30 mg/L after the initiation of PD + HD combination therapy. A previous study showed similar results. In that study, serum β2MG levels were not decreased even after the introduction of combination therapy [18]. Additionally, serum β2MG levels were not significantly reduced with both short-term and long-term combination therapy in that study, with levels of 31.9 ± 6.5 mg/L at 0 months, 31.7 ± 6.9 ($p = 0.8452$) at 6 months, and 30.3 ± 6.3 ($p = 0.1247$) at 12 months.

Although Japanese guidelines for PD recommend that the target serum β2MG level for combination therapy should be below 30 mg/L, introduction of combination therapy failed to achieve this target level in our patients. One of the reasons for the limited decrease in serum β2MG levels was the decline in residual renal function during the course of the study, which is a major elimination route of β2MG in PD patients. Another factor was probably an inadequate HD prescription, e.g., the choice of dialysis membrane, setting of blood flow rate, and time on HD after the combination therapy.

In terms of the factors contributing to the reduction of serum β2MG are serum albumin levels, blood flow during HD sessions, residual renal function (urine volume, renal creatinine clearance, renal Kt/V), and baseline β2MG levels. In this study, β2MG levels were significantly lower at 3 and 12 months in patients with higher albumin levels ($\beta = -0.990$, $p = 0.032$ at 3 months, $\beta = -0.551$, $p = 0.033$ at 12 months). Our treatment protocol is probably one of the reasons for this phenomenon. At our hospital, we replace the dialysis membrane to increase the efficiency of dialysis. A serum albumin level 3.4 g/dL or more is considered as a replacement requirement of dialyzer type. When serum albumin is less than 3.4 g/dL, we don't change the dialysis membrane in order to minimize the risk of albumin loss by high-efficiency dialysis. Hence, it is likely that the high-efficiency dialyzer was positively selected in cases with high albumin levels, resulting in greater clearance of β2MG and a higher Δβ2MG in these patients. Blood flow rate in HD session is an important factor for determining Kt/V and the clearance of low molecular solutes, such as urea. The

Table 2 Factors influencing Δβ2MG

	Univariate analysis ($n=11$)			Multivariate analysis ($n=11$)		
	Correlation coefficient	**95% CI**	***p***	***β***	**95% CI**	***p***
Δβ2MG (0–3 months)						
Age	0.155	(− 0.49 to 0.6907)	0.650			
Body mass index*	− 0.073	(− 0.645 to 0.551)	0.830			
Vintage of PD therapy	− 0.005	(− 0.603 to 0.5967)	0.989			
Hemoglobin*	− 0.162	(− 0.694 to 0.485)	0.635			
Serum albumin*	**− 0.656**	(− 0.901 to − 0.093)	**0.028**	**− 0.990**	**(− 21.016 to − 1.425)**	**0.032**
Blood urea nitrogen*	0.502	(− 0.14 to 0.8469)	0.115			
Creatinine*	− 0.073	(− 0.645 to 0.551)	0.831			
C-reactive protein*	0.174	(− 0.476 to 0.7007)	0.609			
Baseline beta 2 microglobulin	− 0.456	(− 0.829 to 0.1981)	0.159	0.273	(− 0.322 to 0.674)	0.406
Total PD fluid volume*	− 0.089	(− 0.654 to 0.5397)	0.794			
Weekly Kt/V of PD	0.138	(− 0.504 to 0.6815)	0.686			
Blood flow rate of HD session*	− 0.399	(− 0.806 to 0.2641)	0.308	0.301	(− 0.062 to 0.173)	0.279
Kt/V of HD*	− 0.54	(− 0.861 to 0.0886)	0.087			
Renal Kt/V	**0.604**	**(2.231 to 1170.269)**	**0.049**			
Urine volume	**0.623**	**(0.002 to 0.056)**	**0.041**	0.960	(− 0.003 to 0.091)	0.059
Renal CCr	**0.658**	**(0.129 to 1.755)**	**0.028**	− 0.293	(− 1.920 to 1.080)	0.504
Δβ2MG (0–6 months)						
Age	0.221	(− 0.475 to 0.7467)	0.514			
Body mass index*	− 0.489	(− 0.855 to 0.2032)	0.126			
Vintage of PD therapy	0.1	(− 0.565 to 0.6864)	0.756			
Hemoglobin*	0.104	(− 0.562 to 0.6885)	0.761			
Serum albumin*	− 0.36	(− 0.807 to 0.3487)	0.277	− 0.155	(− 8.021 to 4.246)	0.465
Blood urea nitrogen*	− 0.067	(− 0.668 to 0.5874)	0.845			
Creatinine*	− 0.332	(− 0.795 to 0.3763)	0.318			
C-reactive protein*	− 0.298	(− 0.781 to 0.4082)	0.377			
Baseline beta 2 microglobulin	**− 0.764**	(− 0.941 to − 0.259)	**0.006**	− 0.659	(− 0.851 to 0.076)	0.084
Total PD fluid volume*	0	(− 0.63 to 0.6296)				
Weekly Kt/V of PD	0.037	(− 0.607 to 0.6515)	0.914			
Blood flow rate of HD session*	**− 0.609**	(− 0.895 to 0.0335)	**0.047**	0.054	(− 0.096 to 0.110)	0.873
Kt/V of HD*	− 0.487	(− 0.855 to 0.2057)	0.129			
Renal Kt/V*	0.452	(− 141.589 to 722.894)	0.163			
Urine volume*	0.587	(− 0.001 to 0.040)	0.058	0.995	(− 0.007 to 0.074)	0.084
Renal CCr*	0.437	(− 0.315 to 1.451)	0.179	− 0.621	(− 2.403 to 0.788)	0.250
Δβ2MG (0–12 months)						
Age	0.093	(− 0.57 to 0.6827)	0.785			
Body mass index*	− 0.324	(− 0.792 to 0.384)	0.332			
Vintage of PD therapy	− 0.017	(− 0.64 to 0.6193)	0.960			
Hemoglobin*	− 0.093	(− 0.683 to 0.57)	0.786			
Serum albumin*	**− 0.746**	(− 0.936 to − 0.219)	**0.008**	**− 0.551**	**(− 16.559 to − 0.983)**	**0.033**
Blood urea nitrogen*	0.443	(− 0.259 to 0.8387)	0.173			
Creatinine*	− 0.267	(− 0.768 to 0.4359)	0.428			
C-reactive protein*	− 0.276	(− 0.772 to 0.428)	0.411			
Baseline beta 2 microglobulin	**− 0.629**	(− 0.902 to 0.001)	**0.038**	− 0.181	(− 0.685 to 0.438)	0.609
Total PD fluid volume*	0.062	(− 0.591 to 0.6656)	0.856			
Weekly Kt/V of PD	0.099	(− 0.566 to 0.6859)	0.773			
Blood flow rate of HD session*	− 0.336	(− 0.797 to 0.3724)	0.313	− 0.076	(− 0.136 to 0.109)	0.799

Table 2 (continued)

	Univariate analysis ($n=11$)			Multivariate analysis ($n=11$)		
	Correlation coefficient	**95% CI**	***p***	***β***	**95% CI**	***p***
Kt/V of HD*	−0.09	(−0.681 to 0.572)	0.792			
Renal Kt/V*	**0.616**	**(17.093 to 970.907)**	**0.044**			
Urine volume*	**0.616**	**(0.001 to 0.049)**	**0.044**	**0.507**	**(0.005 to 0.036)**	**0.019**
Renal CCr*	**0.616**	**(0.043 to 2.458)**	**0.044**	–	–	–

p-values less than 0.05 are indicated in bold

Correlation coefficient refers to Pearson's correlation coefficient

PD peritoneal dialysis, *HD* hemodialysis

*Compared with data at each time point (3, 6, and 12 months). Multivariable model adjusted for serum albumin, baseline beta 2 microglobulin, and blood flow rate of HD session

relationship between blood flow rate and β2MG reduction has been demonstrated by Leclerc et al. [19]. They showed that the reduction ratio of β2MG slightly but significantly increased from 0.40 ± 0.07 to 0.45 ± 0.06 and 0.48 ± 0.06 when the blood flow rate was increased (300, 350 and 450 mL/min) [20]. Accordingly, our data and this previous report indicating that increasing the blood flow rate is a useful method for increasing the clearance of β2MG suggest that achieving highly efficient HD with a high blood flow rate is recommended.

Interestingly, serum β2MG at 6 and 12 months tended to decrease more in cases with high baseline β2MG (6 months: $r=-0.764$, $p=0.006$; 12 months: $r=-0.629$, $p=0.038$). This is probably a reflection of the appropriate adjustment of the dialysis prescription when β2MG values at baseline were high. The fact that there was a correlation between baseline β2MG levels and blood flow in HD sessions at 6 and 12 months (6 months: $r=0.804$, $p=0.003$, 12 months: $r=0.799$, $p=0.003$) might well support this notion.

In this study, multivariate analysis revealed urine volume correlated significantly with Δβ2MG ($\beta=0.507$, $p=0.019$) at 12 months. Preservation of residual renal function is associated with better long-term survival in dialysis patients and increased serum β2MG clearance and lower serum β2MG [20, 21]. Our data confirmed that the reduction in β2MG was greater in patients with higher residual renal function. Therefore, even in patients with PD + HD combination therapy, preservation of residual renal function is suggested to be important.

Furthermore, we cannot detect the significant difference in background between β2MG increased group and decreased group (Table 3). Also, no statistically significant difference in body weight, serum blood urea nitrogen, serum albumin, hemoglobin, and blood pressure were observed between 0 and 12 months (Table 4). Only serum creatine was significantly lower at 12 months compared to 0 months ($p=0.041$).

Table 3 Comparison of patient backgrounds between the beta 2 microglobulin increase group and the decrease group

	Increased group ($n=2$)	**Decreased group ($n=9$)**	***P* value**
Age	50.0 ± 4	57.8 ± 13.8	0.436
Body mass index	23.1 ± 0.9	25.9 ± 4.6	0.582
Vintage of PD therapy	2.5 ± 1.9	3.6 ± 1.0	0.582
Hemoglobin	10.9 ± 0.4	11.2 ± 1.3	1.000
Serum albumin	3.1 ± 0.1	3.3 ± 0.3	0.436
Blood urea nitrogen	73.8 ± 19.3	47.6 ± 13.4	0.145
Creatinine	13.4 ± 2.5	14.0 ± 4.4	1.000
C-reactive protein	0.1 ± 0.1	0.4 ± 0.7	0.909
Baseline beta 2 microglobulin	32.9 ± 0.4	37.5 ± 7.2	1.000
Total PD fluid volume	8.7 ± 0.8	9.8 ± 2.2	0.582
Weekly Kt/V of PD	1.5 ± 0	1.7 ± 0.3	0.727
Blood flow rate of HD session	235 ± 15	250 ± 27.5	0.582
Kt/V of HD	1.4 ± 0.3	1.5 ± 0.3	1.000
Renal Kt/V	0.01 ± 0.01	0	0.327
Urine volume	200 ± 200	0	0.327
Renal CCr	4.0 ± 4.0	0	0.327

Table 4 Comparison of patients' the data between 0 and 12 months

	0 months	**12 months**	***P* value**
Blood pressure (mmHg) Systolic	140 ± 24	142 ± 20	0.789
Blood pressure (mmHg) Diastolic	80.6 ± 11.2	79.7 ± 13.2	0.863
Body weight (kg)	69.8 ± 10.4	71.4 ± 12.6	0.328
Serum blood urea nitrogen (mg/dL)	58.0 ± 22.5	52.4 ± 17.8	0.248
Serum creatinine (mg/dL)	15.1 ± 4.6	13.9 ± 4.1	0.041
Serum albumin (g/dL)	3.1 ± 0.4	3.2 ± 0.3	0.235
Hemoglobin (g/dL)	10.0 ± 1.5	11.2 ± 1.2	0.013

Hemodialysis prescriptions need to be adjusted to reduce serum β2MG levels in combination therapy with PD and HD. Despite this, however, we observed

that serum β2MG levels did not satisfactorily decrease in our patients. When looking at the changes in β2MG levels of eight patients (age 67.0 ± 7.0 years, PD duration 3.7 ± 1.8 years) who had transferred from PD alone to regular HD (three times weekly using a high performance membrane, 4–5 h each session with QB 200–250 mL/min) at our institution, there were no significant changes in β2MG levels: 30.5 ± 2.2 mg/L at 0 months and 31.1 ± 3.8 at 12 months ($p = 0.697$) (unpublished data) following the switch to HD. Taking these data together, it seems that there is a limitation in respect to the decreasing serum β2MG levels by combination therapy of PD plus once a week HD(4 h).

On the other hand, several previous studies have reported that hemodiafiltration (HDF), especially online HDF, can effectively reduce serum β2MG [22, 23]. Lin CL et al. reported that long term HDF further reduced pre-dialysis serum β2MG levels compared to high flux HD [22]. This suggests that online HDF might be more beneficial than HD using high-flux membranes for β2MG management in PD + HD combination therapy. This needs to be studied in future.

The limitations of this study are the: (1) single-center retrospective design, (2) small number of participants, (3) short observation period, and 4) insufficient bias adjustment for related factors that might contribute to the decrease in β2MG.

Conclusion

Combination therapy of PD and HD might reduce serum β2MG levels, but with marginal efficacy. Our preliminary data indicate that the combination therapy of PD and once weekly HD is not sufficient to significantly decrease serum β2MG levels. Additional HD prescriptions, such as increase in blood flow rate and hemodiafiltration, need to be tested in order to improve β2MG levels in these patients.

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Author contributions
MN presented the idea of the study. All authors participated in the planning of the study and discussed the results. SM, SN, and YT collected the data, and YT and KW analyzed the data. SM, KW, and MN finalized the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
Not applicable.

Declarations

Ethics approval and consent to participate
This study was approved by the research ethics committee of St Luke's International Hospital (Approval Number 21-R156).

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Clinical Engineering Center, St Luke's International Hospital, Tokyo, Japan. [2]Division of Kidney Center, St Luke's International Hospital, 9-1 Akashi-Cho, Chuo-Ku, Tokyo 104-8560, Japan.

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