



## Restless legs syndrome effectively treated with constant-pressure predilution online hemodiafiltration

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### Abstract

**Background** We encountered a case of unstable predilution online HDF due to elevated transmembrane pressure (TMP) when performing constant-speed predilution online hemodiafiltration (HDF) as treatment for restless legs syndrome (RLS) in a dialysis patient. We report the effectiveness of incorporating a newly developed constant-pressure predilution online HDF system as a preventive measure against unstable online HDF and frequent adjustment of settings when treating dialysis patients with RLS.

**Case presentation** A 55-year-old man had suffered from RLS and been undergoing constant-speed online HDF with 45 L target predilution and an ABH-21P hemodiafilter. The symptoms of RLS rated 10 on the International Restless Legs Syndrome Rating Scale (IRLS). The  $\alpha_1$ -microglobulin ( $\alpha_1$ -MG) removal rate was only 27.8%, so the hemodiafilter was subsequently replaced with a PEPA hemodiafilter. However, episodes of elevated TMP exceeding 250 mmHg occurred frequently after the replacement and were managed by reducing dialysate flow rate. Therefore, we incorporated a constant-pressure predilution online HDF that maintains TMP below 200 mmHg. The amount of replacement was maintained at approximately  $43.5 \pm 6.98$  L and the  $\alpha_1$ -MG removal rate was 39.5%, with no need to manually reduce the flow rate. The Alb leakage in dialysate waste was 7.9 g. The patient has maintained an IRLS rating of 0 with no RLS symptoms for the past 4 years.

**Conclusions** Using the constant-pressure mode enabled achieved the clinical endpoint, namely, resolution of RLS with no need to manually reduce the flow rate.

**Keywords** Online HDF · Restless legs syndrome · Constant-pressure predilution

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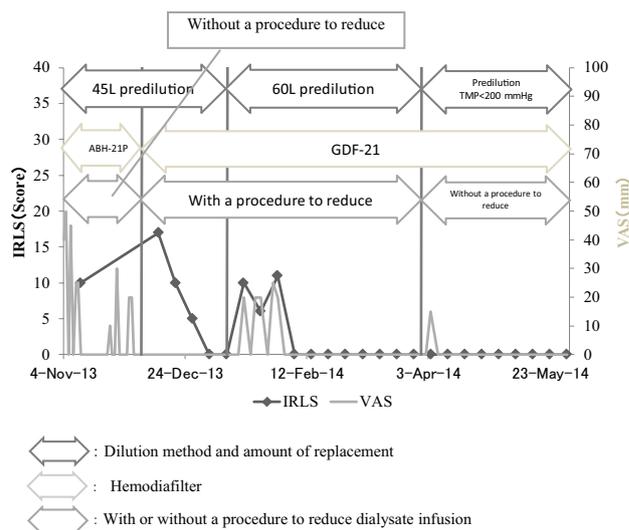
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### Background

Considerable improvement in the symptoms of restless legs syndrome (RLS) is one of the clinical benefits of online hemodiafiltration (HDF), and achieving this effect essentially requires the removal of molecules with molecular weights similar to that of  $\alpha_1$ -microglobulin ( $\alpha_1$ -MG) [1, 2]. We encountered a case of unstable predilution online HDF due to elevated transmembrane pressure (TMP) when performing constant-speed predilution online HDF as treatment for RLS in a dialysis patient, necessitating frequent adjustments of console settings such as the amount of dialysate and TMP. Here, we report the effectiveness of incorporating a newly developed constant-pressure predilution online HDF system as a preventive measure against unstable online HDF and frequent adjustment of settings when treating dialysis patients with RLS.

### Case presentation

A 55-year-old man with diabetes had been undergoing hemodialysis with the GC-110N console machine (Japan Medical Supply Co., Ltd., Hiroshima, Japan) since January 2012. RLS was diagnosed in June 2013 and treatment was initiated with constant-speed online HDF with 45 L target predilution and an ABH-21P hemodiafilter (Asahi-Kasei Medical Co. Ltd., Tokyo, Japan). The patient experienced some relief for 4 months, but the symptoms of RLS returned in November 2013 and rated 10 on the International Restless Legs Syndrome Rating Scale (IRLS) (Fig. 1). The  $\alpha_1$ -MG removal rate was only 27.8% (Table 1), so the hemodiafilter was subsequently replaced with a PEPA hemodiafilter (GDF-21, Nikkiso Co. Ltd., Ishikawa, Japan) in December 2013. However, episodes of elevated TMP exceeding 250 mmHg occurred after the replacement and were managed by reducing dialysate flow rate. This resulted in the replacement of  $40.7 \pm 4.50$  L, with removal of 30.4% of  $\alpha_1$ -MG. The total amount of albumin (Alb) leakage in dialysate waste was 5.3 g. The symptoms of RLS were not improved.



**Fig. 1** The progress of IRLS and VAS when online HDF was performed in each condition. The IRLS and VAS of symptoms decreased using GDF-21. After the substitution method was changed from the constant volume to the TMP controlled one, these scores were also kept in good levels

In January 2014, we attempted constant-speed online HDF with 60 L target predilution instead of 45 L, achieving a replacement volume of  $44.1 \pm 5.0$  L, an 8.4% increase from the previous amount. In addition, the  $\alpha_1$ -MG removal rate increased to 42.8% and Alb leakage was 12.1 g. The IRLS rating reduced to 0, indicating remarkable improvement of symptoms. However, elevated TMP was noted frequently during dialysis sessions, setting off alarms and requiring the staff to decrease TMP by reducing dialysate flow rate. Due to cumbersome dialysis treatment, the actual amount of fluid replaced was less than the original target amount. Therefore, we incorporated a newly developed fully automated console GC-110N with a built-in automated dialysate infusion system (Japan Medical Supply Co., Ltd.) to establish a constant-pressure predilution online HDF that maintains TMP below 200 mmHg. The automated dialysate infusion system regulates TMP on dialysis membranes by automatically adjusting the flow rate based on setup time. Thus, the

**Table 1** Amount of replacement, removal rate, and leakage amount under each condition

	ABH-21P 45 L predilution	GDF-21 45 L predilution	GDF-21 60 L predilution	GDF-21 Predilution TMP < 200 mmHg
Amount of replacement (L)	$44.3 \pm 0.632$	$40.8 \pm 4.50$	$44.1 \pm 5.00$	$43.5 \pm 6.98$
Removal rate of urea (%)	58.5	56.2	56.2	56.5
Removal rate of Cr (%)	50.9	46.5	45.6	45.6
Removal rate of $\beta_2$ -MG (%)	75.2	71.2	71.6	68.8
Removal rate of $\alpha_1$ -MG (%)	27.8	30.4	42.8	39.5
Leakage amount of albumin (g)	2.5	5.3	12.1	7.9

amount of replacement was maintained at approximately  $43.5 \pm 6.98$  L (6.9% increase) and the  $\alpha_1$ -MG removal rate was 39.5%, with no need to manually reduce the flow rate. The Alb leakage in dialysate waste was 7.9 g, which was less than the amount observed during the 60 L constant-speed infusion mode. The patient has maintained an IRLS rating of 0 with no RLS symptoms for the past 4 years.

## Conclusions and discussion

Several studies reported that the prevalence of RLS in the general population was between 5.5 and 15% [3–6]. In addition, hemodialysis patients have shown that the prevalence of RLS was between 12.2 and 23% [7–9]. Sakurai K reported that the 7 hemodialysis cases with RLS showed the alleviation by 35% removal rate of an  $\alpha_1$ -MG and demonstrated the cure of RLS by an  $\alpha_1$ -MG removal rate of 38% or more [1]. In the present case, RLS recurred when the  $\alpha_1$ -MG removal rate was 27.8% with constant-speed online HDF and 45 L target predilution. RLS symptoms disappeared when the rate increased to 42.8% with the use of the 60 L target predilution, but the alarm was set off frequently, requiring adjustments of console settings, and thus making treatment cumbersome. When we instituted constant-pressure predilution online HDF with TMP set at < 200 mmHg, 39.5%  $\alpha_1$ -MG removal was achieved without the need for staff to manually adjust the console settings and the RLS symptoms also disappeared (Table 1). According to Sakurai K [1], uremic toxins whose molecular weights are greater than that of  $\beta_2$ -MG may be involved in the development of clinical manifestations such as insomnia, pruritus, irritability, RLS, anemia, and osteoarticular pain. However, the reason for removing  $\alpha_1$ -MG is not because  $\alpha_1$ -MG itself is toxic, but because  $\alpha_1$ -MG has a molecular weight of 33 kDa and should be used as a biomarker for evaluation of clinical outcomes of HDF. These indicate that the achievement of  $\alpha_1$ -MG removal rate of 38% or more under online HDF treatment led to remove uremic toxin around a molecular weight of 33 kDa and then the disappearance of the symptoms of RLS. Online HDF with high TMP settings is known to induce excessive leakage of Alb [10]. Using the constant-pressure mode enabled reduced Alb leakage compared with the 60 L target predilution (Table 1). In this case, the constant-speed online HDF required cumbersome treatment by the staff and 12.1 g albumin leakage to obtain the reduction of the RLS symptoms. On the other hand, in the constant-pressure mode, even if achieving the reduction of RLS symptoms, it was unnecessary for the staff to be required cumbersome treatment,

and the albumin leakage could be kept as low as 7.9 g. The constant-pressure mode is the most useful treatment mode that can obtain the clinical effect of the reduction of RLS symptoms and reduce the strain of medical staff.

The GC-110N console enables predilution online HDF at constant pressure or speed and also has a postdilution mode. Further study is needed to investigate the appropriate use of each mode, but the availability of this console is beneficial for dialysis patients by offering more treatment options.

## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest

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