Research Article

Influence of Hemofiltration on Intradialytic Plasma Volume Decrease

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Key Words

Dialysis • Hemofiltration • Hypotension • Plasma volume

Abstracts

Background/Aims: Compared with hemodialysis (HD), hemodiafiltration (HDF) reduces the frequency of episodes of intradialytic hypotension. Intradialytic plasma volume decrease (IPVD) induced by ultrafiltration is a leading cause of the episodes, and hemofiltration might have a preventive effect on IPVD. This study examined whether online HDF (ol-HDF) prevented IPVD compared with HD. **Methods:** Online HDF of pre-dilution mode (pre-ol-HDF) and post-dilution mode (post-ol-HDF) and HD were performed in 22 patients on maintenance dialysis. In each session, IPVD was calculated by using an intradialytic change in hematocrit, and IPVD in pre-ol-HDF and post-ol-HDF was compared with that in HD in a crossover manner. **Results:** While the ratios of intradialytic body weight loss to post-dialysis BW (IBWL/BW) in ol-HDF were generally smaller than those in HD, the levels of IPVD and IPVD/IBWL/BW were generally larger than those in HD; the IPVD levels were 0.108 ± 0.058 , 0.113 ± 0.053 , and 0.101 ± 0.057 ($P = 0.67$), and those of IPVD/IWL/BW were 2.21 ± 0.97 , 2.32 ± 0.91 , and 1.98 ± 1.14 ($P = 0.21$) in pre-ol-HDF, post-ol-HDF, and HD, respectively. **Conclusion:** Online mode hemofiltration, in either pre-dilution mode or post-dilution mode, performed in combination with hemodialysis has no preventive effect on IPVD.

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Introduction

Maintenance hemodialysis for end-stage renal disease is generally performed intermittently [1, 2]. During each dialysis session, body weight (BW) gain between dialysis sessions is removed by ultrafiltration. Body fluid removal causes intradialytic plasma volume decrease (IPVD), which is a leading cause of intradialytic hypotension (IDH) [3–5]. Compared with the primary mode of hemodialysis (HD), where only diffusive transport is performed, hemodiafiltration (HDF), a mode of dialysis where convective transport is used

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in combination with diffusive transport [6, 7], reduced the episodes of IDH [8, 9]. Thus, HDF is expected to prevent IPVD. Previously, we found that online HDF (ol-HDF) in either pre-dilution mode (pre-ol-HDF) or post-dilution mode (post-ol-HDF) did not prevent IPVD compared with HD in a retrospective analysis of dialysis sessions [10]. To confirm these findings, we compared the levels of IPVD in pre-ol-HDF and post-ol-HDF with that in HD in a crossover study.

Materials and Methods

Cases and dialysis conditions

We carried out a crossover study involving 22 adult patients (age ≥ 18 years) who were on maintenance dialysis treatment (2–3 sessions per week, 3.5–4 h per session) with either pre-ol-HDF and post-ol-HDF. In each patient, one-off sessions of HD and a different mode of ol-HDF from the mode used in maintenance dialysis were performed. For instance, in a patient on maintenance dialysis with pre-ol-HDF, one-off sessions of HD and post-ol-HDF were performed. In the one-off sessions, the same type of hemodiafilter was used at the same blood flow rate, at the same dialysate temperature, and for the same dialysis session time as in maintenance dialysis for each patient. Blood flow rate and dialysis session time were individually prescribed to achieve a dialyzer clearance of urea to volume of distribution area (Kt/V) of >1.2 in maintenance dialysis [1]. Dry weight (DW) was individually prescribed to maintain cardiothoracic ratio $<52\%$ without pulmonary congestion on chest radiography. Ultrafiltration rate was adjusted in each session to avoid symptomatic IDH.

All sessions were performed with bicarbonate dialysate (sodium 140, potassium 2.0, calcium 1.5, magnesium 1.0, chloride 111, bicarbonate 35, and glucose 8.3 mmol/L) at a dialysate flow rate of 500 mL/min as the first session for the week. Priming and washback procedures were performed using dialysate. For pre-ol-HDF and post-ol-HDF, substitution fluid was replaced at constant rates of 10 and 2.5 L/h, respectively, which are generally used in Japan [2]. This study was approved by the hospital ethics committee and registered on the UMIN Clinical Trials Registry (UMIN000028422). All patients provided informed consent.

Laboratory measures and definitions

Blood sampling was performed just after venipuncture at the session-start (pre-dialysis) and just before washback at the session-end (post-dialysis). Patients were placed lying in a supine position in bed for >20 min before the pre-dialysis sampling, and were not allowed to eat or drink until the post-dialysis sampling [11, 12]. Hematocrit (Ht), albumin (Alb), and sodium (Na) concentrations of the samples were measured. IPVD was calculated as $IPVD = 1 - (\text{pre-dialysis Ht})/(\text{post-dialysis Ht})$ [13]. Pre-dialysis BW gain and post-dialysis BW relative to DW (BW/DW) were used to indicate the fluid excess in each session. Intradialytic BW loss (IBWL) and its ratio to post-dialysis BW (IBWL/BW) were used to indicate the fluid removal during each session.

Statistical analysis

Continuous variables were expressed as the mean $\pm$ standard deviation (SD), and were analyzed by using one-way analysis of variance. All statistical analyses were performed using the SPSS software package (Dr. SPSS II, IBM Corp., Armonk, NY). Probability values of $P < 0.01$ were considered statistically significant.

Table 1. Characteristics of cases (n = 22)

Characteristic	Mean $\pm$ SD or %
Age (years)	66 $\pm$ 10
Sex (% female)	14
Dialysis length (months)	78 $\pm$ 47
Diabetes mellitus (%)	41
Antihypertensives (%)	
Angiotensin blockers	32
Calcium channel blockers	32
Beta-blockers	13
Alpha-blockers	0
Diuretics	41
Blood flow rate (mL/min)	229 $\pm$ 22

Results

Table 1 shows the summary of patient characteristics. Age ranged from 45 to 83 years, and dialysis history ranged from 37 to 236 months. Three patients were female, and 16 patients were receiving treatment for hypertension. Blood flow rates ranged from 200 to 280 mL/min with a median of 220 mL/min.

Pre-dialysis and post-dialysis measurements and intradialytic body fluid status indicators in pre-ol-HDF and post-ol-HDF were compared with those in HD (Table 2). No intravenous fluids were administered in any of the sessions. None of the examined measurements and indicators in ol-HDF differed significantly from those in HD. While BW gain and IBWL/BW in ol-HDF were generally smaller than those in HD, IPVD was generally larger than that in HD. Accordingly, IPVD/IWL/BW in ol-HDF was generally higher than that in HD. IPVD and IPVD/IWL/BW were similar between ol-HDF with similar levels of BW gain and IBWL/BW between them.

Discussion

In this study, IPVD and IPVD/IWL/BW in pre-ol-HDF and post-ol-HDF were generally larger than those in HD. These findings suggested that ol-HDF either in pre-dilution mode or post-dilution mode did not prevent IPVD compared with HD.

In previous studies, IPVD greater than the limit for each patient induced IDH [3–5], and HDF reduced the episodes of IDH compared with HD [8, 9]. However, in our present and previous studies, ol-HDF did not prevent IPVD compared with HD [10]. Therefore, factors other than IPVD prevention could have contributed to the reported IDH reduction by HDF. A thermal effect, namely substitution-fluid-induced lowering of core temperature, could be one such factor [14, 15]. Although we selected ol-HDF where the substitution fluid from dialysate was warmed to body temperature to eliminate a possible thermal effect, ol-HDF might still have provided some thermal effect [7]. Factors that increase blood pressure between dialysis sessions, such as the interdialytic increase in vascular tone and facilitation of the interdialytic vascular

Table 2. Comparison between dialysis modes. Data are shown as mean $\pm$ SD. Alb, serum albumin concentration; BW, body weight; DBP, diastolic blood pressure; DW, dry weight; HD, hemodialysis; Ht, hematocrit; IBWL, intradialytic BW loss; IBWL/BW, IBWL relative to post-dialysis BW; IPVD, intradialytic plasma volume decrease; IPVD/IBWL/BW, IPVC divided by IBWL/BW; Na, serum sodium concentration; pre-ol-HDF, pre-dilution online hemodiafiltration; post-ol-HDF, post-dilution online hemodiafiltration; SBP, systolic blood pressure

Measurement	HD	pre-ol-HDF	post-ol-HDF	P
Pre-dialysis				
Ht (%)	32.0 $\pm$ 3.9	33.0 $\pm$ 3.4	32.7 $\pm$ 3.0	0.42
Alb (g/dL)	3.4 $\pm$ 0.3	3.5 $\pm$ 0.3	3.6 $\pm$ 0.3	0.09
Na (mmol/L)	139.6 $\pm$ 3.0	139.9 $\pm$ 3.1	140.4 $\pm$ 2.7	0.29
SBP (mmHg)	159 $\pm$ 23	160 $\pm$ 23	157 $\pm$ 26	0.73
DBP (mmHg)	85 $\pm$ 15	86 $\pm$ 15	84 $\pm$ 14	0.66
BW gain (kg)	3.2 $\pm$ 1.2	2.9 $\pm$ 1.3	3.1 $\pm$ 1.4	0.36
Post-dialysis				
Ht (%)	35.8 $\pm$ 4.9	37.1 $\pm$ 4.4	37.0 $\pm$ 3.9	0.34
Alb (g/dL)	3.8 $\pm$ 0.5	4.0 $\pm$ 0.3	3.9 $\pm$ 0.4	0.35
Na (mmol/L)	142.3 $\pm$ 1.8	142.2 $\pm$ 1.7	142.3 $\pm$ 1.4	0.96
SBP (mmHg)	147 $\pm$ 27	147 $\pm$ 27	149 $\pm$ 30	0.79
DBP (mmHg)	83 $\pm$ 13	83 $\pm$ 13	79 $\pm$ 14	0.14
BW/DW	1.005 $\pm$ 0.009	1.002 $\pm$ 0.007	1.005 $\pm$ 0.009	0.048
Intradialysis				
IBWL (kg)	2.8 $\pm$ 0.9	2.7 $\pm$ 1.0	2.7 $\pm$ 0.9	0.72
IBWL/BW	0.051 $\pm$ 0.013	0.047 $\pm$ 0.016	0.048 $\pm$ 0.014	0.54
IPVD	0.101 $\pm$ 0.057	0.108 $\pm$ 0.058	0.113 $\pm$ 0.053	0.67
IPVD/IBWL/BW	1.98 $\pm$ 1.14	2.21 $\pm$ 0.97	2.32 $\pm$ 0.91	0.21

refilling from interstitial fluid, might have contributed to the reported reduction in IDH episodes by HDF, since ol-HDF increased pre-dialysis blood pressure compared with HD [9].

While ultrafiltration is the primary determinant of IPVD, other factors could influence IPVD [16–18]. Vascular refilling from interstitial fluid is a major factor, and fluid excess relative to DW may facilitate refilling, and thus decrease IPVD. In the present study, BW gain and BW/DW in HD were generally larger than in ol-HDF, which might have facilitated the refilling during HD sessions and so underestimated IPVD in HD. However, because fluid excess was reported to not influence refilling [19], the possible difference in fluid excess between the modes would not have significantly influenced IPVD.

Intradialytic albumin loss and intradialytic Na change may also influence IPVD by affecting inward oncotic and osmotic forces [17, 20]; intradialytic albumin loss will facilitate IPVD by decreasing inward oncotic force, while intradialytic Na gain will prevent IPVD by increasing inward osmotic force. In the present study, intradialytic Na change in ol-HDF did not differ from the change in HD. However, IPVD could be underestimated in ol-HDF because albumin loss is generally larger in HDF than in HD irrespective of the mode [18]. Nevertheless, recent data suggest that inward oncotic force has little effect on refilling [16]. Therefore, differences in intradialytic albumin loss and intradialytic Na change could not have significantly influenced IPVD in the present study.

Intradialytic erythrocyte loss decreases post-dialysis Ht. Relative post-dialysis Ht decrease leads to IPVD underestimation. Hemoconcentration in dialyzer hollow fibers is a cause of intradialytic erythrocyte loss and is severer in post-ol-HDF compared with HD and pre-ol-HDF, so it follows that post-ol-HDF would have larger intradialytic erythrocyte loss compared with the other modes [6, 7]. Hence, if intradialytic erythrocyte loss had occurred, the findings that IPVD in post-ol-HDF was not smaller than IPVD in HD would have indicated facilitation rather than prevention of IPVD by post-ol-HDF compared with HD.

We could not achieve optimal effectiveness of convective transport in post-ol-HDF [6]; the blood-flow rates generally used in our country are lower than those recommended by the relevant European and American societies [1, 2]. In contrast, we could achieve optimal effectiveness even with low blood-flow rates in pre-ol-HDF; the estimated effective convective rates were >30% of blood-flow even with low blood-flow rates. Because IPVD did not differ between pre-ol-HDF and post-ol-HDF in spite of differences in their effectiveness, this would not have affected the present findings.

The present study has several limitations. Firstly, this report includes a small number of cases in a single center, and may thus be limited by the possibility of selection bias. Secondly, the cases were skewed; for example, few women were included in the study, although this would not have significantly affected the findings. Thirdly, as mentioned earlier, we could not eliminate the potential effect of the difference in weight gain between the dialysis modes. Therefore, future studies with a larger sample size are required to confirm the generalizability of the present findings.

Conclusion

Online mode hemofiltration in combination with hemodialysis has no preventive effect on IPVD, a leading cause of IDH. Therefore, factors other than prevention of IPVD, such as increased vascular tone and enhanced vascular refilling between dialysis sessions would reduce IDH episodes in HDF.

Acknowledgements

MT designed the study, performed the data analysis, and wrote the manuscript. TT, YM, MU, and YO collected the clinical data. All authors read and approved the final manuscript. This study was approved by the Ethics Committee of Shin-Kuki General Hospital.

Disclosure statement

The authors declare no potential conflicts of interest.

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