

## Original Article

## Postdialysis serum sodium changes and systolic blood pressure in patients undergoing online hemodiafiltration and high-flux hemodialysis



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## ABSTRACT

**Background:** Because hemodiafiltration (HDF) involves large amounts of ultra-filtration and substitution fluid infusion, its effects on serum electrolytes may be different from those of hemodialysis (HD). Serum sodium and blood pressures were compared between patients undergoing online HDF and high-flux HD (HFHD).

**Methods:** Thirty-two of 101 patients on HFHD switched voluntarily to online HDF. Their pre- and postdialysis serum measurements were compared with those of the remaining 69 HFHD patients.

**Results:** Online HDF patients had lower pre- and postdialysis systolic blood pressures (SBPs) than HFHD patients (predialysis,  $136 \pm 21$  vs.  $145 \pm 19$  mmHg,  $P < 0.05$ ; postdialysis,  $129 \pm 22$  vs.  $142 \pm 25$  mmHg,  $P < 0.05$ ). Pre- and postdialysis serum sodium concentrations were not significantly different between online HDF and HFHD (predialysis,  $138 \pm 2$  vs.  $137 \pm 3$  mEq/L; postdialysis,  $134 \pm 2$  vs.  $134 \pm 2$  mEq/L). However, the change in serum sodium concentration after dialysis was greater in online HDF than HFHD patients ( $-3.7 \pm 2.2$  vs.  $-2.5 \pm 2.8$  mEq/L,  $P < 0.05$ ). The change in serum sodium concentration was correlated with postdialysis SBP ( $r = 0.304$ ,  $P < 0.005$ ) and pulse pressure ( $r = 0.299$ ,  $P < 0.005$ ). Predialysis SBP ( $r = 0.317$ ,  $P < 0.005$ ) and pulse pressure ( $r = 0.324$ ,  $P = 0.001$ ) were also correlated with the postdialysis serum sodium change.

**Conclusion:** Compared with HFHD, online HDF has a greater serum sodium lowering effect. This might contribute to the ability of online HDF to stabilize both pre- and postdialysis SBP.

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## Introduction

The majority of hemodialysis (HD) patients are hypertensive [1], and increased extracellular fluid volume is an important factor that affects hypertension in this patient population [2].

Thus, controlling body sodium content by reducing sodium intake and/or by increasing sodium output is necessary to reduce hypertension [3]. HD offers sodium removal by the processes of convection (ultrafiltration) and diffusion.

Current maintenance HD procedures include low-flux HD, high-flux HD (HFHD), and online hemodiafiltration (HDF). Online HDF combines the convective clearance of hemofiltration with the diffusive clearance of HD to enhance dialytic removal. Although most centers use HFHD at present, mortality may be improved by the use of high-efficiency postdilution online HDF [4,5].

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We reasoned that because the HDF procedure is accompanied by large amounts of ultrafiltration and substitution fluid infusion, sodium and other electrolyte balances should be affected differently when compared to other HD procedures are performed. In addition, we questioned whether any difference in sodium balance might be associated with changes in blood pressure in HD patients although it is not clear if online HDF affords greater cardiovascular stability than conventional HD [6]. This study was undertaken to compare serum electrolyte profiles and blood pressures between online HDF and HFHD patients.

## Methods

Thirty-two of 101 patients on HFHD switched voluntarily to online HDF in August, 2008. Pre- and postdialysis electrolyte values of patients that remained stable and that adhered to online HDF for 2 years were compared with those of the remaining 69 HFHD patients. The same dialysis machine (Fresenius 5008; Fresenius Medical Care, Bad Homburg, Germany) and membrane (Helixone; Fresenius) were used for the two groups of patients. Blood flow rate ranged from 250 mL/min to 300 mL/min, and dialysate flow rate was 500 mL/min. Dialysate concentrations of sodium, potassium, chloride, and bicarbonate were 138 mEq/L, 2.0 mEq/L, 108 mEq/L, and 33 mEq/L, respectively. In online HDF, the same dialysate was used as the substitution fluid (30 L/session) in the predilution step. Blood pressure was measured in the supine position before HD (predialysis) and after HD (postdialysis) by the cuff-oscillometric method using an automated device (Blood Pressure Monitor, 5008 Therapy System; Fresenius). Pre- and postdialysis blood samples were taken from the arterial limb of the arteriovenous fistula just before the start of dialysis and after slowing blood flow at the end of the dialysis session, respectively. Levels of serum electrolytes were measured using ion-selective electrodes.

Continuous data are described as means  $\pm$  standard deviation. Statistical comparisons between groups were performed using the Mann-Whitney *U* test, and correlations between variables of interest were analyzed by linear regression. Categorical data were analyzed using contingency tables and the  $\chi^2$  test. A *P* value  $< 0.05$  was considered to indicate statistical significance.

## Results

Age of all 101 patients was  $55 \pm 12$  years, and there were no significant differences in age or sex between online HDF and HFHD patients. No significant differences in body weight or body mass index were found between online HDF and HFHD patients. However, the underlying causes of end-stage renal disease were different; more patients in the HFHD group were diabetic (41 vs. 11%,  $P < 0.01$ ), while more patients in the online HDF group had essential hypertension (28 vs. 12%,  $P < 0.05$ ). Duration of dialysis was greater in online HDF patients than in HFHD patients (Table 1).

Dialytic indicators of online HDF and HFHD patients are compared in Table 2. None of the urea kinetic modeling values were significantly different between groups. As expected, however,  $\beta_2$ -microglobulin removal was greater in the online HDF group than in the HFHD group.

Online HDF patients had lower pre- and postdialysis systolic blood pressures (SBPs) than HFHD patients (predialysis,

**Table 1. Demographic features of the patients**

	High-flux HD (n = 69)	Online HDF (n = 32)
Male/female	34/35	21/11
Age (y)	55 $\pm$ 13	55 $\pm$ 10
Body mass index (kg/m <sup>2</sup> )	22.0 $\pm$ 3.6	21.3 $\pm$ 3.0
Underlying disease		
Diabetes mellitus	28	3
Essential hypertension	8	9
Chronic glomerulonephritis	15	7
Others	18	13
Duration of dialysis (mo)*	78 $\pm$ 104	146 $\pm$ 99

\*  $P < 0.01$ , high-flux HD vs. online HDF.

Continuous values are mean  $\pm$  standard deviation. HD, hemodialysis; HDF, hemodiafiltration.

**Table 2. Comparisons of dialytic indicators**

	High-flux HD (n=69)	Online HDF (n=32)
Pre-HD BUN (mg/L)	640 $\pm$ 250	700 $\pm$ 180
Post-HD BUN (mg/L)	180 $\pm$ 80	190 $\pm$ 60
Urea reduction ratio (%)	73 $\pm$ 7	73 $\pm$ 6
Single-pool Kt/V	1.55 $\pm$ 0.29	1.59 $\pm$ 0.27
Pre-HD $\beta_2$ -microglobulin (mg/L)	19.8 $\pm$ 2.5	20.0 $\pm$ 2.3
Post-HD $\beta_2$ -microglobulin (mg/L)*	14.1 $\pm$ 4.1	8.7 $\pm$ 3.1
$\Delta\beta_2$ -microglobulin (%)*	-29.3 $\pm$ 17.5	-51.8 $\pm$ 7.6

\*  $P < 0.01$ , high-flux HD vs. online HDF.  $\Delta\beta_2$ -microglobulin (%) = [(post HD  $\beta_2$ -microglobulin - pre-HD  $\beta_2$ -microglobulin) / pre-HD  $\beta_2$ -microglobulin]  $\times$  100

Continuous values are mean  $\pm$  standard deviation.

BUN, blood urea nitrogen; HD, hemodialysis; HDF, hemodiafiltration.

136  $\pm$  21 vs. 145  $\pm$  19 mmHg,  $P < 0.05$ ; postdialysis, 129  $\pm$  22 vs. 142  $\pm$  25 mmHg,  $P < 0.05$ ), although pre- and postdialysis diastolic blood pressures were not significantly different between the two groups. Adjustments for the duration of dialysis and the presence of diabetes mellitus did not affect the significant differences in pre- and postdialysis SBPs ( $P < 0.05$ ).

Pre- and postdialysis serum sodium concentrations were not significantly different between online HDF and HFHD patients (predialysis, 138  $\pm$  2 mEq/L vs. 137  $\pm$  3 mEq/L; postdialysis, 134  $\pm$  2 vs. 134  $\pm$  2 mEq/L). However, the decrease in serum sodium concentration was larger in the online HDF group than the HFHD group (3.7 vs. 2.5 mEq/L,  $P < 0.05$ ), although net ultrafiltration during the dialysis session was not significantly different. Adjustments for the duration of dialysis and the presence of diabetes mellitus did not affect the significant difference in serum sodium changes ( $P < 0.05$ ). The number and classes of antihypertensive agents prescribed to online HDF versus HFHD patients were not significantly different (Table 3).

Fig. 1 illustrates the correlations between the postdialysis serum sodium change and SBP for all patients. Postdialysis serum sodium lowering correlated with postdialysis SBP ( $r = 0.304$ ,  $P < 0.005$ ) and pulse pressure ( $r = 0.299$ ,  $P < 0.005$ ). It also correlated with predialysis SBP ( $r = 0.317$ ,  $P < 0.005$ ) and pulse pressure ( $r = 0.324$ ,  $P = 0.001$ ).

Finally, pre- and postdialysis serum potassium, chloride, and total CO<sub>2</sub> concentrations were compared between online HDF and HFHD patients. No significant differences were found between the two groups (Table 4). Postdialysis decreases in serum potassium and chloride were not significantly different

**Table 3. Comparisons of pre- and postdialysis blood pressures and serum sodium concentrations**

	High-flux HD (n=69)	Online HDF (n=32)
Pre-HD systolic BP (mmHg) <sup>*</sup>	145 ± 19	136 ± 21
Pre-HD diastolic BP (mmHg)	73 ± 11	73 ± 15
Post-HD systolic BP (mmHg) <sup>*</sup>	141 ± 25	129 ± 22
Post-HD diastolic BP (mmHg)	73 ± 10	73 ± 12
Net ultrafiltration (kg)	1.75 ± 1.07	2.06 ± 1.70
Antihypertensives		
None	31 (44.9%)	16 (50.0%)
ACEI	3 (4.3%)	1 (3.1%)
ARB	29 (42.0%)	7 (21.9%)
CCB	32 (46.4%)	13 (40.6%)
BB	16 (23.2%)	11 (34.4%)
Pre-HD serum Na <sup>±</sup> (mEq/L)	136.5 ± 3.3	137.7 ± 2.4
Post-HD serum Na <sup>±</sup> (mEq/L)	134.0 ± 2.2	134.0 ± 2.2
ΔSerum Na <sup>±</sup> (mEq/L) <sup>*</sup>	-2.5 ± 2.8	-3.7 ± 2.2
ΔSerum Na <sup>±</sup> (%)	-1.8 ± 2.0	-2.7 ± 1.6

\*  $P < 0.05$ , High-flux HD vs. Online HDF.

Continuous values are mean ± standard deviation.

ΔSerum Na<sup>±</sup> (mEq/L) = post HD serum Na<sup>±</sup> - pre-HD serum Na<sup>±</sup>

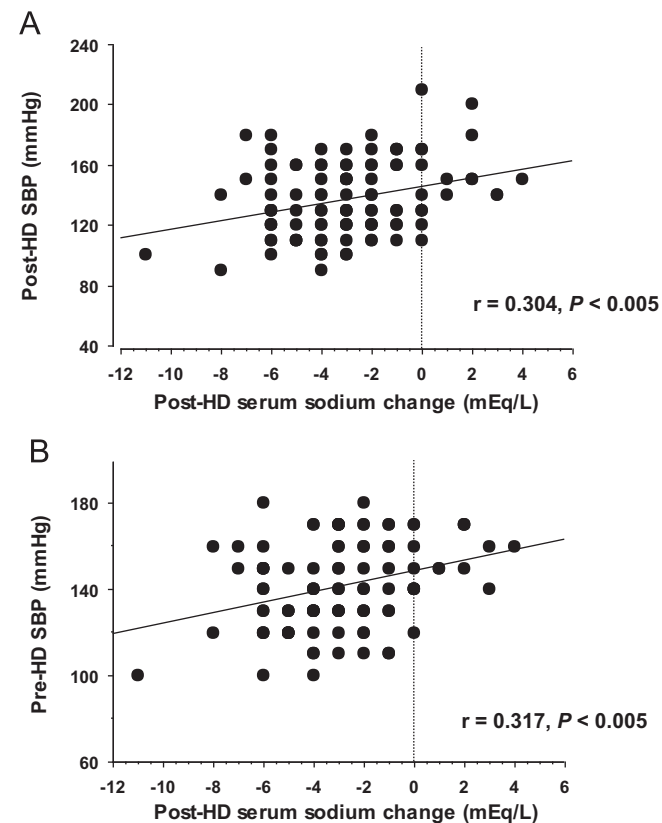
ΔSerum Na<sup>±</sup> (%) = [(post HD serum Na<sup>±</sup> - pre-HD serum Na<sup>±</sup>) ÷ pre-HD serum Na<sup>±</sup>] × 100; ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin II receptor blockade; BB, β-blocker; BP, blood pressure; CCB, calcium channel blocker; HD, hemodialysis; HDF, hemodiafiltration.

**Table 4. Comparisons of pre- and postdialysis serum potassium, chloride and total carbon dioxide (tCO<sub>2</sub>) concentrations**

	High-flux HD (n=69)	Online HDF (n=32)
Pre-HD serum K <sup>+</sup> (mEq/L)	4.7 ± 1.1	5.1 ± 0.6
Post-HD serum K <sup>+</sup> (mEq/L)	3.1 ± 0.5	3.3 ± 0.4
ΔSerum K <sup>+</sup> (mEq/L)	-1.6 ± 0.8	-1.8 ± 0.5
Pre-HD serum Cl <sup>-</sup> (mEq/L)	97 ± 4	98 ± 3
Post-HD serum Cl <sup>-</sup> (mEq/L)	93 ± 2	94 ± 2
ΔSerum Cl <sup>-</sup> (mEq/L)	-4.2 ± 3.6	-4.4 ± 2.7
Pre-HD serum tCO <sub>2</sub> (mEq/L)	22.2 ± 3.4	22.0 ± 2.9
Post-HD serum tCO <sub>2</sub> (mEq/L)	27.5 ± 4.8	27.3 ± 2.6
ΔSerum tCO <sub>2</sub> (mEq/L)	5.2 ± 4.8	5.4 ± 2.9

Continuous values are mean ± standard deviation. No significant differences were found between the two groups.

ΔSerum K<sup>+</sup> (mEq/L) = post HD serum K<sup>+</sup> - pre-HD serum K<sup>+</sup>; ΔSerum Cl<sup>-</sup> (mEq/L) = post HD serum Cl<sup>-</sup> - pre-HD serum Cl<sup>-</sup>; ΔSerum tCO<sub>2</sub> (mEq/L) = post HD serum tCO<sub>2</sub> - pre-HD serum tCO<sub>2</sub>. HD, hemodialysis; HDF, hemodiafiltration.



**Figure 1. Relationship between systolic blood pressures and the postdialysis serum sodium change.** The change in serum sodium after dialysis was significantly correlated with both (A) postdialysis and (B) predialysis systolic blood pressure.

between online HDF and HFHD patients. Similarly, the postdialysis increase in total CO<sub>2</sub> concentration was not significantly different between the two groups (Table 4).

## Discussion

In this study, we investigated if serum electrolyte profiles are different between HFHD and online HDF patients. Whereas serum potassium, chloride, and total CO<sub>2</sub> levels were not significantly different between these two groups of patients, postdialysis serum sodium changes were significantly different (Table 3). Furthermore, the postdialysis serum sodium change was significantly correlated with pre- and postdialysis SBP (Fig. 1).

We postulated that patients on online HDF might have different serum electrolyte profiles than patients on conventional HD because the procedure of HDF involves large amounts of ultrafiltration and substitution fluid infusion. However, no differences in sodium, potassium, or calcium levels were reported between HDF and HD patients when solute balances during HD were assessed using total dialysate/filtrate collections [7]. Our results are consistent with those of previous observational studies that reported no differences in predialysis serum sodium, potassium, or bicarbonate levels between patients undergoing HFHD and online HDF [8,9]. According to Ahrenholz et al, no significant differences in pre- and postdialysis plasma bicarbonate concentrations were found between HFHD and online HDF patients [10].

However, we found that the change in serum sodium concentration after dialysis was significantly larger in online HDF patients than in HFHD patients, despite similar pre- and postdialysis serum sodium concentrations between the two groups. In most of our patients, serum sodium concentrations were actually lowered after HD (Fig. 1). This decrease in serum sodium concentration, expressed in either mEq/L or percent, is likely to reflect sodium removal during HD [11].

Postdialysis serum sodium concentrations are affected by the dialysate sodium concentration; the dialysate sodium concentration used in this study was 138 mEq/L. A dialysate sodium prescription > 138 mEq/L may result in a positive dialysate-to-serum sodium gradient in most patients [12]. However, previous simulation studies have shown that serum sodium concentration decreases during HD using a normal dialysate sodium concentration [13,14]. Net sodium transfer from serum to dialysate can occur, and a negative sodium balance would result in blood pressure changes. In our patients, both pre- and

postdialysis SBPs were significantly correlated with the postdialysis serum sodium change, i.e., sodium removal during HD. Notably, online HDF patients appeared to have lower pre- and postdialysis SBPs and removal of more sodium during dialysis than HFHD patients. Sodium removal would induce a transcellular fluid shift to increase the intracellular fluid volume, which would decrease the extracellular fluid volume and potentially relieve hypertension.

This study had two major limitations. First, sodium balance was not accurately assessed by measuring dietary sodium intake and dialysate sodium removal. Second, we cannot exclude the possibility that factors (e.g., comorbidities, residual renal function, use of diuretics, etc.) other than the HD modality may have affected blood pressures and serum sodium profiles because of our uncontrolled cross-sectional study design.

In conclusion, patients on online HDF had similar pre- and postdialysis serum sodium, potassium, chloride and total CO<sub>2</sub> concentrations to those of HFHD patients. However, online HDF decreased postdialysis serum sodium levels to a greater extent than HFHD. This appeared to stabilize both pre- and postdialysis SBPs in the online HDF patients.

### Conflicts of interest

None declared.

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