

## Original Article

# Effect of dialysate sodium concentration and sodium gradient on patients with maintenance hemodialysis

Yue Zhang, Qiang He, Daqing Hong, Li Wang

Department of Nephrology, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, No. 32, First Ring Road, Chengdu 610072, Sichuan, China

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**Abstract:** Backgrounds: Patients with maintenance hemodialysis (MHD) have a high risk of cardiovascular disease, which is the leading cause of morbidity and mortality. The aim of the present study was to explore the relationship between the sodium gradient and the water load of MHD patients. Methods: Eighty one MHD patients were selected in the study. The serum sodium concentration, sodium gradient, interdialysis weight gain (IDWG), IDWG% of the patients and the incidence of hypotension were analyzed. Correlation analysis was carried out. Results: The serum sodium concentrations were  $138.81 \pm 3.27$  mmol/L and  $137.81 \pm 2.88$  mmol/L before and after dialysis, respectively. The sodium concentration of dialysis solution was 135 mmol/L. The absolute sodium gradient was  $3.92 \pm 2.69$  mmol/L. The absolute sodium concentration difference after dialysis was  $2.79 \pm 2.14$  mmol/L. IDWG was  $2.06 \pm 0.82$  kg and the value of IDWG% was  $3.71 \pm 1.42\%$ . The absolute sodium gradient was positively correlated with IDWG ( $r=0.349$ ,  $P=0.001$ ) and IDWG% ( $r=0.269$ ,  $P=0.013$ ). Dialysis with the lowest IDWG had the least effect on sodium load and water load in patients. Age was negatively correlated with the sodium concentration before dialysis ( $r=-0.349$ ,  $P=0.014$ ), the absolute sodium gradient ( $r=-0.321$ ,  $P=0.031$ ), IDWG ( $r=-0.483$ ,  $P=0.001$ ) and IDWG% ( $r=-0.452$ ,  $P=0.002$ ). Conclusion: The absolute sodium gradient was significantly correlated with IDWG, which contributes to improving water load in MHD patients.

**Keywords:** Hemodialysis, sodium gradient, interdialysis weight gain, water load

## Introduction

Patients with maintenance hemodialysis (MHD) have been experiencing high morbidity and mortality of the cardiovascular disease [1]. The risk factors of the cardiovascular disease in MHD patients mainly include hypertension and water overload [2, 3]. The clinical manifestation of water overload usually includes interdialysis weight gain (IDWG) and IDWG% [4]. The serum sodium concentration before dialysis is usually seen as a set-point of the serum sodium level of the patient and the sodium gradient is the difference between the sodium concentration of the dialysis fluid and the serum sodium concentration before dialysis [5, 6]. However, the effect of dialysate sodium concentration and sodium gradient on MHD patients remains unclear and to be further explored.

High sodium gradient is often associated with increased sodium load [7], and its mechanism need to be further elucidated. The question is whether the lower sodium gradient can

have a better improvement on the sodium load and water load of the MHD patients [8]. Thus, uncovering the mechanism of dialysate sodium gradient on MHD patients in the improvement and prognosis of the patients not only can provide valuable information for the treatment and prognosis of the patients, but also can serve as a new potential biomarker of the patients.

The low sodium gradient may lead to hyponatremia in MHD patients, and it may even affect the stability of hemodynamics in dialysis [9]. Therefore, this study intends to explore the relationship between the sodium gradient and the water load of MHD patients, assuming that the absolute value of lower sodium gradient is associated with lower IDWG.

## Materials and methods

### Subjects

Eighty one MHD patients were selected from March to December of 2013 in our hospital

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**Table 1.** Characterization of clinical data in MHD patients

Items	Values
Total number of patients (n)	81
Age (year)	65.04 ± 11.11
Female (n, %)	42, 51.85%
Dialysis age (month)	89.27 ± 52.68
Serum sodium before dialysis (mmol/L)	138.81 ± 3.27
Serum sodium after dialysis (mmol/L)	137.81 ± 2.88
Absolute sodium gradient (mmol/L)	3.92 ± 2.69
Absolute sodium concentration difference (mmol/L)	2.79 ± 2.14
IDWG (kg)	2.06 ± 0.69
IDWG/Dry weight (%)	3.62 ± 1.10
Incidence of hypotension (%)	0.82 ± 1.02

Note: Maintenance hemodialysis (MHD), Interdialysis weight gain (IDWG).

with hemodialysis of 3 times/week, 4 hour/time and urine <500 ml/day. The inclusion criteria and exclusion criteria were as described in previous studies [10, 11]. The study was approved by the ethics committee of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, performed in accordance with the Declaration of Helsinki, and written informed consent was obtained from all patients and their families before enrollment.

### Data collection

During the study, clinical data including age, sex, dialysis age, medical history, serum sodium, sodium gradient before and after dialysis, IDWG, IDWG% and the incidence of hypotension during hemodialysis were collected and analyzed as described previously [12, 13].

### Statistical analysis

All data were expressed as means ± standard deviation (SD). Statistical analysis was performed using SPSS 17.0 software. A value of  $P < 0.05$  indicates that the difference is significant.

## Results

### Characterization of clinical data in MHD patients

As shown in **Table 1**, the average age of the patients was 65.04 ± 11.11 (40-83) years. The dialysis age of all the patients was 89.27 ± 52.68 (6-228) months. Female patients (42/81) account for 51.85% of total number of the patients. The serum sodium concentrations

before and after dialysis were 138.81 ± 3.27 (130.2-145.0) mmol/L and 137.81 ± 2.88 (132.5-146.0) mmol/L, respectively. Sodium concentration of dialysis solution was 135 mmol/L. The absolute sodium gradient was 3.92 ± 2.69 (0-10.0) mmol/L. The absolute sodium concentration difference after dialysis was 2.79 ± 2.14 (0.1-8.6) mmol/L. IDWG was 2.06 ± 0.69 (0.50-4.20) kg. IDWG% was 3.62 ± 1.10 (1.01-8.42)%.

### Correlation of age with sodium concentration and sodium gradient

As we mentioned above, water overload was usually measured as IDWG and IDWG% [4]. Age negatively correlated with IDWG ( $r = -0.483$ ,  $P = 0.001$ ) and IDWG% ( $r = -0.452$ ,  $P = 0.002$ ). Meanwhile, age was negatively correlated with the absolute value of sodium concentration and sodium gradient before and after dialysis ( $r = -0.363$ ,  $P = 0.014$ ;  $r = -0.321$ ,  $P = 0.031$ ) (**Figure 1**).

### Correlation between sodium gradient and water overload

We found no significant associations between water overload and sodium concentration whether before or after dialysis ( $P > 0.05$ ). Meanwhile, the absolute sodium concentration difference before and after dialysis was not significantly correlated with IDWG ( $r = -0.180$ ,  $P = 0.913$ ) and IDWG% ( $r = -0.022$ ,  $P = 0.381$ ) (**Table 2**).

The absolute sodium gradient was positively correlated with IDWG and IDWG% ( $r = 0.349$ ,  $P = 0.001$ ;  $r = 0.269$ ,  $P = 0.013$ ). When the sodium concentration of dialysis solution and serum sodium concentration was equal (absolute sodium gradient of zero), MHD patients would have the lowest IDWG and IDWG%, which illustrated that dialysis had the least effect on the sodium load and water load of MHD patients (**Figure 2; Table 2**).

### The hypotension incidence analysis

Correlation analysis revealed that no significant association between the hypotension incidence and sodium concentration ( $r = -0.252$ ,  $P =$

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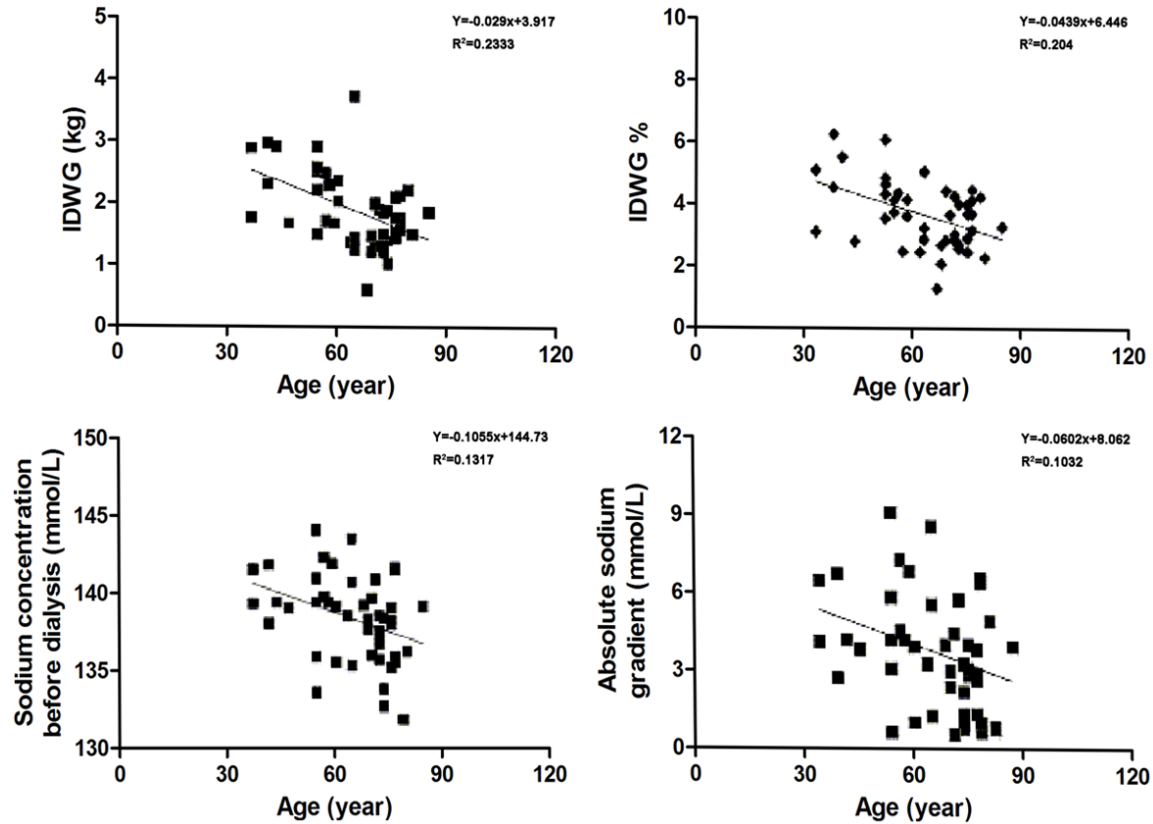


Figure 1. Linear correlation between age and sodium concentration, sodium gradient, IDWG, IDWG%.

0.122), sodium gradient ( $r=-0.232$ ,  $P=0.155$ ), IDWG ( $r=-0.276$ ,  $P=0.088$ ) and IDWG% ( $r=-0.240$ ,  $P=0.141$ ) (Table 2).

### Discussion

Incidence of cardiovascular disease in MHD patients is high, which seriously threatens people's life and living. The present study aimed to explore the relationship between the sodium gradient and the water load of MHD patients. The serum sodium data, sodium gradient, IDWG and IDWG% of the patients before and after dialysis and the hypotension incidence during dialysis were analyzed. Our findings provide solid evidence that the absolute sodium gradient of the MHD patients was significantly correlated with IDWG.

In recent years, in order to maintain the stability of hemodynamics in MHD patients during dialysis, the dialysate sodium concentration was often higher, which also resulted in high sodium gradient. The higher sodium gradient may be associated with more water sodium

retention. Previous studies revealed that IDWG during dialysis significantly correlated with sodium gradient [14, 15]. The reason may be that the higher sodium gradient makes the patients thirstier. When the sodium gradient was high, the serum sodium concentration of the MHD patients after dialysis was increased, thus stimulating hypothalamus and cerebral cortex, and increasing generation of thirst and IDWG [16]. Our results suggested that IDWG and IDWG% of the MHD patients increased along with the increase of sodium gradient, when the sodium gradient was positive, which was consistent with the previous results above.

Whether the lower the sodium gradient, the lower IDWG and IDWG% of the MHD patients in MHD patients? Our results demonstrated that when the sodium gradient was negative, the IDWG increased with the decrease of the sodium gradient, which is not consistent with the above findings [14-16]. When the sodium gradient was negative, the serum sodium concentration in the patients before dialysis was higher than that of the dialysate sodium concentration, and the serum sodium concentration in

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**Table 2.** Correlation analysis among absolute sodium gradient, the incidence of hypotension, IDWG and IDWG%

Clinical index	r	P
Sodium concentration before dialysis and IDWG	0.211	0.062
Sodium concentration before dialysis and IDWG%	0.160	0.071
Absolute sodium gradient and IDWG	0.349	0.001
Sodium gradient absolute and IDWG%	0.269	0.013
Sodium concentration after dialysis and IDWG	0.078	0.629
Sodium concentration after dialysis and IDWG%	0.024	0.880
Absolute sodium concentration difference and IDWG	-0.18	0.913
Absolute sodium concentration difference and the IDWG%	-0.022	0.381
Hypotension incidence and sodium concentration before dialysis	-0.252	0.122
Hypotension incidence and sodium gradient	-0.232	0.155
Hypotension incidence and IDWG	-0.276	0.088
Hypotension incidence and IDWG%	-0.240	0.141

Note: Interdialysis weight gain (IDWG).

the patients after dialysis may be decreased and the colloid osmotic pressure decreased. The decrease in serum sodium in healthy subjects may result in a decrease in the secretion of anti-diuretic hormones, which can increase the urine volume and decrease body weight. However, the activity of renin-angiotensin-aldosterone in some MHD patients may be increased, which could stimulate secretion of anti-diuretic hormone and cause water sodium retention [17, 18]. In this part of the patients, when the sodium gradient was negative (the concentration of sodium in dialysis solution was lower than that of the serum sodium concentration), the serum sodium concentration after dialysis may be significantly decreased with the increase of serum sodium concentration. The activity of renin, anti-diuretic hormone, and IDWG may be significantly promoted, as well. In addition, the negative sodium gradient may lead to osmotic pressure of the dialysis solution lower than serum osmotic pressure, which may affect the ultrafiltration of the MHD patients. However, the hypothesis above needs to be further elucidated.

Some studies demonstrated that the sodium gradient in dialysis was related to the occurrence of hypotension during hemodialysis, and that hypotension can be induced by low sodium gradient and the increase of the sodium concentration of dialysis solution could reduce the incidence of hypotension in hemodialysis [10]. However, it was found that the negative sodium gradient did not increase the incidence of hypotension in dialysis patients compared with that

of the positive sodium gradient group [6]. In our study, there was no significant correlation between the incidence of hypotension and the sodium gradient, which was consistent with the results of the latter study. Its specific mechanism is not yet clear.

We observed the negative correlation between age and sodium concentration before dialysis, the absolute sodium gradient, IDWG and IDWG%. With the increase

of age, the serum sodium concentration of MHD patients decreased, and the absolute sodium gradient decreased, while both IDWG and IDWG% were significantly decreased. Hecking et al. also found that IDWG and IDWG% in the MHD patients with age  $\geq 60$  years were significantly lower than those with age  $< 60$  years [7]. This may be related to the dietary intake of elderly MHD patients, and the elderly patients may have better restriction compliance of salt.

Our study has several limitations. First, the sample size was small, which may bring about research error. Second, the research period was short and a long-term follow-up is needed.

### Conclusion

In conclusion, the absolute sodium gradient in MHD patients was significantly and positively correlated with IDWG, and the changes of sodium concentration in dialysis solution may affect the IDWG of MHD patients. Too low or too high sodium gradient may have an effect on IDWG, which may result in excessive water load and further many complications. Therefore, the individual prescription of the dialysate sodium concentration may improve the water load in MHD patients.

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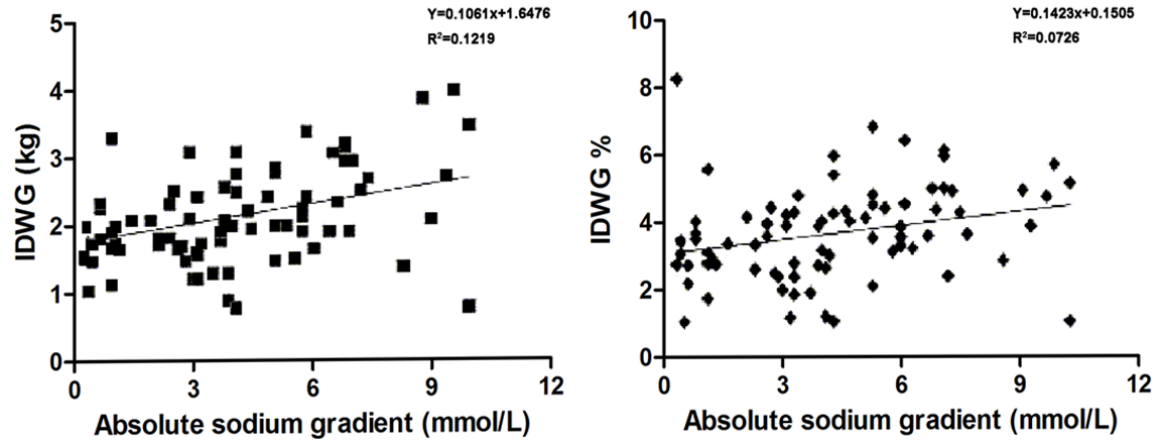


Figure 2. Linear correlation between absolute sodium gradient and IDWG, IDWG%.

### Disclosure of conflict of interest

None.

### Authors' contribution

Conceived and designed the experiments: Y Zhang and L Wang. Performed the experiments and analyzed the data: Q He and DQ Hong. Contributed reagents/materials/analysis tools: L Wang.

**Address correspondence to:** Dr. Li Wang, Department of Nephrology, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, No. 32, First Ring Road, Chengdu 610072, Sichuan, China. Tel: +86-028-87393311; Fax: 13111865150; E-mail: scwangli62@163.com

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