Relationship between Serum Sodium Levels and Circadian Blood Pressure Abnormalities in Patients with Primary Nephrotic Syndrome

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Background

- Ambulatory blood pressure (ABP) monitoring is particularly useful for detecting a non-dipper type hypertension (reduced nighttime BP dip).
- Recent study has shown that non-dipper type hypertension is significantly associated with mortality and poor cardiovascular outcomes, independent of mean BP level.

Salles GF et al. Hypertens 2016.

- Hypertension is frequently observed in patients with nephrotic syndrome (NS).
- Recent studies have shown that the primary enhancement of renal sodium reabsorption contributes to the edema formation in NS patients.

Andersen RF et al. Pediatr Nephrol 2013.
Zachar RM et al. J Am Soc Nephrol 2015.

- To date, however, it is not fully elucidated that change in renal sodium handling contributes to the abnormality of circadian BP in NS patients.

Aim

To determine the clinical factors associated with the night-to-day ratio of ABP (NDR) in NS patients.

Subjects and methods

- The inclusion criteria

i) Patients with apparent onset of NS
ii) Patients with indications for immunosuppressive therapies

- The exclusion criteria

i) Patients who had already achieved remission at the time of the 1st ABP measurement
ii) Patients with a diagnosis of acute kidney injury
iii) Patients with apparent causes or systemic diseases that might induce secondary NS

- Setting

All of the patients consumed a diet containing 6 g/day of sodium chloride during their hospitalization.

- Measurement of ABP

ABP measurement was performed within 7 days after the admission (1st ABP) and after the achievement of NS remission (2nd ABP).

- Definition

The 24-hour ABP: the average of the 24-hour ABP
The daytime ABP: the average of the daytime ABP
The nighttime ABP: the average of the nighttime ABP
The night-to-day ratio of ABP (NDR):
the ratio of the nighttime ABP to the daytime ABP
Nephrotic syndrome(NS):
Urinary protein excretion of ≥3.5 g/day and serum albumin concentration of <3.0 g/dL
NS remission: urinary protein excretion of <3.5 g/day

Abbreviation

ABP; ambulatory blood pressure, **BW**; body weight, **GFR**; glomerular filtration rate, **NDR**; nighttime to daytime ratio of ABP, **NS**; nephrotic syndrome, **RAS**; renin-angiotensin system, **% Increase BW**; change rate in body weight at the time of the ABP measurement compared with that at the time of discharge, **Δ**; change rate in the values before and after the achievement of NS remission.

Results

Table 1. The clinical characteristics of NS patients before remission (N=33)

Clinical findings		
Age	(years)	58 ± 17
Male	(n[%])	24 (73)
% Increase BW	(%)	14.1 ± 9.2
Anti-hypertensive medications used	(n[%])	23 (70)
RAS blockade	(n[%])	11 (33)
Diuretics	(n[%])	18 (55)
Corticosteroids use	(n[%])	14 (42)
Urinary protein excretion	(g/day)	6.7 ± 2.9
Serum albumin	(g/dL)	1.8 ± 0.6
Serum sodium	(mEq/L)	140 ± 3
Estimated GFR	(mL/min/1.73 m^2)	62 ± 21
24-hour ABP	(mmHg)	126/79
Daytime ABP	(mmHg)	127/81
Nighttime ABP	(mmHg)	120/74
NDR		0.93 ± 0.06
Histopathological diagnosis	(n[%])	
Minimal change disease		17 (52)
Focal segmental glomeruloscrelosis		4 (12)
Membranous nephropathy		12 (36)

Figure. Relationship between the serum sodium level and NDR before remission (N=33)

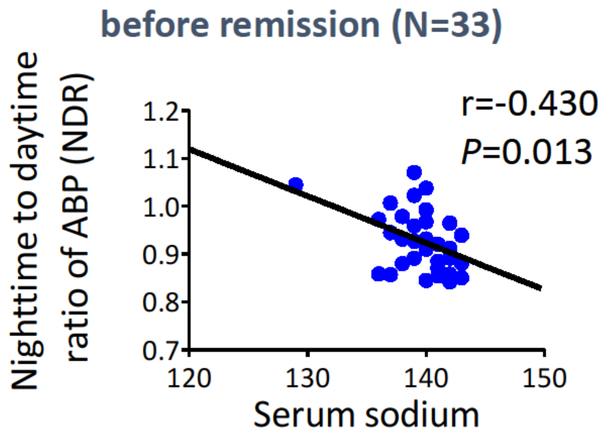

Table 2. Multiple linear regression analysis for the NDR before remission (N=33)

	Univariate		Multivariate	
Variables	r	*P*-value	β	*P*-value
% Increase BW	0.021	0.909	-0.091	0.667
Urinary protein excretion	-0.062	0.733	-0.105	0.588
Serum albumin	-0.081	0.655	-0.027	0.904
Serum sodium	**-0.430**	**0.013**	**-0.462**	**0.016**

Table 3. The clinical characteristics of NS patients before and after remission (N=14)

Variables		Before remission	After remission	*P*-value
Age	(years)	50 ± 18	-	-
% Increase BW	(%)	19.4 ± 9.9	1.1 ± 1.9	<0.001
Number of anti-hypertensive medications used		0.9 ± 0.7	0.5 ± 0.5	0.082
Urinary protein excretion	(g/day)	7.6 ± 3.5	0.1 ± 0.2	<0.001
Serum albumin	(g/dL)	13 ± 5	3.2 ± 0.4	<0.001
Serum sodium	(mEq/L)	139 ± 3	140 ± 2	0.408
24-hour ABP	(mmHg)	130/82	122/78	0.047
Daytime ABP	(mmHg)	132/83	123/79	0.063
Nighttime ABP	(mmHg)	125/77	117/72	0.036
NDR		0.94 ± 0.06	0.93 ± 0.10	0.874

Table 4. Multiple linear regression analysis for the difference rate in NDR before and after remission (N=14)

	Univariate		Multivariate	
variables	r	*P*-value	β	*P*-value
Δ BW	0.055	0.852	0.274	0.578
Δ Urinary protein excretion	0.242	0.404	0.552	0.154
Δ Serum albumin	0.036	0.904	-0.048	0.901
Δ Serum sodium	**-0.603**	**0.022**	**-0.599**	**0.041**

Summary

- In this cross-sectional study, the serum sodium level was identified as a factor associated with the NDR, independent of the % increase BW, serum albumin and urinary protein excretion.
- The ABP, especially nighttime ABP, was markedly decreased after remission, despite reduced number of anti-hypertensive medications used.
- The Δ serum sodium was significantly correlated with the Δ NDR in the patients who were subjected to repeated ABP measurements both before and after NS remission.
- Our results suggest that changes in the renal handling of sodium and water, which might be reflected by the serum sodium level, is involved in the abnormalities of circadian blood pressure in NS patients.

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