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Comparative study of urinary sodium excretion in hypertensives versus normotensives

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Abstract: *Objective:* To examine the pattern of urinary sodium excretion in hypertensive patients and comparison of the results with those from the normotensive subjects; as well this study further quantified the diurnal variations. *Background:* In healthy individuals, there is a diurnal variation in pattern of urinary sodium excretion, maximum sometime around midday and a minimum toward the end of sleep. Hence, this study is conducted to compare the pattern of urinary sodium excretion between hypertensive patients and normotensive subjects. *Material and Method:* The study was a hospital based cross-sectional, observational study. The study group consisted of two subsets, the hypertensive individuals (according to JNC 7^2 criteria), both for indoor and outdoor consultations and the normotensive group consisted of volunteers selected randomly. Study participants provided 8- hour urine collections carefully timed into three periods 6am-2pm, 2pm-10pm and 10pm-6am. *Results:* The mean excretion of sodium was double during morning hours in the normotensive patients (6 a.m. to 2 p.m.) 95.4 vs 45.1 to hypertensive patients and the reversal of this pattern in hypertensive patients where nocturnal excretion (10 p.m. to 6 a.m.) of sodium was almost double 97.6 as compared to their normotensive counterparts 56.9 (p value <0.001). *Conclusion:* Hypertensives have significant under excretion of urinary sodium in the day time and highest excretion during night time, which is a reversal pattern of urinary sodium excretion process in comparison to normotensives.

Keywords: Urinary Sodium Excretion, Diurnal Variations of Urinary Sodium Excretion, Pattern of Sodium Excretion in Hypertension.

Introduction

For decades excess sodium intake has been implicated in the etiopathogenesis of high blood pressure [1]. The two major modifiable risk factors for development of cardiovascular disease are hypertension and diabetes. Complications of hypertension account for 9.4 million deaths worldwide every year. Hypertension is responsible for at least 45% of deaths due to heart disease, and 51% of deaths due to stroke [2]. Slight elevation in blood pressure is associated with cardiovascular morbidity and mortality [3].

Worldwide, raised blood pressure is estimated to cause 7.5 million deaths in the future, about 12.8% of the total of all deaths (WHO global health observatory). This accounts for 57 million disability adjusted life years (DALYS) or 3.7% of total DALYS (WHO Report). Blood pressure levels have been shown to be positively and continuously related to the risk for stroke and coronary heart disease. Globally, the overall prevalence of raised blood pressure in adults aged 25 years and over was around 24% in males and 20.5% among females [4]. It has long been thought that renal sodium handling i.e. its retention is the primary determinant of high blood pressure and investigators suggest that hypertension is the result of an inability of the kidney to excrete salt and water normally [5-6]. High salt consumption also contributes to the development of hypertension and is considered an independent risk factor for vascular remodeling, cardiac hypertrophy, and stroke incidence. Arthur C. Guyton the role of altered salt excretion by the kidney as a central mechanism in the development of hypertension [7]. According to this hypothesis, there is impaired excretion of sodium ions by tubular epithelial cells in the kidney. To maintain salt and water homoeostasis, the body adopts a pressure-natriuresis approach that ultimately leads to an elevation in BP.

Diurnal variations in urinary excretion of sodium, chloride, potassium and water have long been recognized, with excretion of water and electrolytes generally reaching a maximum sometime during mid-day and a minimum sometime during sleep [8-11]. A reversal of the usual diurnal cycle of sodium, chloride, and water excretion (i.e. higher excretion at night) has been reported for persons with several diseases [12-16] like cirrhosis of the liver, congestive heart failure, nephrosis, glomerulonephritis, Cushing's disease, and primary hyperaldosteronism. Investigators have also reported a reversal or flattening of the usual cycle of sodium and chloride excretion in hypertensives [17-18].

In a previous report, Dyer et al. [17] found on average no diurnal variation in excretion of sodium and water in a group of hypertensive men and women, with more than half showing a higher rate of sodium and water excretion at night than during the day. A stronger association between blood pressure and overnight excretion of sodium, compared to daytime or 24-h excretion, has also been reported [19]. In this regard, a study was conducted to find out the association between blood pressure and sodium excretion and to find out any changes in the diurnal pattern of sodium excretion in hypertensive patients as compared to the normotensive.

Material and Methods

Design and participants: The study was a hospital based cross-sectional, observational study. The study group consisted of two subsets, the hypertensive individuals (according to JNC 7[2] criteria) both for indoor and outdoor consultations and the normotensive group consisted of volunteers selected randomly. The duration of study was 18 months. Study participants provided three carefully timed 8- hour urine collections divided into 6am-2pm, 2pm-10pm and 10pm-6am periods. Special attention was paid to completeness of all specimens. Adequacy and accuracy of samples were done by doing urinary creatinine of the samples. Detailed instructions on methods for collection for each time period was included in each urine collection kit.

Statistical Analysis: The recorded data were compiled and entered in a Microsoft Excel and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean+-SD and categorical variables were summarized as percentages. Chi-square test or Fishers exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data is presented by bar diagrams. A P-value less than 0.05 is considered statistically significant. All P-values were two tailed.

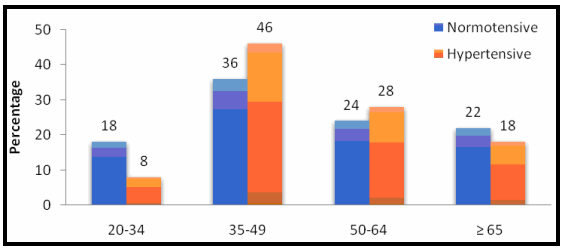
Results

There were 200 participants enrolled in the study. Half of them (100) were hypertensive and the remaining half (100) were normal control. Mean age of normotensive group was 48.3±8.37 in comparison to 47.5±9.45 of hypertensive patients (Table 1).

Table-1: Age distribution of study patients

Age (years)	Normotensive	Hypertensive	P-value
20-34	18	8	0.655
35-49	36	46	
50-64	24	28	
≥ 65	22	18	
Total	100	100	
Mean ± SD	48.3±8.37	47.5±9.45	

Fig-1: Age distribution of study patients

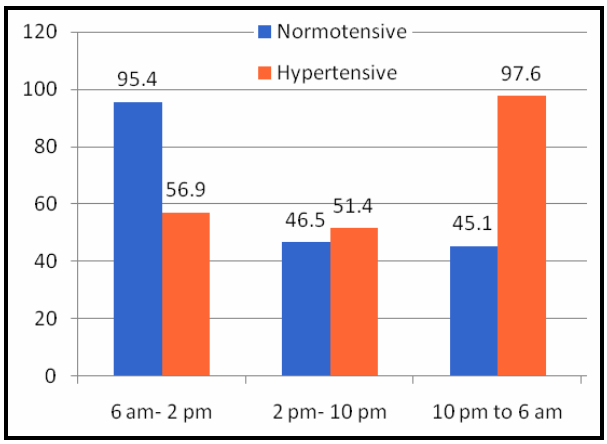


The mean age of normotensive and hypertensive was comparable and the maximum patients were in the age group of 35-64. 8-hourly sodium excretion of normotensive patients revealed a pattern where sodium excretion in morning interval (6 a.m. - 2 p.m.) was almost double (95.4 vs 46.5/45.1) than that of other 8 hourly intervals ($p<0.001$).In the hypertensive patients nocturnal (10 p.m. - 6 a.m.) secretion of sodium was higher (97.6 vs 56.9/51.4) than

the daytime levels (p<0.001), the mean value of sodium excretion during nocturnal intervals were roughly the double of each of other 8-hour intervals (p<0.001) (table 2).

Table-2: Comparison of Urinary Sodium Excretion					
Time Period	Normotensive		Hypertensive		P-value
	Mean	SD	Mean	SD	
6 am-2 pm	95.4	16.82	56.9	17.82	<0.001*
2 pm-10 pm	46.5	11.39	51.4	14.52	
10 pm-6 am	45.1	14.72	97.6	18.73	

Fig-2: Comparison of Urinary Sodium Excretion



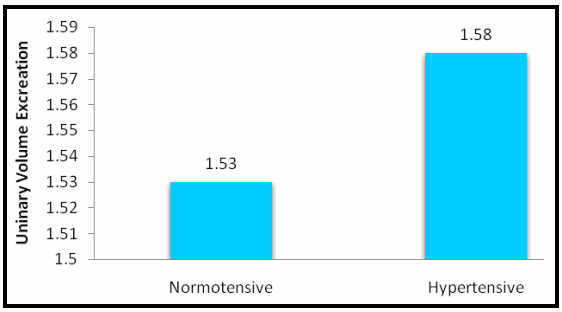
Discussion

A great emphasizes has been laid on association of Sodium excretion and Blood pressure, in this landmark trial. Diurnal variations in excretion of sodium, chloride, potassium, and water have been observed in many studies [10-11]. Water and electrolyte excretion in healthy individuals generally reaches a maximum sometime around midday and a minimum toward the end of sleep [18-19]. However, it has been observed that the hypertensive subjects have higher nighttime sodium excretion rates than normotensive subjects [17] and relative day time retention. In our study, half of the patients belonged to the hypertensive group and the other half was normotensive. The mean age of the patients in hypertensive group (47.5±9.45 years) was comparable to that in the normotensive group (48.3±8.37 years).

However, on comparing the two groups, the number of hypertensive patients was more in the age group of 35-65 years, though this relationship was statistically insignificant. The effect of increasing age on hypertension has been demonstrated by Anderson GH et. Al [20] in his study conducted over 4500 hypertensive patients. Upon collection of carefully timed 8-hour urine, the 24-hour urinary volume excretion was comparable in the hypertensive and normotensive groups, though the urinary volume in hypertensive group exceeded that of the normotensive group, but this difference was not statistically significant (p-0.55) (Table 3).

Table-3: Comparison based on 24 hour urinary volume excretion among two groups				
Group	Mean	SD	Range	P-value
Normotensive	1.53	0.39	1.2-2.1	0.554
Hypertensive	1.58	0.45	1.3-2.4	

Fig-3: Comparison based on 24 hour urinary volume excretion among two groups



Upon comparison analysis of the 8 hourly sodium excretion between normotensive and hypertensives, it was seen that patients with hypertension had significantly higher sodium excretion during the nocturnal hours, particularly from 10pm- 6:00 am, with the loss of circadian rhythm of urinary sodium excretion as was also demonstrated by Dyer et al in year 1987 [17] and has been recently validated at molecular level by Richards et al [21] which showed that mutation own B-mal 1 gene is responsible for the loss of diurnal rhythm in sodium excretion. It was also found that the sodium under excretion occurred during the day time in hypertensive patients as compared to the normotensive patients.

The retention/under excretion of sodium in hypertensive subjects as compared to the normotensive occurred in (6 a.m.- 2p.m) as well as (2 p.m-10 p.m.) intervals however this retention of sodium in hypertensive patients as compared to that of the normotensive patients was more pronounced in the 6 a.m. -2 p.m. interval (1:1.4), this relationship reached statistical significance.

Conclusion

The normal diurnal variation in the excretion of sodium was disrupted in hypertensive subjects. In comparison, hypertensive patients with their normotensive subjects, hypertensive patients had significant under excretion of sodium in day time and highest excretion during the night time. This pattern was the reversal of normal renal handling of sodium which shows a peak of excretion during mid-day. The association of these results with the complications hypertension, if any, needs further research.

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Conflicts of interest: There are no conflicts of interest.

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