A study of the pattern of urinary sodium excretion in patients of essential hypertension versus normotensives A hospital based cross sectional study.

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Abstract:

Introduction:

One of the major modifiable risk factors for development of cardiovascular disease is hypertension¹. 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. Slight elevations in blood pressure are associated with significant cardiovascular morbidity and mortality. There are multiple mechanisms that have been proposed for the development of essential hypertension. One of the mechanisms being retention of salt in the body during day.

High salt consumption and retention contributes to the development of hypertension and is considered an independent risk factor for vascular remodelling, cardiac hypertrophy, and stroke.

Objectives:

Primary: The objective of this study was to examine the associations of essential hypertension with the pattern of urinary sodium excretion and comparison of the results with those from the normotensive subjects.

Secondary: The study further quantified the variations and related them with the severity of hypertension.

Materials and methods:

The study was a hospital based cross sectional observational study conducted over a period of two years. The study group consisted of two subsets, the patients of essential hypertension (according to JNC 7 criteria) where all the other potential causes of secondary hypertension were excluded by detailed investigations and the normotensive group which consisted of volunteers selected randomly. Study participants provided three carefully timed 8-hour urine collections divided into 6am-2pm, 2pm-10pm and 10pm-6am periods which were analysed for Urinary Sodium levels.

Results:

Our study enrolled a total of 100 participants. Half of them suffered from essential hypertension and the other half formed the normal controls. The mean age of the patients in hypertensive group (47.5±9.45) was comparable to that in the normotensive group (48.3±8.37). Among the hypertensive patients, almost the half (22) had nocturnal sodium excretion (10 p.m.- 6 am) exceeding that of the other 8 hour intervals. It was also found that the sodium under extraction occurred during daytime (more pronounced in 6 a.m to 2 p.m shift) in hypertensive patients as compared to the normotensive patients.

Conclusion:

Our results were in accordance with the theory that the hypertensive patients lose their circadian rhythm of urinary sodium excretion and this tool, though cumbersome, can be used to identify patients who have high nocturnal Blood Pressure, and are thus amenable to more organ damage.

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I. Background:

Salt homeostasis and balance plays a paramount role in the development of hypertension² and its retention is considered to be an independent risk factor for vascular remodelling, cardiac hypertrophy, and stroke incidence. Based on the analysis of literature data, it has been concluded that the kidneys and central nervous system (CNS) are two major sites for salt sensing via several distinct mechanisms: 1) [Cl⁻] sensing in
renal tubular fluids, primarily by Na⁺-K⁺-Cl⁻ co-transporter (NKCC) iso-forms NKCC2B and NKCC2A, whose expression is mainly limited to macula-densa cells; 2) Na⁺ sensing in cerebrospinal fluid (CSF) by a novel isoform of Na⁺ channels. Nax, expressed in subfornical organs; 3) sensing of CSF osmolality by mechanosensitive, nonselective cation channels (transient receptor potential vanilloid type channels), expressed in neuronal cells of supraoptic and paraventricular nuclei; and 4) osmolality sensing by volume-regulated anion channels in glial cells of supraoptic and paraventricular nuclei. Such multiplicity of salt-sensing mechanisms likely explains the differential effects of Na⁺ and Cl⁻ loading on the long-term maintenance of elevated blood pressure that is documented in experimental models of salt-sensitive hypertension.

The role of altered salt excretion by the kidney as a central mechanism in the development of hypertension was proposed by Arthur C. Guyton (3). According to Dr. Guyton’s hypothesis, there is impaired excretion of sodium ions by tubular epithelial cells in the kidney. To maintain salt and water homeostasis, the body adopts a pressure-natriuresis approach that ultimately leads to an elevation in BP. These data confirm that the basic problem in conditions leading to alteration in BP lies in the genetic alteration of sodium transport in renal epithelial cells. Several factors including ageing, sympathetic overactivity, toxins, and a low nephron number have been proposed as factors that could ultimately damage the renal tubules and alter epithelial cells, resulting in defective sodium excretion.

II. Objective:

Primary: The objective of this study was to examine the associations of essential hypertension with the pattern of urinary sodium excretion and comparison of the results with those from the normotensive subjects.

Secondary: The study further quantified the variations and related them with the severity of hypertension.

III. Materials and methods:

The study was a hospital based cross sectional observational study. The study group consisted of two subsets, the hypertensives individuals(according to JNC 7 criteria) who came to SMHS hospital, both for indoor and outdoor consultations and the normotensive group consisted of volunteers selected randomly.

The duration of study was 24 months.

The inclusion criteria for the study group was Hypertension according to the JNC 7

The inclusion criteria for controls:

- Volunteers, who were normotensive

The exclusion criteria for study group:

- Patients receiving diuretics
- Patients with liver function abnormalities documented on LFT or USG abdomen.
- Patients with impaired KFT or abnormal routine urine examination
- Congestive heart failure
- Any electrolyte or any acid base disorder

The exclusion criteria for controls:

- Hypertension
- Patients receiving diuretics
- Patients with liver function abnormalities documented on LFT or USG abdomen.
- Patients with impaired KFT or abnormal routine urine examination
- Congestive heart failure
- Any electrolyte or any acid base disorder

Study participants provided three carefully timed 8- hour urine collections divided into 6am-2pm, 2pm-10pm and 10pm-6am periods which were analysed for sodium levels.

Special attention was paid to completeness of all specimens. Detailed instructions on methods for collection for each time period was included in each urine collection kit. Adequacy and accuracy of samples was done by doing urinary creatinine of the samples.
IV. Statistics

The recorded data was compiled and entered in a spreadsheet (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 summarised as percentages. Chi-square test or Fishers exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and pie diagrams. A p-value of less than 0.05 was considered statistically significant. All P-values were two tailed.

V. Results:

Our study enrolled a total of 100 participants. Half of them suffered from essential hypertension and the other half formed the normal controls. The mean age of the patients in hypertensive group (47.5±9.45) was comparable to that in the normotensive group (48.3±8.37). Among the hypertensive group, males outnumbered females by 38:12. This gender ratio was comparable in normotensive group. The urine samples were collected carefully and urinary creatinine was done to ensure the adequacy of the samples.

<table>
<thead>
<tr>
<th>Time Interval</th>
<th>Normotensive</th>
<th>Hypertensive</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 am-2 pm</td>
<td>79.5±17.82</td>
<td>57.2±18.15</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>2 pm-10 pm</td>
<td>52.4±12.45</td>
<td>45.7±15.82</td>
<td>0.021*</td>
</tr>
<tr>
<td>10 pm-6 am</td>
<td>42.7±25.71</td>
<td>35.1±31.74</td>
<td>&lt;0.001*</td>
</tr>
</tbody>
</table>

It was found that the mean excretion of sodium was significantly higher during morning hours in the normotensive patients (6 a.m. to 2 p.m.) 79.5 vs 37.3 in hypertensives and our data showed the reversal of pattern with hypertensive patients where nocturnal excretion (10 p.m to 6 a.m) of sodium was almost double as compared to their normotensive counterparts (p value <0.001). Among the 22 hypertensive patients where nocturnal (10 p.m - 6 a.m) secretion of sodium was higher than the daytime levels, the mean value of sodium excretion during nocturnal intervals was roughly the double of each of other 8 hour intervals. 28 out of 50 of the hypertensive patients had their 8 hourly sodium excretion pattern similar to that of the normotensive patients with high levels during the morning hours (p-value<0.001). Only 4 out of 50 normotensive patients had their nocturnal sodium levels exceeding that of the other 8 hourly intervals, the pattern that had been seen in hypertensive patients. The excretion of majority of the normotensive patients (44/50) revealed a pattern where sodium excretion in morning interval (6 a.m - 2 p.m) interval was double than that of other 8 hourly intervals (p<0.001)

VI. Discussion:

Non-Communicable diseases have taken over the communicable diseases as the leading causes of mortality and morbidity worldwide, hypertension and diabetes being the two most important. WHO projections show that NCDs will be responsible for a significantly increased total number of deaths in the next decade.

Globally, the overall prevalence of raised blood pressure in adults aged 25 and over was around 24% in males and 20.5% among females (4)

As such, over the years scientists and researchers have studied hypertension extensively and have tried to delineate its pathogenesis. Theories about the origin and development of hypertension are varied and blossom repeatedly. These range from mosaic theory where it was stated that the essential hypertension will prove to be not a single disease, but many different diseases of different origin and development to the haemodynamic theory which states that hypertension begins as the increase in cardiac output which in turn increases the pressure on the arterial tree. (5)

The other theories profess the role of increases sympathetic stimulation and baroreceptor reset, with age, in the pathogenesis of the essential hypertension. It is concluded that no one theory is adequate at present.
time to encompass all the known facts. It has been found that the role of eating habits and the sedentary life style has marked influence on the epidemic of hypertension. This was demonstrated in a landmark DASH trial, showing a significant effect of dietary changes over the control of blood pressure. Hence, a great emphasises has been laid on the influence of Sodium content in our diet on Blood pressure. Not only has the significant effect of excess salt intake in our diet on blood pressure been validated by many investigators, but the association between the sodium excretion/retention and blood pressure has also been demonstrated. Data from epidemiological, clinical, and animal experimental studies all indicate a direct causal association between excess salt intake and hypertension. It has long been thought that blood pressure is the primary determinant of nighttime sodium excretion and investigators suggest that hypertension is the result of an inability of the kidney to excrete salt and water normally.

Dyer et al in 1998 conducted a study as a follow-up to the study in HCP hypertensives, to examine further associations of BP with diurnal variation in excretion of sodium, potassium, and water, with control for potential confounding variables including age. In these analyses, SBP and DBP were positively and significantly correlated with 3-day averages of 8-h overnight to 24-h urinary excretion of sodium and potassium, but not with urinary volume or creatinine, with control for age, BMI, alcohol intake, and heart rate. Mean BP differences between highest and lowest quartiles of average ratios, with adjustment for these same variables, were 8.7 and 4.3 mm Hg for SBP and DBP for sodium, and 9.2 and 6.1 mm Hg for potassium. Average ratios for sodium, potassium, and urinary volume were also significantly correlated with age. For those under age 40, mean proportions of 24-h excretion in the 8-h over- night collection corresponded to harmonic means for ratios of 24-h to 8-h overnight excretion of 3.63 for sodium, 4.96 for potassium, and 3.38 for urinary volume, while for men aged 40 and over, mean pro- portions corresponded to lower harmonic means of 3.06, 4.32, and 2.97, respectively.

Positive associations of BP with overnight to 24- h ratios of sodium and potassium in these men indicate that with higher BP, a relatively greater proportion of 24-h urinary sodium and potassium excretion occurred at night. These results also indicate however, that with higher BP, a relatively smaller proportion of 24-h urinary sodium and potassium excretion occurred during the daytime, since the proportion excreted during the day is simply 100 minus the proportion excreted at night. Diurnal variations in excretion of sodium, chloride, potassium, and water have thus been observed in the patients of essential hypertension. Water and electrolyte excretion in healthy individuals generally reaches a maximum sometime around midday and a minimum toward the end of sleep. However, it has been observed that the hypertensive subjects have higher nighttime sodium excretion rates than normotensive subjects and a relative daytime salt retention.

VII. Conclusion:

Though the results of the studies in the past show variable results with regards to diurnal sodium excretion our results were in accordance with the theory that the hypertensive patients lose their circadian rhythm of urinary sodium excretion and this tool, though cumbersome, can be used to identify patients who have high nocturnal Blood Pressure, and are thus amenable to more organ damage.

Bibliography:

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