Renal Sodium Handling in Patients With Untreated Hypertension and White Coat Hypertension

Michel Burnier, Jérôme Biollaz, Jean Luc Magnin, Michel Bidlingmeyer, Hans R. Brunner

Abstract Renal tubular sodium handling was investigated prospectively in 48 normotensive subjects, 53 untreated hypertensive patients, and 13 patients with white coat hypertension using endogenous trace lithium as a marker of proximal sodium reabsorption. A 12-hour daytime ambulatory blood pressure recording was performed in all patients to confirm the diagnosis of hypertension. Patients were included in the white coat hypertension group if their office blood pressure was above 160/90 mm Hg but the mean value of their 12-hour ambulatory recording was lower than 140/90 mm Hg. All participants were studied on their normal diet and ate salt freely. Fractional excretions of sodium (FENa), lithium (FEU), and potassium (FEK) were measured simultaneously before blood pressure recording. FENa was significantly higher in hypertensive patients (0.84±0.05%, P<.05) than in normotensive control subjects (0.60±0.06%), and FEK was comparable in the two groups (15.4±0.65% in hypertensive patients and 17.0±0.9% in control subjects). However, the relation between FENa and FEK was significantly different in normotensive subjects and hypertensive patients (P<.001), so that for a given increase in FENa a smaller increase in FEK was observed in hypertensive patients. In addition, the ratios of urinary lithium to sodium and urinary potassium to sodium were significantly reduced in hypertensive patients, suggesting an increased proximal reabsorption of sodium. Similar alterations in renal tubular sodium handling were observed in patients with white coat hypertension. These results suggest that an increased sodium reabsorption in the proximal tubule may contribute to the maintenance of hypertension and that white coat hypertension might represent a prehypertensive state. (Hypertension. 1993;23:496-502.)

Key Words hypertension, essential • lithium • sodium • hypertension, white coat • renal function

The kidneys play a key role in the regulation of blood pressure and in abnormalities of renal function, including an increase in renal sodium reabsorption, which appears to be pivotal in the development and maintenance of experimental and clinical hypertension. The pressure-natriuresis mechanism is abnormal in all forms of chronic hypertension, suggesting that in hypertensive patients and animals, adequate renal sodium excretion is achieved only at elevated blood pressures.1 The nature of the renal abnormality leading to a rightward shift of the pressure-natriuresis curve in hypertension is still unknown. It may be the consequence of alterations in renal hemodynamics, as renal vascular resistance is almost invariably found to be increased in patients with hypertension, but it could also be due to abnormalities of renal tubular sodium reabsorption.2

So far, an increase in tubular sodium reabsorption leading to sodium retention has been difficult to show conclusively in hypertensive animals or patients. Nonetheless, some evidence in favor of this hypothesis has been accumulated over the past 10 years. The first attempts to characterize renal sodium handling in normotensive and hypertensive animals were done using micropuncture studies. However, the need for anesthesia and surgery, which modify renal hemodynamics and hence renal sodium excretion, has considerably limited the conclusions that can be drawn from such studies.3,4 In the 1980s, several investigators used lithium as a marker of proximal tubular sodium reabsorption to evaluate renal sodium handling in hypertension.2-12 Lithium is freely filtered at the glomerulus and reabsorbed in the proximal tubule in parallel with sodium and water. Although some lithium may be reabsorbed in the loop of Henle in some circumstances, distal tubular handling of lithium is minimal.13 Thus, the fractional excretion of lithium (FEU) may be the best marker of proximal sodium reabsorption available today.

When the fractional excretion of sodium (FENa) and FEU were compared in normotensive and hypertensive rats, tubular sodium handling was found to be altered in hypertensive animals, suggesting a decreased contribution of sodium escaping proximal reabsorption to final sodium excretion in these animals.5 Moreover, a decrease in FEU indicative of an increased proximal tubular sodium reabsorption has been found in two models of genetic hypertension, ie, the spontaneously hypertensive rat and the Dahl salt-sensitive rat.5,12 In humans, Weder6 found patients with essential hypertension to have a lower FEU than normotensive control subjects. A reduced FEU was also measured in the normotensive first-degree relatives of essential hypertensive patients. In contrast to this original report, several other investigators7,10,11 reported no difference or an increase in lithium clearance in hypertensive patients compared with normotensive control subjects. In addition, no increase in proximal sodium reabsorp-

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Characteristics of the Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Controls (n=48)</th>
<th>Untreated Hypertension (n=53)</th>
<th>White Coat Hypertension (n=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>44</td>
<td>51.4</td>
<td>58.4</td>
</tr>
<tr>
<td>Range</td>
<td>21-79</td>
<td>28-78</td>
<td>21-78</td>
</tr>
<tr>
<td>Men/women</td>
<td>26/22</td>
<td>28/25</td>
<td>7/8</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>70±16</td>
<td>74.2±13.3</td>
<td>74.6±14.8</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>24.3±5.0</td>
<td>26.6±3.70*</td>
<td>27.0±5.0</td>
</tr>
<tr>
<td>Office BP, mm Hg</td>
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<tr>
<td>Systolic</td>
<td>126±13.9</td>
<td>168.6±20.9†</td>
<td>165.3±14.5†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>82±5.8</td>
<td>105.5±13.5†</td>
<td>97.7±5.0†</td>
</tr>
<tr>
<td>Ambulatory BP, mm Hg</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>...</td>
<td>157.4±15.9</td>
<td>136.9±14.1†</td>
</tr>
<tr>
<td>Diastolic</td>
<td>...</td>
<td>100.1±10.3</td>
<td>82.7±5.1†</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>86±14</td>
<td>84.3±15.8</td>
<td>80.7±13.6</td>
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<td>Plasma</td>
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<tr>
<td>Sodium, mmol/L</td>
<td>141±2.4</td>
<td>140±2.8</td>
<td>140±2.2</td>
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<tr>
<td>Potassium, mmol/L</td>
<td>4.38±0.39</td>
<td>4.31±0.35</td>
<td>4.37±0.33</td>
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<tr>
<td>Lithium, μmol/L</td>
<td>0.17±0.08</td>
<td>0.18±0.06</td>
<td>0.26±0.22</td>
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<td>Urine</td>
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<td></td>
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<tr>
<td>Sodium, mmol/L</td>
<td>105±50.9</td>
<td>121±55.8</td>
<td>129.5±45.2</td>
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<tr>
<td>Potassium, mmol/L</td>
<td>78.8±37.5</td>
<td>62.5±32.7</td>
<td>70.0±25.7</td>
</tr>
<tr>
<td>Lithium, μmol/L</td>
<td>3.70±2.24</td>
<td>2.92±1.55</td>
<td>3.77±2.37</td>
</tr>
</tbody>
</table>

BP indicates blood pressure. Values are mean±SD.

*P<.05.
†P<.01 vs controls.
‡P<.01 vs untreated hypertension.

The purpose of the present study was to investigate renal sodium handling in untreated hypertensive patients, in patients with white coat hypertension, and in normotensive control subjects using trace lithium as a marker of proximal sodium reabsorption.

Methods

Subjects

The study was conducted in 48 normotensive subjects, 53 untreated hypertensive patients, and 13 patients with white coat hypertension. The characteristics of these three groups are presented in the Table. All participants gave their informed consent.

The normotensive control subjects had a normal blood pressure measured in the sitting position using a mercury sphygmomanometer (phases I through V). They were on their usual diets and had no other known diseases at the time of the study. None were taking drugs, including analgesics or nonsteroidal anti-inflammatory agents.

All hypertensive patients were newly diagnosed, had never received drug treatment for hypertension, and had no evidence of renal or heart disease. Their office blood pressure was greater than 160/90 mm Hg when measured with a sphygmomanometer on at least three occasions. A 12-hour daytime ambulatory blood pressure recording was performed in all patients to confirm the diagnosis of hypertension. For inclusion in this group, the mean 12-hour blood pressure value had to be greater than 140/90 mm Hg. Like control subjects, these patients were on a free sodium diet and were not taking any drugs when investigated.

Patients were included in the white coat hypertension group if their office blood pressure was greater than 160/90 mm Hg at three different occasions but the mean value of their 12-hour ambulatory blood pressure recording was lower than 140/90 mm Hg. These patients were studied under the same conditions as hypertensive patients.

Finally, some results were also obtained from a group of 18 healthy male volunteers maintained on a fixed-sodium diet of 160 mmol sodium and 80 mmol potassium per day for 5 days.

In all the studies cited above, exogenous lithium was administered to obtain measurable concentrations of lithium in plasma and urine. There is now evidence that administration of lithium has acute effects on renal electrolyte handling, the most disturbing being an increase in sodium excretion. The effects of lithium on sodium excretion have been found even at very low plasma lithium concentrations of approximately 0.2 mmol/L. Thus, it is possible that in most previous studies the administration of exogenous lithium interfered with the parameter under investigation, ie, sodium excretion. The determination of natural trace lithium in plasma and urine obviates the need for lithium administration and allows the calculation of lithium clearance and FE_Li under steady-state conditions with no interference.

The purpose of the present study was to investigate renal sodium handling in untreated hypertensive patients, in patients with white coat hypertension, and in normotensive control subjects using trace lithium as a marker of proximal sodium reabsorption.
Experimental Methods

All participants in the study were investigated at the Polyclinique Médicale Universitaire between 7 and 9 AM. After 30 minutes in the supine position, blood was drawn for the determination of plasma sodium, potassium, trace lithium, and creatinine. Plasma renin activity was also determined in hypertensive patients and patients with white coat hypertension. After blood was drawn, a urine sample was obtained to measure the urinary concentrations of sodium, potassium, trace lithium, and creatinine. None of the patients or subjects received additional water to ensure diuresis. In all hypertensive patients, blood and urine samples were taken immediately after the installation of the ambulatory blood pressure recorder.

Sodium and potassium concentrations were measured by flame photometry (Eppendorf) and creatinine concentration by the Jaffé method on an autoanalyzer (Cobas Bio, Hoffmann-La Roche). Trace lithium in plasma and urine was determined by electrothermal atomic absorption spectrophotometry (model 1100B with HGA-700 graphite furnace, Perkin-Elmer). Briefly, plasma samples were deproteinized, and urinary lithium was separated by solid-phase extraction. Ammonium nitrate was used as a matrix modifier. The intraday and interday variabilities were 7% and 10%, respectively, with a quantification limit of the method of 0.043 μmol/L. The fractional excretion of potassium (FEK), FEN, and FEU were calculated by the standard formula: FE = UC/PC - UC/PC, where U and P represent urinary and plasma concentrations of sodium, potassium, and lithium; and U , and P are urinary and plasma concentrations of creatinine, respectively. The fractional reabsorption of sodium in the postproximal tubules (FDR No) was calculated as [(FE - FE No)/(FE No)] x 100. For the determination of plasma renin activity, angiotensin I (Ang I) generated during a standard incubation procedure was trapped and measured by high-affinity antibodies.

Statistical Analysis

All results are expressed as mean±1 SD or SEM when indicated. The statistical significance of differences was evaluated by a one-way ANOVA followed by Fisher's least significant difference test, with a value of P<.05 as the minimum level of significance. A multiple regression analysis was used to compare the relation between FE and FEU in the various groups. The following linear model was fitted to the data: FEU=FE No+FE +b FEU, where a and b are regression coefficients, and the e error term and a1 and a2 are dummy variables taking the value 1 for hypertensive patients and white coat hypertension, respectively, and 0 otherwise. This model was compared with the single linear regression, where a1=a2=0, FEU=(FE No)+b FEU, by the mean of an F test.

Results

The characteristics of the three groups included in the study are presented in the Table. Patients with untreated and white coat hypertension were older than control subjects, but the age range was comparable and the difference was not significant. Patients also had a higher body mass index than control subjects (P<.05). Again, the ratio of urinary potassium to sodium was significantly lower in hypertensive patients, FEU was not significantly decreased in hypertensive patients, and FDR No are presented in Fig 2. FEU was significantly increased in untreated hypertensive patients (0.84±0.05% in hypertensive patients versus 0.60±0.06% in control subjects, P<.05) and was comparable to control subjects in patients with white coat hypertension (0.56±0.1%). FEU was not significantly decreased in hypertensive patients (15.4±6.55% versus 17.0±0.9% in control subjects). The ratio of urinary potassium to sodium was significantly lower in hypertensive patients compared with normotensive subjects (0.58±0.12 versus 1.02±0.13, P=.05). Again, the change did not reach statistical significance in patients with white coat hypertension (0.62±0.25, P=NS).

FE No and FEU, the latter reflecting indirectly proximal sodium reabsorption, and FDR No are presented in Fig 2. FE No was significantly increased in untreated hypertensive patients (0.84±0.05% in hypertensive patients versus 0.60±0.06% in control subjects, P<.05) and was comparable to control subjects in patients with white coat hypertension (0.56±0.1%). FEU was not significantly decreased in hypertensive patients (15.4±6.55% versus 17.0±0.9% in control subjects). However, it was significantly lower in patients with white coat hypertension (11.6±1.7%, P<.05 versus control subjects). FDR No was 96.3±0.3% in control subjects and was reduced to 94.4±0.5% in hypertensive patients.

In patients with white coat hypertension, plasma renin activity was at 0.77±0.21 ng Ang I/mL per hour. In patients with white coat hypertension, plasma renin activity was at 0.77±0.21 ng Ang I/mL per hour.

Urinary sodium concentration was slightly but not significantly higher in hypertensive patients and patients with white coat hypertension. Urinary potassium concentration tended to be lower in hypertensive patients, whereas urinary lithium concentration was comparable in all three groups. However, as shown in Fig 1, the ratio of urinary lithium to sodium was significantly decreased in hypertensive patients compared with normotensive control subjects (0.026±0.003 versus 0.044±0.004, P<.05). In patients with white coat hypertension, this ratio (0.032±0.007) was not significantly decreased when compared with control subjects. Similarily, the ratio of urinary lithium to sodium was significantly lower in hypertensive patients compared with normotensive subjects (0.58±0.12 versus 1.02±0.13, P=.05). Again, the change did not reach statistical significance in patients with white coat hypertension (0.62±0.25, P=NS).

Fig 1. Bar graphs show ratios of urinary lithium to sodium (U/L, top) and potassium (U K) to sodium (bottom) in normotensive subjects (n=48), untreated hypertensive patients (n=53), and patients with white coat hypertension (n=13). Results are mean±SEM. *P<.05 vs normotensive control subjects.
FIG 2. Bar graphs show fractional excretion of sodium (FE\textsubscript{Na}, top) and lithium (FE\textsubscript{Li}, middle) and fractional distal reabsorption of sodium (FDR\textsubscript{Na}, bottom) in normotensive subjects (n=48), untreated hypertensive patients (n=53), and patients with white coat hypertension (n=13). Results are mean±SEM. *P<.05 vs normotensive control subjects. Patients (P=NS) and to 92.3±2.8% in patients with white coat hypertension (P<.05). In normotensive control subjects, the FE\textsubscript{Na}/FE\textsubscript{Li} ratio was 0.036±0.003. This ratio was significantly increased in untreated hypertensive patients (0.056±0.004, P<.05) and patients with white coat hypertension (0.076±0.028, P<.05).

Fig 3 shows the relations between FE\textsubscript{Na} and FE\textsubscript{Li} in the 48 normotensive and 53 hypertensive patients. In addition, the results obtained in 18 normotensive subjects maintained on a high sodium diet are shown. A linear correlation was present in normotensive subjects (y=10.9x+10.5, r=.81, n=48) and hypertensive patients (y=3.7x+12.3, r=.35, n=53). The relation was even better according to the multiplicative model (y=aX\textsuperscript{b}), with a correlation coefficient of .70 in normotensive subjects and .41 in hypertensive patients. The slope of the two regression lines differed markedly (P<.001), so that for a given increase in FE\textsubscript{Li} a larger increase in FE\textsubscript{Na} was observed in hypertensive patients than in normotensive control subjects. In patients with white coat hypertension a weak linear correlation was also found, but the number of patients was too small to establish statistical significance.

The relations between FDR\textsubscript{Na} and FE\textsubscript{Na} in normotensive individuals and hypertensive patients are shown in Fig 4. Again, close correlations were found in both groups (y=-3.73x+98.6, r=-.72 and y=-5.0x+98.6, r=-.83, respectively). The results obtained in normotensive volunteers on a high sodium intake fitted perfectly to the relation of normotensive subjects. No correlation was found between systolic or diastolic blood pressure and FE\textsubscript{Li}.

**Discussion**

Our results show that the relative contribution of the proximal and postproximal tubules to the final excretion of sodium is significantly different in normotensive subjects and untreated hypertensive patients or patients with white coat hypertension. Normotensive subjects are characterized by a steep relation between FDR\textsubscript{Na} and FE\textsubscript{Na} and a flat relation between FDR\textsubscript{Na} and FE\textsubscript{Na}, suggesting a preponderant role of the early proximal tubule in regulating sodium excretion. In contrast, in hypertensive patients proximal sodium reabsorption is increased and the postproximal segments appear to play a greater role in sodium excretion.

To be a reliable estimate of proximal tubular reabsorption of sodium, a substance should have two characteristics. First, its ratio of tubular fluid to plasma concentration at the end of the proximal tubule should...
be very close to 1, and second, none of the substance should be reabsorbed beyond the proximal tubule. Lithium is indeed reabsorbed in parallel to sodium and water in the proximal tubule. Some controversy has been raised about a possible reabsorption of lithium in the postproximal tubules. Lithium may be reabsorbed beyond the proximal tubule in circumstances such as salt depletion. However, postproximal reabsorption is probably limited and unimportant in humans. At the present time, lithium clearance may therefore be considered as the best available estimate of proximal tubular sodium handling in humans.

Since the validation of lithium clearance as a marker of proximal sodium reabsorption, several investigators have used this technique to evaluate sodium reabsorption in hypertension. However, the results of these studies have so far given contradictory results. In subjects performing their usual daily activities, Weder and Langford et al. have found a significantly lower $F_{E \text{Na}}$ in hypertensive patients than normotensive control subjects, whereas in several other studies the $F_{E \text{Na}}$ of hypertensive patients was either higher or similar to that of normotensive subjects. Major differences in methodological approach have been proposed to explain these discrepancies. In particular, posture and salt diet were not controlled in the two studies demonstrating an increased proximal sodium reabsorption in hypertensive patients. Moreover, the hypertensive patients included in Weder's study were significantly younger (mean, 25.2 years) than those enrolled in most other trials.

In the present investigation, proximal sodium reabsorption was also found to be increased in hypertensive patients. Similar to Weder's study, our patients and their control subjects were studied on a free sodium intake under conditions that resembled as close as possible their normal life. All age categories between 20 and 80 years were included, with an equal distribution of men and women, and all blood and urine samples were collected after 30 minutes in the supine position. Because several studies have demonstrated that moderate changes in glomerular filtration rate do not preclude the use of lithium as an indicator of proximal tubular sodium reabsorption, renal function was estimated only by serum creatinine, and patients with abnormal creatinine values were not included. Finally, the presence of hypertension was confirmed by a 12-hour daytime ambulatory blood pressure recording.

In contrast to all previous studies, plasma and urinary trace lithium were measured in the present study. Although the technical skill for the method of atomic absorption spectrophotometry may represent a limitation to a wide use of trace $F_{E \text{Na}}$, this approach offers many advantages. First, there is no need to prescribe exogenous lithium on the day before the experiment. The enrollment of patients is thereby much easier, and in particular women of childbearing age or who are pregnant can be safely investigated. The second major advantage is the lack of interference with sodium excretion. Indeed, it has recently been shown that even low doses of exogenous lithium may modify urinary sodium excretion, the parameter under investigation. Some recent studies have demonstrated that this new approach is very effective in detecting the changes in proximal sodium reabsorption occurring after maneuvers such as head-out water immersion or in diseases such as liver cirrhosis, pericardial tamponade, or acute renal failure. To estimate the proximal reabsorption of sodium, we used $F_{E \text{Na}}$ rather than the clearance of lithium because this approach eliminates one important source of analytic error, i.e., urine flow rate, and reduces the large intersubject variation.

When analyzed as an independent value, $F_{E \text{Na}}$ was slightly but not significantly lower in hypertensive patients than normotensive control subjects. However, $F_{E \text{Na}}$ was significantly higher in hypertensive patients. Because all patients were studied on a free sodium diet, this higher $F_{E \text{Na}}$ most likely reflects a higher sodium intake in hypertensive patients. Because the proximal reabsorption of sodium and hence lithium is dependent on sodium intake, lithium excretion must be corrected for sodium excretion. When urinary lithium concentration was related to sodium excretion, a significant decrease in the urinary lithium-sodium ratio was found in hypertensive patients, suggesting an increase in the proximal reabsorption of lithium in hypertension. If sodium is reabsorbed more avidly in the proximal tubule, the distal delivery of sodium decreases, and hence less potassium is expected to be exchanged in the
distal tubule. This was indeed the case, as the potassium-sodium ratio was significantly reduced in untreated hypertensive patients. Thus, both the lithium-sodium and potassium-sodium ratios support the hypothesis that proximal reabsorption of sodium is enhanced in hypertensive patients.

The comparison of the relations between FE\textsubscript{Na} and FE\textsubscript{U} appears to be the best evidence for an alteration in renal sodium handling in hypertensive patients. Indeed, it is clearly apparent from the relations that the relative contribution of sodium escaping proximal reabsorption to final sodium excretion is decreased in hypertensive patients. Interestingly, the characteristics of the correlations between FE\textsubscript{Na} and FE\textsubscript{U} obtained in normotensive subjects (y = 10.9x + 10.5) and hypertensive patients (y = 3.7x + 12.3) are similar to those found some years ago in normotensive (y = 20.0x + 12.09) and hypertensive (y = 5.22x + 15.13) rats. The relation between FDR\textsubscript{Na} and FE\textsubscript{U}, also indicates that hypertensive patients exhibit a decreased distal sodium reabsorption. This latter finding is compatible with the early observation of Kunau and Lameire, who located the pressure-natriuresis phenomenon in the distal nephron. In both correlations, there is an overlap between hypertensive patients and normotensive subjects, particularly at a low FE\textsubscript{Na}, suggesting that the alteration is best revealed when the patients eat a high salt diet. Similarly, a decrease in FE\textsubscript{U} was found in Dahl salt-sensitive rats only after sodium loading. The overlap may also be due to an inhomogeneity of the hypertensive population. Previous studies performed in various models of hypertensive rats have shown that not all types of hypertensive animals have an increased proximal reabsorption of sodium. A decreased FE\textsubscript{U} was observed mainly in spontaneously hypertensive and Dahl salt-sensitive rats.

Considering the pathogenesis of hypertension, it would be important to know whether the increased reabsorption of sodium in the proximal tubule is the cause or only a consequence of hypertension. Persistent hypertension is characterized by a decrease in renal blood flow, which may result in an increase in proximal reabsorption of sodium. The proximal reabsorption could also be increased in response to a stimulation of the renin-angiotensin system or sympathetic nervous system. We did not measure renal blood flow or plasma catecholamines in this study but found plasma renin activity to be normal in our hypertensive patients. Thus, our results obtained in hypertensive patients do not allow us to answer this very crucial question.

An abnormality of renal tubular sodium handling has also been looked for in normotensive subjects with a positive family history of hypertension or in patients with borderline hypertension to determine whether the renal abnormality precedes or follows the development of hypertension. Weder found a low FE\textsubscript{Na} in normotensive subjects with a positive family history, whereas other researchers found no significant alteration of proximal sodium excretion in hypertensive offspring or patients with borderline hypertension.

We have evaluated the renal handling of sodium in another group of patients susceptible to developing hypertension, ie, patients with white coat hypertension. White coat hypertension is usually defined as a high blood pressure at the doctor's office and normal values when blood pressure is recorded during the patients' daily activities. Yet there is still no generally accepted definition of white coat hypertension because the normal limits of ambulatory blood pressure measurement have not been determined. Moreover, the factors responsible for the development of white coat hypertension and its long-term prognostic significance have not been established. In the present study, we defined white coat hypertension according to two arbitrary criteria, ie, a mean 12-hour daytime ambulatory blood pressure of less than 140/90 mm Hg and a mean office blood pressure, measured at different occasions, of greater than 140/90 mm Hg. In the small group of patients meeting these criteria, FE\textsubscript{Na} was found to be significantly lower than in normotensive control subjects, whereas sodium excretion in the two groups was similar. Conversely, FDR\textsubscript{Na} was significantly reduced in patients with white coat hypertension. Unfortunately, the number of patients enrolled in this subgroup was too small to evaluate adequately the relation between FE\textsubscript{Na} and FE\textsubscript{U}. Nevertheless, when included in the multiple regression analysis, the characteristics of the correlation obtained in this group of patients were significantly different from those of normotensive control subjects and similar to those found in hypertensive patients. Patients with white coat hypertension therefore appear to behave very much like untreated hypertensive patients. These results also suggest that in white coat hypertension, the alteration of renal sodium handling precedes the development of hypertension. This observation certainly deserves further investigation; however, it might considerably change our attitude toward patients with white coat hypertension. Indeed, it is still not known whether white coat hypertension represents an innocuous clinical condition. Our findings suggest that patients with white coat hypertension already share some similarities with patients who have established hypertension. In this respect, our results are in accordance with the recent observation that white coat hypertension is characterized by a mild cardiac enlargement and abnormalities in left ventricular filling similar to persistent hypertension.

In summary, our results show that the reabsorption of sodium in the proximal tubule, evaluated using FE\textsubscript{Na}, is increased in untreated hypertensive patients and that the distal tubule has a greater contribution to the final excretion of sodium in hypertensive patients than in normotensive subjects. These alterations in renal sodium handling can also be observed in patients with white coat hypertension. In these latter patients, the increase in sodium reabsorption may represent one pathogenetic mechanism and a plausible reason to consider white coat hypertension as a prehypertensive state.

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References


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