Abnormal Renal Hemodynamics in Black Salt-Sensitive Patients With Hypertension

Vito M. Campese, Mario Parise, Frederick Karubian, and Roberto Bigazzi

African-Americans with essential hypertension are more prone to the development of renal failure and are frequently salt-sensitive as well. Because alterations of intrarenal hemodynamics are important in the progression of renal disease and because salt-sensitive animal models with hypertension manifest a greater propensity to develop glomerulosclerosis in association with a rise in glomerular capillary pressure, we tested whether the renal hemodynamic adaptation to high dietary Na+ intake differs in salt-sensitive and salt-resistant hypertensive patients. We studied 17 black and nine white patients with essential hypertension who were placed on a low Na+ diet (20 meq/day) for 9 days, followed by a high Na+ diet (200 meq/day) for 14 days. During the last 4 days of each diet regimen, they received 30 mg/day of slow-release nifedipine. Eleven blacks were salt-sensitive, and all whites were salt-resistant. During the low Na+ diet period, salt-sensitive and salt-resistant patients had similar mean arterial pressure, glomerular filtration rate, effective renal plasma flow, and filtration fraction. During the high Na+ intake period, glomerular filtration rate did not change in either group; effective renal blood flow increased in salt-resistant patients (from 455±25 to 524±27.7 ml/min, p<0.01), but it decreased in salt-sensitive patients (from 538±20 to 426±15.8 ml/min, p<0.01); filtration fraction decreased (from 21±1.8 to 19±1.5%) in salt-resistant patients, but it increased (from 19±0.9 to 23±1.5%, p<0.01) in salt-sensitive patients; glomerular pressure decreased (from 58±2.0 to 52±1.5 mm Hg, p<0.01) in salt-resistant patients, but it increased (from 48±1.6 to 58±1.5 mm Hg, p<0.01) in salt-sensitive patients. During the period of high Na+ intake, nifedipine decreased arterial pressure, renal vascular resistance, and filtration fraction and increased renal blood flow in salt-sensitive but not in salt-resistant patients. These studies show that an abnormal renal hemodynamic adaptation occurs in salt-sensitive patients during high Na+ intake. The rise in filtration fraction and in intraglomerular pressure during high Na+ suggests that these renal hemodynamic derangements might be partially responsible for the greater propensity to renal failure in hypertensive African-Americans. (Hypertension 1991;18:805–812)
both in the renal tubular capacity to excrete a sodium load and in renal hemodynamic adaptation to changes in dietary sodium intake between SS and SR hypertensive patients.\(^\text{11}\)

Whether a linkage exists between these renal hemodynamic differences and the greater propensity for black hypertensive patients to develop renal failure remains to be established.

The purpose of this study was to evaluate the renal hemodynamic adaptation to a low and a high dietary sodium intake and to the administration of a calcium channel blocker, nifedipine, in a group of both black and white essential hypertensive patients.

The choice of a calcium channel blocker stems from the postulate proposed by us\(^\text{11}\) and by others\(^\text{12,13}\) that sodium-linked abnormalities in calcium metabolism may be the basis for the systemic and renal hemodynamic abnormalities observed in SS patients with essential hypertension.

### Methods

Twenty-six patients with essential hypertension and normal renal function were included in these studies. Seventeen were black and nine were white. The demographic characteristics of these patients are shown in Table 1.

Exclusion criteria excluded from the study patients with a creatinine clearance less than 80 ml/min, a history of myocardial infarction, congestive heart failure, stroke, diabetes mellitus, liver disease, and women with childbearing potential. Patients were considered to be hypertensive if, during three subsequent clinic visits to the outpatient clinic, their blood pressure was found to be equal to or greater than 140/90 mm Hg. Antihypertensive medications were discontinued at least 2 weeks before the study. Women on birth control pills and patients known to abuse drugs or alcohol were excluded from the study. A diagnosis of secondary hypertension was adequately ruled out by the normal findings of SMA-19, urinalysis, chest x-ray, urinary aldosterone, and renal angiogram when clinically indicated.

After the nature and the purpose of the study were explained and informed consent was obtained, all patients were admitted to the Clinical Research Center of the Los Angeles County-University of Southern California Medical Center for a period of 23 days. Throughout the study, the subjects ingested the same basic diet containing constant amounts of protein (1.3 g/kg), calories (126 kJ/kg), calcium (800 mg/24 hr), and potassium (80 meq/day), while their sodium intake varied. During the first 9 days of the study, patients received a diet containing 20 meq/day of sodium, whereas during the remaining 14 days, all patients received a dietary sodium intake of 200 meq/day. During the first 5 days of the low sodium diet (phase 1) and the first 10 days of the high sodium diet (phase 3), patients received a placebo. During the last 4 days of the low sodium diet (phase 2) and of the high sodium diet (phase 4) patients received nifedipine (Gastrointestinal Transport System [GITS], Pfizer Laboratories, New York) each evening at 8:00 PM. The duration of phase 3 was extended to 10 days to avoid the possibility that residual nifedipine effect from phase 2 might influence the hemodynamic response to high sodium intake. The renal function was evaluated four times: on day 5, 9, 19, and 23 of the study. The subjects were weighed daily at 8:00 AM after they had voided and before they had eaten breakfast. Twenty-four-hour urine collections were obtained daily throughout the study for measurement of creatinine, sodium, and potassium excretion. On each protocol day, the subjects assumed the recumbent position between 7:00 and 8:00 AM, and a venous catheter was inserted into a vein. One hour later, blood pressure and heart rate were measured, and a blood sample was obtained for the determination of serum sodium, potassium, creatinine, and hematocrit. Patients then received a light breakfast, and 1 hour later water diuresis was instituted by giving four 250-ml aliquots of water by mouth every 30 minutes. Glomerular filtration rate (GFR) and effective renal plasma flow (ERPF) were then measured by inulin and para-aminohippurate (PAH) clearances. Loading doses of inulin (40 mg/kg body weight) and of PAH (4 mg/kg body weight) were given, and an infusion of these two compounds (to maintain a serum concentration of 0.2 mg/ml and of 0.02 mg/ml, respectively) was initiated. After 2 hours of infusion, three separate measurements of inulin and PAH clearance were made 15 minutes apart. The clearance rates of inulin and PAH were corrected to a body surface area of 1.73 m\(^2\). Filtration fraction was calculated by

\[
\text{GFR/ERPF} \times 100
\]

The calculation of glomerular pressure and renal segmental vascular resistances was performed according to the analysis used by Gomez\(^\text{14}\) and later modified by Hall et al.\(^\text{15}\). Blood pressure was measured with an automatic recorder (Omega 1000 In Vivo Research Laboratories, Inc, Tulsa, Okla.). Each data point of blood pressure is the mean of three consecutive readings. Mean arterial pressure (MAP) was calculated as the sum of diastolic blood pressure and one third of pulse pressure. Sodium and potassium were determined by a flame photometer (Instrumentation Laboratory, Lexington, Mass.), and creatinine was measured by the Technicon autoanalyzer (Technicon Corp., Ardsley, New York).
Inulin and PAH were measured in plasma and urine by standard methods. The statistical analysis of the data was performed by analysis of variance for comparison between means, and by the Fisher Exact test for multiple comparisons. Relations between parameters were assessed using linear regression analysis. The data are expressed as mean±SEM.

Results

 Patients were divided into two distinct groups based on whether their MAP increased by more than 10 mm Hg on a high dietary sodium intake as compared with MAP during low dietary sodium intake. The 10 mm Hg criterion to divide patients into SS and SR groups was based on our previous observation that during high sodium intake, MAP usually does not increase more than 10 mm Hg in normal subjects without a predisposition for the development of hypertension. Based on this definition, 11 patients were classified as SS, and 15 patients were considered SR.

The clinical characteristics of SS and SR patients are shown in Table 1. The mean age of SS patients was 47±3.0 years and was not different from the mean age of SR patients (52±2.6 years). All SS patients were black, whereas in the SR group, nine were white and six were black. During low dietary sodium intake, SS and SR patients had a similar MAP (100±3.3 versus 102±2.7 mm Hg). During high dietary sodium intake, MAP increased to 114±3.6 mm Hg (p<0.01) in SS patients but remained unchanged (98±2.0 mm Hg) in SR patients. In the latter group, MAP was independent of the level of dietary sodium intake. In the SR group, nifedipine caused no significant change in MAP. On the other hand, in the SS group nifedipine caused a significant fall in the MAP, which fell to levels comparable to those achieved during the low sodium diet (from 114±3.6 to 103±3.2 mm Hg).

Heart rate in SR was higher than in SS patients (70±2.6 versus 62±2.1 beats per minute, p<0.05) during a low but not during a high sodium diet (60±1.3 versus 58±1.7 beats per minute). Nifedipine did not cause a significant change in heart rate during low dietary sodium intake in either group or during high sodium intake in the SS group; however, nifedipine caused a significant increase in heart rate in the SR group during the high sodium diet (from 60±1.3 to 66±1.7 beats per minute, p<0.05). During high dietary sodium intake, heart rate decreased by 10.6±2.1 beats per minute in the SR group but by only 4.4±1.5 beats per minute in the SS group (p<0.02).

Body weight was similar among SS and SR patients during low dietary sodium intake (87±3.8 kg). During high sodium intake, body weight in SS patients increased more than in SR patients (2.4±0.27 versus 0.8±0.26 kg, p<0.01). Nifedipine caused a greater decrease in body weight in SS than in SR patients both during low (-1.1±0.27 versus 0.69±0.12 kg) and during high dietary sodium intake (-0.7±0.19 versus 0.3±0.15 kg), but these differences were not statistically significant. In SS patients there was a significant correlation between the changes in body weight and the changes in MAP, when the data comparing high sodium versus low sodium and high sodium with nifedipine versus high sodium were combined (r=0.68, p<0.001). There was no correlation between changes in body weight and changes in MAP in SR patients (Figure 1). There was no significant correlation between the changes in body weight and MAP observed in either group of patients during the period of low sodium diet plus nifedipine.

The slope of the renal function curve in SS patients was 0.08±0.011 was significantly different from that of SR patients (-0.028±0.013, p<0.005). Nifedipine
improved the slope of the renal function curve to 0.04±0.03 (p=0.08) in SS patients (Figure 2).

GFR was similar between SS and SR patients during all phases of the study. During high dietary sodium intake, ERPF and renal blood flow increased significantly (p<0.05) in SR but decreased (p<0.05) in SS patients. ERPF was significantly higher (p<0.05) in SR compared with SS patients during high (531±26 versus 464±15 ml/min/1.73 m²) but not during low dietary sodium intake. Nifedipine caused a significant (p<0.05) rise in ERPF and renal blood flow in both SS and SR patients during high dietary sodium intake (Table 2).

During high dietary sodium intake, renal vascular resistance tended to decrease in SR patients (from 10,250±727 to 9,485±728 dynes/sec/cm⁵) but increased significantly (p<0.01) in SS patients (from 9,010±495 to 12,383±598 dynes/sec/cm⁵). Nifedipine caused a significant decrease in renal vascular resistance both in SS and in SR patients during high dietary sodium intake (Table 3).

The filtration fraction did not change in SR patients during the four phases of the study, but it increased from 19±0.98% during low sodium to 23±1.49% during high sodium intake (p<0.05) in SS patients (Table 2). There was a significant difference (p<0.01) between SS and SR patients in the changes in filtration fraction from the low to the high sodium diet.

Glomerular capillary pressure was lower in SS patients (p<0.01) during high Na⁺ intake compared with the values during low Na⁺ intake (52±1.5 and 58±2.0 mm Hg, respectively). On the contrary, glomerular capillary pressure in SS patients was higher during high Na⁺ intake than during low dietary Na⁺ intake (58±1.5 versus 48±1.6 mm Hg, p<0.01) (Table 3).

As previously mentioned, the racial composition of the SR group was six blacks and nine whites (Table 4). During low dietary sodium intake, MAP in SR blacks was 95±4.3 mm Hg, which was significantly lower (p<0.05) than in the white population taken alone (106±2.6 mm Hg). During high dietary sodium intake MAP decreased in whites (from 106±2.6 mm Hg to 100±2.5 mm Hg, p<0.05) but did not change in black SR patients. In whites, nifedipine

### Table 2. Mean Arterial Pressure, Heart Rate, Body Weight, Glomerular Filtration Rate, Effective Renal Plasma Flow, Renal Blood Flow, Filtration Fraction, and 24-Hour Urine Sodium Excretion in Salt-Sensitive and Salt-Resistant Patients Measured the Last Day of Each Phase

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Salt-resistant</th>
<th>Salt-sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>Low Na⁺ Low Na⁺+Nif High Na⁺ High Na⁺+Nif</td>
<td>Low Na⁺ Low Na⁺+Nif High Na⁺ High Na⁺+Nif</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>102±2.7 96±2.1 98±2.0 96±2.6 100±3.3</td>
<td>95±3.6 114±3.6* 114±3.6* 103±3.2†</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>81±3.8 80±3.7* 81±3.7 80±3.7 87±4.4</td>
<td>86±4.3* 88±4.2* 88±4.2*</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)</td>
<td>97±6.0 93±6.7 100±6.7 100±5.9 102±5.7</td>
<td>99±6.4 107±7.9 107±7.9 108±7.8</td>
</tr>
<tr>
<td>ERPF (ml/min/1.73 m²)</td>
<td>482±28.8 504±34.5 531±26.6* 570±33.6†</td>
<td>538±20.3 495±27.7 464±15.8* 528±24.2†</td>
</tr>
<tr>
<td>RBF (ml/min/1.73 m²)</td>
<td>831±50.4 853±55.6 854±43.0 919±53.4†</td>
<td>900±34.9 831±42.4 747±31.0* 853±40.5†</td>
</tr>
<tr>
<td>FF (%)</td>
<td>20.8±1.61 18.8±1.20 19.1±1.30 18.0±1.16 19.2±0.98</td>
<td>20.5±1.59 22.8±1.49* 20.6±1.2</td>
</tr>
<tr>
<td>UNa⁺</td>
<td>29±4.6 20±3.3 193±11.3 167±12.7 31±3.5</td>
<td>28±6.0 193±10.9 190±11.3</td>
</tr>
</tbody>
</table>

Nif, nifedipine; MAP, mean arterial pressure; HR, heart rate; bpm, beats per minute; GFR, glomerular filtration rate; ERPF, effective renal plasma flow; RBF, renal blood flow; FF, filtration fraction; UNa⁺, 24-hour urine sodium excretion.

* p<0.05 versus low Na⁺.
† p<0.05 versus high Na⁺.
‡ p<0.05 versus salt-resistant.

### Table 3. Renal Hemodynamic Parameters in Salt-Sensitive and Salt-Resistant Patients With Essential Hypertension

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Salt-resistant</th>
<th>Salt-sensitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal vascular resistance (dynes/sec/cm⁵)</td>
<td>Low Na⁺ Low Na⁺+Nif High Na⁺ High Na⁺+Nif</td>
<td>Low Na⁺ Low Na⁺+Nif High Na⁺ High Na⁺+Nif</td>
</tr>
<tr>
<td>Renal afferent resistance (dynes/sec/cm⁵)</td>
<td>10,259±727 9,485±728 9,542±658 8,815±632*</td>
<td>9,010±495 9,367±606 12,383±598‡ 9,895±480*</td>
</tr>
<tr>
<td>Renal efferent resistance (dynes/sec/cm⁵)</td>
<td>4,322±381 3,937±414 4,524±388 3,929±339</td>
<td>4,601±468 4,171±552 5,712±433‡ 4,403±239*</td>
</tr>
<tr>
<td>Glomerular pressure (mm Hg)</td>
<td>58±2.0 56±1.8 52±1.5† 53±1.6</td>
<td>48±1.6† 48±1.6 58±1.5‡ 54±4.3</td>
</tr>
</tbody>
</table>

Nif, nifedipine.
* p<0.02 versus high Na⁺.
† p<0.01 versus low Na⁺.
‡ p<0.05 versus salt-resistant.
lowered MAP (from 106±2.6 to 97±2.8 mm Hg, *p<0.05*) during low sodium diet and (from 100±2.5 to 97±2.8 mm Hg) during high sodium diet, but this difference was not statistically significant. MAP did not change in black SR patients during the four phases of the study.

There was no difference in GFR, ERPF, renal blood flow, renal vascular resistance, and filtration fraction among either black or white SR patients (Table 3).

**Discussion**

Together, these studies point out substantial differences in the systemic and renal hemodynamic adaptation to a high dietary sodium intake between SS and SR patients with essential hypertension.

For example, during high dietary sodium intake, SS patients not only gained more weight but also displayed a greater rise in blood pressure than did the SR patients. In fact, there was a significant and direct correlation between the increase in body weight and the rise in MAP. This suggests that increased sodium retention may play a role in the rise of blood pressure during sodium loading in black SS patients.

Our findings confirm previous evidence that suggests that hypertensive blacks handle sodium less efficiently than whites. Weinberger et al.\(^1\) have shown that after salt loading with 2.1 of 0.9% NaCl given over a 4-hour period, black hypertensive patients as well as normotensive blacks at risk of becoming hypertensive excrete the salt load more slowly and less completely than whites. These investigators have also compared the blood pressure response to extremes of sodium intake (ranging from 10 to 1,500 meq/day) in both black and white normotensive subjects. Despite similar increases in sodium balance, blood pressure increased significantly more in black than in white patients.\(^19\) Dustan et al.\(^20\) have also reported that SS patients retain more sodium than SR patients when salt loaded after a period of salt depletion.

The slope of the renal function (pressure–natriuresis) curve was significantly lower in the SS patients when compared with the renal function curve of the SR patients, confirming our previous observation.\(^11\) This finding suggests a disturbance in renal tubular sodium reabsorption in the SS group. More importantly, it constitutes a pathophysiological basis for the greater sodium retention and the attendant rise in blood pressure observed during sodium loading in these SS patients. However, the reasons for the shift of the renal function curves and for the lower slope of this relation in the SS patients remain to be established.

Several investigators have proposed that the shift of the renal function curve in hypertension might be due to a genetic defect involving the ability of the kidneys to excrete a sodium load.\(^21,22\) Guyton et al.\(^23\) have proposed that blood pressure increases as a compensatory response to sodium retention to increase filtered sodium load and maintain sodium balance.

The plausibility of this hypothesis in human subjects becomes more apparent when the lower portion of the renal function curve belonging to SS patients is superimposed on the renal function curve of normal subjects. The lower portion of this curve represents the period of blood pressure normalization in the SS patients that occurs during low dietary sodium intake. As blood pressure normalizes with dietary sodium restriction, the two curves approximate each other more closely.

There are exceptions, however, and this hypothesis cannot be applied to all SR patients nor can it completely apply to those SS patients whose blood pressure remains high even during dietary sodium restriction. In these patients, the shift of the renal function curve must be secondary to other mechanisms.

Since a shift of the renal function curve occurs in secondary forms of hypertension and reverses with correction of the underlying cause for the secondary hypertension,\(^24\) it is possible that factors other than a congenital renal defect may account for the shift of
the renal function curve in patients with essential hypertension.

Among the factors that can alter the renal function curve is an increased activity of the sympathetic nervous system. Substantial evidence both in animals and in human subjects suggests that high dietary sodium intake may stimulate the activity of the sympathetic nervous system resulting in water retention and in a rise in blood pressure.

Interestingly, in this study we have shown that a decrease in heart rate is more pronounced in SR as compared with SS patients during high dietary sodium intake, thus giving further indirect support to the notion that abnormalities in autonomic nerve function exist in SS patients with essential hypertension.

Substantial differences in renal hemodynamic adaptation to a high dietary sodium intake also exist between SS and SR patients.

GFR, renal vascular resistance, renal blood flow, and filtration fraction did not change during low or high dietary sodium intake in either black or white SR patients.

In SS patients, on the other hand, there were significant renal hemodynamic changes during high compared with low dietary sodium intake: GFR did not change, renal vascular resistance increased, renal blood flow decreased, and filtration fraction increased.

The rise in filtration fraction suggests the possibility of a parallel rise in intraglomerular pressure in SS patients during high dietary sodium intake. Indeed, calculation of glomerular capillary pressure by the Gomez formulas revealed substantial differences among SS and SR patients. Glomerular capillary pressure decreased during high dietary sodium intake in SR patients, but it increased significantly in SS patients. Although the results obtained with these methods must be regarded as approximation and interpreted with caution, it is of interest that they substantiate the differences in filtration fraction that we have observed in SS and SR patients in response to a high dietary sodium intake.

Since all SS patients in this study were black, the observed abnormalities in renal hemodynamic adaptation to high sodium diet may provide a mechanistic explanation for the greater propensity for the development of progressive renal failure in hypertensive African-Americans.

One can speculate that since the average daily dietary sodium intake in the African-American population approximates that used in these studies, this might lead to a permanent elevation in intraglomerular pressure and to progressive nephrosclerosis and renal failure in these patients.

Animal studies support this concept. Spontaneously hypertensive rats (SHR) and Dahl SS rats (DS/Jr) are two inbred strains genetically predisposed to develop hypertension. Hypertension in the SHR develops spontaneously and independently of the dietary sodium intake, whereas hypertension in DS/Jr rats develops only if these animals are exposed to a high dietary sodium intake. In younger SHR, the superficial nephrons adapt to the rise in blood pressure with an increase in renal afferent arteriolar resistance, thus protecting the glomeruli from the adverse effects of hypertension. The juxtaglomerular nephrons are more susceptible to glomerulosclerosis and proteinuria. This may be because the rise in blood pressure in these animals is associated with a reduction of afferent arteriolar resistance, thereby causing a rise in glomerular capillary pressure.

In addition, other experimental models of SS hypertension in rats manifest accelerated glomerulosclerosis. These models include deoxycorticosterone acetate–salt hypertension, uninephrectomized SHR, the Holtzman post-salt model of hypertension, and the Milan strain of SHR.

All these SS models of hypertension share the characteristic of responding to a rise in systemic arterial pressure with a rise in glomerular capillary pressure.

Before the present study, there was a paucity of data in the literature relating to renal hemodynamics in black hypertensive patients, and most of the articles that were published did not take into account the potential impact of different dietary sodium intakes.

Levy et al showed a significant reduction in renal blood flow and a failure of urinary kallikrein to increase in response to sodium depletion in black hypertensive patients. They also observed by renal angiogram that black hypertensive patients manifested more severe nephrosclerosis than white patients.

Frohlich and coworkers measured cardiac output, plasma volume, and renal blood flow in blacks and whites matched for sex, age, and arterial pressure. They found that blacks had significantly lower renal blood flow and higher renal vascular resistance than did whites.

Messerli et al measured cardiac output, vascular resistance, plasma volume, and total blood volume in a group of racially mixed hypertensive patients, and they found no differences except for slower heart rate in blacks. We observed a faster heart rate in SS than in SR black patients during sodium restriction, but there was no difference among races during high sodium intake.

Lowenstein et al used direct measurements of wedged renal vein pressure to calculate renal interstitial pressure and glomerular capillary pressure with the formulas of Gomez, and found an increase in glomerular capillary pressure in patients with essential hypertension despite an increase in renal afferent resistance. In that study, however, no consideration was given to dietary sodium intake or to race.

Williams and Hollenberg measured renal hemodynamics in a group of patients with essential hypertension and normal plasma renin activity. They found
that a subgroup of patients with essential hypertension failed to modulate their renal blood flow and aldosterone response to angiotensin II in changes in dietary sodium intake. Such patients were termed "non-modulators" by the investigators.44 In so-called non-modulators, renal blood flow failed to increase in response to high dietary sodium intake, whereas in normal subjects and in hypertensive patients with normal renal vascular and adrenal modulation, renal blood flow increased by at least 120 ml/min 1.73 m². Non-modulators also manifested a derangement in the capacity to handle sodium along with an increase in blood pressure during high dietary sodium intake. Obviously, many of the renal hemodynamic characteristics observed in the non-modulators mimic those observed by us in black SS patients. The difference between these two studies is that we have not selected patients with normal plasma renin activity, a criterion that would have excluded most of the hypertensive black patients, who notoriously have reduced levels of plasma renin activity.45

Nifedipine reduced blood pressure more effectively in SS than in SR patients during high dietary sodium intake, and its hypotensive action was significantly correlated with the fall in body weight. This suggests that the antihypertensive effect of this agent may be, at least partly, due to its natriuretic property. The natriuretic action of nifedipine was evident only in SS patients and only during the first 48 hours of treatment. This explains why urinary sodium excretion at the end of phase 4 of the study was not different among SS and SR patients. Nifedipine, at the low doses used in this study, improved but did not normalize the slope of the renal function curve in SS patients. It is possible that higher doses might improve further the slope of the renal function curve. This would lend additional support to the hypothesis of a linkage between abnormalities of sodium and calcium metabolism in SS patients with essential hypertension.11

It is of interest that nifedipine caused a decrease in filtration fraction and a modest, albeit not significant, reduction in glomerular pressure in SS patients during high Na⁺ intake. This observation in human subjects, would not be in keeping with the animal studies that have shown a predominant vasodilatory action of calcium channel blockers on the renal afferent arterioles, actually resulting in an increase in intraglomerular pressure.46,47

It is obvious that a prospective study involving a large number of SS patients (black and white) is needed to establish whether a relation exists between these renal hemodynamic derangements and the greater propensity for the development of renal failure in black hypertensive patients, whether renal failure is more likely to develop in SS black patients than in SR blacks, and whether SS white patients have similar hemodynamic derangements and a similar propensity for the development of renal failure as a result of protracted hypertension as black patients.

In addition, more studies are needed to determine the effect of calcium channel blockers on the renal microcirculation in vivo rather than in vitro.

References


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