Racial Differences in Pressure, Volume and Renin Interrelationships in Essential Hypertension

STEVEN G. CHRYSANT, M.D., PH.D., KOLA DANISA, M.D., DAVID C. KEM, M.D., BONNIE L. DILLARD, P.A., WALTER J. SMITH, P.A., AND EDWARD D. FROHLICH, M.D.

SUMMARY The interrelationships of arterial pressure, plasma volume (PV), and plasma renin activity were studied in 152 consecutive male patients with uncomplicated essential hypertension. Of these, 22 (17 white and 5 black) subjects had normal plasma volumes and because of the small number were not included in the analysis of results. The remaining 130 (35 black and 95 white) patients were classified as having either expanded or contracted plasma volume. A higher percentage of black (43%) than white (21%) subjects were volume expanded (PV > 19 ml/cm) and a lower percentage of blacks (57%) than whites (79%) were volume contracted (PV < 17 ml/cm). There was no significant difference in mean arterial pressure and plasma renin activity between the volume expanded and contracted black patients. In contrast, the white patients with contracted plasma volume had significantly higher arterial pressures (p < 0.05) and plasma renin activity (p < 0.001) than those with expanded plasma volume. More blacks than whites had low plasma renin activity and did not manifest the inverse relationship of plasma renin activity to plasma volume as did the whites. These data confirm and extend previous observations that the relationship between plasma volume and plasma renin activity (PRA) in the male patient with essential hypertension seems to differ between the black and white race. Efforts to explain the low PRA in black patients might be best directed toward those patients with suppressed PRA and with contracted intravascular volume. (Hypertension 1: 136-141, 1979)

KEY WORDS • racial differences • essential hypertension • plasma volume • plasma renin activity

The incidence of essential hypertension is higher in the black than the white race, and more blacks than whites have low renin hypertension. The cause(s) for these racial differences are not clearly understood. Explanations offered for these differences include: the high-salt intake by blacks, the higher incidence of plasma volume expansion in black subjects and the attenuated response of renin release to various stimuli in blacks. Besides race, other investigators have found sex differences in renin release to various stimuli, with women showing resistance to renin release in contrast to men, who do not show such resistance. However, there are not enough data available dealing with the interrelationships between blood pressure, plasma volume and plasma renin activity in black and white patients with essential hypertension studied under similar experimental conditions. Therefore, this study was undertaken to investigate the above interrelationships in black and white male subjects with uncomplicated essential hypertension under the same experimental design.

Materials and Methods

The present investigation included 152 male black and white patients with stable uncomplicated essential hypertension. All patients having any evidence even suggesting secondary hypertension were excluded, and only black patients from the continental United States were included. The protocol was explained to all patients and each gave his informed consent as re-
RACIAL DIFFERENCES IN PV-RENIN IN HYPERTENSION/Chrysant et al. 137

quired by our institutional experimentation committee. All patients studied were either new untreated patients or former patients who had discontinued their treatment on their own for over a month. The investigational protocol consisted of a 3-day observation period on a daily 150 mEq sodium, 100 mEq potassium diet. During this period the arterial pressure and heart rate were determined every 4 hours in the supine (5 min) and standing (2 min) positions by nurses assigned exclusively to the metabolic unit. To obviate subjective error, a precalibrated Doppler recording unit* was used for determination of indirect arterial pressure. Blood pressure was recorded as the mean of two determinations. Each patient had a complete history and physical examination and laboratory investigation. The latter included determination of complete blood count with differential, blood urea nitrogen, and serum creatinine, electrolytes, liver enzymes, cholesterol, uric acid, triglycerides, and fasting blood glucose. A 4-hour glucose tolerance test was also performed. Every patient had an electrocardiogram, hypertensive urogram, and chest x-ray.

Between 6:00 a.m., Day 3 to 6:00 a.m., Day 4, a 24-hour urine was collected for urinalysis and determination of creatinine clearance, and excretion of sodium, potassium and protein. Upon completion of this 24-hour urine collection, while the patient was still supine, blood was withdrawn for determination of plasma renin activity (supine PRA). Then the patient was asked to be up and about for 2 hours and at 8:00 a.m. another blood sample was drawn for plasma renin activity (upright PRA). Subsequently, the patient was sent to the Nuclear Medicine Department for determination of his blood volume by using I31I RISA for plasma volume and 51Cr for red cell mass. Blood samples were withdrawn at 10, 20 and 30 minutes after injection to construct a regression line to zero time for determination of that particular volume measurement. The variability of our method is ± 5%.

The plasma volume was expressed as ml/cm of height. Normal values for men in our laboratory are 18 ± 1 SEM ml/cm height. For the purposes of this study any plasma volume above 19 ml/cm was arbitrarily considered expanded and any below 17 ml/cm was arbitrarily considered contracted.

The data were analyzed by comparing the plasma volume, renin activity and blood pressure between black and white patients and also within each race between volume expanded and contracted subjects using the unpaired t test analysis. Regression analysis was performed comparing mean arterial pressure to plasma volume and upright PRA, and plasma volume to upright PRA. The upright PRA was chosen because the laboratory methods used to measure PRA limit the discrimination of low, normal and high renin subgroups, unless the stimulus of upright posture is used to enhance PRA, and also for better correlation with the ambulatory measurement of plasma volume.

*Arteriosonde-1216, Medical Electronics Division, Hoffman LaRoche Inc., Cranbury, N.J. 08512.

Results

Of the 152 patients studied, 22 (17 white and 5 black) had normal plasma volume and because of the small number, were not included in the analysis of results. Of the remaining 130, 20 white (21%) and 15 black (43%) patients had expanded plasma volume and 75 white (79%) and 20 black (57%) patients had contracted plasma volume (table 1). Of the volume expanded groups, the black patients had higher systolic and diastolic arterial pressures and lower sodium excretion than the white (p < 0.05). There was no difference between these two groups of patients, however, with respect to age, serum creatinine, creatinine clearance, plasma volume and PRA (table 1). Of the volume contracted groups, there was no significant difference between black and white with respect to arterial pressure, sodium excretion, age, serum creatinine, creatinine clearance, or plasma volume with the exception of plasma renin activity, which was significantly higher in the white patients (p < 0.005; table 1). When the subjects were compared within each race, it was found that there was not any significant difference in either arterial pressure or PRA between the volume expanded and contracted black patients. Moreover, the white patients with contracted plasma volume had significantly higher arterial pressures and PRA than whites with expanded plasma volume (fig. 1). And, when the relationship of arterial pressure to plasma volume in the four groups of patients was analyzed, it was found that there was no correlation between pressure and volume in the volume expanded black and white subjects, in contrast to volume contracted black and white patients, who showed a significant inverse relationship between pressure and volume (r = −0.49, p < 0.01 for black;
TABLE 1.  Clinical Findings in Black and White Hypertensive Patients with Expanded and Contracted Plasma Volume (Mean ± SEM)

<table>
<thead>
<tr>
<th></th>
<th>Expanded</th>
<th>Contracted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (no.)</td>
<td>15 (48%)</td>
<td>20 (57%)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>50 ± 2</td>
<td>50 ± 2</td>
</tr>
<tr>
<td>Arterial pressure (mm Hg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>172 ± 7</td>
<td>178 ± 5</td>
</tr>
<tr>
<td>Diastolic</td>
<td>113 ± 4</td>
<td>112 ± 3</td>
</tr>
<tr>
<td>Serum creatinine (mg%)</td>
<td>1.2 ± 0.1</td>
<td>1.3 ± 0.1</td>
</tr>
<tr>
<td>Oreatinine clearance (ml/min)</td>
<td>95 ± 8</td>
<td>94 ± 6</td>
</tr>
<tr>
<td>Plasma volume (ml/cm)</td>
<td>20 ± 0.4</td>
<td>15 ± 0.3</td>
</tr>
<tr>
<td>Plasma renin activity (ng/ml/hr)</td>
<td>0.7 ± 0.2</td>
<td>1.1 ± 0.2</td>
</tr>
<tr>
<td>UN.V (mEq/24 hr)</td>
<td>113 ± 11</td>
<td>142 ± 11</td>
</tr>
</tbody>
</table>

*Significance of differences between black and white hypertensive patients.

$r = -0.51, p < 0.005$ for white; fig. 2). The comparison of arterial pressure to PRA for the four groups of patients showed no correlation between the volume expanded and contracted blacks, and the volume expanded whites. This was in contrast to volume contracted whites who demonstrated a positive correlation between arterial pressure and PRA ($r = 0.30, p < 0.01$; fig. 3). However, the correlation was weak and is probably due to the larger number of volume contracted whites. The comparison between plasma volume and PRA for the four groups of patients showed no correlation in the volume expanded black and white and volume contracted black patients. In contrast, the volume contracted white patients demonstrated a significant inverse relationship between plasma volume and PRA ($r = -0.32, p < 0.005$; fig. 4). This figure also depicts the normovolumic black and white patients to show the spectrum of changes of plasma volume from expanded, normal, contracted, and its relationship to PRA.

![Figure 2](http://hyper.ahajournals.org/) This figure depicts the correlations between mean arterial pressure (MAP) and plasma volume (PV) in black and white hypertensive patients with expanded and contracted plasma volumes. There was no correlation between MAP and PV in the volume expanded subjects, whereas, in those with contracted plasma volume, there was a significant inverse correlation between MAP and PV.
FIGURE 3. In this figure, the relationships between mean arterial pressure (MAP) and plasma renin activity (PRA) are shown. No correlation was observed in the volume expanded blacks and whites and in the volume contracted blacks, whereas the volume contracted whites manifested a significant direct correlation between MAP and PRA.

FIGURE 4. In this figure, the relationships between plasma renin activity (PRA) and plasma volume (PV) are illustrated for the four groups of patients. Again, there was no correlation between PRA and PV for the volume expanded black and white groups and the volume contracted black patients, whereas the white patients with contracted plasma volume manifested a significant inverse relationship. This figure also shows the normovolumic black and white patients and their relationship to PRA.
Discussion

Plasma volume usually falls as arterial pressure increases in male patients with uncomplicated essential hypertension, and PRA increases as plasma volume contracts. This inverse relationship between plasma volume and PRA is not shared by women with essential hypertension. The present investigation confirms those previous observations concerning the interrelationships between mean arterial pressure, plasma volume and PRA in male subjects with uncomplicated essential hypertension and extends them further by demonstrating racial differences in the above interrelationships. In this study, black patients with contracted plasma volumes had similar arterial pressures and PRAs to those with expanded plasma volume. In contrast, the white patients with contracted plasma volumes had significantly higher arterial pressures and PRAs than the volume expanded whites (fig. 1). Also, black patients with contracted plasma volumes did not exhibit an inverse relationship between plasma volume and PRA as did their white counterparts (fig. 4). Plasma renin activity remained low in the majority of black patients in our study. Similar observations have been reported by other investigators. The reasons for this high incidence of low-renin hypertension in the black are not exactly known. One factor accounting for the high incidence of low-renin hypertension in the black is our observation that more blacks than whites with uncomplicated essential hypertension have expanded plasma volumes. Besides the expanded plasma volume being responsible for low-renin hypertension in blacks, other studies have shown that a relatively high percentage of black subjects with uncomplicated essential hypertension manifest an impaired response of renin secretion to various stimuli. Similar impaired response to renin release has also been reported for black normotensive subjects. Possible reasons accounting for these differences could include 1) the suppression of the sympathetic nervous system in such patients, since this system plays an important role in renin release by the kidney; 2) the presence of an increased central blood volume; or 3) a continuous secretion of mineralocorticoids other than aldosterone, leading to volume expansion and suppression of renin release. Although a significant number of black hypertensive patients with expanded plasma volume had low PRA, it is also notable that several blacks with markedly contracted plasma volumes also had low PRA. It is evident, therefore, that low PRA and an expanded plasma volume should not necessarily be considered as a cause-effect relationship. The inverse relationship that we found in our white male patients with essential hypertension between plasma volume and plasma renin activity has been reported previously and is consistent with the physiologic principles governing renin release by the kidney. Since PRA was similar in the black and white patients with expanded volume, the role of volume in these patients must be operative. However, the failure to demonstrate a rising PRA in the volume contracted black patients with essential hypertension suggests that other factors suppressing PRA in these patients could be present. Thus, the simultaneous determination of the two physiological variables (plasma volume and plasma renin activity) should be very helpful in studies attempting to explain the mechanism of suppressed PRA in black patients with essential hypertension. Further efforts to explain this suppressed PRA in blacks might best be directed to those with a contracted plasma volume.

Acknowledgments

We are indebted to Ms. Betty Nordquist for her secretarial assistance, Ms. Fern Brandt, Ms. Dorothy Johnson, Ms. Marilyn Patterson, Ms. Mary Zuckerman and Ms. Beatrice Richardson for nursing assistance.

References

16. Tarazi RC, Dusyan HP, Frohlich ED: Plasma volume and chronic hypertension: Relationship to arterial pressure levels in
Racial differences in pressure, volume and renin interrelationships in essential hypertension.
S G Chrysant, K Danisa, D C Kem, B L Dillard, W J Smith and E D Frohlich

Hypertension. 1979;1:136-141
doi: 10.1161/01.HYP.1.2.136

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/1/2/136

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org//subscriptions/