Salt Sensitivity in Blacks
Salt Intake and Natriuretic Substances

JAMES R. SOWERS, MICHAEL B. ZEMEL, PAULA ZEMEL, FRANCES W. J. BECK, MARY F. WALSH, AND EDWARD T. ZAWADA

SUMMARY Accumulating evidence suggests that hypertension in blacks is manifested in part by impaired renal excretion of salt. Consequently, this study was performed to determine if hypertensive and normotensive black subjects differ in their ability to generate known natriuretic substances. Fourteen normotensive and 11 hypertensive blacks were maintained on constant metabolic diets containing either 40 or 180 mmol of salt per day for 14 days each. During the last 4 days of each salt intake period, urine was collected for measurement of sodium, dopamine, and norepinephrine. On the last day of each 14-day dietary period, blood pressures were measured, blood was collected for measurement of plasma atrial natriuretic factor (ANF) and aldosterone, and urine was collected over 2 hours for measurement of prostaglandin E$_2$ (PGE$_2$). Both the normotensive and the hypertensive groups manifested salt sensitivity; their mean arterial pressure rose by 7 ± 0.2 and 6 ± 0.2%, respectively, when salt intake was increased from 40 to 180 mmol/day. The hypertensive group exhibited decreased ($p < 0.05$) dopamine excretion as compared with the normotensive group for both dietary salt intakes. Plasma ANF levels increased ($p < 0.05$) in the hypertensive group, but not in the normotensive group, with increasing dietary salt. Plasma aldosterone and urinary norepinephrine and PGE$_2$ were comparable in the two groups for both dietary salt intakes. These data suggest that salt sensitivity is not unique to hypertensive blacks but occurs in normotensive blacks as well. Decreased renal production of dopamine may be a pathogenic factor in the development and maintenance of hypertension in blacks. (Hypertension 12: 485–490, 1988)

KEY WORDS • salt sensitivity • atrial natriuretic factor • diet • dopamine • prostaglandins • black population

HYPERTENSION in American blacks, as compared with hypertension in whites, is characterized by a higher incidence of salt sensitivity$^{1-4}$ in spite of the apparent lack of differences in sodium and salt intakes between the two populations.$^5$ The mechanisms involved in the relatively high incidence of salt-sensitive hypertension in blacks are poorly understood. However, an impaired natriuretic response to a salt load in hypertensive blacks could result from a reduced ability to generate natriuretic substances such as dopamine (DA), prostaglandin E$_2$ (PGE$_2$), and atrial natriuretic factor (ANF).

There is a considerable body of evidence suggesting a relationship between renal production of DA and the ability of the kidney to excrete a salt load.$^6-21$ Enhanced dietary salt intake or infusion of saline results in an increase in urinary DA excretion and a decrease in norepinephrine excretion.$^{15-22}$ That the dietary salt or saline-mediated natriuresis is causally linked to renal DA excretion is supported by the observation that administration of carbidopa, the peripheral inhibitor of the enzyme dopa decarboxylase, prevents the increases in urinary sodium in response to dietary salt$^{23}$ and saline infusion.$^{14, 15}$ However, there is evidence that salt loading does not appropriately increase urinary DA excretion in hypertensive patients,$^{24, 25}$ suggesting that decreased renal DA production in response to a salt load may play a role in the pathogenesis and maintenance of hypertension. Data from a recent report by Gill et al.$^{25}$ suggested that salt sensitivity in hypertensive patients with normal renin may be related in part to decreased urinary DA to norepinephrine ratios, particularly with high salt intake.

Since PGE$_2$ synthesis can affect renal blood flow, glomerular filtration rate, and urinary sodium excretion, renal PGE$_2$ has been implicated in the patho-
Materials and Methods

Fourteen normotensive subjects, with a mean age of 34 ± 6 years and a mean arterial pressure (MAP) of 87 ± 2 mm Hg, and 11 hypertensive subjects, with a mean age of 44 ± 8 years and a MAP of 103 ± 5 mm Hg, all having a strong family history of hypertension, took part in this study after informed consent was obtained. All study subjects had normal serum electrolyte levels and creatinine levels below 1.3 mg/dl. Blood pressure criterion for the nonnotensive group was a mean arterial pressure above 90 mm Hg or a supine systolic pressure above 140 mm Hg (or both) after being off all antihypertensive medications for 1 month. During the course of this study the subjects continued all normal activities but ate their meals under supervised conditions in our nutrition-metabolic unit.

This metabolic study was divided into two 14-day periods, in which subjects received a low salt (40 mmol/day for the last 14 days) diet. The high salt (180 mmol NaCl) to the high (180 mmol NaCl) daily sodium intake (see Table 1). Salt sensitivity in this study was arbitrarily defined as an increase in MAP of at least 5% or an increase of systolic pressure of at least 10% in going from the low (40 mmol NaCl) to the high (180 mmol NaCl) daily dietary salt intake (see Table 1). This arbitrary definition is in general accordance with arbitrary definitions of salt sensitivity in two prior dietary studies employing more extreme differences in sodium intake (10-200 mmol; 9-249 mmol). There was an increase of 6 ± 0.2 mm Hg (6 ± 0.2%) in MAP and an increase of 10 ± 0.2 mm Hg (7 ± 1.2%) in systolic pressure in the hypertensive subjects. In the normotensive group there was a mean increase (6 ± 0.2 mm Hg; 7 ± 0.2%) in MAP and an increase (12 ± 0.3 mm Hg; 10.5 ± 1.3%) in systolic pressure with increasing salt intake. Thus, the normotensive group of black subjects was clearly as salt-sensitive as the hypertensive group. Similarly, plasma aldosterone was appropriately suppressed with increasing salt intake, and the suppression was comparable in the two study groups on the two dietary salt intakes (see Table 1).
TABLE 1. Effects of Changing Salt Intake on Urinary Sodium Excretion, MAP, and Plasma Aldosterone in Normotensive and Hypertensive Black Adults

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low salt diet (40 mmol/day)</th>
<th>High salt diet (180 mmol/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NTN</td>
<td>HTN</td>
</tr>
<tr>
<td>Urinary sodium (mmol/day)</td>
<td>40±6</td>
<td>34±2</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>81±3</td>
<td>100±2†</td>
</tr>
<tr>
<td>Plasma aldosterone (ng/dl)</td>
<td>21±5</td>
<td>19±3</td>
</tr>
</tbody>
</table>

Values are means ± SEM. NTN = normotensive; HTN = hypertensive.
*p < 0.001, †p < 0.05, ‡p < 0.01, compared with values on the low salt diet.
†p < 0.05, compared with values in normotensive subjects.

As can be seen in Figure 1, the 24-hour urinary excretion of DA was greater (p < 0.01) for the normotensive subjects than for the hypertensive subjects on both extremes of salt intake. With increasing salt intake urinary DA excretion increased 25% in normotensive and 40% in hypertensive subjects.

Urinary norepinephrine excretion was not different for the two groups on either dietary regimen (see Figure 1). Urinary norepinephrine decreased 29% in normotensive subjects and 40% in hypertensive subjects when salt intake was increased. The urinary DA to norepinephrine ratio was greater in the normotensive subjects than in the hypertensive subjects at the low (222%; p < 0.01), but not the high (140%), salt intake (see Figure 1). This ratio of urinary DA to norepinephrine increased (p < 0.05) only in the hypertensive group in going from a low salt to a high salt intake. There was no correlation between urinary sodium excretion and the urinary DA to norepinephrine ratio in either the normotensive or the hypertensive group.

Plasma ANF levels were greater (p < 0.01) in the hypertensive group on the high salt diet and tended (p = 0.06) to be greater in the hypertensive group on the low salt diet (Figure 2). Although there was no change in ANF levels in the normotensive group, there was a 45% increase (p < 0.05) in ANF levels in the hypertensive group when dietary salt was increased.

Urinary PGE2 excretion was not different in the two groups on either diet (Figure 3). Further, urinary PGE2 excretion did not vary with changing salt intake.

Discussion

Blood pressure in both the black normotensive and hypertensive subjects in this study increased on changing from a relatively low to a high salt intake. This finding is in accord with previous observations.

Figure 1. Effects of changing salt intake on urinary norepinephrine (NE) and dopamine (DA) excretion in black salt-sensitive normotensive (NTN) and hypertensive (HTN) subjects. Values are means ± SEM. Asterisk denotes significant difference from normotensive values (p < 0.01); dagger denotes significant difference from 40 mmol NaCl values.

Figure 2. Effects of changing salt intake on plasma ANF in black salt-sensitive normotensive (NTN) and hypertensive (HTN) subjects. Values are means ± SEM. Asterisk denotes significant difference from normotensive values (p < 0.01) values and significant difference from 40 mmol NaCl values (p < 0.05).
of salt sensitivity in normotensive1, 42 as well as hypertensive 2–5, 43 blacks. It is interesting that the normotensive blacks in this study were as salt-sensitive as the hypertensive subjects. This observation strongly suggests that salt sensitivity is not a phenomenon that characterizes or is limited to the hypertensive population. It has previously been observed that normotensive blacks excrete a short-term intravenous salt load over 24 hours to a lesser extent than do normotensive white subjects. 1, 4 The observation that normotensive relatives of hypertensive subjects also have a blunted natriuretic response to short-term salt load is also consistent with salt sensitivity in the normotensive population. 44

Urinary DA excretion was decreased in the hypertensive subjects as compared with the normotensive subjects on both salt intakes. There was a slight increase in DA with increasing salt intake in both groups. This salt-induced increase in urinary DA excretion is less than that previously observed in normotensive whites,17, 19 which is in agreement with a brief report of a negligible salt-induced increase in DA in West African blacks. 45 White subjects with essential hypertension have also been reported to exhibit lower levels of DA excretion compared with normotensive whites in response to increasing dietary salt intake. 24, 25 Gill et al. 25 observed no increase in urinary DA in salt-sensitive and salt-resistant hypertensive subjects with normal renin in contrast to the rise in urinary DA in normotensive subjects on changing from a low to a high salt intake; although not specified, it is presumed that these patients were white. In line with these data demonstrating decreased urinary excretion of DA with salt loading is the observation that hypertensive whites appear to be more sensitive to the natriuretic and hypotensive effects of DA and DA agonists than normotensive subjects. 46, 47 Thus, hypertensive blacks appear to differ from whites in that they have low urinary DA excretion under low dietary salt conditions but have urinary DA responses to salt similar to those of normotensive blacks. The diminished urinary DA response to dietary salt loading in normotensive blacks as compared with normotensive whites 17, 19 probably reflects the greater prevalence of salt sensitivity in the normotensive black population.

In contrast to our observations for urinary DA, the 24-hour urinary norepinephrine levels were similar in the two study groups on the two salt intakes. Both normotensive and hypertensive groups displayed a small decrease in urinary norepinephrine excretion when placed on the high salt diet. That urinary norepinephrine decreased with increasing salt intake is consistent with previous reports. 1, 8, 48, 49 Changes in urinary excretion of norepinephrine with various salt loads appear to reflect changes in renal sympathetic nerve activity. 14, 50, 51 Stimulation of renal sympathetic nerves or renal arterial infusion of norepinephrine increases tubular absorption of sodium and chloride independently of simultaneous changes in renal hemodynamics. 50–52 Therefore, decreases in renal excretion of norepinephrine associated with a high salt diet may reflect decreased renal sympathetic nerve traffic associated with the renal adaptation to increasing dietary salt. Campese et al. 43 noted that salt-sensitive hypertensive whites failed to suppress plasma norepinephrine levels in going from low to high salt intake. Gill et al. 25 also noted a failure of dietary salt loading to suppress urinary norepinephrine in both normotensive and salt-sensitive hypertensive whites. Thus, salt sensitivity in blacks appears to differ from that in whites in that it is not characterized by a failure of increasing dietary salt to suppress adrenergic activity. Our observations, as well as those of others, 1, 8, 9 of reciprocal changes in renal excretion of DA and norepinephrine in response to dietary salt intake suggest that modulation of renal production of both catecholamines may be important in the renal adaptation to different salt intakes.

Because of the natriuretic effects of DA and the antinatriuretic properties of norepinephrine, the ratio of urinary DA to norepinephrine may be a critical index of the overall net effects of catecholamines on the renal handling of salt. Accordingly, it is important to note that this "natriuretic index" was decreased in hypertensive blacks compared with normotensive blacks on the low salt intake, but not the high salt intake. This observation likely reflects the fact that the normotensive study group was also salt-sensitive and did not appropriately modulate renal catecholamine production in relationship to salt ingestion. In accordance with this concept, Gill et al. 25 noted that this natriuretic index characteristically rose much more strikingly in salt-resistant than in salt-sensitive subjects. However, in the present study the natriuretic index was not correlated with urinary sodium excretion in either the normotensive or the hypertensive group. Weinberger et al. 49 reported that hypertensive subjects may have a lower natriuretic index than normotensive subjects and that the natriuretic index correlated closely with sodium excretion in normotensive subjects when they were subjected to
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various salt intakes. Although race and salt sensitivity were not identified in the article by Weinberger et al., it is quite possible that the normotensive population was not salt-sensitive. Accordingly, the absence of a close relationship between salt intake and excretion and the natriuretic index in the present study may be characteristic of salt sensitivity in both normotensive and hypertensive subjects.

ANF has been implicated in the regulation of renal salt excretion as well as in the control of blood pressure. In this study we observed that salt-sensitive black hypertensive subjects clearly have higher levels of plasma ANF than their normotensive counterparts when studied on a high salt intake. However, when the subjects were studied on a low salt diet, no difference in ANF levels existed between the hypertensive and the normotensive study groups. Several investigative groups have reported elevated levels of ANF in patients with essential hypertension, both treated and untreated. Unfortunately, it is unclear whether these studies were performed under controlled salt intake, and they did not address the issue of salt sensitivity. Kohno et al. reported that salt-sensitive hypertensive subjects demonstrated a greater rise in plasma levels of ANF in response to increasing salt intake than did non-salt-sensitive hypertensive subjects. Increased plasma ANF levels have also been reported in salt-sensitive rats. Atrial secretion of ANF appears to be elicited by volume expansion. Our data are thus consistent with the concept that the kidney in salt-sensitive hypertensive subjects is less effective in excreting a salt load, resulting in greater salt and water retention and a corresponding rise in plasma ANF.

Decreased renal PGE₂ production in blacks with low-renin black hypertension could explain in part both the decreased ability to excrete salt and the low-renin state, as PGE₂ stimulates renin secretion. However, our data suggests that PGE₂ production is comparable in black salt-sensitive normotensive and hypertensive subjects. This observation agrees with that of Campbell et al. who did not observe decreased PGE₂ in low-renin hypertensive subjects. These observations suggest that salt-sensitive hypertensive blacks may have subtle abnormalities in modulating renal PGE₂ production with various salt intakes but that this abnormality probably does not contribute to their salt sensitivity.

Plasma aldosterone levels were comparable in the normotensive and hypertensive groups on both salt intakes. Both DA⁶ and ANF are known inhibitors of aldosterone secretion. Therefore, enhanced ANF secretion and decreased DA production may have resulted in no net alteration in plasma aldosterone concentrations in our black salt-sensitive hypertensive subjects as compared with their normotensive counterparts. Furthermore, comparable salt intake-related alterations in plasma aldosterone levels in the two groups suggest that salt-sensitive hypertension in blacks is not characterized by the nonmodulation of adrenal responsiveness that is observed in young salt-sensitive white hypertensive subjects.

Data from the present study indicate that salt sensitivity may be equally manifested in normotensive and hypertensive blacks. In both groups, this phenomenon may be related in part to a blunted increase in renal DA production in response to increased salt intake, which in turn results in a blunted natriuretic response. The observed reductions in urinary DA and the natriuretic index (DA to norepinephrine ratio) in the hypertensive subjects as compared with normotensive subjects further suggest a greater impairment in natriuretic response among hypertensive blacks.

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References

39. Dray R, Charvonnel B, Maclouf J. Radioimmunoassay of
38. Shenker Y, Sider RS, Ostafin EA, Grekin RJ. Plasma levels of
36. Laragh JH. Atrial natriuretic hormone, the renin-aldosterone
35. Richards AM, Nicholls MG, Ikram H, Webster MWI, Yan-
34. Tan SY, Sweet P, Mulrow PJ. Impaired renal production of
33. McGiff JC, Vane JR. Prostaglandins and the regulation of
32. Sowers JR, Zawada EF. Hypertension in the aged. In:
31. Sowers JR, Zawada ET, Sica DA, eds. Geriatric nephrology and uro-
30. Bolger PM, Eisner GM, Ramwell PW, Slotkoff LM. Renal
29. Stokes JB, Kokko JP. Inhibition of sodium transport by
28. Lee JB, Patak RV, Mookerjee BK. Renal prostaglandins and
27. Kirschenbaum MA, Stein JH. The effect of inhibition of
26. Schnermann J, Briggs JP. Participation of renal cortical
24. Underwood RH, Williams GH. The simultaneous measure-
23. Ball SG, Gunn IG, Douglas HS. Renal handling of dopa,
21. Baines AD. Effects of salt intake and renal denervation on
catecholamine catabolism and excretion. Kidney Int 1982;
20. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
21. Baines AD. Effects of salt intake and renal denervation on
catecholamine catabolism and excretion. Kidney Int 1982;
19. Baines AD. Effects of salt intake and renal denervation on
catecholamine catabolism and excretion. Kidney Int 1982;
18. Baines AD. Effects of salt intake and renal denervation on
catecholamine catabolism and excretion. Kidney Int 1982;
17. Kuchel O, Buu NT, Unger T, Lis M, Genest J. Free and
16. Ball SG, Buu NT, Unger T, Lis M, Genest J. Free and
15. Richards AM, Nicholls MG, Ikram H, Webster MWI, Yan-
14. Bolger PM, Eisner GM, Ramwell PW, Slotkoff LM. Renal
13. Stokes JB, Kokko JP. Inhibition of sodium transport by
12. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
11. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
10. Ball SG, Gun D, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
9. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
8. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
7. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
6. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
5. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
4. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
effects of human alpha atrial natriuretic peptide in healthy
3. Ball SG, Gunn IG, Douglas HS. Renal, hemodynamic, and hormonal
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