Salt-Sensitivity in Borderline Hypertension

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Patients with essential hypertension may often be specifically sensitive to changes in dietary sodium intake when compared with normotensives. The increase in blood pressure with sodium loads is associated with hemodynamic changes, i.e., increased cardiac output and/or increased peripheral resistance. Moreover, abnormalities in the renin-angiotensin-aldosterone system and the sympathetic nervous system in the pressor responses to sodium loading have been identified in essential hypertension. In young patients with borderline hypertension very few detailed studies of hemodynamic and humoral responses to sodium loading or depletion have been reported. To identify factors that may contribute to sodium susceptibility, we studied the hemodynamic and endocrine responses to sodium depletion or sodium loads in young patients with borderline hypertension who are at risk of developing essential hypertension.

In our present study, short-term sodium loading, following a period of sodium depletion with a diuretic, caused blood pressure to rise significantly in 21 young subjects with borderline hypertension but not in 12 normal subjects of comparable age, sex, and body weight. Hemodynamic responses of the borderline hypertensives to sodium loads after sodium restriction showed an increased cardiac index, whereas in the normal subjects whose blood pressure did not significantly increase with sodium loads, cardiac index did not change significantly. Calculated peripheral resistance did not change in either group. These observations are consistent with those of our previous study in which patients with essential hypertension adhered to a high-sodium diet of 249 mEq sodium chloride per day.

The mechanisms by which excessive sodium intake increases cardiac output in borderline hypertensives are not known, but a decreased natriuretic capacity is a characteristic common to all salt-sensitive rats and man. Tobian et al. performed pressure-natriuresis experiments in sodium-sensitive and sodium-resistant rats, and found that kidneys from sensitive rats required greater perfusion pressures to excrete a given amount of sodium than kidneys from resistant rats. In our previous study, the salt-sensitive patients, who had greater increases in cardiac output and blood pressure with sodium loads, showed an impaired ability to excrete sodium compared with the non-salt-sensitive ones. Since in the present study there was a good correlation in borderline hypertensives between the elevation of blood pressure following sodium loads and its decrease on treatment with a diuretic, as previously reported in patients with essential hypertension, it is likely that the sodium retained with loading and that lost with a diuretic is in some way responsible for the increases and decreases in blood pressure. Thus, these results provide further support for the modest volume expansion that occurs with the sodium loads in borderline hypertensives being related to retarded renal excretory responses, which lead to the resultant increase in cardiac output. The sympathetic nervous system and the renin-angiotensin system have important influences over renal sodium excretion. In the present study, plasma norepinephrine and epinephrine, and plasma renin activity levels were consistently higher in borderline hypertensives.
than the levels in normotensives. Therefore, it is possible that in the borderline hypertensives examined in the present study, the adrenergic-angiotensin system may cause difficulty in sodium excretion, leading to increased cardiac output and the resultant BP rise with sodium loads, via sodium retention.

In contrast to the pressor action of sodium, potassium is known to have antihypertensive properties. Although the precise mechanism of the antihypertensive action of potassium remains controversial, its natriuretic properties are thought to play an important role. In the present study, potassium supplementation in borderline hypertensives could attenuate the increase in ventricular volume, stroke volume, and cardiac output with sodium loads, which are clinically available indices of preload. It is suggested, therefore, that in these young borderline hypertensives with impaired renal sodium excretion, potassium loading could prevent the rise in blood pressure with sodium loads by attenuating the increase in cardiac output, mainly as a result of natriuresis.

Since the increments of mean blood pressure did not correlate with changes in cardiac output but correlated well with the changes in total peripheral resistance observed in our present study, the differences in blood pressure must be attributed to differing responses in peripheral vascular resistance. Thus, it is suggested that the fall in peripheral resistance was not adequate to maintain pressure homeostasis with the relatively greater increase in cardiac output with sodium loads in the borderline hypertensives. It has been suggested that autoregulation may contribute to increased vascular resistance during salt and water excess. Another suggestion is that the augmented neurogenic activity may be partly involved in the inappropriately high peripheral resistance relative to the elevated cardiac output with sodium loads.

Recently, studies on cell membrane electrolyte transport have been performed to clarify the pathogenesis of essential hypertension. In patients with diminished sodium excretory capacity, circulating substances ("natriuretic hormone") are produced that inhibit sodium transport in the kidney, thus resulting in the maintenance of sodium homeostasis when they ingest excessive sodium. Such humoral substances may inhibit the ouabain-sensitive sodium-potassium pump. However, sodium transport inhibition would necessarily increase intracellular sodium content, leading to increased vascular resistance, through the increased intracellular calcium. As one possible explanation for the inappropriately elevated peripheral resistance with sodium loads in these borderline hypertensives, we speculate that salt loading in susceptible subjects with borderline hypertension may promote formation or release of such substances which increase vascular contraction and blood pressure. Moreover, potassium may stimulate the ouabain-sensitive sodium-potassium pump, and thus reduce blood pressure by vasodilation, since intraarterial infusion of potassium is known to cause arterial vasodilation, the degree of which is reduced by pre-treatment with ouabain. Although this speculation has not been tested in this study, studies of cell membrane electrolyte transport in borderline hypertensives at increased risk of developing essential hypertension provide new insight into the pathogenesis of essential hypertension. Finally, the mechanisms which regulate sodium-susceptibility in borderline hypertension may be multifactorial, including; age, sex, race, renal function, vascular reactivity, humoral factors, and cell membrane transport.

In summary, we have demonstrated that excessive sodium intake after sodium deprivation produces a significant increase in blood pressure in young subjects with borderline hypertension, but not in age-matched normal subjects, and that the increase in blood pressure could be attributed

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not only to an increased cardiac output but also to the relatively increased peripheral resistance. The increased sympathetic activity and the augmented renin-angiotensin system in young patients with borderline hypertension may be involved in the increased cardiac output, the inadequate fall in total peripheral resistance, and the resultant increase in blood pressure with sodium loads. Potassium supplementation could prevent the elevation of blood pressure with sodium loads by attenuation of the increased cardiac output, possibly as a result of the inhibition of sodium retention.\(^\text{14}\)

REFERENCES


