Ethnic differences in renal handling of water and solutes in hypertension

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Ethnic differences in hypertension are well recognized and have been attributed to several factors, including genetic susceptibility, environmental factors, and lifestyle. This latter increases the likelihood of developing hypertension in some populations by favoring the development of risk factors such as obesity, a low level of physical activity, a high sodium intake, and a low dietary intake of potassium and calcium. Thus, high blood pressure is clearly more frequent among black subjects, and hypertensive disease in black subjects differs from that seen in the white population in several aspects: black hypertensive patients more frequently exhibit salt sensitivity, a tendency toward expanded plasma volume, lower plasma renin activity, and increased renal vascular resistance.1,2 Moreover, difference in the urinary excretion of natriuretic and vasodilatory substances, such as dopamine and prostaglandins, and in sodium-potassium and sodium-lithium countertransport have been reported in black and white hypertensive subjects, suggesting once again that subjects of black descent excrete sodium less efficiently than white subjects, an observation that also explains the increased percentage of salt-sensitive hypertension in the black population.3

However, the important unanswered question remains, “Where within the kidney does the greater sodium reabsorption occur?” The characterization of the molecular mechanisms of several monogenic forms of human salt-sensitive hypertension has focused much of the attention on an increased reabsorption of sodium by the earlier segments of the nephron.4 However, these forms of hypertension are rare, and so far primary disturbances in distal reabsorption of sodium that could explain the increased sodium sensitivity of hypertension in some populations have not been clearly documented in patients with essential hypertension. Several studies have suggested that an increased reabsorption of sodium by the earlier segments of the nephron may be associated with salt sensitivity.5,6 Thus, Pratt et al7 found that amiloride, an inhibitor of the epithelial sodium channel, had a greater blood pressure–lowering effect in white than in black subjects, an observation that also explains the increased percentage of salt-sensitive hypertension in the black population.8

In this issue of Hypertension, Chun et al8 have added another piece to the puzzle by providing some evidence of an increased activity of the Na,K,2Cl channel in the thick ascending limb in young normotensive subjects of black origin of whom ~25% had a family history of hypertension. In this study, black subjects investigated on a free sodium and water intake had a lower 24-hour urinary volume and more concentrated urine measures than white subjects at baseline. In addition, subjects of African origin exhibited lower urinary excretion rates of potassium, calcium, and magnesium. In this study, Chun et al8 used furosemide as a pharmacological tool to investigate the activity of the Na,K,2Cl channel in vivo. Interestingly, they found a comparable natriuretic effect of furosemide in black and white subjects. However, the response to intravenous furosemide was significantly lower in terms of potassium and calcium excretion, suggesting a greater basal activity of the Na,K,2Cl channel in black subjects. The absence of significant difference in furosemide-induced urinary sodium excretion may seem surprising, but one should take into account that the distal segments of the nephron were still able to adapt for the final elimination of sodium to maintain sodium balance and blood pressure. The data of Chun et al.,8 therefore, provide additional evidence that alterations of renal sodium in the loop of Henle segments of the nephron might have some role in the development of hypertension, particularly in black hypertensive subjects. These data should, however, be interpreted with caution. Indeed, whether the response to furosemide solely reflects the activity of the Na,K,2Cl channel could be questioned. Moreover, subjects were not investigated in conditions controlled for sodium, potassium, and calcium intake.

Ethnic differences in the response to antihypertensive therapy are also well recognized.9 Thus, in clinical practice it is generally assumed that diuretics and calcium channel blockers are more effective than blockers of the renin-angio-

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tensin system or β-blockers in lowering blood pressure in black subjects than in white subjects. Yet, dietary salt restriction has been shown to facilitate blood pressure reduction with both blockers of the renin-angiotensin system and calcium antagonists in black subjects, as well as in white hypertensive patients. The data of Chun et al suggest that some aspects of the acute renal response to a loop diuretic also differ among black and white subjects. Interestingly, the finding of a lower urinary volume and of a significant increase in plasma vasopressin levels in black subjects would suggest that an overactive vasopressin system plays a role in the development of essential hypertension in some subjects of African descent. So far, the use of vasopressin receptor antagonists in the treatment of hypertension has been rather disappointing, but only vasopressin V1 receptor antagonists have been investigated in this clinical indication. If water retention does play a role in the development of hypertension, by delaying the excretion of daily ingested fluid and sodium, then partial inhibition of vasopressin V2 receptors with a low dose of a selective V2 receptor antagonist could become an interesting therapeutic approach, as proposed recently by Bankir et al. However, this hypothesis remains to be demonstrated.

In conclusion, the data presented by Chun et al in this issue confirm the need to investigate in more detail the subtle changes in segmental handling of water and solutes occurring early in hypertensive individuals as it becomes increasingly evident that alterations of sodium excretion in subjects prone to develop essential hypertension do not result from an anomaly of a single transport system but rather from a combination of several subtle changes in sodium reabsorption occurring at different sites along the nephron.

Disclosures

None.

References

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