Sodium–Potassium Interaction in Hypertension and Hypertensive Cardiovascular Disease

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Epidemiological evidence suggests that low potassium intake is associated with the probability of occurrence of hypertension and stroke. The short-term response to increased potassium intake is increased sodium excretion as well as increased potassium excretion; the short-term response to increased sodium intake is increased potassium excretion as well as increased sodium excretion. In some experimental studies, increased amounts of potassium have been able to block the noxious influences of sodium. Sodium and potassium must be concomitantly considered in the investigation of the association of either of these cations with hypertension and cardiovascular disease. The chloride ion is also important for sodium's effects; its importance in potassium's effects has not been extensively explored. (Hypertension 1991;17[suppl I]:I-155-I-157)

The interaction of sodium and potassium was the focus of Von Bunge's studies in Germany in the mid-1870s and remains a topic of interest. Von Bunge was concerned that the natriuresis produced by potassium would lead to serious disease. He was relieved to discover that the natriuresis lasted for only a few days; afterwards, the experimental subject returned to sodium balance. Keith and Binger used potassium to produce natriuresis in congestive heart failure in the mid-1920s, and several reports from Canada discussed the hypotensive consequences of potassium salts.

Animal Studies

None of the aforementioned studies were done with modern methods, and there was little interest in the cardiovascular consequences of potassium supplementation until publications by Meneely and Ball and Dahl et al. Meneely and Ball studied Wistar rats on a very high sodium intake. They found that the life expectancy of the rats, which was shortened by the high doses of sodium, was increased back toward the untreated values by concurrent supplementation with potassium. Blood pressure was lowered by potassium supplementation, although the effect was not marked and was not found at all times after the initiation of therapy. In retrospect, the effect on morbidity and mortality was more impressive than it was on blood pressure. Dahl et al studied the effect of potassium supplementation on the salt-sensitive (DS) rats, the strain that he had bred. They used a dose–response study, which demonstrated the interaction between the hypertensive effect of sodium and the hypotensive effect of potassium on the final blood pressure. The effect on mortality seemed to accord with the effect on blood pressure in studies by Dahl et al.

Tobian has used a stroke-prone strain of spontaneously hypertensive rats (SHRSP) to study the effect of potassium. He has discovered that the mortality of the SHRSP is markedly increased by sodium feeding. The increased mortality can be prevented by simultaneous feeding of KCl. The potassium feeding produces a lowering of blood pressure in some but not all of Tobian's studies, and the protection against morbidity and mortality does not seem to rely primarily on the effect of potassium on blood pressure.

Epidemiological Studies on the Relation of Potassium Intake to Blood Pressure

Blacks in the United States consistently have higher blood pressures than whites. Equally as consistently, they excrete less potassium than whites. The decreased urinary excretion is almost surely not the result of a difference in the partition of potassium excretion between urine and other routes in blacks compared with that in whites. The best evidence for this phenomenon is given by Grim et al, who analyzed duplicate meals from whites and blacks and found that the difference in potassium intake between blacks and whites was larger than the difference in urinary excretion of potassium. Similar re-
renal gland to increased amounts of potassium is increased aldosterone secretion. The increase in this secretion limits sodium loss; thus, it blocks (at least partially) the natriuresis that directly results from increased potassium intake. Therefore, this normal homeostatic response inhibits the fall of blood pressure resulting from potassium administration.

**Potassium Response to Sodium Loading**

Increased sodium intake, especially by large amounts, causes increased excretion of potassium. If the sodium intake is large enough, plasma potassium will decrease even if the potassium intake remains normal.¹²

**The Chloride Story**

In recent years, a series of studies by Kotchen et al¹³ and Morris (Kurtz and Morris¹⁴) have suggested that sodium, with anions other than chloride, is relatively ineffective in raising blood pressure. Chloride with cations other than sodium is also ineffective in raising blood pressure. In the reported trials of blood pressure lowering, potassium has been given with chloride as its anion. One must consider the possibility that the KCl is donating its chloride to some sodium that is ingested without chloride. Therefore, the KCl administration could be transforming sodium, which has been ingested without chloride, into potent, blood pressure–raising NaCl. This possibility seems relatively remote, as most sodium is probably ingested as NaCl. However, as noted above, it is possible that those who acquire their sodium by means other than NaCl would lose any blood pressure–lowering effect of the potassium.

Another considered possibility is that the sodium appetite, which is precipitated by the potassium-produced natriuresis, produces enough increased sodium intake to block the hypotensive effect of potassium. In fact, several studies demonstrated a modest increase in steady-state sodium excretion with the potassium-treated group, which was significant in at least one study.¹⁵

**Effect of Very Low Potassium Intake**

Potassium supplementation is usually said to lower plasma renin activity. In our study, potassium supplementation in a black population raised plasma renin activity, presumably because the natriuretic effect of the potassium outweighed the renin-lowering effects of KCl.¹⁶ Krishna et al¹⁷ compared the effects of sodium supplementation in individuals who were on a normal potassium diet with those on a low potassium diet. An amount of sodium that did not induce hypertension in subjects given a normal potassium diet did cause hypertension in subjects given a low potassium diet. The possibility remains that the effect of potassium intake on blood pressure is a threshold one. Above a certain threshold, modest amounts of potassium possibly have little effect. Below this threshold, a low potassium intake serves to sensitize the individual to sodium.
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Research Implications

The aforementioned considerations suggest that the role of potassium should be investigated further.

1) Is there a significant effect of potassium on cardiovascular health that is independent of its effect on blood pressure?
2) Is potassium of primary importance when its intake is very low and of little importance once it passes a certain threshold?
3) Should potassium be given with anions other than chloride?
4) What is the difference between the diets of blacks and whites that results in such low potassium intake in blacks (not discussed above)?
5) How can diets be changed to raise potassium intake if potassium significantly manifests its importance to cardiovascular health?

References

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