Sodium–Potassium Interaction in Hypertension and Hypertensive Cardiovascular Disease

Herbert G. Langford

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.1 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.2

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 Ball3 and Dahl et al.4 Meneely and Ball3 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 impres-

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...sive 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.4 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.5 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,6 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-
Results were found by Frate in diet diaries from a study in rural Mississippi. Evidence that this difference between blacks and whites could be a cause of the greater frequency of hypertension in blacks than whites is given by numerous studies that show a negative correlation between urinary excretion of potassium, or a positive correlation with the urinary sodium/potassium ratio, and blood pressure.

Langford and Watson studied the correlation between blood pressure and urinary excretion of sodium and potassium in 104 black females with a mean age of 20 years. Daily urine specimens were collected for 6 days, and three blood pressures were taken daily for 8 days. The urinary sodium/potassium ratio and diastolic blood pressure were significantly correlated. Walker et al. studied 571 individuals in Baltimore, Md., and found that potassium excretion significantly and negatively correlated with blood pressure. The INTERSALT study revealed a significant negative correlation between blood pressure and potassium excretion and a positive one between the sodium/potassium ratio and blood pressure.

Khaw and Barrett-Connon obtained careful diet histories of middle-aged and older individuals who lived in a prosperous planned community near San Diego, Calif. Although there was a significant negative correlation of potassium intake and blood pressure, a stronger negative correlation was found between potassium intake and stroke.

Effect of Potassium Loading on Blood Pressure

Because potassium is natriuretic, blunts the sodium-produced rise of blood pressure in rats, and is epide-

miologically associated with lower blood pressure, a reasonable expectation is for potassium supplementation to lower blood pressure in humans. The results have been inconsistent. A meta-analysis of most published trials of potassium supplementation showed a small but significant blood pressure-lowering effect. The effect could be considered disappointingly small and of little clinical importance, although it might be important for a given population.

Homeostatic Response to Potassium Loading: A Possible Cause for the Limited Blood Pressure Fall Produced by Potassium

Von Bunge showed that natriuresis after potassium loading was brief. Young et al. systematically explored the effect of potassium loading in dogs. Their results advance an explanation of the limited response of blood pressure to potassium supplementation of a constant sodium diet. Potassium supplementation in intact dogs produced natriuresis that lasted no more than 3 days and was accompanied by a marked increase in aldosterone. Blood pressure did not significantly change. Conversely, when they adrenalectomized the dogs and put them on constant mineralocorticoid replacement, a different sequence of events occurred. Natriuresis was greater and more prolonged, plasma renin activity was higher, and blood pressure fell and remained depressed. The normal response of the adrenal 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.

The Chloride Story

In recent years, a series of studies by Kotchen et al. and Morris (Kurtz and Morris) 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.

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. Krishna et al. 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.
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
2. Addison WLT: The use of sodium chloride, sodium bromide and potassium bromide in cases of arterial hypertension which are amenable to potassium chloride. Can Med Assoc J 1928;18:281–285

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