The Role of Potassium Manipulation in Blood Pressure Control

The state of the art of dietary intervention for control of high blood pressure and prevention of arteriosclerosis is uncertain. The most noncontroversial method is caloric restriction for weight reduction, but long-term normalization of weight is the exception, rather than the rule. Dietary sodium restriction has received considerable attention in recent years. New possibilities of management with potassium manipulation are being explored, based on experimental and epidemiological data. This editorial reviews five recent short-term human trials in England, Austria, and Japan and 10 epidemiological-observational studies conducted worldwide. These indicate that sodium chloride restriction per se or increased potassium intake may be helpful in the prevention of high blood pressure or the lowering of elevated blood pressure for some, but not all, individuals. However, an approach that combines sodium chloride restriction and an increase in dietary potassium holds considerable promise for success, although questions about the nonpharmacological management of hypertension will not be resolved until long-term controlled experiments have been carried out.

Reports from the Hypertension Detection and Follow-up Program in this country, the Australian Management Study of mild hypertension, and a British follow-up study of mild and moderate hypertension have shown that there have been excellent results with pharmacological therapy. For the millions of mildly hypertensive patients, however, the nonpharmacological management of elevated blood pressure levels is the key issue of the 1980s.

Proponents of sodium restriction for the control of elevated blood pressure recommend dietary intervention on the basis of experiments of relatively short duration, usually not exceeding 2 years. Opponents of sodium chloride restriction, such as Sackett, argue that clinical trials of rigorous sodium restriction have shown that this is relatively ineffective as the sole treatment of hypertension. According to Pickering, the possibility exists, “that a very few people respond with a small fall of pressure to salt restriction of the order of 1 g per day.”

Weight reduction remains the treatment of choice, since 60% of patients with essential hypertension are 20% or more over their normal weight, and blood pressure levels are promptly reduced by weight loss. The problem here is one of long-term efficacy, because many patients regain their lost weight.

Therefore, it is appropriate to consider the electrolyte, potassium, which has shown a promising potential for lowering blood pressure in animal studies. As early as 1928, Addison suggested that potassium supplements may be beneficial in treating hypertensive patients. Our knowledge about potassium's possible effect on blood pressure is limited. It is based on three sets of observations: 1) animal experiments, 2) epidemiological comparisons of dietary habits among different populations, and 3) experiments with humans.

Animal Experiments

The results of dietary trials with animals will not be repeated here, but may be summarized as follows: Over the past 25 years, animal experiments have clearly demonstrated that feeding potassium protects unequivocally against the development of hypertension in Sprague-Dawley, Dahl S, and R strain rats as well as dogs and that this treatment lowers blood pressure levels in animals with hypertension.
Epidemiological Studies

Studies of human populations show that life styles and habits have considerable influence on both blood pressure levels and dietary potassium intake. In reviewing a study of two populations in South America, Morgan et al.6 found that different degrees of urbanization correlated with different eating patterns and blood pressure levels. The more urbanized population used more sodium chloride and had higher blood pressure levels. The rural population still used plant ashes (potassium chloride) and retained lower blood pressure levels. Other studies on groups in primitive societies have confirmed that persons with a low salt, high potassium intake remain normotensive and have no rise in blood pressure with age. Abernethy7 noted that primitive tribes usually have a sodium intake of less than 10 mEq per day and that this is regularly accompanied by a high potassium intake of 7800 mg to 11,700 mg (200 to 300 mEq) per day.

In another study, Kesteloot et al.8 compared blood pressure with sodium intake in Belgium and Korea. Blood pressure levels were found to be higher and sodium intake and excretion significantly higher among Koreans than among Belgians. Potassium intake and excretion were lower in Koreans than in Belgians. The authors established a significant negative relationship between potassium and blood pressure level, which is interesting because the drop in blood pressure per millimole (mmol) of electrolyte was about three times more pronounced than the positive effect of sodium. Thus, the use of potassium appears to be a possible dietary tool in the management of blood pressure.

In 1980, Fodor and Rusted9 recorded that a random sample of adult Newfoundlanders showed evidence of a suboptimal dietary potassium intake. Potassium consumption was lower among 51 hypertensive patients (1525 mg/day) than among 93 normotensive persons (1750 mg/day). Sodium intake among Newfoundlanders is very high, since salt fish, salt potatoes, and canned vegetables are staples of the daily diet. In this easternmost island of the North American continent, hypertension is as epidemic as in the traditional southeastern "stroke belt" extending from North Carolina to Georgia.

Other studies (in Evans County, Georgia; Baltimore, Maryland; Washington, D.C.; New Orleans, Louisiana; and Jackson, Mississippi) document the lower potassium intake among blacks in comparison to whites. Blacks in Evans County, for instance, consumed about 50% less potassium than whites, which was obviously related to their inadequate intake of fruits, vegetables, and salads, as well as to the traditionally longer cooking process whereby the intracellular potassium is removed from beef, fowl, and potatoes and discarded with the cooking water. In South Africa, a low potassium intake is associated with the lowest socioeconomic class since the blacks in the upper class have the same diets as whites. A low potassium intake is usually associated with a high sodium consumption; it is tempting to speculate that the higher prevalence of hypertension in blacks compared to whites may be partly explained by this electrolyte imbalance. The VA Study Group10 pointed out that the presence of a considerably reduced potassium excretion was "one of the most striking racial differences... probably reflecting a diminished dietary intake of potassium in blacks compared with whites." However, without vigorous validation in future epidemiological and clinical studies, it is impossible to draw any firm conclusions.

In studies of six male Japanese populations, Ueshima et al.11 analyzed serum potassium and surveyed dietary intake by the 24-hour recall method. There was a significant negative correlation ($r = -0.98$) between the mean serum potassium level and the prevalence of hypertension. The serum potassium level was lowest in Akita where the prevalence of hypertension and the sodium intake were highest. However, potassium intake was also significantly higher. It was suggested that hypertension, and the low serum potassium in Akita, despite high potassium intake, resulted from the high sodium intake which promotes kaliuresis. Generally speaking, for people on a high sodium diet, "sodium is kaliuretic" and "potassium is natriuretic."

The relation of arterial pressure to body sodium, body potassium, and plasma potassium in essential hypertension was studied by Beretta-Piccoli et al.12 Although no dietary histories were recorded, this clinical investigation of 91 hypertensives
and 121 normal controls nevertheless contained data that seem to confirm results obtained in more indirect epidemiological surveys. For example, the mean exchangeable sodium was the same in normal and hypertensive persons when the two groups were matched for leaniness. The exchangeable sodium and total body sodium increased with age in hypertensive, but not in normal, subjects. On the other hand, plasma potassium concentrations, exchangeable potassium, and total body potassium correlated inversely and significantly with blood pressure in hypertensive patients. These correlations were more marked in young patients. The authors suggested that changes in plasma and body potassium are important in the earlier stages of hypertension and that changes in body sodium may become important later.

The British Whitehall long-term epidemiological study was reported on by Bulpitt et al. In this group of people, 2216 men and 1362 women had hypertension, but were not taking antihypertensive medication. After appropriate adjustment for age and body mass, plasma potassium was negatively associated with both systolic and diastolic blood pressure. A decrease of only 1 mmol/liter in women was associated with a systolic blood pressure increase of 7 mm Hg and a diastolic blood pressure increase of 4 mm Hg ($p < 0.001$ for both). In men, the corresponding increases were 4 mm Hg and 2 mm Hg, both significant at $p < 0.05$.

Experiments with Humans

In addition to the animal experiments and the epidemiologic studies, there have been experiments with humans that indicate the usefulness of high potassium and low sodium intake for blood pressure lowering. Some groups were treated either with dietary potassium or sodium manipulation, and other groups were treated by a combination of high potassium and low sodium. The first double-blind experiments with potassium chloride in humans were reported in 1980 and 1981. An Austrian group demonstrated that the addition of 8 g of potassium chloride, with a simultaneous restriction of sodium chloride to 3 g, caused a marked drop in systolic and diastolic blood pressure in contrast to a diet that was restricted in sodium and contained no added potassium chloride. This study involved 2 weeks of crossover experiments on 21 normotensive medical students, half of whom had a family history positive for hypertension.

In England, 12 weeks of experiments with 16 hypertensive and eight normotensive persons resulted in an elevation of systolic and diastolic blood pressure when 6 g of sodium chloride was added to the diet. The blood pressure increase was more marked among the hypertensives than among the normotensive persons. The addition of potassium chloride over 12 weeks resulted in a minor blood pressure increase among normotensive persons, but in hypertensives there was a significant decrease in systolic and diastolic blood pressure levels. The same investigators also experimented for 8 weeks with a group of young men with and without family history of hypertension. They compared the effects on blood pressure using 1) low sodium alone, 2) high potassium alone, 3) low sodium plus high potassium, and 4) normal dietary intake. The blood pressure reduction was most marked when high potassium chloride and low sodium chloride was used. However, this was only true for students with family histories positive for hypertension; in students with a family history negative for hypertension, blood pressure levels were higher.

The results from these two British studies were critically reviewed and reanalyzed. The contrasting behavior of the hypertensive and normotensive groups on the low sodium, high potassium diet in the first study was confirmed. Reanalysis of the second experiment revealed "essentially the same general effects of dietary electrolyte manipulations as before, but the depressor effect of potassium loading was of only marginal statistical significance," since the reviewers found it necessary to remove 16 of the original 23 patients from the analysis. "Some of the clinical data were no longer available to us" was the only explanation given. It is not clear why the research team would carry out a new analysis to reassess the validity of their own previous studies, and then proceed with a third publication. Whatever the reason, the confirmation of existing evidence was a valuable service, particularly when one considers the difficulties in conducting dietary experiments with free living humans.
These results suggest that the fall in blood pressure among hypertensives during the high potassium, low sodium diet was mainly due to the increased potassium intake. Return to their customary diet was associated with a marginal rise in sodium intake but a much greater fall in potassium intake, and their blood pressure levels rose again.

In another publication from Austria, Skrabal et al. studied 20 normotensive students, 11 of whom had a family history positive for hypertension. These workers showed that there was a more marked blood pressure reduction in students ingesting 200 mmol of potassium and less than 4 g of sodium chloride in comparison with students on regular diets or students on a sodium chloride-restricted diet. After adding potassium and keeping total calories the same, a weight reduction of 1 kg was noticeable within 1 week. This was interpreted as due to a loss of extracellular fluid volume and was related to the direct saluretic effect of potassium on the kidneys.

In another study with 20 hypertensive inpatients, Limura et al. observed a significant reduction of body weight, extracellular fluid volume, total exchangeable sodium and mean arterial pressure (from 114 to 103 mm Hg) after 10 days of potassium loading (175 mmol potassium a day for 10 days). They felt that the hypotensive effect of high potassium intake may be caused by a reduction in body fluid volume through augmentation of sodium excretion.

MacGregor et al. followed 13 patients for 2 months without treatment. Their mean blood pressure levels were 154 to 99 mm Hg when they were studied in an 8-week double-blind randomized crossover study. They were treated for 1 month with either slow release potassium tablets (60 mmol/day) or a placebo without alteration of dietary sodium and potassium. For those taking supplemental potassium, their mean supine blood pressure levels had fallen by 4% after 4 weeks. Their urinary potassium excretion was increased from 64 mmol/24 hrs to 118 mmol/24 hrs. The authors concluded that this moderate potassium intake could be achieved by using a potassium-based salt substitute coupled with a moderate increase in vegetable and fruit consumption.

Conclusions

From an assessment of the results of these studies, it is not clear whether the relatively short duration of the experiments is an important factor. The Japanese inpatient study was terminated after 10 days, the Austrian crossover study periods lasted only 2 weeks, and the several English studies lasted between 8 and 12 weeks for each dietary change. We now must ask whether the lowering of blood pressure levels in association with a high potassium diet represents a permanent change.

Such a possibility is suggested by a preliminary report by Dodson et al. indicating a highly significant diastolic blood pressure reduction in 13 of 32 hypertensive patients for as long as 9 months on a diet providing 40 to 50 mmol/day sodium and 80 to 90 mmol/day potassium. The mean diastolic blood pressure levels in the supine position were reduced from 98.3 to 85.0 mm Hg. Nothing, however, is known about the blood pressure of the remaining 19 hypertensive patients.

We feel that data on dietary electrolyte manipulation shows great promise. However, final proof of the hypothesis that adding potassium to a sodium-restricted diet will have a permanent effect on elevated blood pressure levels and be valuable in the primary prevention of hypertension and atherosclerosis will require further extended investigations. In addition to the background of well publicized animal experiments and a wealth of epidemiological observations, it is now time for vigorously conducted long-term intervention studies. These should include high school students and high risk groups with a propensity for the development of hypertension, particularly the black population.
References

2. Sackett DL. Letter to the editor. CMAJ 1980;122:1131
4. Addison W. The uses of sodium chloride, potassium chloride, sodium bromide and potassium bromide in cases of arterial hypertension which are amenable to potassium chloride. CMAJ 1928;18:281–285
6. Morgan T, Myers J, Carney S. The evidence that salt is an important aetiological agent, if not the cause, of hypertension. Clin Sci 1979;57:459s–462s
7. Abernethy JD. Sodium and potassium in high blood pressure. Inst of Food Technologists 1979;57–59

We acknowledge the contributions of the reviewers of this editorial and their helpful suggestions and valuable criticisms.

Siegfried Heyden
Sigrid J. Nellus
Kenneth A. Schneider
Duke University Medical Center
Durham, North Carolina

The role of potassium manipulation in blood pressure control.
S Heyden, S J Nelius and K A Schneider

doi: 10.1161/01.ATV.3.4.302

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/3/4/302.citation