Sodium and Potassium Intake and Blood Pressure

GRAHAM A. MACGREGOR, F.R.C.P.

SUMMARY There is increasing circumstantial evidence that the very high sodium diet combined with low potassium intake that most Western communities now eat may be, at least in part, responsible for the prevalence of high blood pressure. This circumstantial evidence combined with animal evidence has been considered sufficient in some countries to make a general recommendation to reduce sodium intake. If high sodium intake is an important cause of high blood pressure, it is not clear at the present time how it may do so. In this report, evidence is reviewed for one hypothesis suggesting an inherited defect in the kidney's ability to excrete sodium in patients who are going to develop essential hypertension, together with evidence for a raised concentration of an inhibitor of sodium transport. In patients with established hypertension, moderate restriction of sodium intake appears to lower blood pressure and moderate potassium supplementation to also lower blood pressure. While further evidence is required, particularly long-term studies, it would seem prudent to recommend to patients with essential hypertension or a strong family history of hypertension that they restrict dietary sodium intake moderately and increase dietary potassium intake by the consumption of more fruits and vegetables and, perhaps, the use of a potassium-based salt substitute. This regimen could obviate or reduce the need for drug treatment in some patients with mild to moderate hypertension. (Hypertension 5 (supp III): III-79-III-84, 1983)

KEY WORDS • sodium intake • diet • potassium • kidney • heredity • transport inhibitor • epidemiology • natriuretic hormone

THERE is considerable controversy about the role of sodium, first, as a cause of essential hypertension and, second, whether its reduced intake has any effect on established high blood pressure. Potassium intake may play a protective role in preventing the development of essential hypertension and/or ameliorating it when it is established. From an evolutionary point of view, sodium is a vital cation; one of its major functions is to regulate the extracellular fluid volume. Over the centuries, because of the obvious difficulties of obtaining sodium away from the sea, mammals have developed powerful mechanisms to conserve sodium in both urine and sweat and have also developed an instinctual appetite to seek out sodium. We have acquired the ability to obtain salt both from the sea and from mines and have found that it can be used to preserve food during the winter. It is therefore not surprising that salt has become an extremely important material, with great religious importance in early civilizations and great economic significance. In most developed countries, consumption of sodium is extremely high, around 100-400 mmols/day compared to the 5 to 10 mmols/day eaten by our ancestors during evolution and by individuals in communities today where salt is not freely available.\(^1\)\(^-\)\(^3\) Concurrent with this large increase in salt intake has been a smaller but nevertheless potentially important reduction in potassium intake, partly from reduced consumption of fruits and vegetables and partly from eating processed foods, which have potassium removed during processing. It is probable that potassium intake has fallen from 100 to 250 mmols/day previously to an average in most Western communities today of between 30 to 80 mmols/day. Does this high sodium/low potassium diet predispose us to the development of high blood pressure?

Epidemiological Evidence of the Influence of Salt and Potassium on Blood Pressure

There is considerable epidemiological evidence from studying different communities that differences in sodium and potassium intake among communities are important determinators of the whole populations' blood pressure levels.\(^1\)\(^-\)\(^4\) All of these studies can be criticized,\(^5\) but no study has produced evidence against the concept. More recent studies in which potassium excretion has also been measured suggest that within a particular community there may be a direct relationship between potassium excretion or the sodium/potassium ratio in the urine and blood pressure.\(^6\)\(^-\)\(^7\) None of these studies, however, is likely to demonstrate clearly that altering sodium intake or potassium intake is going...
Yet there are persuasive studies where communities have changed their salt or potassium intake, such as the Kenya study in which Samburu soldiers were given a daily 16 g salt ration; a rise in blood pressure resulted, part of which was ascribed to the increase in salt intake.8 An ongoing study of an African rural tribe, some of whom have migrated to cities, has shown that blood pressure is higher in urban environments and that perhaps at least part of the rise in blood pressure is related to the increase in urinary sodium and fall in urinary potassium that occurs in urban environments.9

A Possible Mechanism for Sodium Causing High Blood Pressure?

The mechanism whereby a high sodium intake might cause high blood pressure is not certain, but most authors agree that there must be some defect in the kidney’s ability to excrete sodium. This could give rise to retention of sodium and water, increased cardiac output, and, by autoregulation, increased peripheral resistance. However, the fact that plasma volume and extracellular volume are not raised in essential hypertension, but tend to be reduced, makes this explanation unlikely. On the whole, experimental evidence is against this concept, and also does not explain the increasing evidence of abnormalities of sodium transport in patients with essential hypertension.

In particular, there is evidence of inhibition of the ouabain-sensitive component of the sodium pump.10-12 There is also evidence from kidney cross-transplantation experiments in animals that, in inherited hypertension in the rat, the kidney carries the underlying message for the later development of high blood pressure.

This abnormality in the kidney of the rat is most probably a difficulty in excreting sodium.13-15 In humans, de Wardener and MacGregor16, 17 suggested that those who were going to develop essential hypertension might have inherited a kidney that is less able to excrete sodium (fig. 1). The high sodium diet that we eat in the West would give rise to a transient increase in blood volume, triggering the release of natriuretic hormone that would inhibit sodium transport in the tubule of the kidney, thereby increasing sodium excretion and restoring sodium balance back toward normal. Blaustein18 has suggested that a raised level of a circulating sodium transport inhibitor could increase intracellular calcium concentration,18 by inhibiting sodium transport across the smooth muscle cell of the arteriole, and thereby increase the sensitivity or tone of the arteriole. Eventually, this would result in an increased peripheral resistance and the development of high blood pressure. The rate and severity of the hypertension would therefore depend on the extent of the kidney’s defect in excreting sodium and the amount of sodium in the diet. An inhibitor of Na+-K+-ATPase has been demonstrated in normal human plasma, the level of which was related to sodium intake.19 Two studies20, 21 have shown that the ability of plasma to inhibit Na+-K+-ATPase is raised in patients with essential hypertension, as has another study22 in which normotensive white cells incubated in hypertensive plasma acquired the same abnormality as the hypertensives’ own white cells. The protective effect of an increase in potassium intake on sodium-induced hypertension could perhaps be explained apart from potassium’s well-known natriuretic effect, by potassium stimulating the sodium pump of either the smooth muscle cell of the arteriole or the

**Figure 1.** Sequence of events to explain a postulated inherited defect in the kidney’s ability to excrete sodium, the observed rise in the concentration of a circulating sodium transport inhibitor, rise in salt intake, and the rise in peripheral resistance in essential hypertension.
sympathetic neuronal junction. Potassium is known to oppose the effect of ouabain and could therefore oppose the raised levels of the circulating inhibitor of Na⁺-K⁺-ATPase. In vitro, it is known that ouabain increases norepinephrine output from nerve terminals and reduces its reuptake, thus raising the amount of norepinephrine available to react with receptor cells on the affected cell membrane. It is possible, therefore, that the increase in sympathetic activity that has been reported in some patients with essential hypertension, which also occurs with salt loading, could be due to an increased concentration of the circulating sodium transport inhibitor.

**Should the Whole Population Reduce Sodium Intake or Increase Potassium Intake?**

Recommendations in the U.S.A., Belgium, and, more recently, the United Kingdom that the whole population should reduce sodium and increase potassium intake are based not on direct experimental evidence but on animal and epidemiological evidence. Many decisions by public health officials have to be made before there is overwhelming scientific evidence. Previous public health measures such as vaccination for smallpox, provision of clean water, and drainage at the time of the cholera and typhoid epidemics in Europe in the 19th century were taken under similar circumstances. Indeed, the medical hierarchy at the time opposed some of these changes, and evidence of their benefit only came retrospectively. If communities are successful in altering the sodium/potassium ratio in their diet, careful observation of these communities may provide the evidence to justify the action that has already been taken. However, alteration of sodium/potassium intake may only affect a small proportion of the community, i.e., 10% to 20% of those who already have or are going to develop high blood pressure. Rose, however, has pointed out that the benefits achieved by current blood pressure treatment would be equalled by a downward shift of the whole blood pressure distribution of the population by only a few mm Hg, since the risks from high blood pressure increase throughout the range and do not start at a particular diastolic or systolic pressure. However, reducing sodium intake for a few days does not lower blood pressure in normotensive subjects, largely because of an immediate compensatory rise in renin release, but a small study where potassium intake was doubled by the use of slow potassium for 1 month did show a small fall in blood pressure in normotensive subjects.

**Established Hypertension**

Once blood pressure is raised, removing the cause does not necessarily lower the blood pressure level to normal. Nevertheless, it has been known since the early 1900s that severe restriction of sodium intake to around 10 mmols/day does cause a substantial fall in blood pressure in patients with severe and/or malignant hypertension. In particular, the Kempner rice and fruit diet, which was not only low in sodium but high in potassium and low in protein, was an effective way of lowering blood pressure but was extremely monotonous and most patients were not able to stick to it. Studies in which sodium intake was increased from 10 mmols/day to around 25 to 35 mmols/day caused the blood pressure to return toward treatment levels. It was therefore assumed that less severe sodium restriction would not lower blood pressure and, with the advent of diuretics, sodium restriction was abandoned by many physicians. A more modest reduction of sodium intake, achieved by simply not adding salt to food and avoiding high sodium foods has been claimed to lower blood pressure in patients with mild to moderate hypertension, but these studies have been criticized for their lack of adequate controls, their open nature, and the methodology of the blood pressure measurement.

We therefore conducted a double-blind randomized crossover study of the effect of modest restriction of dietary sodium intake on unselected patients with mild to moderate essential hypertension. We instructed 19 patients with mild to moderate essential hypertension who had been under care of the Blood Pressure Unit for some months to halve their sodium intake by not adding sodium to the food and avoiding sodium laden foods. After 2 weeks of sodium restriction during which their urinary sodium levels fell from 191 ± 19 mmols/24 hrs to 83 ± 11 mmols/24 hrs, they entered into a double blind randomized crossover study of Slow Sodium tablets for 1 month against identical matching placebos for another month. The number of Slow Sodium tablets that each patient took was estimated to restore sodium intake back to the subject’s usual intake. With sodium restriction, there was a significant fall in blood pressure; with placebo, the blood pressure remained at the same level. With the increase in salt intake with Slow Sodium, where urinary sodium was restored back to their normal diet, blood pressure rose. The percentage fall in blood pressure on the 4th week of placebo compared to the 4th week of Slow Sodium was 6.1%.

Our study, therefore, clearly demonstrated that moderate restriction of sodium intake significantly lowered blood pressure, and that its effect approximately equaled the effect of a single antihypertensive drug such as a diuretic or beta-blocker (fig. 2).

Amery and coworkers demonstrated some time ago that moderate sodium restriction is additive to diuretic therapy, and it is known that salt loading blunts the blood pressure lowering effect of diuretics. A more recent study has shown that moderate sodium restriction is additive to other drugs including beta-blockers. The immediate blood pressure lowering effect of sodium restriction, like a diuretic, is offset by the rise in renin and angiotensin II that sodium loss stimulates. Interfering with the release of renin or blocking the formation of angiotensin II would therefore be expected to be especially effective in combination with sodium restriction. Use of drugs that block the renin system, particularly the angiotensin converting-enzyme inhibitors, combined with moderate sodi-
drop in blood pressure. However, it has not as yet been clearly demonstrated that potassium supplementation is additive to the effect of sodium restriction. Nevertheless, based on the current evidence such as it is, it would seem prudent to advise patients with essential hypertension whether on treatment or not to restrict sodium intake, or at the very least, not to add salt to their food or to the cooking and to avoid sodium-laden foods. An increase in potassium intake can be achieved by the greater consumption of fresh fruit, vegetables, and cereals, i.e., making the diet more natural. This may carry other benefits apart from the increase in potassium intake, particularly from the higher fiber and lower saturated fat content of the diet. Use of a potassium-based salt substitute may be helpful for some patients following a low sodium diet and could at the same time increase potassium intake.

All of these studies in patients demonstrate a blood pressure drop in small groups of patients. The studies have been criticized for the short length of time in which the diets were altered. However, one study that has been continued for a longer period of time showed an increasing effect of moderate sodium restriction with time, and it is certainly possible that moderate sodium restriction might prevent the progressive rise of blood pressure that can occur in patients with essential hypertension. Nevertheless, further studies of the

"FIGURE 2. Average systolic and diastolic pressure and urinary sodium excretion in 19 patients with essential hypertension on a normal diet, 2 weeks after a restricted sodium diet, and at 2-weekly intervals during the randomized crossover study of Slow Sodium vs placebo. Patients were not receiving any drug therapy. ***p < 0.001; **p < 0.01; *p < 0.05, comparing equivalent measurements on Slow Sodium to placebo. †p < 0.001, comparing a normal diet to 2 weeks of dietary sodium restriction.

"FIGURE 3. Average systolic and diastolic pressures and urinary potassium excretion before and during treatment with potassium and placebo. *p < 0.05; **p < 0.025; ***p < 0.001, comparing equivalent measurement on Slow K to placebo."
effect of dietary alteration of sodium and potassium intake in patients with essential hypertension must be done and are much more easily done than lifelong preventive community studies.

Future studies need to concentrate on whether increasing potassium intake is additive to the effect of moderate sodium restriction and whether patients can comply with the alteration of the diet over a longer period of time, as well as which type of patient responds best to dietary alteration. It is probable that the mechanism of the immediate fall in blood pressure with sodium restriction in patients with high blood pressure is different from the mechanism by which sodium causes a gradual rise in blood pressure over many years. Part of the immediate fall in blood pressure with sodium restriction is due to the lack of compensatory rise in angiotensin II with sodium loss, and it is already known that sodium restriction is more effective in low renin patients. There is increasing evidence that drug treatment of mild hypertension is beneficial. Approximately 10% to 20% of the population in the West have a diastolic pressure over 90 mm Hg. The cost of blood pressure lowering drugs could become extremely large. Alteration of dietary sodium and potassium intake could play an important role in containing drug costs in the future.

References
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Discussion

DISCUSSANTS: A. SALVETTI
G. MACGREGOR
POOLE
G. WATT

SALVETTI: What happens to normotensive subjects being exposed to the same regimen?

MACGREGOR: Short-term sodium restriction in normals shows no fall in blood pressure because of the reactive rise in renin and thereby angiotensin II. We do not know the long-term effect of restricting sodium intake, particularly if you start at an early age.

SALVETTI: It is a really big problem in our population to restrict salt intake below 100 mg/day. So I think that diuretic treatment is very important in our population.

WATT: I think the most important point about Dr. MacGregor's study is the initial level of blood pressure of the patients studied, which was 98 mm Hg diastolic supine and 108 mm Hg diastolic standing after 8 weeks of observation, giving an average of 103 mm Hg. It is probable, therefore, that the referral pressures were outside the mild hypertension range. The mean level of blood pressure during the 4th week of sodium restriction was 96.5 mm Hg. I make three points; first, the patients were not in the mild hypertension range; second, pressure was not adequately controlled; and third, if sodium restriction cannot control pressure without additional drug therapy, it loses much of its attraction for many patients.

MACGREGOR: Before treating any patient, one must exclude individuals who respond to placebo. In your study, there was a large decrease in blood pressure whether salt was restricted or not, and your patients did not have mild hypertension. I agree that our study was in patients with mild to moderate hypertension, as we stated in the title of the paper. In this group of patients we demonstrated a significant fall in blood pressure with moderate sodium restriction, roughly equivalent to the effect of a diuretic.

POOLE: Could you tell us about the daily calcium intake of your patients and comment on the work of McKerron and colleagues as to whether calcium in an important dietary factor whose deficiency promotes hypertension and whose supplementation reduces blood pressure?

MACGREGOR: It is not appropriate to comment at present. We are doing studies on altering calcium intake in normals and hypertensives and the effects of changing sodium balance on ionized calcium.

WATT: To respond to the comments that our patients did not have mild hypertension, Dr. MacGregor appears to be entertaining all possible explanations of our data other than the most reasonable one, namely, that reducing sodium intake to less than 60 mmol/day had no effect on blood pressure in patients with pressures consistently in the range 90-99 mm Hg. We have good evidence to show that the patients in our study correspond to roughly the 90th percentile of the blood pressure distribution in our population, which is mild hypertension in anybody's language.

MACGREGOR: During your study, the average diastolic pressure was 83 mm Hg. This is not mild hypertension by anyone's definition. We have now looked at your individual responses and because of the skewed nature of your randomized crossover study, we applied nonparametric statistics and found a significant effect of sodium restriction in your study.
Sodium and potassium intake and blood pressure.

G A MacGregor

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