Hypertension and Sodium Intake

Diederick E. Grobbee

Department of Epidemiology and Biostatistics, Erasmus University Medical School, Rotterdam, The Netherlands

The Chinese "yellow" emperor was the first to report that high salt intake makes the pulse hard (1). Subsequently, in particular in the second half of this century, numerous studies have examined the dietary sodium intake in relation to hypertension. The possibility of such an association was raised by the observation by Dahl and others that the average sodium intake across populations was related to the prevalence of hypertension within those populations (2-5). However, low sodium populations tend to live in remote areas and are relatively unaffected by Western culture, thereby differing in many aspects of lifestyle as well as in other social and environmental factors from high sodium countries, leading to a possible ecologic fallacy in drawing causal inference from cross-cultural associations. In the INTERSALT study, the association between sodium and blood pressure was studied using standardized protocols in 52 samples of men and women drawn from defined populations from 32 countries around the world, including data on 10,079 individuals (6,7). Whereas body mass index and alcohol intake emerged as strong determinants of hypertension, the findings on urinary sodium excretion as a measure of intake were more ambiguous. The reported significant cross-population association between urinary sodium and blood pressure level was dependent on four remote populations with an extremely low sodium intake. When restricted to the other 48 centers, no linear association was present. Even so, sodium excretion appeared to be related to the blood pressure slope with age, suggesting that, in a high sodium environment, blood pressure increases more strongly with advancing age than in low sodium populations. Part of the explanation for this discrepancy is that the analysis of slope was based on within-center data rather than from a cross-center comparison. Importantly, in spite of its rigorous methodology, INTERSALT remains susceptible to some of the biases inherent to any interpopulation comparison.

Studies conducted within populations are limited in number and, in several of these, no association between sodium excretion and blood pressure was found. In a recent meta-analysis of intrapopulation studies, it was estimated that a difference in intake of sodium of 100 mmol was associated with a blood pressure that was on average 2 to 3 mm Hg higher (8). Unfortunately, in within-population analyses, two obvious confounding variables—other dietary factors and physical activity—are
also often not included. In the largest within-population study to date, the Scottish Heart and Health Study (9), the relationship between sodium and blood pressure disappeared after adjustment for age, gender, height, weight, pulse rate, alcohol consumption, and potassium excretion.

Some studies were carried out specifically to address the potential influence of sodium intake on blood pressure change over time. In a cohort study of 233 children between ages 6 and 16 years who were followed for a period of more than 6 years, a clear effect of sodium intake on blood pressure change could not be determined, in contrast to associations of blood pressure change with potassium and sodium to potassium ratio (see following) (10). Cross-sectional studies on sodium intake and blood pressure level in children have hardly shown any association (11). The age of participants in the INTERSALT study ranged from 20 to 59 years. Additional analyses from the INTERSALT study have similarly indicated that the association between blood pressure and sodium intake was more pronounced in the elderly (12). It appears that the elderly are, in general, more sodium-sensitive than middle-aged and younger subjects based on results from other studies (13). However, a randomized intervention study in newborn infants showed a small but significantly increased blood pressure change on a relatively high sodium intake (14). This could indicate a sensitivity to sodium in the first months of life and, for example, results from the immature kidney at that stage. When maintained, such an effect could have a sizable impact on blood pressure later in life.

From these observational data, an association between blood pressure level, prevalence of hypertension, and sodium intake appears to be present, although of limited magnitude, at least in the range of sodium intake commonly observed in Westernized societies. Still, even a small association of a nutrient and blood pressure on a population scale may have an important impact on cardiovascular disease rates (15). Moreover, certain groups may be particularly sensitive to a high sodium intake, notably the very young and the elderly. However, the findings on sodium suggest that certain other environmental and lifestyle factors may be at least as important although perhaps less intensively studied so far.

RESULTS FROM TRIALS

An article generally considered to have provided the first experimental data on salt and blood pressure, was published in 1904 by Ambard and Beaujard, in which emphasis was on chloride rather than sodium. In recent decades, several well-controlled trials on sodium restriction in hypertensive and normotensive subjects have been reported. In a pooled analysis, we considered 13 randomized studies on moderate sodium restriction (16). In these studies (5 were double blind), participants were aged between 16 to 70 years. The duration of the intervention ranged from 12 to 730 days and the change in sodium achieved ranged from 21 to 70 mmol per day. The average reduction in systolic blood pressure was 3.6 mm Hg (range —0.5 to —10.0) and in diastolic blood pressure, 2.0 mm Hg (3.2 to —7.0). In agreement
with the observational findings, older subjects and patients that had more severe hypertension showed more marked changes in blood pressure. These findings were confirmed by a subsequent larger meta-analysis (17). Apart from "typical," or average, effects of sodium restriction, meta-analyses may provide data on dose–response or threshold effects of the intervention. Most trials in which the achieved sodium intake was still above approximately 50 mmol per day have shown little effect, suggesting that a threshold for effects on blood pressure may indeed be present around that level of intake.

SODIUM SENSITIVITY

Findings in both observational studies and trials suggest that individuals vary in their blood pressure response to differences in sodium intake. To detect subgroups of hypertensive subjects in whom dietary sodium restriction is particularly effective, it is important to know characteristics and mechanisms of sodium sensitivity. Many potential markers have been suggested and the importance of some of these factors, notably the activity of the renin–angiotensin system, appears well established from studies and has a known pathophysiologic basis (18,19). Some indicators of sodium sensitivity have been inferred from cross-sectional observations or from experimental studies in which subjects were compared who showed a fall or rise of blood pressure on a change in sodium intake. Because no clear bimodality exists in blood pressure responses to increases or decreases in sodium intake, the classification of responders (sodium-sensitive) and nonresponders (not sodium-sensitive) depends on arbitrary cut-off points in an otherwise Gaussian distribution: the normal probability fallacy (20). Only a few studies have used rechallenges to confirm sensitivity to sodium in particular subgroups (21,22). Apart from advanced age, black race, low plasma renin activity and a blunted renin response, and possibly diabetes, there are, as yet, no well-defined and practically useful characteristics to discriminate sodium-sensitive from nonsensitive subjects.

CONCLUSION

There is substantial data indicating that the level of sodium intake is related to the blood pressure of individuals. The average effect of differences in sodium intake in the range of dietary sodium characteristic of westernized societies is small, around 0.02 to 0.05 mm Hg per mmol sodium. There is hardly any doubt that drastic reductions in sodium intake to as low as 20 mmol per day will reduce blood pressure levels in hypertensive subjects. Compliance to this intervention is, however, problematic. More modest restriction of sodium is documented to reduce systolic and diastolic blood pressure by a few mm Hg. There appears to be a marked heterogeneity in response. Yet, apart from age and black race, there are few easily measurable and established indicators for sodium sensitivity that the practicing physician may use to select patients for advice on sodium intake. More research in this area is
clearly needed, and determining the efficacy of sodium restriction in hypertensive
patients is still a matter of trial and error.

In hypertensive patients, a direct comparison of the efficacy of sodium restriction
to other nonpharmacologic interventions has rarely been conducted. Swales recently
estimated that a reduction of 66 mmol sodium per day to achieve a 1 mm Hg
reduction of blood pressure would equal the effect of 1.5 glasses of alcohol less and
the loss of 0.5 kg body weight (23).

Although noted as early as the mid-1870s (24), knowledge on the interaction
between intake of sodium, chloride, potassium, and other electrolytes in its effects
on blood pressure is still limited. A more integrated approach to the study of dietary
electrolytes and blood pressure is clearly indicated. To examine the potential positive
interaction of reduced sodium, increased potassium, and increased magnesium in-
take, and improve compliance to sodium restriction in hypertensive patients, we
recently conducted a double blind randomized trial on the long-term blood pressure
effects of a low sodium/high potassium/high magnesium mineral salt in elderly
patients with moderate hypertension. In this study, a clear fall in both systolic and
diastolic blood pressure could be demonstrated, whereas the dietary intervention
was well tolerated (25).

Systematic and well-controlled studies on efficacy and safety as well as on mecha-
nisms and determinants of sensitivity are still few compared to the work devoted
to pharmacologic intervention. However, given the importance of knowledge on
dietary determinants of hypertension and the potential for relatively inexpensive and
tailored intervention, this lack of interest is not justified and more work needs to
be supported.

ACKNOWLEDGMENTS

Portions of this work were supported by the Netherlands Heart Foundation. The
text is, in part, adapted from Grobbee DE. Electrolyte intake and human hyperten-

REFERENCES

1. Veith I. The yellow emperor’s classic in internal medicine (translated from Huang Ti Nedi Ching
2. Dahl LK. Possible role of salt intake in the development of essential hypertension. In: Cottier P,
143–56.
6. INTERSALT Cooperative Research Group. INTERSALT: An international study of electrolyte ex-
cretion and blood pressure: results for 24 hour sodium and potassium excretion. BMJ 1988; 297:
DISCUSSION

Dr. Ginsberg: I was intrigued by your observations in the newborns, who were exposed briefly to different sodium levels and had changes in blood pressure that persisted after decades. I suppose an alternative hypothesis to explain that might be that the early exposure changed their appetite for sodium or in some way led to more permanent changes in how their body handles sodium subsequently. I wonder whether they have been studied from that point of view.

Dr. Grobbee: That is a very good point, and indeed we should be careful not to conclude on the basis of the blood pressure differences only that it is the initial intervention that is responsible. It may be that the initial intervention induced something else, like salt preference for example, that could explain the finding. We do not have a good way of measuring that, unfortunately. We did measure the current sodium and potassium excretion in these children and that was not different from control. However, we have data to suggest that in young
hypertensive subjects, the kidney hemodynamics are changed, though it remains surprising to us that there is a difference after such a long period (1).

Dr. Wolf: This was a salt restriction versus normal salt intake, and you said that there was a difference in blood pressure but no difference in the urinary excretion of sodium or potassium. Which group had a blood pressure that was closer to an average 15-year-old? Were the salt-restricted ones lower and the regular ones higher?

Dr. Grobbee: We are speaking about small differences, so it is difficult to judge which is closer to the average. But it is important to realize that, at the time the initial study was done, the low-sodium group was on formula feeds that provided half the usual sodium intake, but after that trial, the manufacturer changed their formulas so that the low-sodium formula became the standard formula. Nonetheless, I think it is very difficult to say what is normal.

Dr. Ganten: Potassium and magnesium supplementation has been advocated by the group in Finland as well. There is always a problem of taste with high potassium salt. Do you have any problems in this regard?

Dr. Grobbee: That is very true. I have been interested in this low salt and the Finnish variant of that for some time but the problem is that the taste is not too good. It is rather bitter and most people do not like it as a replacement for common salt. Also, there have not really been controlled studies for the Finnish salt, so it was all a bit unclear. One interesting recent development was the availability of a natural salt that is found in Iceland, not a mixture from the laboratory, and that salt has a good taste. In our blinded study, the majority of participants liked foodstuffs using this salt and, in fact, there was a preference for the mineral salt cheese that was also confirmed by the manufacturer. So it is a good salt and it was easy to use as a replacement, even over this relatively long period.

Dr. Guesry: Does the Icelandic salt have the same sodium chloride, potassium chloride, and magnesium chloride composition?

Dr. Grobbee: It is slightly different from the Finish salt.

Dr. Scott: Can you comment on a recent paper which I think has been published by Professor Alderman in New York, indicating that a low salt diet may actually have increased the risk of myocardial disease.

Dr. Grobbee: I am rather skeptical about reports that sodium restriction in the usual range might have hazards. It seems unlikely to me and there is not much good evidence. One explanation for the findings could be that those patients that had a myocardial infarct at some stage in the past were advised to change their sodium intake, and that is then reflected in a possible association between low sodium and heart attack risk. My impression from other published reports is that there is little basis for expecting major risks associated with modest restrictions in sodium intake in the way they can be achieved in a population.

Dr. Scott: I have a second question. Given the current scientific evidence and the current debate, do you think it is justifiable to base public health policy on restricting the salt intake of the whole population as opposed to the hypertensive population as recommended in the UK? Do you think the evidence could justify that kind of rather dramatic recommendation?

Dr. Grobbee: I am not too optimistic about this either. I think that the effects of changes in sodium intake in a range of 50 or 60 mmol/day—which would be a major achievement if possible—would not show much in terms of changes in population blood pressure distribution. So it would make more sense to reserve that for the high risk approach and try to find the patients who respond best. On the other hand, as I said, there is nothing wrong with reducing the sodium content of food.

Dr. Ornstein: I want to congratulate you for this study because you obtained a 5 mm Hg decrease in blood pressure on average, and in 40%, you achieved a reduction of 7.5 mm Hg,
which is obviously important. The only drawback I see is that about two thirds of the subjects could detect to which group they belonged. Most of your subjects were elderly and would be expected to have reduced salt sensitivity. I think there is a risk that younger people would be less likely to accept the changes you introduced.

Dr. Grobbee: You are quite right that this was an elderly population and from the trials we knew that elderly people would respond better to changes in sodium intake, which they did. It is difficult to say what would happen with younger subjects. We did a much shorter study some years ago in adolescents where we also changed sodium and potassium intake, and we did see an effect of the combined intervention which was significant but small.

Dr. Ornstein: I am less worried about the blood pressure reducing effect than about the taste effect. Didn’t the young people react more strongly?

Dr. Grobbee: I don’t really have formal research data on this. The group that participated in the trial was very satisfied with the salt and those of us in the laboratory who were younger than the participants and tasted the foodstuffs were enthusiastic too. I think it tastes good and there is not much difference from common table salt, so it should also be well tolerated in younger age groups.

Dr. Guesry: You made the classical statement that, at the population level, a reduction of sodium intake by 1 mmol would lead to a certain reduction in average blood pressure, but I think it is fair to say that not all mmols of sodium are equal—I mean in the sense that if you plot blood pressure and sodium intake, you have a sigmoid curve, and changes in millimolar concentrations at the two ends of the curve do not have the same effect as a change in the linear part of the curve. Do you agree with this?

Dr. Grobbee: Yes, I agree with that, and in a way it was reflected in my estimates of what would be achieved by alterations in sodium intake; they are not estimates of the best possible effect.

Dr. Guesry: But I think this has a bearing on the question from Dr. Scott, because depending on the intake of the population, a reduction of intake of few mmol may or may not have an impact on blood pressure.

Dr. Grobbee: It seems that there is likely to be an effect in everyone, albeit small. There is another problem that could be raised in this respect and that is just by assumption that we predict that the whole distribution will shift to lower levels of blood pressure if we change, for example, sodium intake. What could also happen is that the shape of the distribution changes and that only in one part of the distribution curve do people move to the middle. There are no data to support either of these two views and such data are unlikely to be generated because it is not feasible to do studies to show this. For me, the main argument is that in any event the effect is likely to be very small, at least in a range that we are able to achieve in society.

REFERENCE