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Review Article

Salt Reduction in a Population for the Prevention of Hypertension

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Abstract

Hypertension is one of the major risk factors for cardiovascular disease, the prevention of which is acknowledged to be critically important. Human beings are the only animal species which consume large quantities of salt, and their consumption has increased with the advancement of civilization. Many observational and interventional epidemiologic studies have demonstrated that a high intake of salt results in elevation of blood pressure, and that a salt-reduced diet induces blood pressure reduction in patients with hypertension as well as in individuals with normal blood pressure. Reduced salt intake, blood pressure reduction, and a remarkable decrease in mortality due to stroke in Japan are important examples of this effect. A decrease in the mean blood pressure in an entire population can contribute significantly to decreased incidence of cardiovascular diseases. A population-based strategy for preventing hypertension, including a salt-reduced diet, is therefore desirable. Proposed measures include public health education by the mass media, reduced salt content in processed foods, salt reduction in foods served by schools or organizations and at restaurants, and labeling of salt content. Further studies are needed of population-wide salt reduction methods, and the effectiveness of such methods.

Key words: blood pressure, hypertension, salt, prevention, population strategy

Introduction

Hypertension has been acknowledged as one of the greatest risk factors for cardiovascular diseases. Particularly in Asian countries, where mortality and morbidity due to stroke are higher than those in Western countries, measures against hypertension are considered very important in the prevention of cardiovascular diseases (1–3). Although the prevalence of hypertension has been decreasing in Japan, hypertension still affects a majority of the elderly, and drug therapies for hypertension have greatly added to medical costs. The conquest of hypertension is still a major challenge.

It is now clear that various environmental factors contribute to the etiology of hypertension, and the causal relationship between salt intake and hypertension was recognized quite a long time ago. A salt-reduced diet is now an established method for preventing and treating hypertension, and has been recommended in several guidelines for the treatment and prevention of hypertension (4–9). For example, the WHO/ISH guideline (1999) (4) and the JNC7 guideline (2003) (USA) (5) both recommend that patients with hypertension, as well as all adults, should take less than 6 g of salt per day. The guideline issued by the Japanese Society of Hypertension in 2000 recommends a salt intake of less than 7 g per day (6) (Table 1). In "Kenko Nippon 21 (Healthy Japan 21)", introduced in 2000, the Japanese Ministry of Health, Labor and Welfare set a goal of reducing the mean salt intake in the general Japanese population to less than 10 g per day by 2010.

This review article discusses the discovery of the relationship between salt intake and hypertension, both observational and interventional epidemiologic studies which clarified the relationship between salt and blood pressure (BP) or between salt reduction and BP decrease, and the effects of a population-based strategy of salt reduction for the prevention of hypertension and cardiovascular diseases.

Human history and salt

The diet of terrestrial wild animals includes only small quantities of salt (sodium chloride). The dietary salt intake for carnivorous and herbivorous animals is estimated to be about 2 g and 0.5 g per day per 60 kg body weight respectively. Stone Age humans are considered to have consumed 1–3 g salt per

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Table 1 Recommendations on salt intake in various guidelines related to hypertension

Guidelines	Recommendation for salt intake per day	Target population
World Health Organization—International Society of Hypertension Guidelines for the management of hypertension (1999)	Less than 6 g (or less than 100 mmol of sodium)	BP 140/90 or higher
Japanese Society of Hypertension Guidelines for the management of hypertension (2000)	7 g or less	BP 130/85 or higher
The JNC 7 (2003)	Less than 6 g (or less than 100 mmol of sodium)	All adults aged 18 years or older
National High Blood Pressure Education Program working group report on the primary prevention of hypertension, the U.S. (1993, 2002)	Less than 6 g (or less than 100 mmol of sodium)	General population

day, and similar quantities are still consumed by primitive populations (10). In the INTERSALT study, the Yanomamo tribe, a tribe indigenous to the Amazon, showed almost zero urinary sodium excretion, and their mean systolic BP (SBP) was about 100 mmHg for men and about 90 mmHg for women. No one in the tribe was afflicted with hypertension or showed elevation of BP with age. Primates such as chimpanzees, gorillas and orangutans show similar BP patterns. It has been postulated that human SBP should also range from 70 to 100 mmHg.

The salt intake of humans has increased with the advance of civilization. At the dawn of civilization, salt was precious, and securing salt was a symbol of power. In the 17th century, aristocrats in northern Europe were said to flaunt their affluence by a daily salt consumption of as much as 50 to 60 g. Later, as salt was produced in increasing quantities and more cheaply, it was used for preserving foods, resulting in an increased salt intake in the whole population. It was not until a few hundred years ago, a short period in terms of human history, that people living in civilized countries began to regularly consume salt in large quantities. Over the last few decades, people living in the northern part of Japan consumed as much as 20 to 30 g of salt per day (11). When compared with the BP of wild animals or of primitive man, BP levels considered to be "normal" in civilized countries may actually be hypertensive, with high salt intake making a great contribution (12). The following is a scientific explanation based on epidemiologic studies.

Observational studies of salt and BP

In 1960, Dahl authored a famous study on the relationship between salt intake and BP in populations in various parts of the world, including Japan (13). He reported that people living in northern Japan consumed about 30 g salt per day and had an almost 40% prevalence of hypertension, whereas Alaskan natives consumed less than 5 g of salt per day and had a prevalence of almost zero. However, the design of this study has been criticized. Gleibermann later demonstrated the relationship between SBP and salt intake in a number of populations whose gender and age were matched (14).

These studies were conducted by collecting data from individual investigations of various populations, and were not standardized for BP determinations or dietetic investigations. BP determinations vary with the method of measurement, and dietetic investigators have found it difficult to evaluate salt intake. Therefore, the international INTERSALT study was conducted, using 52 populations in 32 countries (a total of 10,079 participants), with strictly standardized BP measurement and evaluation of salt intake by 24-hour urinary sodium excretion determination (15–17). The INTERSALT study found that urinary sodium excretion was significantly related to individual BP and to age-dependent BP elevation, after adjustment for age, gender, obesity and alcohol consumption (Fig. 1). It was estimated that a decrease in sodium excretion by 100 mmol (equivalent to about 6 g salt) lowered SBP by 2.2 mmHg, and that SBP and diastolic BP (DBP) were reduced by 10–11 mmHg and 6 mmHg, respectively, between 25 and 55 years of age—a period of 30 years. The INTERSALT study became a landmark observational study of salt intake and BP.

The remarkable decrease in the mean BP and mortality due to stroke in the Japanese population represents one of the most significant cases of descriptive epidemiologic observations, compared to analytical studies. During the period of 1950 to 1960, mortality due to stroke in the Japanese population was markedly high by international standards, but has now been drastically reduced to one-fifth of the previous level, presumably largely due to a steady decrease in the mean BP of the population. This decrease in BP was not only found in the elderly, but also in the middle-aged and younger generations. The Japanese National Survey of Cardiovascular Diseases showed that in the 30 years from 1971 to 2000, the mean SBP for Japanese men aged 40 to 49 decreased by 3.6 mmHg, from

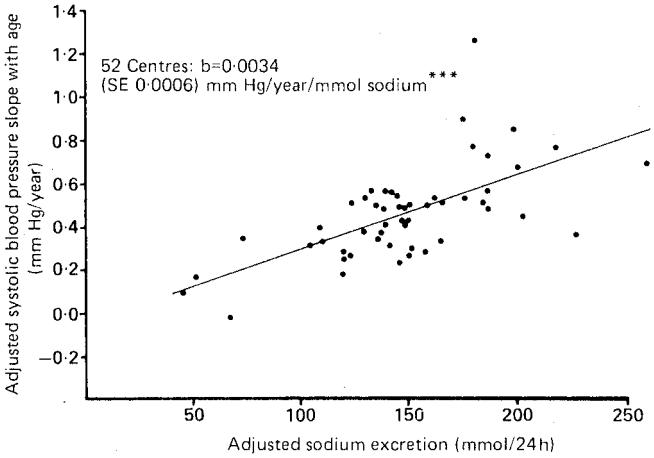

Fig. 1 Cross-center plots of systolic blood pressure slope with age and median sodium excretion and the fitted regression line for 52 centers of the INTERSALT study (adjusted for age, sex, body mass index, and alcohol intake) (15). *** $p<0.001$

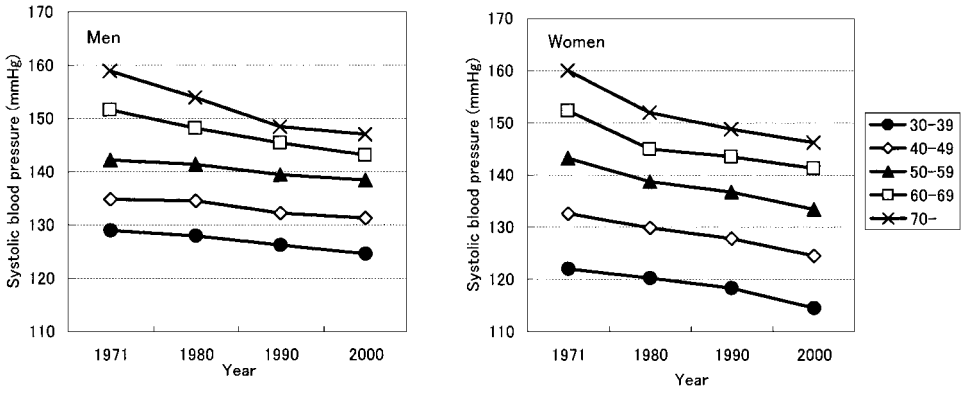

Fig. 2 Trends of mean systolic blood pressure in Japanese men and women by age groups, the National Survey of Cardiovascular Diseases of Japan (1971–2000).

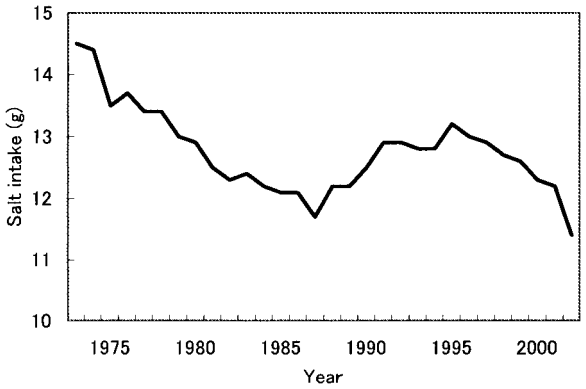

Fig. 3 Trend of mean salt intake in the Japanese, the National Nutrition Survey of Japan (1973–2002).

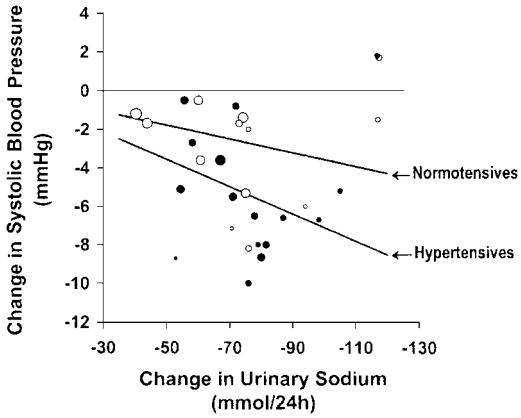

Fig. 4 Relationship between the net change in urinary sodium excretion and systolic blood pressure in 28 randomized trials (25). The open circles represent normotensives and the solid circles represent hypertensives. The slope is weighted by the inverse of the variance of the net change in systolic blood pressure. The size of the circle is in proportion to the weight of the trial.

134.8 mmHg to 131.2 mmHg, and for women aged 40 to 49 it decreased by 7.7 mmHg, from 132.6 mmHg to 124.8 mmHg (Fig. 2) (18–19). As the mean BP decreased in the whole population, including the younger generations, such a phenomenon cannot be explained merely by the widespread use of antihypertensive agents, but may be largely due to a change in the Japanese lifestyle and dietary habits. BP decreased despite other risk factors such as increased obesity (excluding young women), decreased physical activity, and an increase in alcohol consumption. A reduced consumption of salt may have contributed significantly to this decrease (20). The National Nutrition Survey revealed that the daily salt intake of the Japanese decreased by 3.1 g, from 14.5 g in 1973 to 11.4 g in 2002 (Fig. 3)—less than half of the estimated intake in the 1950s (21). Sasaki reported that the salt-reduced diet campaign since the 1950s resulted in a decrease in BP in Japanese school children 20 years later (22). However, one report has also suggested that recent BP decrease in Japan may be due to an increase in potassium intake and a decrease in the sodium-potassium ratio (23).

Interventional studies of salt reduction and BP

Epidemiologic studies based on observation have revealed a relationship between salt intake and BP, but there are various other confounding factors. Many intervention studies have already been conducted which confirmed the effect of salt reduction on BP. Cutler et al. performed a meta-analysis of 32 randomized controlled trials dating from 1973 to 1993, which studied the effect of salt intake reduction on BP (24). A total of 2,635 adult participants were subjected to meta-analysis, which revealed that salt reduction of 4.5 g (77 mmol) typically resulted in a 4.8-mmHg decrease in SBP in subjects with hypertension and a 1.9-mmHg decrease in normotensive subjects. The meta-analysis concluded that salt reduction was effective in decreasing BP. He et al. summarized trials of salt reduction conducted to date, and suggested that a greater salt reduction offered a greater decrease in BP, regardless of whether the subjects were hypertensive or normotensive (Fig. 4) (25). There have been several other meta-analysis studies (26–27).

The TOHP is a well-known multi-center U.S. study in which the effects of nonpharmacologic interventions on BP were evaluated in subjects with a high normal BP (28). A total of 2,182 adult men and women participated in an 18-month randomized controlled trial to evaluate body weight reduction, salt intake reduction, stress management, supplemental calcium and magnesium, and other measures. The risk of developing hypertension was decreased by 51% in the body weight reduction group (mean body weight reduction was 3.9 kg), and by 24% in the salt reduction group (mean salt reduction was 2.6 g), as compared with the control group. The group or individual

instructions were recognized to be helpful in reducing salt intake, and a long-term antihypertensive effect was also confirmed (29). The TONE randomized controlled trial evaluated the effect of body weight reduction and salt reduction in elderly patients who had received medical treatment (30–31). Medication was discontinued after 3 months of education on body weight and salt intake reduction, to evaluate the progression of hypertension and the risk of resumption of medication over the subsequent 29-month follow-up period. The progression and risk were decreased by 31% in the salt reduction group (mean salt reduction was 2.3 g), and by 53% in the group with combined salt reduction and body weight reduction (mean body weight reduction was 4.5 kg), as compared with those in the control group.

The DASH diet, in which vegetables, fruits and low-fat dairy products are increased and total fats and saturated fats are decreased, has been shown to have BP-lowering effects (32–33). This diet has already been included in the JNC 7 guideline for hypertension (5). The DASH Sodium Study evaluated the effects of the DASH diet combined with salt reduction on BP. It reported that a reduction of daily salt intake from 8 g to 4 g, with consumption of the DASH diet for 4 weeks, lowered SBP by 11.5 mmHg in subjects with hypertension, and by 7.1 mmHg in normotensive subjects (34). The combination of the DASH diet with salt reduction is thought to be an ideal dietary pattern for treating and preventing hypertension.

The impact of salt reduction on hypertension and cardiovascular diseases in a population

The intervention studies of the effects of salt reduction on BP in individuals were on a small scale and over a short term. An intervention study of the effects of salt reduction on the development of cardiovascular diseases in a population requires a large-scale study with long-term follow-up, and making an intervention with salt reduction alone in a large population entails technical difficulties and ethical problems. Therefore, no such intervention study has been so far reported nor is likely to be attempted (35). Descriptive or observation-based epidemiologic data are effective in studying the effect of salt reduction on the development of cardiovascular diseases. Some cohort studies of the risks of cardiovascular diseases or death in relation to salt intake have reported negative results, but the methodology of these studies may be suspect (36). By contrast, some recent reports (37–38) have shown positive results. Studies done in Finland demonstrated that when salt intake was increased by about 6 g (100 mmol), the risk of death from coronary heart disease was 1.56 times greater and the risk of death from cardiovascular diseases was 1.36 times greater, after adjustment by multivariate analysis.

One of the most important issues in this summary is the effects of salt reduction on an entire population. The recent guideline on primary prevention of hypertension emphasized that salt reduction is needed, not only for elderly patients with hypertension, but also for the whole population, including individuals with normal BP (7–8). This concept was proposed by Rose (39–40). The effects of salt reduction have been confirmed both in individuals with hypertension and in those with

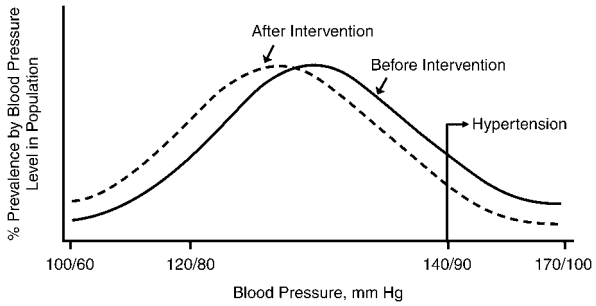

Fig. 5 Effects of a population-based intervention strategy on the distribution of blood pressure. In the population strategy, a blood pressure-lowering intervention is applied to the entire community (modified from a reference (8)).

normal BP. Thus, when salt reduction is attained in a whole population, the distribution of BP in the population is shifted to the right, resulting in a decrease in mean BP levels (Fig. 5). As is apparent in Figure 5, the prevalence of hypertension is also decreased. From the data of the INTERSALT study, Stamler et al. calculated that a mean decrease in salt intake in a population of 5.8 g (100 mmol) would result in a mean decrease of 2.2 mmHg in SBP (41). From the data of the Framingham Heart Study, Cook et al. calculated the effect of a mean decrease of the DBP in the population of as little as 2 mmHg (42). The calculation predicted that the prevalence of hypertension would be decreased by 17%, the risk of stroke decreased by 15%, and the risk of coronary heart disease decreased by 6%. These effects were substantial, and almost equivalent to the results expected if medication had been given to all patients with hypertension.

WHO researchers have recently made a cost-effectiveness analysis of government policies on BP and cholesterol, namely, non-personal health interventions such as a request for salt reduction in processed foods, and personal interventions such as medication for high-risk patients (43). This non-personal health intervention is a population-based strategy which includes the voluntary cooperation of manufacturers in reducing salt content in processed foods, enforcement of related laws and regulations, and public education by mass media. According to this analysis, the non-personal health intervention was cost-effective in reducing cardiovascular diseases and prevented more than 21 million DALYs (disability-adjusted life years) worldwide. Combined therapy for the high-risk group, for which risk had increased by more than 35% in 10 years, was also cost-effective, and was estimated to prevent the occurrence of cardiovascular diseases worldwide by 50%. Thus, every country should introduce cost-effective and population-based policies such as salt reduction.

To accomplish population-wide salt reduction

As proposed by the National High Blood Pressure Education Program in the U.S. (8), the following approaches should be applied as population-based intervention strategies, including salt reduction, for primary prevention of hypertension:

1. An educational program for the general public in which broadcast and print media are used to disseminate clear, simple,

concise, and action-oriented messages about the effect of salt on health. The message must reach the entire population, including children and elderly people.

2. Food manufacturers will be requested to reduce salt content in processed foods. In Japan, where less salt is consumed through processed foods than in the U.S., salt consumption through processed foods is expected to increase in future. It may be necessary to mandate labeling of salt content in processed foods or to legislate the restriction of salt content.

3. Salt reduction is to be further promoted at schools, work sites and hospitals or in catering outlets such as restaurants. Allow informed choice by specifying salt content in the menu or by providing a salt-reduced menu.

4. All medical personnel, including physicians, nurses, public health nurses, school nurses, nutritionists and pharmacists should work together and should be trained to provide guidance on salt intake reduction, as well as body weight management, physical activities and smoking cessation.

Salt intake reduction and BP reduction in the entire Japanese population is an important historical achievement of which we can be proud. However, investigations of the effects of population-based intervention by improving dietary habits, including salt intake reduction, have not been fully successful (44–46) and are still in the early stages of research, and the development of specific methods and the validation of the effect will be a great challenge in the future (47–50). The HIPOP Study appearing in this issue is the first controlled trial conducted in Japan to scientifically validate a population-based intervention by means of lifestyle modification (51–52), in which salt intake reduction was also evaluated (53). We hope that many research results, including ours, will accumulate over time and be used to prevent hypertension and cardiovascular diseases.

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