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BLOOD PRESSURE MECHANISM

Salt Intake and Blood Pressure Levels: Is the Concept Valid?

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ABSTRACT

Globally, sodium intake has increased over the years, and it is seen in all ages, both genders, and in various ethnic groups including Indians. High dietary salt is a major contributor to the increasing incidence of hypertension, with an estimated 30% of hypertension attributed to high salt intake. Salt intake in the developed countries largely comes from prepackaged and processed foods, shelf-stable food, and bakery items. In the Asian communities, the contributing source is in the form of added table salt and in cooking. Sodium balance is maintained by increasing the arterial blood pressure, resulting in a pressure natriuresis and increased urinary sodium excretion in the presence of high sodium chloride intake. Low sodium intake to less than 3 gm/day leads to activation of renin–angiotensin–aldosterone system.

Recently, there have been reports about the deleterious effects of low blood sodium, and there is recognition of the concept of a J-shaped curve. Weak research methodologies with the use of methods like single spot urine samples and single 24-hour urine sodium excretion to estimate usual salt intake have been likely to influence the J curve in the studies so far. In this context, two trials were undertaken in Trials of Hypertension Prevention (TOHP), which implemented sodium reduction. There was no evidence of a J-shaped or nonlinear relationship, and direct relationship with total mortality was demonstrated even at the lowest levels of sodium intake and consistent with a benefit of reduced sodium and sodium/potassium intake on total mortality over a 20-year period.

This review summarizes an overview of current understanding of the concept of salt in hypertension. Dietary sodium is the most accepted and time-tested intervention in prevention and treatment of hypertension, which needs to be implemented but with an unresolved issue of more aggressive salt intake reduction on cardiovascular events.

Keywords: Blood pressure, Hypertension, Salt, Sodium chloride.

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INTRODUCTION

Salt has been of historic value from ancient days when used for preserving food and meat, for trade and taxes, and played a role in rebellions and wars. High dietary salt is a major contributor to the increasing incidence of hypertension, with an estimated 30% of hypertension attributed to high salt intake. Increased blood pressure and reducing dietary salt is estimated to be one of the most effective strategies to improve nation's health.[1] Over the years, the dietary sodium intake has increased from 1 gm/day in the era of hunter gatherers to 9 to 12 gm/day in the population of today's world. The World Health Organization recommends a maximum intake of 2 gm per day and a 30% reduction in population sodium intake by 2025.[2]

An average intake of salt per adult is approximately 10 gm/day (sodium 4,000 mg/day), with reported higher intakes in the Asian continent.[3] Salt intake in the developed countries largely comes from prepackaged and processed foods, shelf-stable food, and bakery items. In the Asian communities, the contributing source is discretionary in the form of added table salt and in cooking. The nutritional transition in the third world countries with globalization of the food industry will increase the salt burden in processed foods.[4,5]

Using a validated food frequency questionnaire, dietary profiles of 6,907 adults aged ≥20 years, from a cluster of 42 villages in Kancheepuram district of Tamil Nadu State in Southern India, were assessed. More than half (57.1%) exceeded the limit of salt intake.[6]

SALT IN HEALTH AND DISEASE

Sodium intake around the world is well in excess of physiological need (i.e., 10–20 mmol/day). Most adult populations have mean sodium intake >100 mmol/day, and for many (particularly the Asian countries) mean intake is >200 mmol/day.[7] Human dietary salt intake has increased tenfold over the last few hundred years.[8,9] In sodium-deficient states, salt consumption is driven by salt appetite – an innate and motivated behavioral response that drives a human or animal to seek and ingest salt-containing foods and fluids.[10-12] Salt appetite is a state where normally aversive concentration of salt is readily consumed. Many animals have evolved specialized mechanisms for detecting and ameliorating deficits in

body sodium. However, under usual circumstances, the ambient salt diet is in excess of physiological need, and in humans, it has been difficult to distinguish innate salt appetite and salt need from salt preference.[13] The hunger for salt is also influenced by taste, culture, social custom, the widespread availability of salt, and habit independent of the need for salt.[14] Heterogeneity exists in the human blood pressure response to alterations in sodium and extracellular fluid balance and the mechanisms that have been invoked for them.[3]

SALT AND BLOOD PRESSURE

Reducing dietary salt has been shown to lower blood pressure and the risk of cardiovascular disease (CVD).[3,4,] Salt has the potential to increase arterial pressure through various neural, endocrine/paracrine, and vascular mechanisms.[4] When there is a high NaCl intake, sodium balance is maintained by increasing the arterial blood pressure, resulting in a pressure natriuresis and urinary sodium excretion increases. The physiological consequence of low sodium intake to less than 3 gm/day is activation of renin–angiotensin–aldosterone system. Interestingly, hyperinsulinemic state also stimulates the resorption of sodium,[8] and glycemia contributes to an sustained antinatriuretic action of insulin. This may have relevance in the developing countries with high prevalence for diabetes.

The role of sodium in CVD and salt restriction in the management of hypertension has become a little controversial in recent times, and it has been pointed in some studies that stringent salt restriction may be detrimental. Data from 23 cohort studies and 2 follow-up studies of randomized controlled trials concluded that both low and high sodium intakes are associated with increased mortality, consistent with a U-shaped association between sodium intake and health outcomes. The hazard ratios (HRs) of total mortality and CVD for low *vs* usual sodium intake were 1.10 [confidence interval (CI), 1.01–1.22] and 1.11 (CI, 1.01–1.22) respectively. The corresponding HRs for high *vs* usual sodium exposure were 1.16 (1.03–1.30) and 1.12 (1.02–1.24).[5] Moreover, 24-hour collection of urine is considered to be the best assessment of salt intake, and a high sodium intake is typically defined by urinary sodium excretion of more than 150 mmol per day.

The study by Graudal et al[5] extends 2013 Institute of Medicine report by identifying a specific range of sodium intake (2645–4945 mg) associated with the most favorable health outcomes, within which variation in sodium intake is not associated with variation in mortality (Table 1).

POPULATION-BASED STUDIES

Large body of observational studies is increasingly complemented by well-designed randomized trials that have shown the benefits of lower salt intake.[18]

Dietary Approaches to Stop Hypertension Sodium Trial[19]

This trial is the most often quoted trial for the effect of reduced sodium intake to very low levels less than 1.5 gm/day over 30 days, adhering to low salt specified meals. Despite being a small study, it effectively showed a blood pressure reduction.

INTERSALT STUDY

This is a multicentric study of electrolyte excretion and blood pressure that reported blood pressure change of 0.94/0.03 mm Hg/1 gm of 24-hour urinary sodium excretion.[20] INTERSALT data also showed a correlation between salt consumption and the rise in blood pressure with age. INTERSALT failed to demonstrate a significant association when the primitive societies of Yanomamo Indians and tribes in Africa with low life expectancy were excluded.

International Study on Micronutrient and Blood Pressure (INTERMAP)

Lower salt intake and smaller sodium/potassium ratio resulted in lowering blood pressure in population.[21]

CURES – 53 STUDY

In the South Asian urban population, the mean dietary salt intake (8.5 gm/day)[22] was positively associated with

Table 1: Guideline recommendations

World health organization	Reduction to <2 gm/day sodium (<5 gm/day salt) in adults[15]
Indian Guidelines on Hypertension 2013	Dietary sodium restriction to <6 gm salt or <2.4 gm sodium (expected systolic blood pressure reduction of 2–8 mm Hg)
	Dietary Approaches to Stop Hypertension eating plan
AHA/ACC Lifestyle Management Guideline 2013	Consume no more than 2,400 mg of sodium/day
	Reduction of sodium intake to 1,500 mg/day can result in even greater reduction in blood pressure[16]
JNC VIII 2014 Guideline for management of high blood pressure in adults	Endorsed the lifestyle modifications recommended by the evidence-based recommendations of the Lifestyle Work Group[17]

AHA: American Heart Association; ACC: American College of Cardiology; JNC: Joint National Committee

hypertension on multiregression analysis. Reduction of 3 gm/day predicted a fall in blood pressure of 3.6 to 5.6/1.9 to 3.2 mm Hg (systolic/diastolic) in hypertensives and 1.8 to 3.5/0.8 to 1.8 mm Hg in normotensives.

PROSPECTIVE URBAN–RURAL EPIDEMIOLOGICAL (PURE) STUDY

For each 1 gm increase in mean sodium intake, systolic blood pressure increased by 2.63, 1.72, and 0.71 mm Hg for sodium intakes of >5, 3 to 5, and <3 gm/day respectively.[23] The PURE study demonstrated a U-shaped curve for salt intake and events.

In a prospective population study, involving 3,681 participants without CVD, systolic blood pressure, but not diastolic pressure, changes over time aligned with change in sodium excretion, but this association did not translate into a higher risk of hypertension or CVD complications. Lower sodium excretion was associated with higher CVD mortality.[24]

Coronary heart disease (CHD) policy model has been used to quantify the benefits of potentially achievable, population-wide reductions in dietary salt of up to 3 gm (1200 mg of sodium) per day. Reducing dietary salt by 3 gm per day is projected to reduce the annual number of new cases of CHD by 60,000 to 120,000, stroke by 32,000 to 66,000, and myocardial infarction by 54,000 to 99,000 and to reduce the annual number of deaths from any cause by 44,000 to 92,000. All segments of the population would benefit, with blacks benefiting proportionately more, women benefiting particularly from stroke reduction, older adults from reductions in CHD events, and younger adults from lower mortality rates.[25]

SALT AND BLOOD PRESSURE LIMITATIONS OF THE AVAILABLE EVIDENCE

- Food and Salt Industry competing commercial financial interests
- Likelihood of study bias due to both random and systematic errors of hidden sodium in processed foods
- Day-to-day variation in diet may negatively impact a 24-hour diet question chart
- Reverse causation theory. Inclusion criteria in studies involve subjects with existent diseases like diabetes mellitus and hypertension, who may consume low salt, which may influence morbidity and mortality
- Weak research methodology with the use of methods like single spot urine samples to estimate usual salt intake

NEW EVIDENCE ON SALT AND MORTALITY

In context with the above evidence limitations, two trials, phase I (1987–1990), with 741 participants over 18 months, and phase II (1990–1995), with 2,382 participants over 36 months, were undertaken in TOHP, which implemented sodium reduction but without control intervention.[26,27]

Researchers estimated that three 24-hour collections would improve accuracy to 75% compared with sodium ingestion and that seven would be needed to improve accuracy to 92%.

The Trials of Hypertension Prevention (TOHP) study used up to seven excretion measurements from prehypertensive adults 30 to 54 years of age. A total of 251 deaths occurred, representing a nonsignificant 15% lower risk in the active intervention (possibly due to insufficient power) as compared with 272 deaths in those not assigned to an active sodium intervention. There was a linear association between average sodium intake and mortality, with an HR of 0.75, 0.95, 1.00, and 1.07 (p trend ¼ 0.30) for <2,300, 2,300 to <3,600, 3,600 to <4,800, and >4,800 mg/24 hour respectively; and with an HR of 1.12 per 1,000 mg/24 hours. There was no evidence of a J-shaped or nonlinear relationship.

The study concluded a direct relationship with total mortality, even at the lowest levels of sodium intake and consistent with a benefit of reduced sodium and sodium/potassium intake on total mortality over a 20-year period. The TOHP trial participants did not previously have comorbid conditions like hypertension, diabetes, or CVD, and these reduced the problem of reverse causation. Evidence of the safety or efficacy of low sodium intake (<2.3 gm/day) was not commented upon, as low sodium intake was not achieved in the intervention group.

Recent studies have invited substantive controversy and have drawn significant criticism from the scientific community for many limitations in research design and methods, misinterpretation of study results, and potential conflicts of interest of the authors.[28] Uncertainties exists on whether reducing sodium intake below 2300 mg/day either decreases or increases CVD risk in the general population.[28] For these reasons, the World Hypertension League and supporting organizations have made an urgent call for quality research on salt intake and health and listed important issues that could be addressed in setting standards for research on sodium (salt) intake and health.[29]

CONCLUSION

Excess salt consumption leads to increase in blood pressure, which in turn increases the CVD and translates to mortality. The lowering of salt intake from high to moderate level is definitely beneficial in people with hypertension. The current available evidence does not support aggressive population-based strategies for low-salt diet. In this context, two trials were undertaken in TOHP, which implemented sodium reduction. There was no evidence of a J-shaped or nonlinear relationship

Table 2: What is the existent knowledge?

Adult populations have mean sodium intake >100 mmol/day, and for many (particularly the Asian countries), mean intake is >200 mmol/day
Sodium balance is maintained by increasing the arterial blood pressure resulting in a pressure natriuresis and increased urinary sodium excretion in the presence of high sodium chloride intake
U-shaped curve for salt intake and events in population-based studies, but with the limitation of using urine spot sodium as a marker for salt intake
Available evidence does not support aggressive population-based strategies for low-salt diet

Table 3: What is new?

24-hour collection of multiple urine sodium sample is considered to be the best assessment of salt intake
Direct relationship with total mortality, even at the lowest levels of sodium intake and consistent with a benefit of reduced sodium and sodium/potassium intake on long-term total mortality
No evidence of a J-shaped or nonlinear relationship between sodium intake and mortality
Prospective data required on safety or efficacy of low sodium intake less than 2.3 gm/day and the more aggressive target of 1.5 gm/day

and direct relationship with total mortality was demonstrated, even at the lowest levels of sodium intake and consistent with a benefit of reduced sodium and sodium/potassium intake on total mortality over a 20-year period.

Larger studies comparing varying levels of salt intake to blood pressure and CV outcome are needed to clarify and understand the optimal sodium intake to prevent CV events (Tables 2 and 3).

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