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Is Salt a Culprit or an Innocent Bystander in Hypertension? A Hypothesis Challenging the Ancient Paradigm

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ABSTRACT

For decades the notion that an excessive consumption of salt (NaCl) leads to hypertension has persisted. However, this idea is based on opinion, not scientific proof. Despite this, every health organization, agency, and clinicians around the world have been advising salt restriction, especially to hypertensive patients. The present review article suggests that the consumption of a high-salt diet is not the cause of hypertension and that there are other factors, such as added sugars, which are causative for inducing hypertension and cardiovascular disease.

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Hypertension is defined by a systolic blood pressure that is ≥140 mm Hg and a diastolic blood pressure that is ≥90 mm Hg.[1] The etiology of hypertension is multifactorial in nature, resulting from the combination of both genetic and environmental factors.[2]

In recent decades hypertension has been ranked as one of the leading causes of worldwide disability-adjusted life years.[3] According to a study conducted by Kearney et al,[4] more than 1 billion adults worldwide (approximately 25%) have hypertension. Other estimates suggest this number will climb to 29% by 2025.

A linear relationship between blood pressure levels and cardiovascular and cerebrovascular mortality was observed by the Prospective Studies Collaboration.[5] The association between blood pressure and cardiovascular morbidity and mortality is present even below the present cut-off for hypertension, which was confirmed in the Framingham study.[6]

In the literature it is often said that an excessive intake of salt (NaCl) can lead to hypertension.[7-11] In general, the average daily salt intake is more than 6 g (2400 mg of sodium), with approximately 95% of the global population consuming somewhere between 7.5 and 12.5 g of salt.[12]

Some European and Asian countries consume slightly more than 12 g of salt (4800 mg of sodium) per day.[13] In India most people consume at least 11 g of salt per day,[14,15] but this may have to do with the hot climate of India, which can induce salt loss of up to 6 g per day (mostly from sweat).[16] Despite these important nuances, various government institutions and bodies recommend population-wide sodium restriction.[17-20]

The World Health Organization (WHO) recommends an intake of <2000 mg sodium per day.[19] Canada's 2010 Sodium Working Group suggest sodium intake of <2300 mg/d,[17] whereas the American Heart Association suggests an even stricter sodium intake (<1500 mg/d).[21] The recently published 2015 Dietary Guidelines for Americans recommend a sodium restriction of <2300 mg/d.[22] The Food and Agricultural Organisation of the United Nations has published food-dietary guidelines for Indians, which suggested that the salt intake should be <2400 mg/d.[23]

India, along with other member states of the WHO, has adopted a target of reducing the mean population salt consumption up to 30% by 2025.[15] This reduction in salt

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intake is targeted with a belief that this will lead to a decrease in blood pressure levels, with the assumption that this will translate into a reduction in cardiovascular events.[24]

Previously, on the basis of a meta-analysis, it was suggested that a reduction in dietary salt intake of up to 6 g per day could help reduce the systolic/diastolic blood pressure by 7/4 mm Hg in hypertensives and 4/2 mm Hg in normotensives.[24] However, recently, DiNicolantonio et al[12] have proposed the idea that added sugars, not salt, is the real culprit for causing hypertension.

If this hypothesis is proved to be correct, then it would be a great relief for the entire population, especially cultures that rely on saltier dishes (such as the Indian population), probably helping them to prevent dehydration in the heat.[14,16] The present article reviews the literature and hypothesizes that 1) salt intake not may not be an important etiologic factor for hypertension; 2) salt restriction paradoxically may cause hypertension and cardiovascular events; and 3) dietary sugar is the more problematic white crystal inducing hypertension.

CLINICAL SIGNIFICANCE

- There is no definitive proof that a normal salt intake causes hypertension.
- The evidence in the literature suggests that sugar, not salt, is the principal driver of hypertension and cardiovascular disease.

HYPERTENSION IN THE INDIAN POPULATION

Hypertension is a serious public health threat on healthcare systems and cardiovascular health status in India.[25,26] Twenty-four percent of all coronary heart disease and 57% of all stroke deaths in India are attributed to hypertension.[27]

According to the 2008 WHO estimates, the prevalence rate of hypertension in the Indian population was 32.5% (33.2% in men and 31.7% in women).[28] The studies, including the 2005 Global Burden of Hypertension,[4] the 2010 Global Burden of Disease,[29] and the 2011 WHO Noncommunicable Diseases India-specific data,[28] showed an alarming rise in hypertension in the Indian population.

The prevalence rate of hypertension in India has been approximately 25% in urban areas and 10% in rural areas, according to recent studies.[27,30-32] Hence, to curb this deadly disease, the Indian Government has started the National Program for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke for prevention and control of disease at the root cause.[33]

WHY HAS HYPERTENSION BEEN ON THE RISE IN INDIA?

The consumption of added sugars may be a culprit driving the increased prevalence of hypertension in India.[34] Other risk factors include age, race, family history, tobacco, alcohol, a low potassium intake, vitamin D deficiency, stress, and high salt diet.[35] However, salt may simply come along with more added sugars; in other words, salt may be an "innocent bystander" rather than a causative agent in hypertension.

CAN LOW-SALT DIETS CAUSE HYPERTENSION, CARDIOVASCULAR EVENTS, AND OTHER UNINTENDED CONSEQUENCES?

In the last 4 to 5 decades, patients with hypertension were given advice to cut down their intake of salt and increase exercise. Yet these recommendations are contradictory, because exercise or physical work (particularly when done in a warm or hot environment) on a low-salt diet causes a 10-fold increased risk of heat exhaustion and prostration (characterized by nausea, vomiting, tachycardia, hypotension, vertigo, dehydration, and collapse).[36] Moreover, following the advice to consume <2300 mg of sodium per day can lead to negative sodium balance, as well as negative calcium and magnesium balance.[37] Thus, low-salt diets may predispose to calcium and magnesium deficiency and all the negative consequences that come with it (including osteoporosis, hypertension, cardiovascular events, arrhythmias, coronary vasospasm, sudden death, and more). Furthermore, recent studies suggest that sugar, not salt, is the likely dietary culprit causing hypertension.[12]

ASSUMED PATHOPHYSIOLOGY BEHIND SALT-INDUCED HYPERTENSION

One of the first and most comprehensive explanations around the association between salt intake and hypertension was given by Guyton et al.[38] They suggested that sodium balance is regulated by the pressure-natriuresis mechanism. Sodium loading was found to be associated with an increase in blood pressure levels, which returned to previous values after regulation of extracellular volume and pressure-natriuresis. However, some individuals have difficulties in eliminating excess sodium, and for the same pressure-natriuresis effect they need to have higher blood pressure, potentially leading to more chronic expansions of extracellular volume, followed by higher cardiac output with tissue perfusion that exceeds metabolic needs. Peripheral tissue vasculature counteracts by activating auto-regulatory vasoconstriction, leading to an increase in peripheral resistance.[38,39] However, the fact that some people tolerate dietary sodium whereas others do not suggests that an underlying factor that is independent of dietary sodium causes "salt-sensitive" hypertension. Interestingly, the renin–angiotensin–aldosterone system (RAAS) plays a major role in regulating sodium–blood pressure response, and dietary sugar (fructose in particular) seems to affect the kidneys in a way that creates salt-sensitive hypertension.[40,41]

CAN SALT CAUSE HYPERTENSION?

The human brain (hypothalamus) is wired to maintain salt (sodium) balance and hence controls our salt intake.[12,42,43]

The biological reason behind this tight homeostatic regulation is that the maintenance of normal sodium levels in the extracellular fluid is required for life and for cellular processes to function properly. The transition process from marine milieu to land-based existence required the evolution of cells that were able to simulate the salty environment of their progenitor cells that existed in sea water. Our remote prehuman hominin ancestors were probably mostly vegetarian (with a diet consisting of, eg, plants, herbs, fruits, and nuts) that were low in sodium.[44,45] However, these early hominins were likely consuming insects, organs, blood, and other animal-based foods when available, which will dramatically increase the overall salt intake. Additionally, salt was considered the essence of life, and if anything was eaten without salt, it was considered to lack an essential element.[44,46,47]

Hence, sodium was an important factor that was conserved in our body with the help of our brain and kidneys. Extracellular fluids had to be kept sodium-rich, whereas intracellular fluids had to be kept relatively free of sodium, allowing cellular and vascular volumes to be maintained. Hence, when sodium levels are low, blood volume is low, which signals the body to ingest more salt and water.[42] Interestingly, in hot tropical countries adequate salt intake was necessary to acclimate to the salt loss through sweat, leading to a higher salt intake.[44]

In other words, bodily need drives salt intake. In fact, the low-salt advice may lead to salt cravings and an overconsumption of more processed foods to obtain the salt our physiology desires.[12] However, nowadays, to get the salt our body needs we end up consuming salty processed foods (instead of naturally salty foods) and thus consume a greater amount of harmful dietary substances (eg, excess calories, added sugars, harmful fats, and artificial flavorings).[12] Indeed, low-salt diets may inadvertently cause us to eat more added sugars. When we are deficient in salt there is an enhanced craving for it, but this does not mean we are addicted to salt.[42,43,48,49]

SALT: THE ANCIENT CRYSTAL THAT ALLOWS INCREASED CONSUMPTION OF VEGETABLES

According to the Salted Food Addition Hypothesis, if salted foods are consumed daily this can lead to salted food addiction. However, if this were true the intake of salt would be increasing rather than remaining in a biologically determined narrow range, which has occurred throughout numerous countries over the last 50 or more years.[12] Despite this overlooked issue with the hypothesis, many still believe that salting foods can lead to overeating and its related complications.[50] What is overlooked is that adding salt to bitter or bland foods, like vegetables or nuts, will probably increase their consumption because salt enhances flavor. Moreover, a higher intake of vegetables and nuts for example, is associated with a reduction in the risk for hypertension and cardiovascular events.[51-58]

Salt (sodium) "appetite" is an evolutionary conserved mechanism that is approximately 100 million years old.[59] It drives us to seek out and obtain salt when we need it.[42] An intake of sodium between 3000 and 5000 mg/d also helps to keep the RAAS and sympathetic nervous system (ie, noradrenaline and adrenaline) suppressed, which places the least amount of stress on bodily organs.[60,61] In short, a person's salt intake is controlled by need but also to ensure homeostasis.

SALT RESTRICTION CAN LEAD TO INSULIN RESISTANCE

Physicians around the world generally ask hypertension patients to restrict salt intake, without being aware of the unintended consequences. Salt restriction has been observed to cause an increase in insulin (hyperinsulinemia) and C-peptide levels,[62-64] which can worsen insulin resistance.[65]

However, the increase in insulin levels on low-salt diets could be due to a reduced insulin-independent clearance of glucose or due to the higher angiotensin-II levels that can lead to a decrease in blood flow to the liver, which is responsible in clearing insulin from the blood stream.[63,66,67] Regardless, the increase in insulin levels caused by insulin resistance can lead to increased fat mass accumulation and obesity, causing hypertension.

It was also observed that a high-salt diet stimulates insulin-independent glucose uptake without interfering with insulin sensitivity,[68] which can be due to an increase in number of glucose transporters (GLUT-1, GLUT-4, or both) in adipocytes because of a high-salt diet.[63] Hence, a high-salt diet can induce protection from the harmful effects of a diet high in sugar, which is the likely primary dietary culprit behind obesity, atherosclerosis, and subsequently hypertension.

DOES A HIGH-SALT DIET CAUSE FLUID OVERLOAD?

DiNicolantonio et al[69] have revealed how an overconsumption of added sugars can lead to fluid and salt overload, whereas dietary salt is more of an innocent bystander in this phenomenon.[69] It is observed that most patients with essential hypertension have normal blood volume and body sodium but an increase in peripheral vascular resistance.[70,71] However, salt restriction may worsen peripheral vascular resistance, and consuming normal salt intakes, as compared with low-salt intakes, may actually improve peripheral vascular resistance,[72] suggesting that salt may not be an etiologic factor for hypertension.

Moreover, diets high in salt do not seem to lead to an overall rise in total body water content.[73] Additionally, serum sodium levels are infrequently found to be high, whereas a low-sodium level is a very common electrolyte abnormality in both the inpatient and outpatient setting, which suggests that some patients may indeed benefit from

consuming more salt rather than less. Perhaps more importantly, 80 million Americans are now prediabetic, and another 20 million have type 2 diabetes. In fact, abnormal glucose homeostasis and elevated serum glucose levels (generally from decades of consuming diets high in added sugars and other refined carbohydrates) are one of the most pressing public health concerns worldwide. Chronically elevated glucose levels can lead to an increase in inflow of water from tissue cells to the intravascular space, leading to an increase in intravascular volume, which if not compensated for, may lead to hypertension.[74] In addition, an overconsumption of added sugars/refined carbohydrates has been shown to reduce nitric oxide (possibly leading to increased peripheral vascular resistance), increased oxidative stress, activation of the RAAS, and increased insulin levels—all of which sets the stage for chronic elevations in blood pressure.[12]

ADDED SUGARS AND HYPERTENSION

Certain evidence suggests that added sugars, not salt, may be a dietary culprit for causing hypertension.[69] Antar et al[75] concluded that 56% of nondiabetic patients with arteriosclerosis have abnormal glucose tolerance, linking elevated glucose levels with atherosclerosis. They found that a diet high in sugar leads to an increase in the level of all major fractions of serum lipids.[75] One study concluded that "…modest intake of dietary sucrose is associated with cardiovascular adaptations that may further burden a heart already compromised by the presence of systemic hypertension."[76] In other words, overconsuming added sugars may not only lead to hypertension but also to cardiovascular disease.

Daily consumption of fruit juice (composed mainly of free sugars) is also associated with a higher central blood pressure.[77] Animal and human studies show that a diet high in sucrose or fructose can increase blood pressure.[12,78-80]

Perhaps the best evidence comes from a meta-analysis of randomized, controlled trials that showed that a diet high in sugar, as compared with a low-sugar diet, for just a few weeks causes an increase in blood pressure of approximately 7.6/6.1 mm Hg.[81] Hence, a diet high in added sugars leads to numerous metabolic disturbances, reflected by hyperlipidemia, fluid overload, insulin resistance, and hypertension.

HIGH-SALT DIETS ALONE ARE UNLIKELY TO CAUSE HYPERTENSION

Dietary salt has been considered as one of the most important etiologic causes of hypertension. However, according to a study conducted by Hall,[82] increasing salt intake in individuals with normal kidney function "usually does not increase arterial pressure much because the kidneys rapidly eliminate the excess salt and blood volume is hardly altered." Other studies also mention the same principal, saying that individuals with normal kidney functions eliminate excess dietary salt with ease.[83-86]

In the 20th century, Allen and Sherrill conducted a study and observed that prolonged blood pressure reduction was seen in only 60% of 180 patients with hypertension when salt intake was restricted to less than 2 g per day. However, they did not find any significant increase in blood pressure when the individuals were administered 10-20 g of salt for 2 weeks in 3 patients with normal blood pressure.[71] Other studies were conducted that showed similar results.[87,88] Kawasaki et al[89] further stated that "Salt loading alone or with injection of desoxycorticosterone acetate (DOCA) virtually never increases blood pressure significantly in normal subjects."

In contrast, studies even suggest that higher salt loads can decrease blood pressure.[90] Luft et al[91] suggested that "sympathetic nervous system activity appears to decrease with sodium loading in normal subjects. These responses may have facilitated the excretion of massive salt loads in normal subjects and may have modulated the increases in blood pressure." Low-salt diets can also lead to vasoconstriction,[92] and consuming more salt in normotensives can lead to vasodilatation.[93]

High-salt diets have also been blamed for increasing serum sodium levels, causing chronic volume retention and hypertension.[94] However, studies fail to show that patients with hypertension have an increase in extracellular volume. Surprisingly, elevations in extracellular concentrations of sodium, even for 6 days, are unable to increase blood pressure in animals.[95,96] Moreover, a higher-salt diet does not seem to lead to over-retention of water.[73,97]

Most importantly, a meta-analysis of almost 170 studies noted that sodium restriction only lowers blood pressure by approximately 1%-3% in normotensives and 3.5%-7% in hypertensives[98]; however, restricting sodium increases aldosterone, renin, noradrenaline, and blood lipids. It is hard

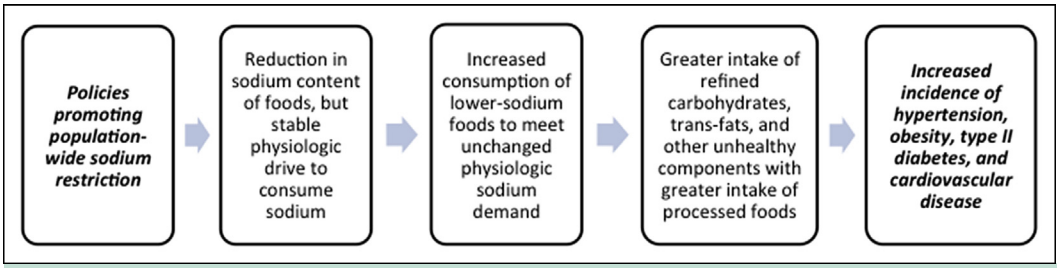

Figure How sodium restriction may lead to hypertension, obesity, type 2 diabetes, and cardiovascular disease.[12]

to justify dietary sodium restriction when the overall cardiovascular risk seems to worsen rather than improve when all risk factors are taken into account.

Hence, the overall evidence in the literature suggests that salt is not the primary culprit but an innocent bystander in hypertension. There is no proof that the potential benefits of dietary salt restriction outweigh the risks. The hypothesis that sodium restriction may lead to hypertension, obesity, type 2 diabetes, and cardiovascular disease is depicted in **Figure**.[12]

CONCLUSION

The cumulative body of evidence suggests that the overconsumption of salt is not the primary cause of hypertension, whereas added sugars are more likely the true culprit. Salt restriction may actually worsen overall cardiovascular health through numerous counter-regulatory mechanisms, and may lead to other unintended consequences (insulin resistance, type 2 diabetes, and obesity). Clinicians should advise their hypertensive patients to cut down on the intake of added sugars (sucrose and high fructose corn syrup) and refined carbohydrates such as white flour, and make dietary salt less of an issue.

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