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# Review Article

## Revisiting Salt Sensitivity and the Therapeutic Benefits of Salt Restriction in Hypertension

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### Abstract

The effects of excessive dietary salt on blood pressure (BP) vary in certain individuals, with some developing a hypertensive response to salt loading (salt-sensitive individuals), while some do not experience any increase in BP (salt-resistant individuals). There are mechanisms that enable an individual to adapt to a high-salt load, and hypertension develops only when the kidney's ability to excrete excess salt is impaired. At present, there are no clinically practical tests available to determine salt sensitivity, and more research is needed so that in the future, a drug specifically working on salt sensitivity will be developed. The effects of high salt diet on gut bacteria and its relationship with diet and disease is an exciting new area of research. Nonpharmacologic and lifestyle modifications, delving on weight loss, exercise (that promotes physical fitness), diet (especially Dietary Approaches to Stop Hypertension diet), and other nutrients (such as potassium and flavonoids) should be emphasized to both hypertensive as well as non-hypertensive patients. The next generation should be taught to not only limit their salt intake but also they should learn to eat healthy to prevent chronic diseases later in life. Clinicians should, therefore, play a more active role in promoting lifestyle changes, most especially dietary salt restriction, and empower patients to take charge of their health, keeping in mind that the strongest benefit can be attained by doing lifestyle interventions in its totality.

**Key words:** Gut microbiome in salt-sensitive hypertension, non-pharmacologic and lifestyle interventions, salt in hypertension, salt sensitivity, therapeutic lifestyle changes

### Introduction

Hypertension is a major health problem with a high prevalence, putting the patient at risk for cardiovascular disease. Many factors contribute to the high prevalence rate of hypertension, namely poor diet, excess body weight (overweight and obese), alcohol abuse, physical inactivity, aging, stress, plus socioeconomic determinants, and inadequate access to health. Among these, dietary salt intake remains to be one of the most important contributing factors to the development of hypertension.<sup>[1]</sup>

### Salt and Sodium

Salt plays a major role in the civilized world. It is mainly used as food flavoring, in addition to spices, and also as food preservative. It is also used as antiseptic. There was a time when it was even used as a form of currency for trading.<sup>[2]</sup>

In the United States, it is usually referred to as sodium, while in most scientific literature, it is commonly referred to as salt (sodium chloride). Salt contains 40% sodium and 60% chloride. Sodium is an important mineral because it is involved in many

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essential processes in the body. It is needed for nerve impulse conduction, muscle contraction, and relaxation, as well as water and electrolyte balance.<sup>[3]</sup>

Sodium is found naturally in certain foods such as eggs and vegetables. Among the sources of salt in the diet, the highest contribution is from packaged and processed foods, comprising about 75–80%, including restaurant foods. Only 10–12% is naturally-occurring, 5% comes from added salt during cooking, and another 5% added as condiment at the table.<sup>[4]</sup>

Despite efforts to educate patients on the ill effects of excessive salt in the diet, especially in hypertensive individuals, clinicians still face a very challenging task due to the ubiquitous nature of salt. It is essential that patients get a clear understanding of what salt/sodium is and what is the salt content of various food sources.

### Salt and Hypertension

The human body only needs an estimated 500 mg of sodium to perform its vital functions. Yet, most people consume a lot more than what is needed.<sup>[3]</sup> With a high-salt diet, there will be consequent water retention, and this will entail an increase in the blood pressure (BP) to excrete the excess salt.

In the normal individual, a sequence of events leads to the return of arterial pressure to near normal levels as follows: An increase in salt intake will produce an increase in extracellular fluid volume, which, in turn, will increase arterial pressure. This increase in BP will increase blood supply to the kidneys, thereby reducing renin and angiotensin, leading to a decrease in renal retention of water and salt, and a return of extracellular volume to near normal levels. This eventually leads to a decrease of BP to almost normal levels.<sup>[5]</sup>

With any increase in arterial pressure, there is a consequent pressure natriuresis which aims to increase excretion of sodium and water through the kidneys. Hypertension develops only when the kidney's ability to excrete sodium becomes impaired.<sup>[6]</sup>

### Salt-sensitive and Salt-resistant BP

As stated previously, sodium is important because it is involved in certain processes in the human body, performing essential cellular functions, regulation of fluids and electrolytes, with consequent maintenance of an optimal BP. However, the question remains, why do some individuals develop a hypertensive response to a high-salt diet, while some do not. The body's natural response is to excrete dietary salt through an increase in BP, or what is called pressure natriuresis, but some individuals are able to do so without needing an increase in arterial BP. Individuals who develop an increase in BP with a high-salt load are said to be "salt sensitive," while those who do not are "salt resistant." The underlying mechanism is complex, involving both genetic and environmental influences.<sup>[6]</sup>

It has been estimated that in hypertensive individuals, 50% are salt sensitive. On the other hand, 25% of normotensives are

also noted to be salt sensitive. If no intervention is done, such as lifestyle and dietary changes, there is a chance that these normotensive individuals who are salt sensitive will become hypertensive in the future. Other ill effects of a high-salt diet include stomach cancer, kidney disease, and an adverse effect on metabolism causing obesity.<sup>[7]</sup>

The clinical significance of the salt-sensitive phenotype is that it serves as a strong cardiovascular risk factor for cardiovascular morbidity and mortality, independent of chronic hypertension. Prognostic implications are said to be as strong as other traditional risk factors. In this regard, more research should be done, especially on drugs that act directly on the causes of salt sensitivity itself and not on hypertension only. As of now, there are no practical tests that can be used clinically. The present laboratory techniques are too costly and hard to do, making it impractical for clinical use.<sup>[8]</sup>

### The Gut Microbiome and Probiotics

An intriguing concept that is still in the experimental stage is the role of the gut microbiome in patients who develop hypertension in relation to a high-salt diet. If validated, it could probably lead to newer treatments directed at salt sensitivity itself.

In animal studies, foods with high-salt content have been shown to have an adverse effect on gut health, causing tissue inflammation and autoimmune disease.<sup>[9]</sup> One study has shown that a high-salt diet causes depletion of *Lactobacillus murinus*, such that subsequent treatment with the same prevented aggravation of salt-induced hypertension.<sup>[10]</sup>

Aside from depletion of *L. murinus*, too much salt can also stimulate inflammation, leading to hypertension in the long run. The researchers from the Massachusetts Institute of Technology showed that probiotics can potentially reverse the effects of too much salt in the diet. The exact mechanisms are still unclear, and more research should be done in the future to learn about the relationship between gut bacteria, diet, and disease.<sup>[11]</sup>

### Dietary Salt Restriction and its Effects on Hypertension

Dietary sodium has been associated with an elevation in BP in various clinical, epidemiological, and experimental studies. Hence, it was considered good advice to reduce salt intake in the diet through various means, and in this regard, patient education plays a major role. A reduction in salt intake has been shown to lower BP, more so in the elderly, in obese individuals, and in African Americans.<sup>[12]</sup>

Since our dietary/eating patterns are considered as learned behavior, there is a possibility that the taste for salty diets can revert back to a lower salt diet. It has been shown that as people are slowly given a lower salt diet, the preference for salty foods also changes. However, consumers find it hard to avoid dietary salt mainly due to the preponderance of salt in packaged and processed foods. Restaurant food is also known to contain high

levels of salt to make the food more palatable to majority of consumers.<sup>[13]</sup>

In addition to sodium's direct BP effects, the benefits of dietary salt restriction extend to improvement in response to certain antihypertensive medications. A low sodium diet will improve BP-lowering effects of most hypertension medications with the exception of calcium channel blockers. It can also decrease potassium loss associated with the use of diuretics. More importantly, it has been shown that there is a better response to angiotensin-converting enzyme inhibitors or angiotensin receptor blockers if patients stick to a low-salt diet.<sup>[14,15]</sup>

### Non-pharmacologic Therapy of Hypertension with Focus on Salt Restriction

Almost all hypertension guidelines recommend dietary salt restriction, but the levels may vary: the World Health Organization (2013) recommends <2000 mg/day of sodium, while the United States Department of Agriculture (2015) recommends ≤2300 mg/day of sodium, and the American Heart Association set their recommendation at an upper limit of 1500 mg/day of sodium.

Salt reduction in the diet entails a change in behavioral pattern as well. In certain cases, it might be helpful to employ the services of a dietitian for reinforcement. The internet is replete with good and bad advice, and it would be better if they are counseled on how to seek accurate and reliable information.

Most guidelines emphasize the need for non-pharmacologic therapy and lifestyle modifications in addition to pharmacologic therapy for hypertension. Therefore, clinicians should play an active role in promoting lifestyle changes, most especially dietary salt restriction. Patients should be made aware that significant BP reductions can be realized with more stringent lifestyle modifications, empowering them to take charge of their health.

There is a linear relationship between weight loss and BP; hence, it should be maintained through proper diet and exercise. If weight is regained, the BP benefit will be lost. Exercise, or any physical activity, should promote physical fitness, which is the physiological benefit that patients get from exercise. However, it should be stressed that only modest exercise is needed to realize benefit for BP reduction since physical activity reaches a plateau beyond which there is no more benefit for the BP. Hence, heavy and strenuous exercise is not actually recommended for BP control. On a positive note, a desirable side effect of exercise is weight loss.<sup>[12]</sup>

With regard to diet, majority still recommend the Dietary Approaches to Stop Hypertension (DASH) diet. The DASH diet (rich in fruits and vegetables, with the use of low-fat dairy products, and low in saturated fats) is independently effective in reducing BP. Likewise, the addition of mineral nutrients, especially an increase in potassium intake, has been shown to help in reducing cardiovascular risk. Flavonoids from cocoa and berries have been shown to have a modest effect on BP.<sup>[12]</sup>

### Summary

Excessive salt intake has been shown to increase BP eventually leading to sustained hypertension. There are mechanisms that enable an individual to adapt and respond to a high-salt diet, but those who are salt sensitive will eventually develop hypertension if left untreated. Even in persons who are not hypertensive, the recommendations to lower salt intake still apply. In theory, sodium reduction by producing lowering of BP can reduce cardiovascular disease. The new concept exploring the relationship between gut bacteria, diet, and disease is promising.

It is imperative that the future generations should be taught not only to limit their salt intake but also, more so, they should learn to eat healthy to avoid developing chronic conditions such as hypertension, diabetes, and obesity. Most guidelines emphasize the need for more stringent lifestyle modifications in all stages of hypertension. Clinicians should, therefore, play a more active role in promoting lifestyle changes, most especially dietary salt restriction, and empower patients to take charge of their health, keeping in mind that the strongest benefit can be attained by doing lifestyle interventions in its totality.

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