Dietary sodium and blood pressure: interactions with other nutrients

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ABSTRACT This paper reviews the evidence that salt sensitivity of blood pressure is related both to the anion ingested with sodium as well as to other components of the diet. In several experimental models of salt-sensitive hypertension and in humans, blood pressure is not increased by a high sodium intake provided with anions other than chloride. Salt-induced increase of blood pressure depends on the concomitant ingestion of both sodium and chloride. Both epidemiologic and clinical evidence suggest that sodium chloride-induced increases of blood pressure are augmented by diets deficient in potassium or calcium. In experimental animals, a high intake of simple carbohydrates also augments sodium chloride sensitivity of blood pressure. These observations indicate that the effect of dietary sodium on blood pressure is modulated by other components of the diet. Am J Clin Nutr 1997;65(suppl):708S–11S.

KEY WORDS Chloride, potassium, calcium, sucrose, hypertension

INTRODUCTION

It has generally been assumed that the salt sensitivity of blood pressure is specifically related to dietary sodium intake. However, recent evidence indicates that the anion ingested with sodium has an important effect on the subsequent blood pressure response. Blood pressure responses to sodium chloride are also modulated by the intake of other nutrients, including potassium, calcium, and sucrose. We briefly review the evidence for the contribution of these nutrients to the salt sensitivity of blood pressure.

CHLORIDE

In the Dahl salt-sensitive (S) rat, we showed that selective dietary sodium loading, in the absence of chloride loading, fails to produce hypertension (1, 2). Although animals fed a high-sodium chloride diet (8%) develop significant hypertension, in animals fed an identical sodium load provided as sodium bicarbonate or other nonchloride salts of sodium, arterial pressure does not increase above that in control animals with a usual (1%) sodium chloride intake. The failure of selective dietary sodium loading to produce hypertension is not related to differences of body weight or net sodium balance.

Similar observations have been made in several other models of experimental hypertension. Luft et al (3) reported that supplementation with sodium chloride in drinking water causes a modest but significant increase of arterial pressure in stroke-prone spontaneously hypertensive rats (SHRs), whereas an equivalent sodium load, primarily in the form of sodium bicarbonate, does not. In Sprague-Dawley rats, hypertension induced by chronic intraperitoneal infusion of angiotensin II is augmented by a high dietary intake of sodium chloride but not by equimolar sodium loading provided as sodium citrate (4).

Hypertension also does not develop in the deoxycorticosterone acetate (DOCA)-salt rat fed sodium bicarbonate or other nonchloride salts of sodium in contrast with animals fed sodium chloride (5–7). However, a diet containing a combination of sodium iodide and sodium bromide induces hypertension more readily than do other nonchloride sodium salts in DOCA-treated rats, suggesting that chloride’s effect on blood pressure, in conjunction with sodium, may be related to some property common to halides (8).

We also evaluated the effect of selective dietary chloride loading without sodium on the development of hypertension in Dahl S rats. Selective chloride loading (provided as glycine chloride), like selective sodium loading, fails to produce hypertension, whereas animals fed a comparatively high amount of chloride provided as sodium chloride become hypertensive (9). Additionally, in salt-sensitive SHRs, compared with animals fed high amounts of sodium chloride, the development of sodium chloride-induced hypertension is attenuated by high-chloride diets provided as glycine chloride and choline chloride (10).

Limited evidence suggests that the salt sensitivity of blood pressure also depends on high intakes of both sodium and chloride in humans. More than 45 y ago, Grollman et al (11) and Dole et al (12) observed that dietary supplementation with ammonium chloride failed to increase blood pressure in hypertensive humans after dietary sodium chloride restriction had decreased blood pressure. In 1929, Berghoff and Geraci (13) reported that blood pressure increased in seven hypertensive persons with high sodium chloride intakes but not with high sodium bicarbonate intakes. This observation was subsequently confirmed. In five hypertensive patients, Shore et al (14) reported that sodium chloride feeding induced a greater rise in blood pressure than did sodium phosphate feeding. Similarly,
Kurtz et al (15) reported that blood pressure was increased by a high sodium chloride intake but not by equimolar sodium loading provided as sodium citrate in five sodium chloride-deprived men with essential hypertension.

Thus, in four experimental models (Dahl S rat, chronic angiotensin II-infused rat, DOCA-salt rat, and stroke-prone SHR) and in humans, the full expression of sodium chloride-dependent hypertension requires the concomitant provision of high dietary intakes of both sodium and chloride. Selective feeding of sodium without chloride or chloride without sodium either fails to produce hypertension or, in the case of salt-sensitive SHRs fed a high-chloride diet, delays its development.

Several of these studies highlight the importance of expansion of the extracellular fluid volume for the development of sodium chloride–sensitive hypertension, because extracellular fluid or plasma volumes are expanded by dietary sodium chloride but not by nonchloride salts of sodium (6, 15). Further studies with these diets should provide additional information about mechanisms by which dietary sodium chloride increases arterial pressure.

**POTASSIUM AND CALCIUM**

Both epidemiologic and clinical evidence suggest that dietary deficiencies of potassium or calcium potentiate sodium chloride sensitivity of blood pressure. Several surveys document a significant inverse correlation between dietary potassium and blood pressure, and this association is particularly prominent in the presence of a high–sodium chloride diet (16–20). The ratio of urinary sodium to potassium (Na:K) is a stronger correlate of blood pressure than either sodium or potassium alone. Results of clinical trials suggest that an increased potassium intake decreases blood pressure in patients with hypertension (16–18, 21–24), and the antihypertensive effect of potassium is more pronounced in persons consuming a high sodium chloride intake (25, 26). Potassium loading also prevents or ameliorates the development of sodium chloride–induced hypertension in several animal models (18, 27).

Similar to potassium, within and among populations, there is an inverse association between dietary calcium intake and blood pressure (28–32). In the data from the first National Health and Nutrition Examination Survey, dietary Na:K was correlated with blood pressure at low but not high calcium intakes (33). In clinical trials, reductions of blood pressure by increased dietary calcium have been modest and inconsistent (29, 30, 34–46). However, a low calcium intake may amplify the effect of a high sodium chloride intake on blood pressure, and calcium supplementation blunts the effect of a high sodium chloride intake on blood pressure (37–40). High dietary calcium also preferentially lowers blood pressure or attenuates the development of hypertension in sodium chloride–sensitive experimental models (40). Although other mechanisms have been proposed, the blood pressure–lowering effects of potassium and calcium may be related to their antinatriuretic capacity (39, 41).

**SUCROSE**

Simple-carbohydrate feeding (sucrose, glucose, or fructose) increases blood pressure in several normotensive strains of rats, including Sprague-Dawley, Wistar-Kyoto, Wistar, and Dahl S rats (42–50). Sucrose feeding also augments the development of hypertension in SHRs and in a rat model of adrenal regeneration hypertension (51–54).

Increasing evidence suggests that sucrose potentiates the sodium chloride sensitivity of blood pressure. In earlier studies, Hall and Hall (51, 52) reported that the addition of sucrose to a 1%–sodium chloride drinking solution augmented the development of both adrenal regeneration hypertension and hypertension after unilateral nephrectomy, and this augmentation was attributed to increased salt consumption in sucrose-drinking rats. However, more recent evidence suggests that the capacity of sucrose to potentiate the effect of dietary sodium chloride on blood pressure in both normotensive rats and SHRs is not accounted for by higher sodium chloride intakes in sucrose-fed animals (44, 45, 54, 55). We reported recently that arterial pressure is increased by a high sucrose intake in a controlled balance study in Sprague-Dawley rats with high (4%) but not low (0.45%) sodium chloride intakes (56). The sodium chloride intake was identical in sucrose-drinking and water-drinking animals fed high amounts of sodium chloride.

Potentiation of sodium chloride sensitivity by sucrose may be related to an antinatriuretic effect of sucrose. A high sucrose intake induces volume expansion, and hypertension develops more readily in unilaterally nephrectomized animals than in intact animals (57). In addition, renal sodium retention occurs during the development of sucrose-induced hypertension in SHRs (58).

Simple carbohydrate feeding induces several metabolic changes, including insulin resistance and increased sympathetic nervous system activity (56). An association between insulin resistance and salt sensitivity of blood pressure has also been observed in several experimental models of hypertension, in human essential hypertension, and in both the human and experimental models of obesity (59). Conceivably, the antinatriuretic effect of a high sucrose intake may be mediated by the insulin-resistant state, increased neural activity, or both.

**PRACTICAL IMPLICATIONS**

The recognition that the sodium chloride sensitivity of blood pressure is dependent on the intakes of both sodium and chloride will have only a limited effect on recommendations for sodium consumption. Most dietary sodium is consumed as sodium chloride, and in practical terms, a recommendation for sodium restriction will translate into sodium chloride restriction. Nevertheless, mineral water and processed foods may contain nonchloride salts of sodium such as sodium bicarbonate and monosodium glutamate. Data in rodent models of hypertension and limited data in humans suggest that ingestion of these salts will have less effect on blood pressure than does sodium chloride. However, efforts to restrict chloride but not sodium intakes may be limited by taste preferences as well as by safety concerns. A chloride deficiency syndrome has been described in infants fed chloride-deficient but not sodium-deficient diets (60). Clinical features of this syndrome include loss of appetite, failure to thrive, hematuria, and severe hypokalemic metabolic alkalosis.

Both epidemiologic and clinical evidence suggest that diets low in potassium or calcium content amplify the effect of a
high sodium chloride intake on blood pressure. Consequently, it is prudent to recommend adequate [ie, the recommended dietary allowance (61)] intakes of both potassium and calcium because of a potential effect on blood pressure as well as for other health reasons. In rodents a high intake of simple carbohydrates also potentiates the capacity of sodium chloride to increase blood pressure. However, the interaction between sucrose and sodium chloride has not been evaluated in humans and should be a fruitful area for future study.

REFERENCES