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Health Risks of Dietary Salt

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Review Article

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Abstract

Besides raising the blood pressure dietary salt is responsible for several other harmful effects. The most important are a number which, though independent of the arterial pressure, also harm the cardiovascular system. A high salt intake is also responsible for increase in the mass of the left ventricle, thickens and stiffens conduit arteries and thickens and narrows resistance arteries, including the coronary and renal arteries. It also increases the chance of strokes, the severity of cardiac failure and platelets aggression. In renal disease, a high salt intake increases the rate of renal functional deterioration. Apart from its effect on the cardiovascular system dietary salt has an effect on calcium and bone metabolism, which highlights the finding that in post-menopausal women salt intake controls bone density of the upper femur and pelvis. Dietary salt controls the incidence of carcinoma of the stomach and there is some evidence which suggests that salt is associated with the severity of asthma in male asthmatic subjects. The intake of salt in our diet must be on balance, because the high Salt intake is associated with the occurrence of stomach cancer, Osteoporosis, Obesity, Kidney Stones, Kidney Disease, Ménière's Disease, Diabetes, Liver problems, cardiovascular disease, Inflammation and sleep problems, and not just Hypertension.

Keeping the above facts in mind the Objectives of the present review study was to clarify what is the diseases and harmful effects of high salt intake in addition to Hypertension and to explain the relationship between high salt intake and these diseases and problems.

Keywords: Dietary salt; Left ventricular mass; Conduit and Resistance arteries; Strokes; Renal function; Bone mass

Introduction

High blood pressure is the greatest cause of heart attack and heart failure and is a major risk for coronary heart disease. Dietary salt seems to be a single important factor in raising the blood pressure. Throughout history the human race only consumed the sodium naturally present in food and the daily intake was about 10mmol/day [1]. It is less than 5000 years ago that use of salt started as an additive to food and the present intake of between 100 to 400mmol/day is therefore a considerable, and in evolutionary terms, latest increase [2.3].

An argument which lasted about 100 years over the proof that suggested that hypertension is somewhat due to the present high intake of salt is now been solved. There is a common understanding that dietary sodium plays an important role in determining the blood pressure of populations, the number of individuals who have a raised blood pressure, and its severity, and that it is

responsible for much of the rise in blood pressure that occurs with age [4]. The previous debate, however, concealed the considerable evidence that in addition to raising the blood pressure dietary salt has other harmful effects, several of which in the cardiovascular system are independent, though additive, to the effect of the hypertension, and some of which seem to be as important as the rise in arterial blood pressure.

Cardiovascular Effects

Left ventricular mass: In human beings there is a correlation between left ventricular mass and cardiovascular mortality and morbidity irrespective of the blood pressure [5-7]. In normal blood pressure subjects left ventricular mass and diastolic blood pressure have been found to be positively correlated with urinary sodium excretion [8,9]. In two other researches with normal BP groups followed up for 3 to 8 years the baseline left ventricular mass and wall thickness were found to be significantly related to the following development of hypertension [5]. In an experimental study, Normotensive rats were given 1% saline for few weeks, they were found to develop an increase in heart weight due to an increase in left ventricular mass without raising the blood pressure [10,11]. In both normotensive humans and the rat therefore, left ventricular mass is positively correlated to the salt intake which, in normal conditions is equivalent to the dietary salt intake.

The correlation of left ventricular mass with salt intake in essential hypertension is well indicated in that in such patients 24-h sodium excretion is an independent determinant for relative wall thickness, and is a strong determinant than the blood pressure [9-14]. These researches have been proved utilizing ambulatory blood pressure observation [8].In subjects with hypertension associated with type I diabetes multiple regression analysis found dietary sodium intake as an independent predictor of left ventricular mass, whereas there was no significant association between left ventricular mass and the blood pressure [15].

It was found that the increase in left ventricular mass correlated with essential hypertension could be decreased by lowering the intake of salt [8,16,17]. The Treatment of Mild Hypertension Study Research Group [25] depicted a significant correlation between the decrease in salt intake and the left ventricular mass. In the complete study group lowering salt intake was the only factor which was significantly correlated with a reduction in left ventricular mass. Similarly in the two-kidney one-clip hypertensive rat a low sodium diet can reverse the myocardial hypertrophy and certain enzyme changes, in the absence of a significant change in blood pressure [18,19].

Conclusion: There is a close link between urinary sodium excretion and left ventricular mass in both man and the rat which is independent of hypertension. In hypertensive patients a reduction in salt intake reduces left ventricular mass independent of a change in blood pressure.

Vessels: An elevated sodium intake, in both humans as well as experimental animals, increases the stiffness of conduit arteries and the activity of resistance arteries, and both become hypertrophied [20,21]. Stiffness of conduit arteries, measured as an increase in pulse wave velocity [22] or pulse pressure [23] is a high risk factor and an independent predictor of cardiovascular problems. Tobian was the first to show that in various forms of experimental hypertension in the rat a high salt intake induces structural alterations in cerebral and renal vessels independent of the blood pressure [24,25]. Recent researches in humans have shown that a moderate reduction in salt intake reduces the stiffness and thickness of the arterial wall, which is not dependent on the blood pressure [26].

In one early research in subjects in a rural community in China, pulse wave velocity in the lower aorta, the arms and the legs was, after adjustment for blood pressure, consistently lower than in a group in an urban community on a higher salt intake [27]. Likewise, the pulse wave velocity of a group of normotensive subjects who lowered their salt intake for a mean of about 2 years was significantly lower than that of a control group, independent of the blood pressure [26].

The structural changes in intramyocardial coronary arteries induced by a high salt diet are associated with a number of metabolic changes including an increased generation of reactive oxygen species [28] which, among other effects, oxidize nitric oxide thus reducing its dilator effect [29,30] and the arteriolar response to acetylcholine [31].

Because a rise in salt intake is usually accompanied by a small rise in plasma sodium and plasma sodium leads to essential hypertension [32] it is possible that the effect of a small change in sodium concentration on *in vitro* cultures of endothelial cells may also be relevant to a consideration of the effect of dietary salt on vessels *in vivo*. For example, increasing the sodium concentration of the culture fluid of cultured myocardial myocytes and

vascular smooth muscle by 6 m M/l for 5 days causes hypertrophy [33]. The researchers responsible for this finding also demonstrated that raising the sodium concentration of the fluid bathing cultured human umbilical vein endothelial cells by 6 m M/l (from 142 to 148mmol/l) for 5 days raises their content of cellular protein and total RNA. When exposed to a sodium concentration of 152mmol/l (ie, an increase of 10 m M/l) there is first, after 2 h incubation, a transient increase in cfos proto-oncogenic mRNA expression. After 3 days there is a general increase in mRNA expression of several factors which are related to hypertrophy [34]. Conclusion: Dietary salt intake controls the hardening of the larger conduit arteries, the reactivity of the smaller resistance vessels and the wall thickness of both. An elevated intake is responsible for an increase in collagen deposition and an increased generation of reactive oxygen species inside the arterial walls. A reduced salt intake reverses these changes. Small variations in the concentration of plasma sodium which can induce hypertrophying effects on cultured vascular endothelium which are responsible for these changes.

Cardiac failure: Cardiac failure in correlation with essential hypertension is the end product of several harmful aftereffects of dietary salt [35]. Primarily there is systolic dysfunction due to the salt induced hypertension [36]. Some older patients may develop diastolic dysfunction due to impaired ventricular filling; this usually precedes systolic dysfunction and is due to the collagen deposition and fibrosis of the ventricle which are closely linked with salt intake. Also, increase in the size of the muscle mass due to high salt intake, due to the hypertrophy and deposition of collagen and fibrous tissue, thickening of the coronary arteries as a result of high intake of dietary salt, which can be detected as an inappropriate coronary blood flow [37,38]. Myocardial function is further impaired by the increase in cardiac output which results in part from increase in right auricular pressure due to high salt intake. The weight gain which is associated with the salt and water retention due to cardiac failure also increases cardiac work. Decreasing salt intake in patients with heart failure is generally used and results in an improvement of symptoms similar to that of the diuretics. As of now, there has been no controlled trials of salt restriction in heart failure.

Stroke: The higher the salt intake, the greater are the chances of strokes [39,40]. Statistical analyses calculated from the urinary electrolyte data obtained from a study (from persons aged 20 to 40 years) and from the age and gender-specific stroke mortality data from 25 countries around the world [41] showed that there is no significant correlation between either the systolic or the diastolic pressure and risk of stroke but there was a significant relationship between stroke mortality and urinary excretion of sodium in males, and the Na/K ratio in females [42]. These results are in accordance with those calculated for a study in 12 European countries where sodium excretion was not significantly related to systolic blood pressure; it was related to risk of stroke [43]. The picture of the mechanism responsible for the correlation between dietary salt and strokes is not clear but may, somewhat, be related to conduit artery thickness and stiffness, and platelet reactivity.

Conclusion: Stroke mortality is strongly correlated to dietary sodium intake which is independent of the blood pressure.

Platelets: In a research in normal males platelet aggregation induced by adenosine 5'-diphosphate was statistically greater when put on a high salt intake [44]. In the same way, in normal females an increase in salt intake from 10 to 200mmol/day was associated with a significant rise in platelet aggregation [45]. In two groups of males with and without a genetic history of hypertension an increase in salt intake also increased the blood pressure of those with a genetic background but platelet aggregation increased in both groups, though it rose more in those with a genetic history [46].

The consequence of salt intake on adrenaline-induced platelet aggregation and α-2 adrenergic receptors on platelet membrane fraction has been measured in patients with essential hypertension. The reciprocation was linked to the correalted changes in blood pressure. In those subjects where there was a rise in blood pressure, platelet aggregation also rose as did the number of α-2 adrenergic receptors [47].
Conclusion: In normal males and females, with and without a genetic background of hypertension and in subjects with essential hypertension, salt intake affects platelet aggregation. These changes as a result of salt intake in platelet reactivity may be a bond between salt intake, thrombotic strokes and heart attack.

Renal function: It has been estimated that an increased salt intake from 1 to 8% for a week to 16 weeks raises the blood pressure and the size and weight of the kidneys in the salt-sensitive and -resistant rat [48] and the SHR and its control the WKY rat [11]. The effect was seen highest in the Dahl salt-sensitive and the SHR rats.

In human subjects with high blood pressure an increase in salt intake frequently increases the rate of glomerular filtration, vascular resistance, calculated intraglomerular capillary pressure and excretion of protein [49]. In normal humans the effect of a high salt intake ranges from no noticeable effect or a slow renal vascular resistance, a few have a similar reaction to that which occurs in those hypertensive patients who have a high glomerular filtration [49-51].

Non-Cardiovascular Effects

Bone density and renal stones: Excretion of sodium through urine and therefore sodium intake controls the urinary output of calcium [52,53]. A rise in dietary salt intake simultaneously leads to increased urinary calcium which in the long term may lead to calcium deficiency from bone [54]. a study done on a group of healthy men and women aged 20/79 years found that the more the sodium intake the more is the loss of urinary calcium and the excretion of hydroxyproline [55], an increase in dietary sodium of 100mmol/day was associated with an increase in calcium excretion of 0.6/1mmol. In older healthy humans a rise in salt intake for 2 to 10 days increases the excretion of calcium in urine, hydroxyproline, cyclic AMP and deficiency of calcium in bones [56-58]. An increase in dietary salt and the resultant increase in calcium excretion also stimulate an increase in 1,25 $(OH)_2D_3$ which seems to be increased by a rise in parathyroid hormone. A rise in salt intake from 70 to 170mmol/day in elderly women increases their calcium loss [59] and a modest reduction in salt intake reduces urinary calcium excretion [60]. The results that in the elderly urinary sodium excretion controls the urinary excretion of calcium and some aspects of bone metabolism suggests that dietary sodium intake may be a factor for reduction in bone thickness that happens in the old age.

The consequence of salt intake on the bones, however, is likely to be pertinent throughout the life of a person. A research done on 380 girls early in adolescence, confirmed the close link between urinary sodium and calcium excretion, has depicted that urinary calcium has a negative effect on total body calcium and total body bone density. It is concluded as a result, that the attainment in young age of a reasonable peak bone mass, which has a notable bearing on the prevalence of osteoporosis after the menopause, is put to risk by a high sodium intake during early adolescence [61]. In women after menopause, one research [62] found, from the effect of a few days rise in sodium intake, that an increased intake of 50mmol/day for 10 years would deplete the calcium stores by about 7.5% which is in accordance another researcher's [63] finding in another group of post-menopausal women, studied for 2 years, that urinary sodium excretion is inversely correlated to bone density. Statistical analysis also revealed that both dietary calcium and urinary sodium excretion are significant determinants of the reduced bone mass happening over the 2 years [64]. The results also suggested that if the daily excretion of sodium were reduced to one half it would have an identical effect on diminishing bone mass to that of increasing calcium intake by 891 mg/day. No bone loss appeared at the hips when calcium intake was above 1768 mg/day or the urinary sodium excretion was below 92mmol/day.

Another retrospective study was performed in population using 24-h diet recalls, for a 2-year period between 1973 and 1975, and a mineral density investigation between 1988 and 1991. No effect of sodium intake on bone mineral density was seen other than for a small significant preventive effect of a lower sodium intake on the distal radius of men [65]. Another research [66] however, did find an inverse correlation between forearm mineral density and 24-h sodium excretion in post-menopausal females. A following 9-month period of sodium restriction (by only 30mmol/day) in a sub-sample failed to depict any alteration in bone mineral density. A high sodium intake is also indicative of the pathogenesis and treatment of high calcium excretion in urine in both children and adults [67,68] and of calcium expenditure in corticosteroid treated patients [69].

It is possible that the relation between urinary sodium excretion to bone density in patients with essential hypertension may be more significant than in normal blood pressure controls. When the children of hypertensive parents are given a high salt diet they tend to have a greater urinary calcium excretion than children from normal parents [70]. Over a follow-up study of 3.5 years in 3676 white women from 66 years of age to 91 years the rate of bone loss in the femoral neck, adjusted for age, initial bone density, weight, smoking and regular use of hormone replacement therapy, the rate of bone adherence increased with the blood pressure measured at base line.In animals the SHR and Milan hypertensive rats are also more likely to get bone loss than their normal controls [71]. Thiazide diuretics which cause a reduction in calcium excretion when given to populations with and without hypertension reduce the number of bone fractures [72,73].

In as much as kidney stones are known to be correlated with an increased urinary excretion of calcium it is possible that the salt-induced increase in urinary calcium excretion in SHR and essential hypertension is responsible for their greater risks of renal stones [74-76].

Conclusion: In normal individuals salt intake has an impact on urinary calcium excretion and bone turnover. In essential hypertension and hypertensive strains of rat urinary calcium excretion is raised, there is an increase in bone rate of replacement and the bones of the SHR and the Milan hypertensive rat tend to be at risk of osteomalacia. In old age women after menopause urinary sodium excretion controls calcium excretion positively and bone density negatively. It is also possible that the increase in kidney stones in essential hypertension and the SHR is due to the rise in urinary calcium excretion as a result of high salt intake.

Carcinoma of the stomach: Of all the risk factors correlated with cancer of the stomach, which is the second most common cancer globally, the relationship to salt is the most intense [77]. Randomly selected 24-h urine collections from a group of 39 subjects selected from 24 countries were obtained from a research. Median sodium excretion levels were made consistent for age and sex between the ages of 20 and 49 years and averaged for each country. Ecological correlation-regression analyses of the levels of sodium excretion in relation to national mortality rates caused by stomach cancer were found to be highly significant in men and women.

A high consumption of salt in the diet of both humans and experimental animals is known to be a risk factor for gastritis and when combined with known gastric carcinogens advances their carcinogenic effect [78]. One such promoter appears to be *Helicobacter pylori*, which has been known to be correlated with development of gastric cancer from gastritis [79]. Also a high salt diet promotes *Helicobacter pylori* growth and development [80]. Prospective researches have shown a positive correlation between *Helicobacter pylori* and gastric cancer constituting to a two-to three-fold increase in risk [81].

Conclusion: Cancer of the stomach is highly correlated to dietary sodium intake.

Asthma: Researches from England and Wales have depicted that there is a strong association between the sale of table salt and risk of asthma in men and children [82]. There are two interventional randomized double-blind, placebo controlled and crossover studies in men with mild to moderate prevalence of asthma, showing the effect of changing the sodium intake for several weeks. There were 27 patients in the first trial and 36 in the second one. The severity of the asthma was measured in one trial whereas, in another, the airway's response to histamine was assessed [83]. In both these small trials it was found that a rise in dietary sodium, 80mmol/day in one and 204mmol/day in the other, was responsible for a rise in both the severity of the asthma and bronchial reactivity. In another randomized crossover trial in 17 male asthma patients, there were three levels of sodium intake, each for 2 weeks. The highest difference in intake was 118mmol/day. The only thing observed was peak expiratory flow which was assessed by the subjects themselves in their own homes. No changes in peak expiratory flow were observed [84].

An experimental study on a small group of men with mild to moderate asthma revealed that bronchial reactivity was strongly correlated to 24-h urinary sodium excretion, allowing for the effect of age, allergy and smoking [85]. Few other observational studies on comparatively larger groups of normal men and boys did not showed a correlation between urinary sodium excretion and bronchial reactivity to methacholine [84-86].

Conclusion

High salt intake may be a risk factor for male patients with asthma. There is no evidence that salt intake effects bronchial responsiveness in normal individuals.

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