

Review Article

Dietary Management of Hypertension

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ABSTRACT

Dietary management with reduced sugar and salt intake and supplementation with B vitamins such as B6 and with anti-oxidant vitamins such as vitamin C and E, and lipoic acid has the potential to lower blood pressure in persons with essential hypertension. Moderate intake of ethanol may also produce an anti-oxidant effect, lower blood pressure, and provide cardiovascular protection. Through these dietary measures we may prevent one of the underlying causes of hypertension, elevated tissue aldehydes. Excess aldehydes can

bind sulphydryl groups of membrane proteins, altering membrane calcium channels and increasing cytosolic free calcium, peripheral vascular resistance, and blood pressure. In hypertension there is increased oxidative stress which can lead to a further increase in reactive aldehydes. Insulin resistance and glucose intolerance are also common features of hypertension. Dietary management can improve carbohydrate metabolism, reduce oxidative stress and tissue aldehydes, and lower blood pressure.

KEYWORDS: dietary management, hypertension

INTRODUCTION

Essential hypertension in humans may develop through a combination of genetic and environment factors^[1,2]. It has been suggested that abnormalities in carbohydrate metabolism may underlie the etiology of the clinical course of hypertension^[1,3-5]. Diet has long been under investigation as a potential effector of blood pressure. A diet high in sugar can give rise to hyperlipidemia, insulin resistance and hypertension^[1]. Persons with a genetic sensitivity would be particularly vulnerable to the adverse effect of a high sugar diet^[5-7]. There is strong evidence that points to excess dietary salt as a major factor contributing to the development of hypertension. Glucose intolerance and insulin resistance are also associated with salt sensitivity^[2,8]. Dietary high salt in people with glucose intolerance may lead to further impairment of glucose metabolism, increased oxidative stress and hypertension. Dietary management through lower sugar and salt intake and increased consumption of vitamins which increase anti-oxidant capacity, may prevent insulin resistance, oxidative stress and hypertension.

SUGAR INDUCED HYPERTENSION**Evidence for Sugar-Induced Hypertension in Animal Models**

Rats given a diet high in fructose have elevated fasting insulin and glucose, elevated insulin

response to oral glucose load, significantly elevated triglycerides, and elevated blood pressure^[9-12]. Similar hyperinsulemia, hypertriglyceridemia and hypertension have also been demonstrated in dogs fed a high fructose diet^[13]. Vasdev et al have shown that Wistar-Kyoto (WKY) rats develop hyperinsulemia and hypertension associated with renal arterial hyperplasia when consuming a diet with only 10% of total calories as fructose^[14].

Long term sucrose feeding in rats also results in impaired glucose and increased blood pressure^[15,16]. Monkeys fed a high sucrose diet show increased serum cholesterol and enhanced blood pressure response to a high salt diet^[17]. Evidence points to the fructose component of sucrose as the agent which is actually causing the insulin resistance and hypertension. Dogs show an increase in triglycerides, fasting insulin, insulin resistance and blood pressure when fed a high fructose diet but not when fed a similar high glucose diet^[13]. Similar insulin sensitivity is induced in WKY rats fed a high fructose diet while rats fed a high glucose diet showed no changes^[18]. These studies indicate that it is the fructose component of sucrose that is the most harmful.

Addition of high salt to a high sucrose diet causes even more marked elevation in blood pressure in both Spontaneously Hypertensive Rats (SHR) and WKY rats^[19]. However, Sprague Dawley

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rats (SD) given a high sucrose diet combined with low salt diet do not develop hypertension. High sucrose intake appears to elevate blood pressure only with normal or high dietary salt intake^[20].

Sugar induced hypertension and insulin resistance in rats is related to the relative genetic sensitivity of the rat strain involved. Long term high sucrose diets elevate insulin and blood pressure most dramatically in SHR, with an intermediate response in WKY rats and moderate elevation in Wistar rats^[16,21]. A fructose enriched diet increases plasma triglycerides, insulin and blood pressure in both WKY and SHR rats but the magnitude of these changes is much greater in the genetically sensitive SHR^[22].

Increased Cardiovascular Risk with High Sugar Diet in Humans

American consumption of "added" sugars has risen dramatically in recent years, from 13% of calories in 1989 to 16% in 1996^[23]. Estimations from food disappearance data indicate that the level of sucrose in the American diet is 15-21% of total calories or about 10% fructose^[18,24]. High fructose sweetening in soft drinks accounts for almost half of the total added sugars in the U.S. diet and consumption of soft drinks has increased dramatically in recent years, particularly among adolescents^[23]. Fructose accounts for 50% of the calories of soft drinks^[25].

In animal models, it has been clearly shown that a high sugar diet can produce both hyperlipidemia and elevated blood pressure, the two major coronary heart disease risk factors. There is also considerable evidence to show that humans consuming a high sugar diet are at increased risk of cardiovascular disease. Early evidence came from a study of Israeli Yemenites. Yemenites living in Israel 25 years or more have a significant increase in the incidence of atherosclerosis, ischemic heart disease and diabetes compared to recent Yemen immigrants. One of the major difference in the diet consumed in Yemen and that in Israel is that carbohydrates consumed in the Yemen consisted solely of starches with almost no sugar while in Israel, sucrose accounted for 25 to 30% of total carbohydrates^[26]. Using market consumption of foods in a multinational study, Grant showed a relationship between the fraction of the diet derived from simple sugars and ischemic heart disease mortality rates^[27]. Sweeteners are particularly highly associated with ischemic heart disease mortality for women between the ages of 35 and 64 years^[28].

Nikkila has suggested that dietary sucrose is one of the factors responsible for increased obesity, diabetes and heart disease in the U.S^[29].

Undoubtedly, the fructose component of the sucrose molecule is the major cause of sucrose-induced insulin resistance. Healthy adult males given a diet high in fructose for just 1 week developed a significant reduction in both insulin binding and insulin sensitivity^[30].

A diet high in carbohydrate is not, in itself, a risk factor. Epidemiological studies provide abundant evidence that, in rice-eating populations of the world, hypertriglyceridemia is rare^[31]. Healthy subjects show significantly increased triglycerides and VLDL after intake of a high sucrose or high fructose diet but show no adverse changes on a corresponding high starch diet^[32,33]. Dietary carbohydrate as starch actually improved triglyceride levels in patients with elevated levels while dietary sugar exacerbated the condition^[31]. Adults age 35 - 55 years consumed two diets for 6 weeks in cross-over design containing either 30% of calories as sucrose or wheat starch. Sucrose feeding produced an increase in serum insulin, insulin/glucose ratio and insulin response to sucrose load compared to starch^[5].

Persons with a genetic susceptibility towards impaired glucose metabolism will be particularly sensitive to the adverse effects of a high sucrose or high fructose diet. Adverse responses to high sucrose diet have been shown to be of greater magnitude in carbohydrate-sensitive subjects^[5]. Carbohydrate sensitive adults given a high sucrose diet develop significantly elevated plasma cholesterol, LDL, triglycerides and blood pressure after 5 to 6 weeks^[6,7].

SALT-INDUCED HYPERTENSION

Sucrose and sodium are common constituents in the diet of modern society. Much evidence has accumulated and appears irrefutable that excess sodium can contribute to the development of hypertension and heart disease. Sodium-dependent hypertension has been documented in well controlled animal and human investigations^[2]. Yanomamo Indians and Xingu of Northern Brazil, who do not eat salt, have no hypertension, nor does their blood pressure rise with age, as it does with all accultured populations^[34,35]. Since almost everyone in western countries ingests a high sodium diet, the fact that only about half will develop hypertension suggests a variable degree of sensitivity to sodium. Obviously, both heredity and interaction with environmental factors are involved.

The term "salt sensitivity" implies that some individuals respond to a high salt intake with an increase in blood pressure and others (salt resistant individuals) do not. Fifty-one percent of hypertensives and only 26% of normotensives are salt-sensitive. Patients with essential hypertension

have been classified as salt-sensitive and salt-resistant according to their blood pressure response to the level of salt intake. Salt-sensitive subjects become hypertensive or their hypertension worsens when exposed to a high salt diet; whereas, salt-resistant individuals do not exhibit important blood pressure changes when going from low to high salt diet, or vice versa^[2]. Animal models of human essential hypertension including Dahl salt-sensitive rats, SHR and WKY rats respond to low and high salt diets with blood pressure changes similar to humans^[21,36-38].

Evidence of Salt-induced Hypertension in Animals

It was shown as early as 1957 that increasing dietary salt causes a progressive rise in blood pressure in rats. Rats fed a diet with only 0.15% salt (dry weight of food) live significantly longer than rats fed greater amounts of dietary salt. The average North American diet is about 0.25% salt on a dry weight basis. A diet with 0.15% salt would provide an average man consuming 2500 Kcal with about 300 mg of sodium or about 750 mg of NaCl /day. A study of a colony of chimpanzees found that the progressive addition of salt to their largely natural diet, resulted in a gradual rise in their blood pressure over 20 months. The amount of salt in the chimps' diet was similar to that found in a typical North American diet. This significant rise in blood pressure was completely reversed within six months after being returned to their natural diet. The evidence in animals shows that simply increasing dietary salt is sufficient to cause increased blood pressure and decreased life expectancy in virtually all animal studies^[8].

Insulin resistance is a common feature of SHRs, Dahl salt-sensitive rats and WKY rats^[21,36-38]. Dahl salt-sensitive rats which have insulin resistance, develop severe hypertension on a high salt diet, where Dahl resistant rats do not. Dahl salt-sensitive rats on a low salt diet become hypertensive and show insulin resistance when given a high sucrose diet. SHR and WKY rats, when given a high salt diet, show a significant increase in blood pressure when compared with their respective control rats on a low salt diet. Both SHR and WKY rats demonstrate an additive increase in blood pressure when given a high salt and sugar enriched diet^[21]. Salt-sensitivity and sugar sensitivity are genetically associated conditions and both are related to insulin resistance and altered glucose metabolism.

Insulin Resistance in Salt-sensitive Essential Hypertension

Hyperinsulinemia resulting from insulin resistance is now recognized as an independent risk factor for

cardiovascular disease. Insulin can increase renal tubular sodium reabsorption and hyperinsulinemia could contribute to a rise in blood pressure by causing sodium retention. Hyperinsulinemia has been suggested to contribute to the pathogenesis of salt-sensitive hypertension^[39].

In a recent study, salt-sensitive essential hypertensive patients exhibited a reduced insulin sensitivity index compared with salt-resistant hypertensive subjects. An inverse relationship between the insulin sensitivity index and a twenty-four hour mean blood pressure was greater with high salt diet. It was concluded that salt-sensitive essential hypertensive patients are more insulin resistant than salt-resistant patients^[40-42]. In healthy normotensives with a family history of essential hypertension, the steady-state glucose-to-insulin ratio was almost twice as high in the salt-sensitive as in the salt-resistant subjects. Thus, insulin-mediated glucose disposal is reduced in otherwise healthy lean normotensive salt-sensitive subjects, indicating that insulin resistance is present in these hypertension-prone individuals before development of hypertension^[43,44].

In another study of essential hypertensives, salt-sensitive patients manifested increased serum levels of total cholesterol, LDL-cholesterol, and increased urinary albumin excretion when compared with salt-resistant patients^[39]. Salt-sensitivity could be considered a marker for increased cardiovascular risk in patients with essential hypertension. There is a direct correlation between insulin level and salt sensitivity. Hyperinsulinemia due to higher dietary salt intake in salt-sensitive essential hypertensives could contribute to an increase in blood pressure by sodium retention, increased sympathetic activity and vascular hypertrophy. Reduced vasodilatory effects of insulin and increased vascular reactivity have been described in insulin resistant states. Salt sensitive subjects react to sodium load with an increase in blood pressure and sympathetic nervous system activity (vasoconstriction), with consequent worsening in insulin-mediated glucose disposal and hyperinsulinemia. The increase in blood pressure due to salt-sensitivity and the hyperinsulinemia due to insulin resistance may derive from a common mechanism, in which case each phenomenon could represent different tissue-specific response to the same salt- or sugar-induced stimulus.

ROLE OF ALDEHYDES AND OXIDATIVE STRESS

There is increasing evidence that glucose intolerance and insulin resistance play a key role in the pathogenesis of essential hypertension in

humans. Abnormalities in glucose utilization are estimated to exist in 25% of the general population and in up to 80% of subjects with essential hypertension^[1,3,4]. Insulin resistance is also a common feature of SHR, Dahl salt-sensitive rats and fructose-induced hypertensive rats^[36,38,45-48]. If glucose metabolism through the glycolytic pathway is impaired, as in insulin resistance, there will be a build up of glyceraldehyde, glyceraldehyde-3-phosphate with further metabolism to methylglyoxal, a highly reactive ketoaldehyde^[49,50]. Methylglyoxal itself inhibits the glycolytic pathway which leads to further insulin resistance and production of excess aldehydes^[51].

Aldehydes react nonenzymatically with sulfhydryl and amino groups of proteins and inhibit their function. Protein sulfhydryl groups are necessary for the proper functioning of L-type calcium channels^[52,53]. Disruption of vascular calcium channels by aldehyde binding to critical sulfhydryl groups, can raise cytosolic free calcium levels and lead to increased peripheral vascular resistance and hypertension^[54,55] (Fig. 1). Rats consuming a high fructose diet (10% of calories) have elevated tissue levels of aldehydes and develop hypertension^[56]. Tissues aldehydes are also elevated in spontaneously hypertensive rats, a model of insulin resistance and essential hypertension^[57].

Increased oxidative stress occurs in salt-induced hypertensive rats, spontaneously hypertensive rats and in human hypertensives leading to increased lipid peroxidation^[58-64]. Peroxidation of unsaturated fatty acids such as linolenic acid results in the formation of aldehydes such as 4-hydroxypentenal, 4-hydroxyhexenal, 4-hydroxynonenal and malonaldehyde^[65-67]. These highly reactive aldehydes have been shown to inhibit key enzymes of the glycolytic pathway^[68]. Altered glucose metabolism leads, in turn, to further production of excess metabolic aldehydes causing both hypertension and increased oxidative stress (Fig. 1). Excess metabolic aldehydes may also act through binding and inactivation of endothelial proteins, altering endothelial function and inhibiting nitric oxide synthase. High levels of aldehydes can also increase sympathetic activity.

It has been shown that the aldehyde binding amino acid, N-acetyl cysteine, can normalize tissue aldehyde levels and blood pressure in spontaneously hypertensive rats^[56]. In addition to directly binding aldehydes, N-acetyl cysteine can also act as an antioxidant to prevent further oxidative stress and formation of aldehydes due to lipid peroxidation^[69]. N-acetyl cysteine when given in the diet to fructose-induced hypertensive rats, completely normalized plasma elevated insulin

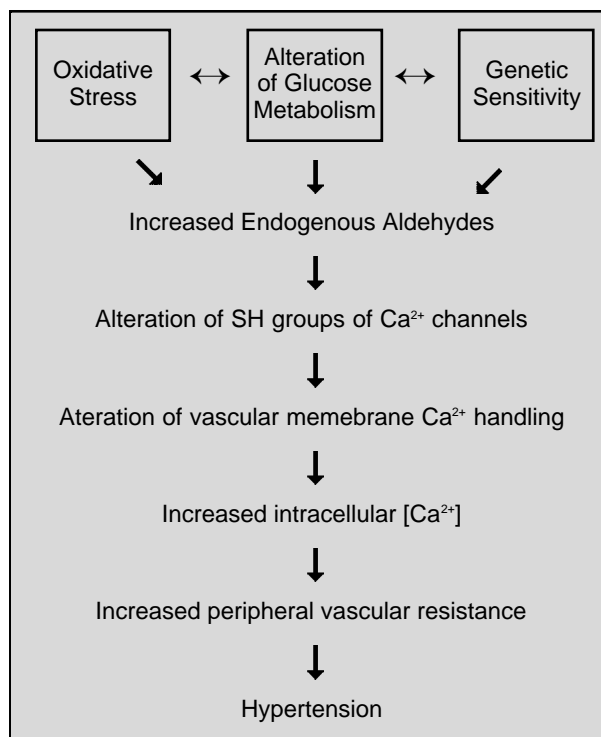


Fig. 1: Factors Important in the Pathogenesis of Hypertension

levels, tissue aldehydes, cytosolic free calcium and blood pressure^[56]. Control of excess metabolic aldehydes and oxidative stress may be critical to the control of essential hypertension.

DIETARY MANAGEMENT OF HYPERTENSION

DASH II (Dietary Approach to Stop Hypertension) study showed unequivocally that reducing sodium intake from a baseline of 8.4 gm of salt (144 mmol of sodium) per day, first to 6 gm of salt (106 mmol of sodium) per day and then to less than 4 gm of salt (less than 66 mmol of sodium) per day, lowered blood pressure levels significantly. For those consuming a typical American diet, systolic blood pressure fell 6.7 mmHg and diastolic blood pressure fell 3.5 mmHg after going from a high sodium diet to a low sodium diet. More than two-thirds of this benefit was obtained by reducing salt intake from the current government-recommended level of 6 gm per day to less than 4 gm per day, a level that is difficult to achieve without special food preparation. In this trial, participants were provided with all their food, including snacks and cooked meals. In westernized societies only about 10% of dietary salt comes naturally from foods consumed. Another 15-25% comes from the salt shaker and about 75% comes from processed foods and meals eaten away from home^[8].

The DASH II trials emphasize a diet consisting of fruits and vegetables, low-fat dairy, high fibre

grain, modest portions of lean meat and reduced salt. This study has important implications for practicing physicians in the dietary management of hypertension. Hypertensive patients on the DASH II diet had a reduction in mean systolic blood pressure of 11.5 mmHg which is comparable to what can be achieved by antihypertensive drug therapy. This DASH II diet is low in both simple sugars and salt and this may be one of the factors that leads to lower blood pressure^[70,71].

Fruits and vegetables are major sources of vitamins such as Vitamin B6, and anti-oxidants such as Vitamin C, Vitamin E, and lipoic acid. These vitamins also may be important contributing factors to the anti-hypertensive effects of the DASH diet.

Vitamin B6

Cysteine reacts with aldehydes forming small stable compounds which can readily be excreted in bile and urine. This aldehyde binding ability has been demonstrated to lower elevated tissue aldehydes and prevent hypertension in both spontaneously hypertensive and fructose-induced hypertensive rats^[14,57]. Vitamin B6 is a co-factor for two enzymes, cystathione b-synthase and cystathionase, involved in the metabolic synthesis of cysteine from methionine^[72,73]. A diet deficient in vitamin B6, when given chronically to rats, leads to a decreased activity of these two enzymes in the liver^[74,75]. Rats given vitamin B6 deficient diet also had lower plasma cysteine levels^[73]. Dietary supplementation of vitamin B6 should stimulate the activity of these enzymes and increase the endogenous synthesis of cysteine from methionine. In hypertensive animals and humans, increased production of cysteine would lead to more efficient excretion of metabolic aldehydes, normalizing vascular calcium channels and endothelium function and lowering blood pressure.

Supplementation of vitamin B6 in the diet of fructose induced hypertensive WKY rats has been shown to lower elevated cytosolic calcium, attenuate adverse renal vascular changes and lower blood pressure accompanied by a significantly lowering of tissue aldehyde conjugates^[76]. Vitamin B6 supplementation attenuated hypertension in both sucrose-fed rats and Zucker obese rats, two other models of insulin resistance hypertension^[77]. Vitamin B6 may also act to lower blood pressure by lowering production of excess aldehydes through improved glucose metabolism. Improvement in glucose tolerance after vitamin B6 administration has been reported in gestational diabetes^[78,79].

Prospective studies in humans suggest that low intake of vitamin B6 contributes to risk of

myocardial infarction and coronary heart disease and it has been suggested that dietary supplementation above current recommended daily allowance may attenuate this risk^[80,81]. Oral supplementation of vitamin B6 has also been shown to lower blood pressure in hypertensive patients^[82].

Vitamin C

Ascorbic acid (vitamin C) may also be effective in increasing endogenous levels of cysteine. It is a cofactor in enzyme conversion of cystine to cysteine^[83]. It has been shown to increase insulin stimulated glucose metabolism in healthy subject and type-2 diabetics^[84,85]. Dietary supplementation of ascorbic acid in mice, rats, guinea pigs and humans leads to increased tissue levels of glutathione, the storage form of cysteine^[85-87]. Glutathione is depleted in the tissues of SHR and in human hypertensives^[88,89]. Studies in humans have shown an inverse relationship between vitamin C blood levels and blood pressure^[90-92]. Increased dietary intake of vitamin C is also associated with decreased cardiovascular risk^[93-95]. Dietary supplementation of vitamin C in spontaneously hypertensive rats lowers blood pressure, cytosolic Ca²⁺, plasma insulin, and tissue aldehydes conjugates and prevents adverse renal vascular changes^[96-100]. Vitamin C may act to decrease tissue aldehydes and lower blood pressure by 1) increasing tissues levels of glutathione and cysteine, 2) increasing antioxidant activity, and 3) improving insulin stimulated glucose metabolism.

Vitamin E

Vitamin E (a-tocopherol), being lipid soluble, is found within the phospholipid bilayer of cell membranes where it protects against lipid peroxidation. It has been recognized as one of the major natural antioxidants^[101,102]. Studies have shown vitamin E to have several potentially cardioprotective effects^[103-105]. By decreasing lipid peroxidation, it lowers tissue aldehydes levels and could play a role in reducing elevated blood pressure caused by excess endogenous aldehydes in insulin resistance hypertension. Vitamin E supplementation produces a significant improvement in insulin mediated glucose utilization in health people, type-2 diabetics and essential hypertensive humans^[106,107]. This action of vitamin E may be due to decreased oxidative stress and sparing of tissue glutathione^[108,109]. Glutathione has been shown to increase insulin secretion in patients with impaired glucose tolerance^[110]. It has been well documented that vitamin E levels are lower in essential hypertensive patients, as well as

spontaneously hypertensive rats compared to normotensive^[59,66,111-113]. Low vitamin E levels may be a predictor of preeclampsia in pregnant women^[114]. In SHR, dietary supplementation with vitamin E significantly lowers elevated tissue aldehydes, cytosolic free calcium and blood pressure^[100,115].

Evidence for the direct effect of vitamin E on cardiovascular health in humans is more problematic. The U.S. Nurses' Health Study and the U.S. Health Professionals' Follow-up Study found a 34% and 39% reduction, respectively, in the risk of having a cardiac event for those taking vitamin E supplements. The Iowa Women's Health Study found a 47% reduction in cardiac mortality^[116]. However, randomized control trails have not shown conclusive evidence for primary prevention of hypertension or cardiovascular disease^[117].

Lipoic Acid

Alpha-lipoic acid is a unique short chain fatty acid with two sulphur atoms which are converted to sulphhydryl groups in dihydrolipoic acid, its reduced form. It is metabolically active in both the oxidized and reduced form^[118-120]. Lipoic acid may act similarly to cysteine to bind excess aldehydes for excretion and spare glutathione. Administration of lipoic acid to mice leads to increased tissue levels of cysteine and glutathione^[121].

Lipoic acid functions as a cofactor in key mitochondrial enzymes controlling glucose oxidation^[122]. In insulin resistance, where tissue aldehydes are elevated, lipoic acid increases insulin stimulated glucose metabolism^[123-125]. In one recent multicenter, placebo-controlled trial, Type 2 diabetic patients showed a significant improvement in glucose disposal after 4 weeks of lipoic acid supplementation^[124]. Treatment of insulin-resistant Zucker rats with lipoic acid increased both oxidative and non-oxidative glucose metabolism with improvement in insulin resistance^[125,126].

Alpha-lipoic acid treatment attenuates tissue oxidative stress and lowers plasma lipids, vascular reactivity, alteration in vascular morphology and blood pressure in streptozotocin-induced diabetic rats and deoxycorticosterone acetate salt-induced hypertensive rats. Supplementation with vitamin E and lipoic acid protect the aged rat heart against ischemia reperfusion injury^[127-129]. Dietary lipoic acid supplementation in both SHR and fructose-induced hypertension in WKY rats lowers blood pressure along with insulin, glucose and tissue aldehyde conjugates and prevents adverse renal vascular changes^[130,131]. Lipoic acid may lower blood pressure and protect against cardiovascular disease by lowering tissue aldehydes, decreasing oxidative stress, increasing endogenous cysteine levels and stimulating glucose metabolism.

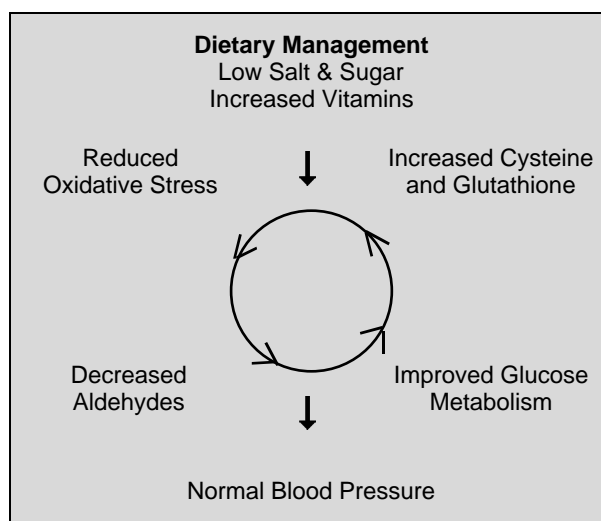


Fig. 2: Dietary Approaches to Control Hypertension

Thus dietary management by lowering salt and sugar intake as well as supplementation with an adequate mix of vitamins can be used to normalize blood pressure (Fig. 2).

Moderate Ethanol Consumption

There is strong epidemiological evidence that consuming 1-2 alcoholic drinks per day in humans is associated with a diminished risk of death from coronary artery disease and ischemic stroke^[132-135]. There is some suggestion that in humans a low ethanol intake of 1-2 drinks may lower blood pressure, while a higher intake (> 30 g alcohol per day) can cause elevated blood pressure^[136-139]. In WKY rats chronic high ethanol intake causes significantly elevated blood pressure along with elevated tissues acetaldehyde levels^[140,141]. In contrast, chronic daily intake of 0.5% ethanol in drinking water (equivalent to 1-2 drinks/day in humans) has been shown to have an anti-hypertensive effect in SHR. In these animals, low ethanol intake actually lowered tissue aldehyde levels along with cytosolic free calcium and systolic blood pressure^[142].

This paradoxical effect of low ethanol intake may be due to a difference in ethanol metabolism at different levels of consumption. Ethanol is metabolized by two pathways; mitochondrial alcohol dehydrogenase (ADH) which produces nicotinamide adenine dinucleotide reduced form (NADH) and by the microsomal ethanol oxidizing system (MEOS) which utilizes nicotinamide adenine dinucleotide phosphate reduced form (NADPH)^[143]. MEOS has a relatively high km for ethanol compared to ADH and thus normally ADH accounts for the bulk of ethanol oxidation at low ethanol levels. The NADH produced may increase tissues levels of cysteine by converting cystine to cysteine through an NADH dependent enzyme^[144].

A low km isoenzyme of alcohol dehydrogenase which operates at very low concentrations of ethanol has been recently identified in human blood vessels^[145]. A metabolic pathway present in blood vessels which is sensitive to low ethanol concentration and capable of producing a reductive environment (NADH) would reduce oxidative stress and prevent lipoprotein oxidation and could account for the protective effect of low ethanol intake on atherosclerosis and coronary artery disease seen in humans. Chronic daily low ethanol intake may also have an anti-hypertensive effect through a similar mechanism^[142].

SUMMARY

Insulin resistance, glucose intolerance and oxidative stress are common features of coronary artery disease, diabetes mellitus and essential hypertension. There is an increasing body of evidence suggesting that these abnormalities develop through a combination of genetic and environment factors. Hypertension is a clinical endpoint of an underlying genetic disorder combined with a nutritional imbalance caused largely by an excessive intake of salt and sugar. Persons with genetic susceptibility would be particularly sensitive to the adverse effect of a high sugar or high salt diet. In such individuals, inadequate nutritional intake of essential vitamins may compound this effect. In healthy people, the present recommended daily allowance (RDA) of vitamins such as B6, E, C and lipoic acid, may be sufficient to maintain normal glucose metabolism and reduced oxidative stress. However, for genetically sensitive individuals, particularly those consuming a high sugar or high salt diet, vitamin supplementation greater than the RDA may be necessary to prevent insulin resistance, oxidative stress and hypertension.

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