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Relationship between diet and blood pressure in a representative Mediterranean population

■ **Summary** *Background* Hypertension is strongly associated with cardiovascular and renal disease. However, despite the efforts made to control hypertension via drug treatment, prevalence of controlled hypertension could be considered

low. *Aim of the study* We performed the present study to investigate dietary habits among groups with different blood pressure status (normotensive, non-medicated hypertensive, medicated hypertensive) and to analyze the association between blood pressure and intakes of selected nutrients in normotensive and non-medicated hypertensive subjects ($n = 1357$), and furthermore in those undergoing hypertension drug treatment ($n = 210$; controlled and non-controlled). *Methods* The present cross-sectional, population-based survey (Gerona, Spain) included cardiovascular risk measurements and analysis of dietary intake with corresponding questionnaires. *Results* Nutrient intake was similar among groups of different blood pressure status after adjusting for sex, age and energy consumption. Multiple linear regression analysis, after adjustment for several confounders, showed that dietary intake of sodium was directly related to blood pressure. The same was seen for the sodium to potassium ratio and both were independent of

hypertension drug treatment. In contrast, an inverse association was observed between blood pressure and dietary calcium intake. Moderate sodium (< 2400 mg Na/d) intake reduced the risk of hypertension by 30 % and 52 % (Odds ratio 0.70; 95 % CI 0.52–0.94, respectively) in normotensive and non-medicated hypertensive subjects. Furthermore, moderate sodium in combination with a calcium intake of more than 800 mg/d reduced the risk of inadequate blood pressure control, by 52 % (Odds ratio 0.48; 95 % CI 0.24–0.95) in subjects undergoing hypertension drug treatment. Controlled hypertension subjects have a significantly higher calcium intake than non-controlled. *Conclusion* These results emphasize the importance of diet and overall of sodium intake as non-pharmacological approach in the prevention and treatment of hypertension.

■ **Key words** blood pressure – diet – nutrients – hypertension – mediterranean

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Introduction

Hypertension is a major risk factor for cardiovascular heart disease and stroke [1, 2]. There is evidence of a relationship between serum lipids and blood pressure [3].

Furthermore, a combination of hyperlipidemia and hypertension increased the risk of CHD in a potentiating rather than in an additive manner [4].

Prevention and management of hypertension are enormous challenges for public health organizations both at an individual and at population level. Prevalence

of hypertension (defined as ≥ 140 mm Hg and/or ≥ 90 mm Hg, or undergoing drug therapy after diagnosis) in Spain is 45.1 %. However, only 15.5 % of patients undergoing drug therapy were controlled [2]. For these reasons, efforts to reduce the prevalence and enhance control of hypertension have been focussing on non-pharmacological approaches that lower blood pressure. Dietary approaches seem to be promising since several nutrients have been inversely associated with blood pressure [5]. Also, dietary intervention has been shown to reduce substantially blood pressure not only in normotensive, but also in hypertensive patients [6].

The aim of the present study was to evaluate dietary habits among groups with different blood pressure status (normotensive, non-medicated hypertensive, medicated hypertensive) in a representative sample of a Spanish Mediterranean population, and to analyze the association between blood pressure and intakes of sodium, potassium, magnesium, and calcium in normotensive and non-medicated hypertensive subjects, and in those undergoing hypertension drug treatment.

Methods

■ Study population

Non-institutionalized Spanish men and women, between the ages of 25 and 74, participated in a population-based cross-sectional study conducted in the province of Gerona from September 1994 to January 1996. Details of the survey methods have been previously described [7]. In brief, 3,000 subjects were randomly selected from the general population of Gerona, according to the 1991 census, with a two stage sampling stratified by sex and five age groups. After excluding census errors, 2,404 eligible subjects were left: 1,748 (72.7 %) agreed to participate. Body mass index was calculated as weight divided by squared height (kg/m^2), and obesity was defined as $\text{BMI} \geq 30$.

■ Blood collection

Blood samples were obtained after a 14-hour fast. Serum was immediately frozen at -120°C in liquid nitrogen for transportation, and stored at -80°C for final conservation. Total cholesterol and high-density lipoprotein (HDL) cholesterol were analyzed by standardized enzymatic methods. Low-density lipoprotein (LDL) cholesterol was calculated by the Friedwald equation. Hypercholesterolemia, and hypertriglyceridemia were defined as total cholesterol ≥ 5.69 mmol/L, and triacylglycerols ≥ 2.27 mmol/L, respectively.

■ Questionnaires

Current alcohol intake was recorded separately by asking participants how many glasses of wine, bottles of beer, and drinks or shots of brandy or similar beverages, were consumed during the previous week. Food intake was reported on a validated 72-hour recall [8]. This questionnaire was administered by a trained interviewer. The 72-hour recall was conducted by a trained interviewer. During the dietary recall interviews participants were requested to describe precisely their food and non-alcoholic beverage intake during the previous three days. Each food listed was characterized by a full description of the usual serving size. Energy consumption and dietary intakes of macro- and micronutrient were calculated from the 72-hour recalls with the software Diet Analysis Nutritionist IV (N Squared Computing, San Bruno, SA). The database of this software was supplemented with 130 food items from Spanish food composition tables.

In brief, the validity of a questionnaire, i. e., its ability to classify study subjects according to a rank of nutrient intake, was reflected by several parameters: a) Pearson's correlation coefficients (0.42 for the 72-hour recall); b) intraclass correlation coefficients (0.55 for the 72-hour recall), and c) the proportion of correct classification (average of 37 % for the 72-hour recall) into the same and extreme quartile and that of misclassification (average 5.3 % for the 72-hour recall). Furthermore, the range of correlation coefficients between dietary intakes of protein, β -carotene, and selenium and its corresponding biomarkers in plasma, were comparable with those found by other dietary assessment methods [8].

A precision scale of easy calibration was used for weight measurement. Readings were rounded to 200 g. Individuals wore underwear. Height was measured in the standing position and measurements rounded to 0.5 cm. Body mass index (BMI) was determined as weight divided by squared height (kg/m^2).

Blood pressure (BP) determination was performed using a periodically calibrated mercury sphygmomanometer. The operator followed a certification process in the measurement technique at central laboratory and all determinations were made by the same person. A cuff adapted to upper arm perimeter (young, adult, obese) was selected for each participant, who was seated with the arm palm upwards and elbow resting on the table. Radial pulse was taken for 30 seconds. Measurements were performed after 5 minutes rest to avoid possible alterations produced by anxiety or the exercise. Systolic blood pressure (SBP) was recorded at the start of Korotkoff phase I and diastolic (DBP) at the start of Korotkoff phase V. Two measurements were taken: the interval between the first and second was at least 20 minutes. The value used was the arithmetic mean of both determinations.

The hypertension questionnaire of the MONICA-WHO study (World Health Organization) was used, in which participants were asked whether any health-care personnel had informed them that their blood pressure was high and whether they had taken any control medication in the previous two weeks. From these data and the blood pressure found during examination (i.e., mean of these measurements obtained with standard methods by certified operators), the participants were classified as normotensive (systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg), non-medicated hypertensive (systolic blood pressure \geq 140 mm Hg and/or diastolic blood pressure \geq 90 mm Hg) and medicated hypertensive. The latter were considered controlled when systolic blood pressure < 140 mm Hg and diastolic blood pressure < 90 mm Hg.

Statistical analysis

Analysis of means by a general linear model (GLM) was used to calculate the main characteristics of the participants. Analysis of co-variance (ANOVA) was used to estimate dietary intake according to blood pressure status (normotensive, non-medicated hypertensive, medicated hypertensive). A post hoc Bonferroni correction for multiple comparisons was carried out to determine differences in nutrient intake between controlled and non-controlled hypertension medicated groups. The odds ratio of inadequate blood pressure control (systolic blood pressure \geq 140 mm Hg and/or diastolic blood pressure \geq 90 mm Hg) for recommended daily calcium and moderate sodium intakes was analyzed with logistic regression adjusted for sex, age, BMI, smoking and alcohol drinking status.

Linear regression analysis was carried out after adjusting for the above mentioned potential confounders to analyze the association of systolic and diastolic blood pressures with sodium, calcium, potassium, and magnesium intakes. To analyze the association of blood pressure and nutrient intake independently of hypertension drug treatment, we performed linear and logistical regression analysis for two groups. First in normotensive and non-medicated hypertensive participants ($n = 1357$) and second in medicated hypertensive participants ($n = 210$). Furthermore, medicated hypertensive participants were distinguished in hypertension controlled and non-controlled. Analysis of the data was conducted using SPSS for Windows (version 9.0) statistical software package (SPSS Inc, Chicago, IL). In all statistical tests performed P values of < 0.05 were considered significant.

Results

Main characteristics of the subjects are shown in Table 1. Generally, more men than women were hypertensive, and hypertensive subjects were significantly older than normotensive. Significantly more normotensive than hypertensive subjects smoked, whereas less medicated hypertensive subjects consumed alcohol in comparison to normotensive and non-medicated hypertensive subjects. Furthermore, significantly more non-medicated and medicated hypertensive subjects had higher LDL-cholesterol and HDL-cholesterol than normotensive subjects. Also, more hypertensive subjects were obese.

More men than women were aware of hypertension, but did not undergo drug therapy (Table 1). Cardiovascular risk factors were the same among medicated and non-medicated hypertensive subjects, with the exception for obesity.

Age- and sex-adjusted energy consumption was significantly higher among non-medicated hypertensive than medicated hypertensive subjects. Further adjustment for energy intake showed no differences of macronutrient and micronutrient intake among groups (Table 2). Alcohol consumption was significantly higher in the non-medicated hypertensive than in the medicated hypertensive group.

Multiple linear regression analyses revealed a highly significant inverse correlation between calcium intake and systolic and diastolic blood pressure in the non-hypertension medicated study population (Subjects on hypertension drug treatment not included.) (Table 3). Sodium intake and the sodium to potassium ratio were directly associated with diastolic blood pressure, whereas magnesium intake showed a direct association with systolic blood pressure. Most importantly, the cor-

Table 1 Characteristics of participants

	Normotensive $n = 986$	Non-medicated hypertensive $n = 371$	Medicated hypertensive $n = 210$
Men (%)	47.7	53.1	43.3
Women (%)	52.3	46.9	56.7
Age (years)	45.1 \pm 12.5	58.6 \pm 11.1	62.0 \pm 9.6
Body mass index	25.7 \pm 4.3	27.8 \pm 4.2	28.7 \pm 4.4
Smoker (%)	30.2	15.4	9.0
Alcohol consumer (%)	61.3	61.5	45.2
Hypertriglyceridemia (%) ¹	5.9	9.7	9.7
LDL cholesterol risk (%) ²	31.4	47.7	47.8
HDL cholesterol risk (%) ³	14.0	16.1	19.2
Obesity (%) ⁴	13.4	24.7	34.9

¹ Hypertriglyceridemia: \geq 2.27 mmol/L

² LDL cholesterol risk: LDL cholesterol > 4.15 mmol/L

³ HDL cholesterol risk: HDL cholesterol for men < 0.91 mmol/L, and for women < 1.09 mmol/L

⁴ Obesity: BMI \geq 30

relation between blood pressure and mineral intake was not only seen in the non-hypertension medicated study population but was also found in the medicated hypertensive subjects (Table 3).

Age- and sex-adjusted energy consumption and nutrient intake of controlled and non-controlled hyperten-

Table 2 Average daily age- and sex-adjusted energy and nutrient intake (further adjusted for energy consumption) according to hypertension status

	Normotensive n = 986	Non-medicated hypertensive n = 371	Medicated hypertensive n = 210
Energy (MJ)	9.12	9.37 ¹	8.90
Carbohydrates (%) [*]	42.9	42.5	42.8
Fat (%) [*]	35.3	35.4	34.9
Protein (%) [*]	21.8	22.1	22.3
Saturated fat (%) [*]	11.9	11.8	11.6
Unsaturated fat (%) [*]	23.4	23.6	23.3
Cholesterol (mg)	407.8	413.3	424.2
Dietary fiber (g)	17.5	17.4	17.3
Vitamin C (g)	161.5	159.5	155.6
β-Carotene (mg)	1536.6	1567.7	1538.6
α-Tocopherole	4.7	4.6	4.6
Potassium (g)	3641	3628	3641
Calcium (mg)	987.2	953.8	963.8
Sodium (mg)	2141	2216	2113
Na/K	0.60	0.62	0.59
Alcohol (g/d)	24.1	27.7	18.6

¹ $p < 0.05$ between hypertension non-medicated and hypertension medicated (Bonferroni)

^{*} In percentage of energy intake

Table 3 Association between systolic (SBP), diastolic (DBP) blood pressures and selected mineral intake

Variable	SBP			DBP		
	B	SE	p	B	SE	p
Normotensive and non-medicated hypertensive subjects (n = 1357)						
*Model 1	$r^2 = 0.361$			$r^2 = 0.230$		
Na/K	3.11	1.84	0.090	3.32	1.20	0.006
*Model 2	$r^2 = 0.374$			$r^2 = 0.245$		
Calcium (10 mg)	-0.0036	0.002	0.020	-0.0023	0.001	0.018
Potassium (10 mg)	-0.0016	0.001	0.094	-0.0001	0.001	0.872
Sodium (10 mg)	0.0006	0.001	0.316	0.0010	0.000	0.008
Magnesium (10 mg)	0.0030	0.011	0.006	0.0119	0.007	0.111
Medicated hypertensive subjects (n = 210)						
*Model 1	$r^2 = 0.091$			$r^2 = 0.054$		
Na/K	17.660	6.853	0.011	7.627	3.682	0.040
*Model 2	$r^2 = 0.117$			$r^2 = 0.096$		
Calcium (10 mg)	-0.0116	0.006	0.057	-0.0068	0.003	0.034
Potassium (10 mg)	-0.0016	0.003	0.621	0.0021	0.002	0.872
Sodium (10 mg)	0.0063	0.002	0.003	0.0037	0.001	0.001
Magnesium (10 mg)	0.0125	0.038	0.742	-0.0267	0.200	0.186

* Adjusted for sex, age, BMI, smoking and drinking status

sive subjects, is shown in Table 4. No significant differences in energy and macronutrient intake between both groups were observed. However, the intake of polyunsaturated fatty acids was significantly lower and intake of calcium significantly higher in the controlled medicated hypertension group than in the non-controlled medicated hypertension group. The ratio of sodium to potassium intake in the controlled group was lower than in the non-controlled group; however, this difference did not reach statistical significance ($p = 0.09$).

Consuming less than 2400 mg of sodium, or less than 2400 mg sodium, but more than 800 mg calcium, reduced the risk of subjects of the non-hypertension medicated study population of being hypertensive to 0.70 and 0.68, respectively (Table 5) in comparison to subjects with higher sodium and/or less calcium intake. The relative risk of inadequate blood pressure control (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg) for subjects undergoing drug therapy was a dependent on the sodium and calcium intake: a reduction of the sodium intake below 2400 mg in combination with a calcium intake of more than 800 mg/d reduced this risk by 52 % (Table 5). Dietary intake of magnesium (≥ 350 mg/d for men and ≥ 280 mg for women) and potassium (≥ 3500 mg/d) were not significantly related to hypertension.

Table 4 Average daily age- and sex-adjusted energy and nutrient intake of non-controlled and controlled medicated hypertensive subjects (n = 210)

	Controlled n = 49	Non-controlled n = 161
Energy (MJ)	8.46	8.42
Carbohydrates (%) [*]	42.9	43.5
Fat (%) [*]	34.5	34.3
Protein (%) [*]	22.6	22.2
Saturated fat (%) [*]	11.7	10.9
Unsaturated fat (%) [*]	22.8	23.4
Cholesterol (mg)	377.2	380.9
Dietary fiber (g)	18.2	18.0
Vitamin C (g)	171.7	161.5
β-Carotene (mg)	1606.8	1523.3
α-Tocopherol	4.6	4.7
Potassium (g)	3.7	3.5
Calcium (mg)	975.6 ¹	884.5
Magnesium	359.3	350.5
Sodium (mg)	1755	1889
Na/K	0.48	0.54
Alcohol (g/d)	15.1	15.0

¹ Significantly different (p < 0.05) between groups.

^{*} In percentage of energy intake

Table 5 Odds ratio and 95 % confidence interval of hypertension according to certain amounts of calcium, sodium, magnesium and potassium intake

	Odds ratio	(95 % confidence interval)
Normotensive and non-medicated hypertensive subjects (n = 1357)		
Calcium RDA ¹	0.85	(0.63–1.13)
Moderate sodium intake ²	0.70	(0.52–0.94)
Moderate sodium intake + calcium RDA ³	0.67	(0.50–0.91)
Magnesium RDA ⁴	0.91	(0.63–1.31)
Potassium RDA ⁵	1.05	(0.79–1.39)
Medicated hypertensive subjects (n = 210)		
Calcium RDA ¹	0.57	(0.27–1.19)
Moderate sodium intake ²	0.56	(0.22–1.39)
Moderate sodium intake + calcium RDA ³	0.48	(0.24–0.95)
Magnesium RDA ⁴	0.59	(0.38–1.47)
Potassium RDA ⁵	0.75	(0.25–1.41)

Odds ratio was adjusted for age, sex, BMI and alcohol and smoking status.

¹ Intake of ≥ 800 mg/d

² Intake of < 2400 mg/d

³ Intake of calcium ≥ 800 mg/d and sodium of < 2400 mg/d

⁴ Intake of magnesium ≥ 350 mg/d for men and ≥ 280 mg for women

⁵ Intake of potassium ≥ 3500 mg/d

Discussion

In this study, we analyzed the effects of nutrients on blood pressure in a representative sample of a Mediterranean population, specifically grouped for blood pressure status: normotensive, non-medicated hypertensive and medicated hypertensive. Nutrient intake was similar among normotensive, non-medicated hypertensive,

and medicated hypertensive subjects. Blood pressure was related to calcium and sodium intake and to the sodium to potassium ratio, but independent of drug treatment. The most important finding of this study is that moderate sodium intake reduced the risk of inadequate blood pressure control (systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg) in normotensive and non-medicated hypertensive subjects by 30 %. Moreover, this dietary regimen in combination with a calcium intake above 800 mg/d was also associated with lower blood pressure in already diagnosed and treated subjects. In the latter subjects we found a risk reduction of 44 %.

Hypertension is strongly associated with cardiovascular and renal disease [9]. The incidence of other cardiovascular risk factors in hypertensive subjects in the present study was high. Hypertension in addition with other cardiovascular risk factors increase the risk of CHD in a potentiative rather than in an additive manner [4]. This reflects the seriousness of hypertension for public health policy. However, despite the efforts made to control hypertension via drug treatment, prevalence of controlled hypertension could be considered low. Therefore, efforts to reduce hypertension have focused on non-pharmacological approaches to reduce blood pressure in addition to drug treatment. The importance of the diet to reduce blood pressure has been shown previously [6]. In the present study we observed a very similar overall nutrient intake pattern among all groups with different blood pressure status. However, medicated hypertensive subjects showed lower sodium intake and alcohol consumption than normotensive and non-medicated hypertensive subjects. Reducing sodium intake and alcohol consumption are two main recommendations for hypertensive patients established by national guidelines [10]. These dietary guidelines seem to have actually affected the behavior of the informed patients, and resulted in the observed lower sodium intake and alcohol consumption in the hypertension medicated group. However, the lack of significant differences in the nutrient intake among the groups suggest that either dietary recommendations by the physician are too limited or incomprehensive, therefore not translated into a change of dietary habits, or the patients do not follow these recommendations.

Intakes of several nutrients have been associated with hypertension. Particularly dietary intakes of sodium, calcium, magnesium, and potassium affected blood pressure [5]. There is an abundance of scientific evidence demonstrating a direct correlation between sodium intake, sodium to potassium ratio and blood pressure [11, 12]. Furthermore, ecological analyses indicate that the association between sodium intake and stroke risk is stronger than the corresponding relationship between sodium intake and blood pressure level which may also imply a direct effect of sodium intake

and stroke risk [13, 14]. In the present study, sodium intake and the sodium to potassium ratio were directly related to diastolic blood pressure in normotensive and non-medicated hypertensive subjects. Additionally, in medicated hypertensive patients (on an average 65 years) a direct association between sodium intake, sodium to potassium ratio and systolic and diastolic blood pressures was observed. This is particularly of interest since reducing overall sodium intake in older hypertensive subjects substantially lowers blood pressure [15]. According to our results, systolic blood pressure increased by 3.15 mm Hg and diastolic blood pressure by 1.85 mm Hg with each 500 mg of sodium intake in medicated hypertensive patients. In clinical trials, 100 mmol reduction of dietary sodium intake was associated with an average reduction of 1.4 mm Hg to 2.5 mm Hg in diastolic blood pressure [16]. In the present study a reduction of sodium intake below 2400 mg/d decreased significantly the risk of having systolic and/or diastolic blood pressures above 90 mm Hg and 140 mm Hg in normotensive and non-medicated hypertensive subjects by 30 %, and, although not statistically significant, by 44 % in subjects undergoing hypertension drug treatment. These findings underline the importance of reduced sodium intake, particularly in elderly people.

Lower blood pressure as a response to reduced dietary sodium intake is strongly related to sodium sensitivity [17]. Furthermore, it has been shown that age is directly associated with sodium sensitivity [18, 19] and this association appears to be stronger in hypertensive than normotensive subjects [18]. In the present study, we observed stronger associations of systolic and diastolic blood pressures and sodium intake in medicated hypertensive than in normotensive and non-medicated hypertensive participants. This finding might be explained by the higher age and salt sensitivity of medicated hypertensive subjects.

Urinary samples were not collected in the present study although this would have been the most accurate way to estimate dietary sodium intake. Because dietary assessments generally underestimate sodium intake, results of the association between sodium intake and blood pressure, presented in this study, have to be cautiously interpreted. Although discretionary sodium use (table and cooking) is one reason for the underestimation of sodium intake, previous studies suggest that this did not account for the vast majority of sodium intake [20].

Low dietary calcium intake is associated with an increased prevalence of hypertension in several epidemiological studies [21]. In the present study, systolic and diastolic blood pressures were inversely associated with calcium intake in the normotensive and non-medicated hypertensive group and also in the medicated hypertensive group. However, in the latter group the inverse association between systolic blood pressure and calcium intake was not statistically significant ($p = 0.057$). Furthermore, moderate sodium in combination with a calcium intake of more than 800 mg/d reduced the risk of inadequate blood pressure control, by 52 % in subjects undergoing hypertension drug treatment. Additionally, controlled hypertension subjects have a significantly higher calcium intake than non-controlled. These results are in line with previous findings on the role of calcium on blood pressure.

The association of sodium and calcium intake with blood pressure was moderate in the present study. However, Cooke and colleagues [22] concluded that a 2 mm Hg reduction in diastolic blood pressure could reduce the incidence of coronary heart disease by up to 6 % and the incidence of stroke and transient ischemic attack by up to 13 %. A reduction of 1 % to 3 % in the average blood pressure of the Spanish population could bring about a decline in the prevalence of hypertension of 5 % to 7 % [2]. Therefore, moderate changes in dietary habits may have an important impact on high blood pressure related diseases.

In conclusion, the sodium to potassium ratio and dietary intakes of calcium and sodium were related to blood pressure independently of hypertension drug treatment. Furthermore, moderate sodium (< 2400 mg Na/d) intake reduced the risk of hypertension in normotensive and non-medicated hypertensive subjects. Moreover, moderate sodium in combination with a calcium intake of more than 800 mg/d reduced the risk of inadequate blood pressure control significantly in subjects undergoing hypertension drug treatment. These findings emphasize the importance of diet as a non-pharmacological approach on the prevention and treatment of hypertension.

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