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Familial predisposition to hypertension and the association between urinary sodium excretion and blood pressure in a population-based sample of young adults

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Abstract

The reasons for the inconsistent association between salt consumption and blood pressure levels observed in within-society surveys are not known. A total of 157 normotensive subjects aged 18 to 35 years, selected at random in a cross-sectional population-based survey, answered a structured questionnaire. They were classified as strongly predisposed to hypertension when two or more first-degree relatives had a diagnosis of hypertension. Anthropometric parameters were obtained and sitting blood pressure was determined with aneroid sphygmomanometers. Sodium and potassium excretion was measured by flame spectrophotometry in an overnight urine sample. A positive correlation between blood pressure and urinary sodium excretion was detected only in the group of individuals strongly predisposed to hypertension, both for systolic blood pressure ($r = 0.51$, $P<0.01$) and diastolic blood pressure ($r = 0.50$, $P<0.01$). In a covariance analysis, after controlling for age, skin color and body mass index, individuals strongly predisposed to hypertension who excreted amounts of sodium above the median of the entire sample had higher systolic and diastolic blood pressure than subjects classified into the remaining conditions. The influence of familial predisposition to hypertension on the association between salt intake and blood pressure may be an additional explanation for the weak association between urinary sodium excretion and blood pressure observed in within-population studies, since it can influence the association between salt consumption and blood pressure in some but not all inhabitants.

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- Familial predisposition to hypertension
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- Salt sensitivity

Introduction

The role of dietary salt on the pathogenesis of essential hypertension and the effect of salt-restricted diets on the treatment of already hypertensive individuals are surrounded by controversies (1-4). One of them is the discrepancy between the strong correlation between salt consumption and blood pressure observed in studies conducted across societies (ecological model) and the weak association observed in within-society surveys (cross-sectional model). A measurement bias of the usual amount of salt consumption, the regression dilution bias (5), and an overadjustment for body mass index in multivariate models (6) have been proposed to explain the weakness of the association between salt and blood pressure in within-society surveys. We hypothesized that the inheritable difference in the response to salt load, similar to that identified in experimental studies of salt manipulation (7-10), could be an additional explanation for the inconsistent association between salt consumption and blood pressure observed in cross-sectional investigations.

Material and Methods

A total of 1089 subjects (92% of those eligible), identified by cross-sectional, population-based, multi-stage probability sampling, were selected in Porto Alegre, a city with more than 1.2 million inhabitants in southern Brazil, from 1990 to 1992. A more detailed description of this survey has been published elsewhere (11,12). Data were collected with a structured and pre-tested questionnaire after obtaining informed consent. The participants were questioned about their knowledge of relatives with a medical diagnosis of hypertension. Sitting blood pressure was determined with aneroid sphygmomanometers (Diasyst - Montagem e Comércio Ltda., São Paulo, SP, Brazil), following standardized recommendations (13), using a cuff sized for non-obese adults. The sphygmomanometers were calibrated periodically against mercury sphygmomanometers. The average of two determinations obtained on the day preceding the overnight urine collection and corrected according to arm circumference (14) was used in the analysis. A sample of 398 individuals chosen at random collected an overnight (12 h) urine sample at home, following detailed oral and written instructions. Urinary sodium and potassium concentration was measured by flame spectrophotometry (15) and the total amount excreted in 12 h was calculated according to urinary volume. In order to study individuals prior to the development of hypertension, we restricted our final sample to 157 subjects aged 18 to 35 years who declared not to have a medical diagnosis of hypertension.

The participants who informed to have two first-degree relatives with a medical diagnosis of hypertension were classified as strongly predisposed to hypertension. The individuals in all other conditions were classified as not strongly predisposed. In approximately 50% of the participants selected for this analysis, the history of familial predisposition to hypertension could be checked directly with their parents or first-degree relatives and, in most cases, confirmed the information obtained during the interview. In the remaining cases, the first-degree relatives were not evaluated because they could not be reached or because they had died. The correlation between the amount of sodium and potassium excreted in 12 h and both systolic and diastolic blood pressure was evaluated by the Pearson correlation coefficient in the whole sample and in groups stratified by familial predisposition to hypertension. Systolic and diastolic blood pressure of groups characterized by familial predisposition (yes or no) and the amount of sodium excreted in 12 h (classified as more or less than the median excretion of the whole sample) were compared by analysis of covariance, allowing for interaction and

controlling for skin color, age and body mass index. A P value of 0.05 or less was regarded as statistically significant.

Results

A total of 27 individuals (17.2%) reported having at least two first-degree relatives with a medical diagnosis of hypertension, and constituted the group strongly predisposed to hypertension. The remaining 130 subjects (82.8%) were classified as not strongly predisposed. The characteristics of the subjects classified by familial predisposition to hypertension are presented in Table 1. The participants with familial predisposition were older, had more frequently a non-white skin color, and had higher systolic and diastolic blood pressure and body mass index. Almost all individuals with a non-white skin color were mulattoes or blacks. The remaining characteristics had similar distribution in both groups.

A direct and positive linear correlation between overnight urinary sodium excretion and systolic and diastolic blood pressure was observed only in individuals strongly predisposed to hypertension (Table 2). This correlation was absent in the whole sample and when the familial predisposition was defined by the presence of only one first-degree relative with a medical diagnosis of hypertension (data not shown).

The median overnight urinary sodium excretion for the whole sample was 61.0 mEq. The individuals excreting this amount or less were arbitrarily classified as excreting low amounts of sodium. Those excreting amounts higher than the median were classified as excreting high amounts of sodium. Systolic and diastolic blood pressures were significantly higher in subjects with both strong familial predisposition and high overnight urinary sodium excretion compared to individuals with strong predisposition excreting low amounts of sodium, and individuals not strongly predisposed excreting either low or high amounts of sodium, after controlling for age, skin color and body mass index (Figure 1).

Table 1 - Characteristics of the groups classified according to familial predisposition to hypertension.

Data are reported as means ± SD or as N (%). NS: Comparison between groups was not significant (chi-square test).

Characteristics	Familial predisposition to hypertension		P
	Strong (N = 27)	Not strong (N = 130)	
Age (years)	28 ± 5.6	25 ± 5.0	0.02
Male	9 (33.3)	62 (47.7)	NS
More than 6 years at school	14 (51.9)	86 (66.2)	NS
Non-whites	6 (22)	12 (9)	0.05
Systolic blood pressure (mmHg)	124 ± 17.4	118 ± 11.9	0.03
Diastolic blood pressure (mmHg)	77 ± 15.1	72 ± 10.4	0.05
Heart rate (bpm)	75 ± 8.6	77 ± 10.6	NS
Body mass index (kg/m^2)	24.7 ± 4.6	23.0 ± 3.7	0.05
Waist-hip ratio	0.8 ± 0.07	0.8 ± 0.07	NS
Overnight sodium (mEq)	68.2 ± 32.4	67.5 ± 36.6	NS
Overnight potassium (mEq)	14.8 ± 8.8	14.3 ± 7.8	NS
Alcohol consumption (g per day)	12.0 ± 24.1	13.3 ± 45.0	NS

Table 2 - Pearson correlation coefficient between overnight urinary sodium excretion and systolic and diastolic blood pressure in individuals classified by familial predisposition to hypertension.

NS: Not significant.

Familial predisposition	Systolic blood pressure		Diastolic blood pressure	
	r	P	r	P
Strong (N = 27)	0.51	<0.01	0.50	<0.01
Not strong (N = 130)	-0.08	NS	-0.16	NS

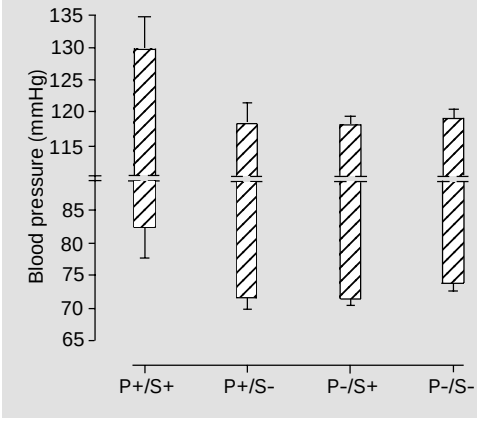

Figure 1 - Influence of familial predisposition to hypertension and sodium load on systolic and diastolic blood pressure of young, non-hypertensive adults. Systolic pressure: F = 4.64, P = 0.033; diastolic pressure: F = 7.61, P = 0.007, for the interaction between familial predisposition and sodium load, adjusted for age, skin color and body mass index. P: Familial predisposition, + = strong, - = not strong; S: sodium load, + = above the median, - = below the median.

Discussion

In this investigation, conducted on a population-based random sample of young, non-hypertensive, free-living adults from an urban region in southern Brazil, we observed that the association between the overnight urinary excretion of sodium and systolic and diastolic blood pressure was influenced by familial predisposition to hypertension independently of other risk factors for hypertension. The subjects with at least two first-degree relatives with hypertension had higher blood pressure, even if not in the hypertensive range, only when they were excreting larger amounts of sodium during the night following the day of blood pressure measurement. The amount of sodium excreted during this night was not associated with blood pressure in individuals without a strong history of hypertension among their relatives. These associations were not biased by the fact that the hypertension-prone individuals were older, had a higher body mass index and were more frequently non-white, since these potential biases were controlled in the multivariate analysis.

Our study has certain limitations which merit discussion and require that their results should be regarded as preliminary findings. First, the overnight urinary output of sodium has not been recognized as an indicator of the pattern of sodium consumption. It has been proposed that it is necessary to measure urinary sodium excretion for 5 to 14 days to identify the usual pattern of salt consumption in order to study its association with blood pressure (16). Our findings, however, were based on an almost simultaneous determination of blood pressure and sodium ingestion, i.e., blood pressure was measured on the day preceding the overnight urinary measurement, when the sodium excreted during the following night was being consumed.

The positive correlation observed in subjects strongly predisposed to hypertension is in agreement with the interpretation that there is an instantaneous association between blood pressure and urinary sodium excretion (2,17-19), and with the theory of "pressure diuresis" (20). The subjects with a familial predisposition to hypertension would require higher blood pressure, and consequently higher renal flow, to be able to eliminate a sodium load. As a consequence, this would result in extracellular volume expansion, an increase in cardiac output and subsequently in vascular peripheral resistance. The recurrence of this phenomenon along the years would predispose to arteriolar hypertrophy and sustained a blood pressure rise (21). This mechanism could be synergistic with other causes of arteriolar hypertrophy, such as those induced by norepinephrine, vasopressin, angiotensin, insulin and others (22,23).

The restriction to young normotensive adults employed in our analysis allowed us to observe the association between blood pressure and urinary sodium excretion before the development of hypertension, which may attenuate this association due to the development of an autonomous elevation in peripheral resistance.

The subjects with a lower intensity of familial predisposition to hypertension, defined by the presence of only one first-degree relative with hypertension, did not present any trend towards a positive correlation between urinary sodium excretion and blood pressure in our study. This observation is in agreement with the interpretation that the predisposition to hypertension is only identified through interviews when two first-degree relatives are hypertensive (24). The weakness of the measurement of familial predisposition to hypertension through questionnaires has been recognized as a potential measurement bias, and cannot be excluded in our survey. The fact that in approximately 50% of the participants the history of hypertension could be confirmed by the next of kin suggests that our main findings are not biased. Anyway, if a proportion of those

classified as not strongly predisposed to hypertension had real predisposition (one unknown relative with hypertension), the measurement bias would be on the conservative side, since it would weaken the magnitude of the association. This reason would also explain the similarity observed between the groups without and with intermediate familial predisposition to hypertension.

In conclusion, familial predisposition to hypertension can be an additional explanation for the weak association between urinary sodium excretion and blood pressure in within-population studies, since it can influence the association between salt consumption and blood pressure in some but not all inhabitants.

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