

Autonomic abnormalities demonstrable in young normotensive subjects who are children of hypertensive parents

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Abstract

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Although a slightly elevated office blood pressure (BP) has been reported in several studies, little is known about the prolonged resting blood pressure, heart rate (HR) and baroreflex sensitivity (BRS) of prehypertensive subjects with a family history of hypertension. Office blood pressure, prolonged resting (1 h) BP and HR were measured in 25 young normotensives with a positive family history of hypertension (FH+) and 25 young normotensives with a negative family history of hypertension (FH-), matched for age, sex, and body mass index. After BP and HR measurements, blood samples were collected for the determination of norepinephrine, plasma renin activity and aldosterone levels, and baroreflex sensitivity was then tested. Casual BP, prolonged resting BP and heart rate were significantly higher in the FH+ group ($119.9 \pm 11.7/78.5 \pm 8.6$ mmHg, $137.3 \pm 12.3/74.4 \pm 7.9$ mmHg, 68.5 ± 8.4 bpm) compared to the FH- group ($112.9 \pm 11.4/71.2 \pm 8.3$ mmHg, $128.0 \pm 11.8/66.5 \pm 7.4$ mmHg, 62.1 ± 6.0 bpm). Plasma norepinephrine level was significantly higher in the FH+ group (220.1 ± 104.5 pg/ml) than in the FH- group (169.1 ± 63.3 pg/ml). Baroreflex sensitivity to tachycardia (0.7 ± 0.3 vs 1.0 ± 0.5 bpm/mmHg) was depressed in the FH+ group ($P < 0.05$). The FH+ group exhibited higher casual blood pressure, prolonged resting blood pressure, heart rate and plasma norepinephrine levels than the FH- group ($P < 0.05$), suggesting an increased sympathetic tone in these subjects. The reflex tachycardia was depressed in the FH+ group.

Key words

- Heart rate
- Blood pressure
- Baroreflex sensitivity
- Family history of hypertension

Introduction

In a previous study (1), we demonstrated that young normotensives with a positive family history of hypertension (FH+) have higher total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglyceride levels, as well as higher office blood pressure when compared with young normotensives with a

negative family history of hypertension (FH-). A slightly elevated office blood pressure in normotensive subjects with a family history of parental hypertension has been reported (2-4). This blood pressure elevation may be considered as a permanent abnormality characterizing a prehypertensive stage early in life (1,5). Since white-coat hypertension may be present in this population, a

prolonged resting continuous blood pressure measurement in the absence of a doctor or nurse may be useful to better characterize the blood pressure behavior of this population. Increased sympathetic activity may be a possible mechanism for alterations in blood pressure regulation (6). Blood pressure regulation largely depends on baroreflex function, but the reflex tachycardia by nitroglycerine injection has not yet been studied in subjects with a family history of parental hypertension. The goal of the present study was to evaluate the prolonged resting heart rate, blood pressure, norepinephrine level and baroreflex sensitivity (BRS) of young normotensives with a positive family history of hypertension.

Material and Methods

Twenty-five young normotensives with a positive family history of hypertension (FH+) and 25 young normotensives with a negative family history of hypertension (FH-) were included in this study. They were healthy normotensive medical students whose office blood pressure was less than 140/90 mmHg on two different occasions. The parents with a positive or negative history of hypertension were identified by evidence of antihypertensive treatment in their medical records or by direct blood pressure measurements. A positive family history of hypertension was considered to be present when at least one of the parents was hypertensive. The groups with FH+ and FH- were matched for age, gender, race and body mass index (Table 1).

After an overnight fast, subjects were admitted to the laboratory and continuous arterial blood pressure was measured noninvasively using the Finapres finger-cuff method for one hour in the supine position (baseline measurements). Blood samples were then collected for measurements of noradrenaline by high performance liquid chromatography, and of plasma renin activity and aldosterone levels by radioimmunoassay. After blood pressure and heart rate recovery, BRS to unloading of the baroreceptors was evaluated by recording cardiac acceleration in response to nitroglycerin-induced fall in blood pressure. BRS to loading of the baroreceptors was evaluated by recording cardiac slowing in response to acute hypertension induced by phenylephrine (bolus of 100 µg). Baroreflex slopes were calculated by plotting the heart rate (bpm) against the preceding peak systolic arterial pressure (mmHg).

Results are reported as means \pm SD. Data concerning categorical variables (gender, race) were analyzed by the chi-square test. The intergroup differences in mean values were assessed by the Student *t*-test. A value of $P < 0.05$ was taken as the level of statistical significance. All participants signed an informed consent approved by the Ethical Committee from the Hospital das Clínicas, University of São Paulo.

Results

Mean office blood pressure, resting continuous arterial blood pressure and heart rate measured noninvasively by the Finapres finger-cuff method were higher in the offspring of hypertensive families than in the offspring of normotensive families (Table 2). Plasma noradrenaline was higher ($P < 0.05$) in the FH+ group (220.1 ± 104.5 pg/ml) than in the FH- group (169.1 ± 63.3 pg/ml). Plasma renin activity (1.1 ± 1.0 vs 1.0 ± 0.9 ng ml⁻¹ h⁻¹) and aldosterone levels (10.7 ± 2.9 vs 9.2 ± 3.8 ng/ml) did not differ between the FH+ and FH- groups. Baroreflex sensitivity to

Table 1 - Age, gender, race and body mass index (BMI) of the subjects studied.

Variables	Negative family history of hypertension (N = 25)	Positive family history of hypertension (N = 25)
Age (years)	20.9 \pm 2.1	20 \pm 1.5
Gender	16 males, 9 females	18 males, 7 females
Race	18 whites, 7 orientals	20 whites, 5 orientals
BMI, kg/m ²	22.1 \pm 2.1	22 \pm 2.2

tachycardiac responses was significantly ($P < 0.05$) depressed in the FH+ group (0.7 ± 0.3 bpm/mmHg) when compared with the FH- group (1.0 ± 0.5 bpm/mmHg). Baroreflex sensitivity to bradycardiac responses (1.1 ± 0.5 bpm/mmHg vs 1.2 ± 0.5 bpm/mmHg) did not differ between the FH+ and FH- groups.

Discussion

The major finding of this study was that young normotensives with a positive family history of hypertension had not only higher office blood pressure but also increased prolonged resting heart rate and blood pressure. Elevated office blood pressure in young normotensives with a positive family history of hypertension has been frequently reported; however, the association with prolonged resting elevated systolic and diastolic blood pressures observed here is new. Indeed, we observed a difference in systolic and diastolic office blood pressures of approximately 7 mmHg between groups and the difference in systolic (9 mmHg) and diastolic (8 mmHg) blood pressures persisted during prolonged resting measurement (1 h). Since the differences obtained with the two methods were similar, the values provided by the Finapres method seem to reflect the real pressure values, even when inaccuracies may occur during prolonged measurement (7). The increase in blood pressure during prolonged resting suggests a true sustained elevated blood pressure, characterizing a permanent abnormality in the prehypertensive stage, rather than a white-coat hypertension reaction during casual measurement as previously thought (8). Moreover, the higher heart rate during prolonged resting, associated with a 30% increase in plasma norepinephrine levels, suggests an increased sympathetic activity in the prehypertensive stage in the group with a positive family history of hypertension. Increased norepinephrine levels, indicating an enhanced sympathetic activity,

were described by Masuo et al. (9) in a longitudinal study involving young nonobese men that presented a rise $\geq 10\%$ in blood pressure after ten years of age.

Regarding the baroreflex control heart rate, although the FH+ subjects had a depressed tachycardiac response to nitroglycerine, they showed a normal bradycardiac response to phenylephrine. Depressed baroreflex sensitivity to bradycardia was described by Iwase et al. (10) when the phenylephrine test was used, but was not detected by Ditto and France (11) and Ravogli et al. (5), when the neck chamber method was used. Our data indicating an impairment of the baroreflex control of the tachycardia, but not of bradycardia, is somewhat unexpected, since a parasympathetic mechanism is primarily involved in baroreflex control of heart rate, while control of vascular resistance mainly reflects sympathetic activity (12). There are experimental reports in the literature (13,14) indicating that the baroreflex control of the bradycardiac responses is first impaired, before attenuation of the tachycardiac responses is demonstrable. In this respect, it should be mentioned that changes in sympathetic or vagal tone alone can alter the dynamic response to vagosympathetic stimulation (15). Otherwise, if the impairment of the baroreflex control of the heart rate is secondary to a depression of the afferent component of the baroreflex pathway, usually observed in chronic hypertension (16,17),

Table 2 - Casual blood pressure, prolonged resting blood pressure and heart rate of normotensive subjects.

Data are reported as means \pm SD. SBP, Systolic blood pressure; DBP, diastolic blood pressure. * $P < 0.05$ compared with control group (Student t-test).

Variables	Negative family history (N = 25)	Positive family history (N = 25)
Casual SBP (mmHg)	112.9 \pm 11.4	119.9 \pm 11.7*
Casual DBP (mmHg)	71.2 \pm 8.3	78.5 \pm 8.6*
Resting SBP (mmHg)	128.0 \pm 11.8	137.3 \pm 12.3*
Resting DBP (mmHg)	66.5 \pm 7.4	74.4 \pm 7.9*
Resting HR (bpm)	62.1 \pm 6.0	68.5 \pm 8.4*

both the baroreflex-mediated bradycardia and tachycardia should be depressed. Therefore, the impairment observed here only in the tachycardiac response is more likely to depend on an alteration in the efferent pathway of the baroreflex due to a downregulation of the sympathetic system determined by its chronic overactivity. The reduced baroreflex sensitivity may also be secondary to a sympathetic pressor reflex, as demonstrated in dogs (18). To explain baroreflex alteration, it should also be mentioned that Koskinen et al. (19) observed that LDL-

cholesterol level and BRS were inversely correlated. As we demonstrated before, young normotensives with FH+ have higher total cholesterol, LDL-cholesterol, VLDL-cholesterol and triglyceride levels. In conclusion, the increased blood pressure and heart rate observed here in the offspring of hypertensive parents, associated with our previous demonstration that they also exhibit increased cholesterol and triglyceride levels, emphasize the importance of genetic influence on the prehypertensive phase of hypertension.

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