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ARTICLE

HEIGHTENED BLOOD PRESSURE, BUT NOT PULSE RATE, RESPONSE TO ORTHOSTATIC CHALLENGE IN NORMOTENSIVE SUBJECTS WITH FAMILY HISTORY OF HYPERTENSION

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ABSTRAK

Cardiovascular illnesses begin with cardiovascular system structural and functional abnormalities. It causes cardiovascular system overreactions to stress. This study compared cardiovascular responses to postural shift in normotensive participants with and without a hypertension family history. Male and female normotensive young adults with (n=16) and without (n=14) hypertension parents performed postural adjustments from supine to standing in a quasi-experimental study. Right after standing, systolic and diastolic blood pressure and pulse were measured. Chi square was used to compare the proportion of participants with increased cardiovascular responses in the two groups. Postural alterations significantly increased the proportion of normotensive patients with higher systolic (≥3.5 mm Hg) or diastolic (≥2 mm Hg) blood pressure responses compared to those without a parental history of hypertension. The proportion of subjects with elevated pulse rate (≥12 bpm) in response to postural alterations was not significantly different across groups. Orthostatic challenge from supine to standing raises blood pressure but not pulse rate in normotensive young adults with family history of hypertension.

Keywords: Blood pressure; Heart rate; Cardiovascular reactivity; Orthostatic; Family history of hypertension.

АБСТРАКТ

Сердечно-сосудистые заболевания начинаются со структурных и функциональных отклонений в сердечно-сосудистой системе. Это вызывает чрезмерную реакцию сердечно-сосудистой системы на стресс. В этом исследовании сравнивались реакции сердечно-сосудистой системы на постуральный сдвиг у нормотензивных участников с семейным анамнезом гипертонии и без него. В квазиэкспериментальном исследовании мужчины и женщины молодого возраста с нормотензией (n=16) и без гипертензии (n=14) выполняли постуральную перестройку из положения лежа в положение стоя. Сразу после вставания измеряли систолическое и диастолическое артериальное давление и пульс. Для сравнения доли участников с повышенной реакцией сердечно-сосудистой системы в двух группах использовался критерий Хи-квадрат. Постуральные изменения значительно увеличили долю нормотензивных пациентов с повышенным систолическим (≥3,5 мм рт. ст.) или диастолическим (≥2 мм рт. ст.) артериальным давлением по сравнению с теми, у кого родители не страдали гипертонией. Доля испытуемых с повышенной частотой пульса (≥12 уд/мин) в ответ на постуральные изменения существенно не различалась между группами. Ортостатический вызов из положения лежа в положение стоя повышает артериальное давление, но не частоту пульса у нормотензивных молодых людей с семейным анамнезом гипертензии.

Ключевые слова: Артериальное давление; частота пульса; сердечно-сосудистая реактивность; ортостатика; семейный анамнез гипертонии.

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INTRODUCTION

Cardiovascular reactivity is a set of changes in cardiovascular parameters, such as blood pressure, heart rate, and other hemodynamic parameters, in response to a stressor. Cardiovascular reactivity is a non-invasive method to detect the pre-clinical state of cardiovascular disease. Pre-clinical cardiovascular disease state is the pathogenic change in the cardiovascular structure and function that can progress into cardiovascular diseases, such as hypertension, myocardial infarct, and stroke.[1]

Essential hypertension occurs more frequently in individuals with family history of the disease.[2] Subjects with family history of hypertension have higher prevalence and incidence of hypertension than those without.[3-4] Normotensive subjects with family history of hypertension can be regarded as a pre-hypertensive model. To identify the functional changes in the cardiovascular system before high blood pressure occurs is important because when hypertension has already occurred, the initial changes may be obscured by adaptations invoked by the rising pressure.[5]

Postural change from supine to standing position is among various stimuli to stimulate cardiovascular system. The orthostasis challenges the cardiovascular system to the effect of gravity to the blood.[6] It was reported that orthostatic hypotension is associated to an increased risk of hypertension, coronary heart disease and stroke.[7] In the opposite, orthostatic hypertension will cause hemodynamic stress, lead to vascular damage and is associated also to an increased risk of developing hypertension.[8-9]

This study was aimed to examine the cardiovascular responses to postural changes from supine to standing in pre-hypertensive model, i.e., normotensive subjects with family history of hypertension, as compared to normotensive subjects without family history of hypertension.

This study found that proportion of heightened blood pressure, but not pulse rate, responses to postural changes was significantly higher among normotensive subjects with family history of hypertension than those without family history of hypertension.

MATERIAL AND METHODS

Study Design This was a quasi-experimental study between-subjects design, which compared cardiovascular reactivity to postural changes from supine to standing in healthy normotensive subjects with and without family history of hypertension. The subjects of this study were normotensive men and women aged between 18 – 30 years (pre hypertensive age) who lived in The Special Province of Yogyakarta. This study used convenience sampling as the sampling method. Sample size was calculated by suing the formula:

$$n = \left(\frac{Z_\alpha \times S}{\overline{X}_1 - \overline{X}_2} \right)^2$$

In which:

n = the size of each sample

Zα = the value obtained from the table of standard values that corresponds to the level of confidence. For a 95% confidence level, the value is 1.96.

S = standard deviation

$x_1 - x_2$ = the difference between the means of two sets of observations

From the above formulation, the calculated sample size as followed:

$$n = \left(\frac{1.96 \times 40}{20}\right)^2 = 15.366 \sim 16$$

Blood pressure and pulse rate were measured during pre-test (supine) and test (standing). In this study we used a delta change score as a measure of cardiovascular reactivity, which was calculated as the difference

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between the cardiovascular parameters measured in the test and pre-test periods. Mean ± standard deviation was used to summarize the subjects' characteristics. Exaggerated cardiovascular responses was defined as subjects' systolic blood pressure, diastolic blood pressure and pulse rate responses that was above the median value of each cardiovascular parameters respectively in responses to postural changes.

Selection criteria, Inclusion criteria. The subject's age was between eighteen to thirty years old. Female subject had body mass index < 27.3 kg/m^2 and male subject had body mass index < 27.3 kg/m^2. The subject had systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg in concordance with the criteria of normotensive subjects based on Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[10]

Exclusion criteria. Subjects reported whether she/ he had renal diseases, hormonal disturbances or neuropsychiatric disorder. Family history of hypertension. Family history of hypertension was defined by parental hypertension. Subjects were considered having family history of hypertension if she/ he reported that either her/ his father or mother or both had one of the following criteria: high blood pressure (SBP > 140 mmHg or DBP > 90 mmHg), being diagnosed hypertension, being on medication for hypertension. Subjects were considered not having family history of hypertension if she/ he reported that her/ his father *and* mother did *not* have all the following criteria: high blood pressure (SBP > 140 mmHg or DBP > 90 mmHg), being diagnosed hypertension, being on medication for hypertension.

Postural change. In the pre-test period, subject took a rest in a supine position for ten minutes. At the end of the rest period, cardiovascular parameters were measured for two times. The two closest measurements were being averaged. In the test period, subject stood quickly by the side of the bed. During standing, the subject should not move. Cardiovascular parameters were measured immediately when the subject stood.

Cardiovascular parameters. Systolic blood pressure (SBP), diastolic blood pressure (DBP), and pulse rate were measured by using a non-invasive, automatic vital sign monitor device TM2551 P (A & D Co. Ltd., Tokyo, Japan). Blood pressure measurement was done above the brachial artery of the participants' dominant hand.

Data handling. Microsoft Office Excel 2019 was used for data reduction and Statistical Package for Social Sciences version 16.0 (SPSS Inc., Chicago, USA) for data summarize and analysis. Data reduction. Delta change score rather than absolute value was chosen to control the baseline level. The magnitude of the reactivity measured by delta change score was not necessarily dependent upon the baseline value. Moreover, delta change score yield reliable measures of blood pressure and heart rate reactivity to laboratory stimuli. A delta change score of cardiovascular reactivity was calculated by subtracting the cardiovascular parameters measured in the pre-test period from the cardiovascular parameters measured during the test period.

A summary of the data. In order to summarize the results, the mean and standard deviation were given. A study of the data. An independent t-test was utilized in order to ascertain the mean difference in the features of the subjects who were belonging to the two groups. In order to assess the proportional difference between the two groups in terms of the participants' systolic blood pressure, diastolic blood pressure, and heart rate in response to orthostatic challenge, chi-square was utilized. Statistical significance was determined to be attained when the P value was less than 0.05.

RESULT

Thirty volunteers with normal blood pressure were included in this investigation. The samples were comprised of two groups: the group of normotensives who did not have a family history of hypertension (without FHoH), which consisted of fourteen subjects, and the

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group of normotensives who had a family history of hypertension (with FHoH), which consisted of sixteen individuals. Both groups did not differ significantly ($p>0.05$) in the terms of age, body mass index, systolic blood pressure, diastolic blood pressure and pulse rate (Table 1).

Table 1. Subjects Characteristics

Variable	Without FHoH (n=14)	With FHoH (n=16)
Age (years)	22.43 ± 2.87	23 ± 3.01
BMI (kg/m^2)	21.4 ± 1.55	19.89 ± 2.12
SBP (mm Hg)	116.86 ± 5.22	116.37 ± 7.56
DBP (mm Hg)	79 ± 4.99	78.44 ± 6.13
Pulse rate (bpm)	74.28 ± 7.84	73.125 ± 6.73

Note: FHoH = family history of hypertension; BMI = body mass index; SBP = systolic blood pressure; DBP = diastolic blood pressure; bpm = beats per minute. Data are summarized as mean ± standard deviation.

Following postural change, the delta change score of systolic blood pressure, diastolic blood pressure and pulse rate were calculated. The median of delta scores of systolic blood pressure, diastolic blood pressure and pulse rate were 3.5 mm Hg, 2 mm Hg, and 12 bpm, respectively. These median values were used to define the exaggerated cardiovascular reactivity to postural change.

Based on the median of the delta change score, whether any significant differences in the proportion of exaggerated cardiovascular reactivity to postural change were presented between normotensive subjects with and without family history of hypertension were analyzed. Normotensive subjects with family history of hypertension had significantly higher proportion of exaggerated cardiovascular response to postural change in systolic blood pressure ($p=0.001$) and diastolic blood pressure ($p=0.001$), but not pulse rate ($p=0.44$) (Table 2a-c).

Table 2. Proportion of exaggerated systolic blood pressure response to the postural change in normotensive subjects with and without family history of hypertension

ΔSBP	Without FHoH (n=14)	With FHoH (n=16)
≥3.5 mm Hg	2	13
<3.5 mm Hg	12	3

Note: FHoH = family history of hypertension; Δ = delta change score; SBP = systolic blood pressure.

Table 3. Proportion of exaggerated diastolic blood pressure response to the postural change in normotensive subjects with and without family history of hypertension

ΔDBP	Without FHoH (n=14)	With FHoH (n=16)
≥2 mm Hg	2	12
<2 mm Hg	12	4

Note: FHoH = family history of hypertension; Δ = delta change score; DBP = diastolic blood pressure.

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Table 4. Proportion of exaggerated pulse rate response to the postural change in normotensive subjects with and without family history of hypertension

ΔPR	Without FHoH (n=14)	With FHoH (n=16)
≥12 bpm	3	6
<2 bpm	11	10

Note: FHoH = family history of hypertension; Δ = delta change score; PR = pulse rate; bpm = beat per minute.

DISCUSSION

This is the first study that reported orthostatic hypertension in normotensive subjects with family history of hypertension (Table 2a; Table 2b). Orthostatic hypertension is defined as the rise of systolic blood pressure >20 mm Hg in standing position after immediately move from supine position.[13] The criteria of orthostatic hypertension in our study, however, was based on the median value of both the delta systolic blood pressure response (≥3.5 mm Hg) and the delta diastolic blood pressure response (≥2 mm Hg) to postural changes across all the subjects in this study.

Normotensive subjects with family history of hypertension have been regarded as a prehypertension model. They are not developed yet high blood pressure; however, they already have structural and functional changes in the cardiovascular system. Therefore, they show exaggerated cardiovascular reactivity in response to various laboratory stimuli or real-life stressors. The family history of hypertension is known as an unmodified risk factor to hypertension.[1,5]

During postural change from a supine to a standing position, gravity load increases transmural pressure in the vein in the lower extremities. Both mean arterial and venous blood pressure increase linearly with vertical distance below the heart level and would reach 180 mm Hg and 90 mmHg, respectively. When the individual does not move during standing, around 500 mL of blood is pooled in the venous capacitance vessels of the lower extremities, which further reduces venous return. Therefore, stroke volume decreases, and pulse pressure drops.[6]

The aortic and carotid baroreceptors detect the decrease in pulse pressure whereas the veno-atrial stretch receptors detect the drop in venous return. The impulses are transmitted to the nucleus tractus solitarius through the IXth and Xth nerve fibres. In turn, the nucleus tractus solitarius will inhibit the cardiac-inhibitatory center and stimulate the cardiac-acceleratory centre. As the results, heart rate and contractility increase to limit the fall in the cardiac output as the venous pressure drops. There is also marked vasoconstriction in the skeletal muscle, splanchnic and renal vascular beds to raise total peripheral resistance. These compensatory adjustments prevent mean arterial blood pressure to heavily fall during postural change, which can affect the cerebral circulation. In fact, during postural change the systolic blood pressure slightly increases, diastolic blood pressure sharply rises and mean-arterial blood pressure transiently falls.[6]

Regarding orthostatic hypertension, two mechanisms or theory are proposed to explain it. First is the vascular adrenergic hypersensitivity theory. Second is the nephroptosis theory. Vascular adrenergic hypertension is related to excessive venous pooling, with an initial drop in cardiac output followed by overcompensation of sympathetic activity with an excessive release of catecholamines. Nephroptosis is related with activation of the renin-angiotensin-aldosterone system as the perfusion pressure to the kidney drops during postural changes.[11-12]

Several evidence show that young male normotensive subjects of hypertensive parents have hyperactive sympathetic nervous system, as assessed by diastolic blood pressure response to cold pressor test and handgrip exercise, as compared to young male normotensive subjects of normotensive

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parents. The activity parasympathetic nervous system does not differ significantly between young male normotensive subjects of normotensive and hypertensive parents. It was also reported that normotensive young adults with family history of hypertension have exaggerated cardiovascular reactivity to physical test (cold pressor test), but not to mental test (arithmetic test), as compared to normotensive young adults without family history of hypertension. It is known that norepinephrine is the main neurotransmitter involved in cold pressor test, whereas epinephrine is dominant humoral response during mental test. Moreover, normotensive subjects with family history of hypertension demonstrates significantly higher norepinephrine level as compared to normotensive subjects without family history of hypertension. The excretion of epinephrine, systolic blood pressure and diastolic blood pressure were significantly higher in women with positive parental history of hypertension than in women with negative parental history of hypertension.[12-15] The evidence support vascular adrenergic hypersensitivity theory, rather than nephroptosis theory, in explaining normotensive subjects with family history of hypertension as the pre-hypertensive model. Furthermore, previous studies suggest that the activation of sympathetic nerves, rather than the activation of sympatho-adrenal system, occurred in normotensive subjects with family history of hypertension.

CONCLUSION

Normotensive subjects with family history of hypertension show heightened systolic blood pressure and diastolic blood pressure to postural changes, which can be regarded as having orthostatic hypertension. This finding supports vascular adrenergic hypersensitivity theory.

DECLARATIONS

Conceptualization and research design were conceived by IMJ; Data collection and measurement were done by WA; Data analysis and interpretation were conducted by WA and IMJ; Critical revision and review of the manuscript was performed by IMJ.

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This study has received ethical approval from the Health Research Ethics Committee of Faculty Medicine Universitas Muhammadiyah Surakarta No. 3579/B.2/KEPK-FKUMS/V/2021. This study was conducted following the declaration of Helsinki. Moreover, informed consent forms were duly signed by all participants. The datasets used and/or analysed during the current study are available in our institutionalized database.

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