Indices of autonomic nervous system activity in women with mild hypertension in the perimenopausal period

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Abstract

Background: Hypertension is more common after menopause. Increased incidence of hypertension can be attributed to autonomic nervous system dysfunction. The relationship between the parameters of heart rate variability (HRV), the levels of norepinephrine (NE) and leptin, and the menopausal status is still poorly understood, although there is some evidence suggesting distinct influence of estrogens on the above-mentioned indicators.

Aim: To characterise the influence of menopause on indices of autonomic nervous system activity in women with mild hypertension.

Methods: We recruited 112 women aged 45 to 55 years with mild essential hypertension confirmed by 24 h ambulatory blood pressure monitoring. The study population was divided into two groups – postmenopausal (A, n = 61; age 51,03 ± 1,39 years) and premenopausal (B, n = 51; age 50 ± 2 years). None of the women had organ damage, other risk factors, inflammation diseases, were on estrogen replacement therapy or oral contraceptives. In all patients we assessed the leptin and NE levels. The HRV time-domain and spectral parameters were analysed from Holter ECG recordings.

Results: After menopause we observed, among others, the lower values of total power, VLF, HF (ms, %), LF (%) and LF:HF 24 h. The level of NE as well as the concentration of leptin were higher in postmenopausal rather than premenopausal women.

Conclusion: Higher activity of sympathetic nervous system and higher levels of leptin in hypertensive women after menopause may suggest their participation in the pathogenesis of hypertension in this group of patients.

Key words: menopause, hypertension, heart rate variability, leptin, norepinephrine

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Introduction

The relationship between menopause and hypertension has been studied for years. However, so far this association has not been fully understood. Increased sympathetic system activity plays an important role in aetiology of hypertension. The most common methods of assessing sympathetic system activity are heart rate variability (HRV) and measurements of catecholamine levels in blood plasma. Neuroendocrine abnormalities are in close relation to metabolic disorders and they contribute together to development of hypertension and its complications. Leptin is believed to be an important factor connecting sympathetic system overactivity with hypertension [1, 2].

The aim of the present study was to assess function of the autonomic nervous system, leptin and noradrenaline levels as well as their correlation in a group of women with mild hypertension after menopause and in the premenopausal period. The aim of the study was also to determine the relationship between the biochemical parameters mentioned above and autonomic system activity.

Methods

Studied population

One hundred twelve women aged 45 to 55 years studied between June 2004 and November 2005 were included in the analysis. An inclusion criterion was a diagnosis of idiopathic mild hypertension. The diagnosis was made on the basis of blood pressure measurements in a physician's office and automated blood pressure monitoring (ABPM) results (SpaceLabs 90207) [3]. Patients did not use any antihypertensive treatment for the 4 weeks before study.

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The studied population was divided into two groups: postmenopausal women and women with regular menstrual cycles. Determination of postmenopausal state was based on the interview (minimal time interval between menopause and study entry was 6 months) and was confirmed by measurements of plasma sex hormone levels: 17-beta--oestradiol (below 50 pg/ml) and FSH (over 30 IU/l). In women with regular menstruation all measurements were performed in the follicular phase of the cycle.

The following patients were excluded from the study: individuals with organ damage [3], other risk factors – obesity, type 2 diabetes mellitus, current smoking or smoking during the last 3 years, inflammatory and chronic diseases (autoimmunological and cancer), women who were taking hormonal medications (hormone replacement therapy or hormonal contraceptives). The study protocol was approved by the local ethical committee. Included patients obtained precise information about the purpose and nature of the study. All patients gave written consent to participate in the study.

Blood pressure measurements and physical examination

Blood pressure measurements were performed with a mercury sphygmomanometer according to the ESC and ESH guidelines [3]. ABPM was performed with a SpaceLabs 90207 device (SpaceLabs Inc., Redmond, Washington, USA) – measurements were obtained every 15 min during daytime hours (between 6 a.m. and 10 p.m.) and every 20 min during the night (between 10 p.m. and 6 a.m.). Physical examination was extended by anthropometric measurements including adipose tissue measurements with a Maltron BF-905 Body Fat Analyser and Tanita Omron. Body mass index (BMI) and waist-to-hip ratio (WHR) were also measured.

Biochemical analysis

All blood samples for biochemical analysis were obtained in the morning between 7:30 and 8:00 a.m. after 30 min rest, in the supine position, at least 12 h after the last meal. Blood was drawn though previously obtained venous access. After centrifugation samples were frozen at –70°C until biochemical analysis was performed. For measurement of leptin levels Quantikine® Human Immunoassay was used (R&D System) with the sandwich method and two monoclonal antibodies. The sensitivity of the test was below 7.8 pg/ml and the reference value was between 3 877 and 77 273 pg/ml. Noradrenalin Elisa (DRG Instrument GmbH) kit was used for noradrenaline concentration analysis. The sensitivity of the test was 20 pg/ml and the upper reference value in EDTA plasma was 600 pg/ml.

24-hour continuous ECG Holter monitoring

The 24-hour continuous ECG Holter monitoring with the analysis of HRV was performed using an analogue recorder (Marquette Electronics) with data storage on a tape cassette. Analysis of the recordings was done with dedicated software (DRG) according to the ESC and NASPE guidelines [4].

Statistical analysis

Database construction and statistical analysis was performed with Statistica for Windows 6.0 PL (StatSoft Inc., Tulusa, Oklahoma, USA) using the following methods: Shapiro-Wilk test, Student's t-test, χ^2 test, Spearman rank correlation, stepwise regression analysis and multiple regression analysis.

Results

Baseline clinical characteristics of the study group are presented in Table I. The mean leptin concentration in the whole studied population was 4.34 ± 0.27 log pg/ml. In menstruating women the higher BMI was, the higher the leptin level that was observed ($\beta = 0.60$; $p < 0.000001$), and it was lower when lower oestradiol level was present ($\beta = -0.26$; $p = 0.04$) Significant correlations of leptin in the whole studied population are presented in Table II.

In the multivariate analysis after adjustment for age, BMI, WHR, percentage of adipose tissue and its mass, duration of hypertension, mean blood pressure (of the measurements performed on the first and second visit and the result obtained from ABPM), as well as for biochemical results such as FSH, oestradiol, noradrenalin concentrations and time domain and frequency domain variables of heart rate, the relation between leptin levels and studied parameters remained statistically significant ($p < 0.05$).

The mean concentration of noradrenaline in the whole studied population was 439.76 ± 170.40 pg/ml and was higher in women after menopause when compared to regular menstruating women (487.58 ± 170.32 vs. 382.57 ± 153.40 pg/ml; $p = 0.0009$). There was an association between noradrenalin level and systolic blood pressure measured at the second visit and the diastolic pressure measured at the first visit. Noradrenalin level increased with increasing age of the studied patients. In the whole group there was a relationship between noradrenaline concentration and age, sex hormone levels (FSH and oestradiol) as well as total cholesterol level. Significant correlations for noradrenaline are presented in Table III.

In the multivariate analysis after adjustment for age, BMI, WHR, percentage of adipose tissue and its mass, the duration of hypertension, mean blood pressure (of the measurements performed on the first and second visit and the result obtained from ABPM), as well as for biochemical results such as FSH, oestradiol, leptin concentrations and time domain and frequency domain

Table I. Baseline clinical characteristics of the studied women

	Total n = 112	Postmenopausal n = 61	Premenopausal n = 51	p
Age [years]	50.7 ± 1.8	51.0 ± 1.4	50.4 ± 2.2	0.06
BMI [kg/m^2]	26.6 ± 2.8	26.9 ± 2.7	26.2 ± 2.8	0.22
WHR	0.8 ± 0.05	0.81 ± 0.05	0.78 ± 0.05	0.0005
FAT Omron [%]	35.1 ± 5.8	35.8 ± 5.9	34.8 ± 5.9	0.92
FAT Maltron [%]	32.3 ± 7.0	32.3 ± 7.0	32.3 ± 7.1	0.99
FAT Maltron [kg]	23.2 ± 7.0	23.6 ± 6.9	22.8 ± 7.1	0.58
FSH [mIU/ml]	39.8 ± 36.6	66.9 ± 28.7	7.4 ± 4.3	< 0.0000001
Oestradiol [pg/ml]	50.6 ± 50.5	18.3 ± 9.8	89.3 ± 52.5	< 0.0000001
Duration of hypertension [months]	14.2 ± 5.7	15.3 ± 5.5	12.8 ± 5.7	0.02
SBP (1st visit) [mmHg]	150.8 ± 4.4	151.7 ± 4.1	149.7 ± 4.5	0.54
DBP (1st visit) [mmHg]	92.9 ± 2.8	93.2 ± 2.8	92.6 ± 2.8	0.24
SBP (2nd visit) [mmHg]	151.2 ± 4.4	152.2 ± 3.9	150.0 ± 4.6	0.58
DBP (2nd visit) [mmHg]	92.5 ± 2.5	92.6 ± 2.7	92.3 ± 2.2	0.46
SBP 24 h [mmHg]	132.9 ± 6.4	133.9 ± 6.8	131.8 ± 5.7	0.09
DBP 24 h [mmHg]	82.2 ± 7.4	81.9 ± 8.8	82.6 ± 5.4	0.62
SBP day [mmHg]	136.8 ± 7.9	137.2 ± 8.9	136.4 ± 6.7	0.58
DBP day [mmHg]	86.8 ± 7.4	86.1 ± 8.3	87.7 ± 6.6	0.20
SBP night [mmHg]	122.8 ± 9.6	124.1 ± 11.0	121.2 ± 7.4	0.10
DBP night [mmHg]	74.0 ± 7.4	74.7 ± 8.8	73.3 ± 5.2	0.32

Abbreviations: BMI – body mass index, WHR – waist to hip ratio, FAT – fat tissue, SBP – systolic blood pressure, DBP – diastolic blood pressure

variables of heart rate, the relation between noradrenaline levels and studied parameters remained statistically significant ($p < 0.05$).

Heart rate variability results are presented in Tables IV and V. Mean HR for 24 hours correlated with mean systolic blood pressure measured on the second visit ($\beta = 0.21$; $p = 0.02$); with higher mean systolic blood pressure measured on the second visit, lower time domain variables were observed: SDNN 24 h ($\beta = –0.22$; $p = 0.02$), SDANN 24 h ($\beta = –0.19$; $p = 0.04$) and SDNNI 24 h ($\beta = –0.20$; $p = 0.03$). The SDNNI values were also influenced by age ($\beta = –0.19$; $p = 0.04$). With higher HRV for 24 hours, lower level of FSH was observed ($\beta = –0.44$; $p = 0.000004$). This component increased when oestradiol concentration increased ($\beta = 0.28$; $p = 0.002$) and with decreasing noradrenaline concentration ($\beta = –0.18$; $p = 0.22$). The normalised component of HF was influenced not only by FSH levels ($\beta = –0.39$; $p = 0.0001$) and oestradiol ($\beta = 0.22$; $p = 0.02$) but also by age ($\beta = –0.17$; $p = 0.03$) and the value of systolic blood pressure measured during the second visit ($\beta = –0.19$; $p = 0.04$). A higher LF:HF ratio for 24 h was noted when higher FSH and noradrenaline levels were present ($\beta = 0.39$; $p = 0.00005$ and $\beta = 0.18$; $p = 0.02$, respectively)

Table II. Correlation between leptin and other parameters

	Leptin log [log pg/ml]	
	r	p
BMI [kg/m^2]	0.64$^{\#}$	< 0.000001$^{\#}$
	0.59*	0.000001*
	0.67**	< 0.000001**
FAT Omron [%]	0.73$^{\#}$	< 0.000001$^{\#}$
	0.73*	< 0.000001*
	0.81**	< 0.000001**
FAT Maltron [%]	0.70$^{\#}$	< 0.000001$^{\#}$
	0.69*	< 0.000001*
	0.80**	< 0.000001**
FAT Maltron [kg]	0.77$^{\#}$	< 0.000001$^{\#}$
	0.76*	< 0.000001*
	0.81**	< 0.000001**
WHR	0.43$^{\#}$	0.000002$^{\#}$
	0.45*	0.0002*
	0.28**	< 0.05**
LF component [%] night	0.22$^{\#}$	0.02$^{\#}$
	0.21*	< 0.05*
	0.20**	< 0.05**

Abbreviations: see Table I
$^{\#}$ for the whole study group
** for group A*
*** for group B*

Table III. Correlation between noradrenaline and other parameters

	Noradrenaline [pg/ml]	
	r	p
Age [years]	0.23#	0.02#
	0.46*	0.0006*
	0.21**	< 0.05*
FSH [mIU/ml]	0.24#	0.009#
	0.22*	< 0.05*
	0.21**	< 0.05**
Oestradiol [pg/ml]	–0.24#	0.01#
	–0.23*	< 0.05*
	–0.21**	< 0.05**
SBP (1st visit) [mmHg]	0.20#	0.04#
	0.20*	< 0.05*
	0.20**	< 0.05**
SBP (2nd visit) [mmHg]	0.28#	0.003#
	0.25*	< 0.05*
	0.23**	< 0.05**
TP log 24 h [log ms^2]	–0.20#	0.03#
	–0.20*	< 0.05*
	–0.20*	< 0.05**
HF component log 24 h [log ms^2]	–0.27#	0.004#
	–0.29*	< 0.01*
	–0.23**	< 0.05**
HF component [%] 24 h	–0.23#	0.02#
	–0.22*	< 0.05*
	–0.21**	< 0.05**
LF:HF ratio, log 24 h	0.25#	0.007#
	0.25*	< 0.01*
	0.21**	< 0.05**
HF component log day [log ms^2]	–0.27#	0.005#
	–0.27*	< 0.01*
	–0.22**	< 0.05**
HF component [%] day	–0.30#	0.002#
	–0.29*	< 0.01*
	–0.25*	< 0.05**
LF:HF ratio, log day	0.27#	0.004#
	0.26*	< 0.01*
	0.23**	< 0.05*
LF component log night [log ms^2]	0.28#	0.003#
	0.26*	< 0.01*
	0.22**	< 0.05**
LF component [%] night	0.27#	0.005#
	0.26*	< 0.01*
	0.23**	< 0.05**
LF:HF ratio, log night	0.26#	0.006#
	0.24*	< 0.05*
	0.22**	< 0.05**

 # for the whole study group
** for group A*
*** for group B*

and when lower oestradiol level was noted (β = –0.30; p = 0.001). All significant correlations for the whole study group are presented in Tables VI and VII.

In the multivariate analysis after adjustment for age, BMI, WHR, percentage of adipose tissue and its mass, the duration of hypertension, mean blood pressure (of the measurements performed on the first and second visit and the result obtained from ABPM), as well as for biochemical results such as FSH, oestradiol, leptin and noradrenalin concentrations, the relation between variables obtained from 24-hour continuous ECG Holter monitoring and studied parameters remained statistically significant (p < 0.05).

Discussion

Leptin

Disturbances of neurohormonal systems play a key role in the aetiology of hypertension after menopause. One of the postulated mechanisms responsible for blood pressure increase is elevated leptin concentration.

The role of leptin in the pathogenesis of idiopathic hypertension has not been yet established. Some authors found higher leptin level in patients with hypertension as compared to individuals without hypertension [5]. Other investigators did not confirm these results [6]. However, analysis of the relationship between blood pressure and leptin concentration in patients with hypertension and in subjects with normal blood pressure showed a significant positive correlation between leptin levels and systolic [6] as well as diastolic [6, 7] blood pressure. The whole group in our study had mild hypertension, which was not treated before. In this homogeneous group no relation between leptin concentration and blood pressure measured either in the physician's office or by ABPM was observed.

Women in the postmenopausal period had higher leptin level as compared to women with regular menstruations. We observed an increase of leptin level with lower oestradiol concentration in both study groups, which confirms the association between leptin level and women's hormonal status. These data are consistent with other reports [8, 9]. However, the opinions about the influence of menopause on leptin levels are conflicting. So far, most published data showed results similar to those presented by us [10, 11]. Some studies negate higher level of leptin in women in postmenopausal state as compared with regular menstruating women [12]. However, the study by Douchi et al. [12] included women without hypertension, at various ages (between 19 and 75 years), and leptin concentrations were measured by radioimmunoassay. Moreover, the authors did not take into consideration the lack of normal distribution of leptin concentration, which might have influenced the results of their study.

Increased leptin concentration after menopause is believed to be associated with sympathetic overactivity [13]. The results of previous studies indicated that leptin and increased activity of the sympathetic system act together in the pathogenesis of hypertension. This hypothesis has been confirmed by documenting the correlation between leptin and mean HR in 24 h

Table IV. Comparison of HRV parameters between studied groups

	Total n = 112	Postmenopausal n = 61	Premenopausal n = 51	p
HR mean	77.4 ± 6.6	79.9 ± 5.3	74.5 ± 6.9	< 0.00001
HR max.	133.0 ± 16.7	136.5 ± 19.2	130.1 ± 13.7	0.04
TP log 24 h [log ms^2]	3.3 ± 0.2 (1995.3)	3.3 ± 0.2 (1778.3)	3.4 ± 0.1 (2511.9)	< 0.000001
VLF component log 24 h [log ms^2]	3.1 ± 0.2 (1122.0)	3.0 ± 0.2 (977.2)	3.1 ± 0.2 (1349.0)	< 0.001
HF component log 24 h [log ms^2]	2.5 ± 0.4 (302.0)	2.2 ± 0.3 (166.0)	2.8 ± 0.2 (616.6)	< 0.000001
LF component 24 h [%]	26.5 ± 12.2	32.1 ± 12.3	19.8 ± 8.0	< 0.000001
HF component 24 h [%]	18.4 ± 11.8	11.9 ± 8.6	26.2 ± 10.3	< 0.000001
LF:HF ratio, log 24 h	1.1 ± 0.2 (12.9)	1.2 ± 0.2 (17.4)	1.0 ± 0.1 (9.1)	< 0.000001

Table V. Comparison of day and night HRV parameters between studied groups

	Total n = 112	Postmenopausal n = 61	Premenopausal n = 51	p
SDNN/day [log ms]	1.9 ± 0.1 (83.2)	1.9 ± 0.1 (79.4)	2.0 ± 0.1 (91.2)	0.01
pNN50/day [log ms]	0.7 ± 0.5 (4.9)	0.6 ± 0.5 (3.9)	0.8 ± 0.5 (6.3)	0.04
LF component day [log ms^2]	2.6 ± 0.3 (426.6)	2.7 ± 0.3 (489.8)	2.6 ± 0.3 (354.8)	< 0.01
HF component day [log ms^2]	2.4 ± 0.4 (239.9)	2.2 ± 0.4 (151.4)	2.6 ± 0.3 (416.9)	< 0.000001
LF component [%] day	26.9 ± 15.0	31.7 ± 14.0	21.3 ± 14.2	< 0.001
HF [%] day	17.1 ± 12.0	11.7 ± 10.8	23.4 ± 10.3	< 0.00001
LF:HF ratio day, log	1.1 ± 0.3 (13.8)	1.3 ± 0.3 (19.1)	1.0 ± 0.2 (9.8)	< 0.00001
LF component log night [log ms^2]	2.6 ± 0.3 (380.2)	2.7 ± 0.3 (501.2)	2.4 ± 0.3 (269.2)	< 0.00001
HF component log night [log ms^2]	2.4 ± 0.4 (245.5)	2.2 ± 0.4 (166.0)	2.6 ± 0.3 (389.1)	< 0.00001
LF component log [%] night	25.6 ± 13.6	32.2 ± 12.8	17.6 ± 9.7	< 0.00001
HF component [%] night	18.8 ± 14.1	13.9 ± 13.3	24.7 ± 12.8	< 0.0001
LF:HF ratio night, log	1.12 ± 0.25 (13.18)	1.25 ± 0.24 (17.78)	0.95 ± 0.14 (8.91)	< 0.00001

in patients with hypertension [14]. In the present study, we did not confirm a relationship between leptin level and mean HR from 24 h. Our results are consistent with the study by Puciłowska et al. [15]. On the other hand, in our patients we observed a correlation between leptin concentration and another marker of sympathetic system activity – LF oscillations during the night expressed in normalised units. Our results are similar to those obtained by Paolissa et al. [16].

Noradrenaline

Increased activity of the sympathetic system is considered to be one of the elements responsible for increased cardiovascular risk with increasing age [17]. Our study revealed a relationship between noradrenaline level and age of the studied women. Noradrenaline concentration was higher in postmenopausal female patients with mild hypertension as compared with regularly menstruating patients. These data suggest that

Table VI. Selected correlations between HRV indices and other parameters

	HR mean [/min]		SDNN log 24 h [log ms]		SDNNI log 24 h [log ms]	
	r	p	r	p	r	p
FSH [mIU/ml]	0.35#	0.0002#	–0.06#	0.56#	–0.11#	0.23#
	0.29*	< 0.05*	0.18*	0.10*	–0.23*	0.06*
	0.22**	< 0.05**	–0.06**	0.60**	–0.01**	0.80*
Estradiol [pg/ml]	–0.39#	0.00003#	0.02#	0.80#	0.19#	0.049#
	–0.35*	< 0.05*	0.16*	0.23*	0.18*	0.06*
	–0.27**	< 0.05**	0.20**	0.18**	0.01**	0.80**
Duration of hypertension [months]	0.27#	0.005#	–0.15#	0.10#	–0.11#	0.23#
	0.42*	0.0006*	–0.27*	0.04*	–0.25*	0.05*
	0.23**	< 0.05*	0.04**	0.80**	–0.14**	0.32**
SBP 1 visit [mmHg]	0.20#	0.03#	–0.15#	0.10#	–0.13#	0.16#
	0.20*	<0.05*	–0.22*	0.09*	–0.23*	0.08*
	0.21**	<0.05**	–0.05**	0.80**	–0.03**	0.80**
DBP 1 visit [mmHg]	0.24#	0.01#	–0.16#	0.08#	–0.23#	0.014#
	0.26*	0.04*	–0.19*	0.09*	–0.28*	0.03*
	0.22**	< 0.05**	–0.12**	0.40**	–0.26**	< 0.05**
SBP 2 visit [mmHg]	0.26#	0.007#	–0.14#	0.14#	–0.13#	0.19#
	0.30*	0.02*	–0.20*	0.11*	–0.28*	0.03*
	0.25**	< 0.05**	0.02**	0.80**	–0.10**	0.50**
DPB 2 visit [mmHg]	0.22#	0.02#	–0.22#	0.02#	–0.23#	0.015#
	0.27*	0.04*	–0.21*	< 0.05*	–0.23*	< 0.05*
	0.24**	< 0.05**	–0.22**	< 0.05**	–0.24**	< 0.05**

Abbreviations: see Table I
 # for the whole study group
** for group A*
*** for group B*

Table VII. Selected correlations between HRV indices and other parameters

	TP log 24 h [log ms²]		HF component log 24 h [log ms²]		LF component log 24 h [log ms²]	
	r	p	r	p	r	p
FSH [mIU/ml]	0.43#	0.000003#	–0.66#	< 0.000001#	0.20#	0.04#
	0.32*	< 0.05*	–0.35*	0.01*	0.18*	0.10*
	0.25**	< 0.05**	–0.26**	<0.05**	0.12**	0.08**
Estradiol [pg/ml]	0.43#	0.000003#	0.62#	< 0.000001#	–0.20#	0.03#
	0.28*	< 0.05*	0.25.*	< 0.05*	–0.01*	0.50*
	0.25**	< 0.05**	0.24**	< 0.05**	–0.01**	0.42**
NE [pg/ml]	–0.20#	0.03#	–0.27#	0.004#	0.08#	0.42#
	–0.21*	< 0.05*	–0.29*	< 0.05*	0.08*	0.56*
	–0.20**	< 0.05**	–0.25**	< 0.05**	0.01**	0.61**
	HF component [%] 24 h		LF component [%] 24 h		LF:HF ratio, log 24 h	
	r	p	r	p	r	p
FSH [mIU/ml]	–0.61#	< 0.000001#	0.46#	<0.000001#	0.64#	< 0.000001#
	–0.39*	< 0.05*	0.37*	<0.05*	0.38*	< 0.05*
	–0.29**	< 0.05**	0.31**	<0.05**	0.32**	< 0.05**
Estradiol [pg/ml]	0.57#	< 0.000001#	–0.47#	< 0.000001#	–0.64#	< 0.000001#
	0.41*	< 0.05*	–0.35*	< 0.05*	–0.27*	0.04*
	0.31**	< 0.05**	–0.29**	< 0.05**	–0.22**	< 0.05**
NE [pg/ml]	–0.23#	0.02#	`0.18#	0.06#	0.25#	0.007#
	–0.26*	< 0.05*	0.10*	0.44*	0.28*	<0.05*
	–0.22**	< 0.05**	0.16**	0.25**	0.22**	<0.05**

Abbreviations: see Table I
 # for the whole study group
** for group A*
*** for group B*

female sex hormones influence sympathetic system activity in older women. In the light of these results, it can be stated that different mechanisms are responsible for higher cardiovascular risk in menstruating women and in women after menopause [18].

Orshal et al. on the basis of experimental studies suggested that oestrogens can substantially modulate sympathetic system activity [19]. Our study confirmed a relationship between female sex hormones and sympathetic system activity. Mercuro et al. [20] also found higher noradrenaline levels in blood plasma of postmenopausal women as compared to regularly menstruating females.

In addition, in our study noradrenaline concentration correlated with the mean systolic blood pressure measured in the physician's office. Masuo et al. [21] demonstrated that patients with hypertension (blood pressure 140-158/90-94 mmHg) have higher noradrenaline concentration than individuals with normal blood pressure values. In our study noradrenaline level correlated positively also with parameters reflecting sympathetic activity, and there was a negative correlation with parameters of parasympathetic system activity, which is consistent with the results of previous studies [22, 23].

24-hour continuous ECG Holter monitoring

The results of our study indicate that oestrogens increase activity of the parasympathetic system, as is confirmed by other authors [24, 25]. Another crucial factor which affects the parameters of HRV is age. In our study there was an association between older age and lower values of SDNNI from 24 h and with the normalised HF component, which confirms observations made by Umetani et al. [26].

A relationship between HR and systolic as well as diastolic blood pressure measured at the first and second visit as well as between hypertension duration was observed in our study group. Moreover, a negative correlation between systolic and diastolic blood pressure measured at the first and second visit and SDNNI value for 24 hours was observed. It was demonstrated that patients with mild hypertension had sympathetic system overactivity [27] and in individuals who developed hypertension, increase in heart rate occurred far earlier than elevated blood pressure. These results suggest that dysfunction of the autonomic nervous system is the key element of the pathogenesis of hypertension [28]. Our observation confirmed the relationship between time domain variables and mean blood pressure, which was described earlier by Virtanen et al. [29].

Conclusions

Compared with regularly menstruating females in postmenopausal women with mild hypertension higher levels of leptin and noradrenaline as well as higher values of LF oscillation and lower values of HF oscillation were observed. These results indicate autonomic system dysfunction, and suggest that changes in concentrations of these hormones together with impaired autonomic system function play a role in the pathogenesis of hypertension in this population.

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Wskaźniki aktywności układu autonomicznego u kobiet z łagodnym nadciśnieniem tętniczym w okresie okołomenopauzalnym

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Streszczenie

Wstęp: Związek pomiędzy menopauzą a rozwojem nadciśnienia tętniczego jest przedmiotem badań od szeregu lat. Pomenopauzalny wzrost częstości nadciśnienia tętniczego przypisuje się m.in. dysfunkcji autonomicznego układu nerwowego. Zależności pomiędzy parametrami zmienności rytmu serca (ang. *heart rate variability*, HRV), stężeniami noradrenaliny (NE) i leptyny oraz menopauzą są nadal słabo znane, chociaż część badań sugeruje silny wpływ estrogenów na wymienione wskaźniki.

Cel: Ocena wpływu menopauzy na wskaźniki aktywności układu autonomicznego u kobiet z łagodnym nadciśnieniem tętniczym.

Metody: Badaniem objęto 112 kobiet w wieku 45–55 lat z pierwotnym łagodnym nadciśnieniem tętniczym, potwierdzonym 24-godzinnym monitorowaniem ciśnienia tętniczego (SpaceLabs 90207). Badane kobiety podzielono na dwie podgrupy: kobiety w okresie pomenopauzalnym (grupa A – n = 61, wiek 51,03 ± 1,39 roku) oraz regularnie miesiączkujące (grupa B – n = 51; wiek 50,37 ± 2,19 roku). Kwalifikację do grupy kobiet w okresie pomenopauzalnym oparto na danych z wywiadu (czas od wystąpienia menopauzy minimum 6 miesięcy) i potwierdzono na podstawie oceny osoczowych stężeń hormonów płciowych: 17-beta-estradiolu (poniżej 50 pg/ml) i hormonu folikulotropowego – FSH (powyżej 30 IU/l). Do badania nie włączano chorych z powikłaniami narządowymi, innymi czynnikami ryzyka, chorobami zapalnymi, zażywających leki hormonalne. U wszystkich chorych oceniono stężenia leptyny (ELISA, DLP00 Biokom) oraz NE (ELISA, EIA-2049 DRG MedTek). Parametry analizy czasowej i częstotliwościowej HRV oceniono na podstawie 24-godzinnego zapisu EKG (rejestrator DRG MedTek).

Wyniki: U kobiet po menopauzie obserwowano m.in. niższe wartości zmienności całkowitej, składowej VLF, oscylacji HF wyrażonych w jednostkach mocy widma i procentowych oraz wyższe znormalizowanej składowej LF i wskaźnika LF/HF z okresu całej doby. Stężenie NE było wyższe u kobiet po menopauzie w porównaniu z kobietami regularnie miesiączkującymi (487,58 ± 170,32 *vs* 382,57 ± 153,40 pg/ml; p = 0,0009), podobnie jak stężenie leptyny (4,39 ± 0,22 *vs* 4,29 ± 0,32 log pg/ml; p < 0,05).

Wnioski: Większa aktywność układu sympatycznego i wyższe stężenia leptyny u kobiet z nadciśnieniem tętniczym po menopauzie przemawiają za ich udziałem w patogenezie nadciśnienia tętniczego w tej grupie.

Słowa kluczowe: menopauza, nadciśnienie tętnicze, HRV, leptyna, noradrenalina

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