

BLOOD PRESSURE AND HAEMODYNAMICS MAYER WAVES IN DIFFERENT PHASES OF OVARIAN AND MENSTRUAL CYCLE IN WOMEN

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WOMEN**

Summary

The goal of the research is to investigate the special effect of ovarian-menstrual cycle phases on the level of women's blood pressure and characteristics of Mayer waves. 77 women aged 18-19 were tested under condition close to the state of basal metabolism in follicular phase (I), ovulation (II) and luteal phase (III) of ovarian-menstrual cycle. In phases II and III, the increase of mean and diastolic blood pressure level, in comparison with phase I in the prone position at rest and with psycho-emotional loading, were observed. The distinctions between variation parameters of R-R interval duration, stroke volume and its synchronization in phases II and III, in comparison with phase I, were observed in the prone position at rest, during tilt-test and with psycho-emotional loading. The substantial level of relationship between the power of Mayer waves and mean and diastolic blood pressure, mainly in phase I under conditions of all types, is observed. The maximum peak amplitude of stroke volume spectrogram is associated with pressure levels in the range of 0.04-0.15 Hz (ρ from -0.33 to -0.64). The obtained results indicate the possible participation of spontaneous baroreflex sensitivity characteristics in keeping blood pressure level in women.

Key words: blood pressure; spontaneous baroreflex sensitivity, Mayer waves, ovarian-menstrual cycle.

INTRODUCTION

In 1876, S. Mayer discovered slow waves in the oscillation of blood pressure (BP) at the frequency of 0.1-0.15 Hz in anesthetized rabbits. Later, the waves became known as “Mayer waves” (Cohen *et al.* 2013, Finucane *et al.* 2010). These waves are rather stable. In humans, they are located at a frequency of about 0.1 Hz, which does not depend on gender, age and body position according to some investigations (Bertram *et al.* 2005). Later, similar oscillations for other haemodynamics indicators were found (R-R interval duration, stroke volume (BSV), etc.) (Cheng *et al.* 2004 Elstad *et al.* 2011). The level of spontaneous baroreflex sensitivity, an indicator associated with features of keeping BP, is determined in the range of frequencies close to Mayer waves (Finucane *et al.* 2010). However, the relationships of AP and the features of haemodynamics indicator oscillations in this range are investigated insufficiently.

At the same time, the indicators of heart rhythms variability (HRV) and central haemodynamics in different physiological conditions have some features stipulated by gender factors. The phase of ovarian and menstrual cycle (OMC) is found to have a sufficient effect upon HRV in the women of reproductive age both at rest and with various loading (Yildirim *et al.* 2002). Such effects are found to change sufficiently haemodynamics indicators stipulated mostly by hormonal changes during OMC. The relationships of AP and the features of Mayer waves have not been studied yet.

Methods

77 women aged 18-19 were tested under the conditioned close to the state of basal metabolism in the prone position, at tilt test and during the test of psychic-

emotional stress (Makarenko 1999). All the women studied for humanitarian specialties at the Cherkasy National University. The main selection criteria were the lack of acute and chronic diseases, the normal trend of ovarian-menstrual cycle, the age of 17-19, the lack of taking hormonal contraceptives.

Each woman was tested three times: in follicular phase (I), ovulation (II) and luteal phase (III) of ovarian-menstrual cycle.

The women with regular ovarian-menstrual cycle took part in the study. Cycle phases were determined according to anamnesis, taking basal body temperature and using a set of inkjet ovulation tests “Solo” (IND Diagnostic, Inc., Canada). The confirmation of the reliability of cycle phase changes (optional) were performed by ultrasound diagnostics. Basal temperature taken rectally was increased by 0,5-0,8 °C in luteal phase.

Analytical methods

Systolic and diastolic BP (BP_s and BP_d respectively) was measured with Korotkov auscultation method by mercury tonometer (“Riester”, Germany). Mean blood pressure (BP_m) was calculated with Hickam formula; struck volume (BSV) – with Kubichek formula (Kubichek *et al.* 1970) by the signals of differentiated impedance rheogram by all the realizations (beat-to-beat) during 5 minutes (Fig.1).

The spectral and cross-spectral analysis of cardiointervalogram was performed in “CASPICO” program (copyright certificate of Ukraine №11262) according to international standards of 1996 (Anonymous 1996). The power of R-R and BSV oscillations spectrum was calculated in standard frequency ranges of very low frequencies of 0-0.04 Hz (VLF), low frequencies of 0.04-0.15 Hz (LF),

high frequencies of 0.15-0.4 Hz (HF), general oscillation power of 0-0.4 Hz (TP), normalized power in the range of 0.15-0.4 Hz (HF_{norm}). Besides, spectral and cross-spectral density and the frequency of the highest amplitude oscillation peak of t-R-R and BSV in LF range (Kovalenko 2005) were estimated in the prone position at rest for 5 minute records, at tilt test from the 2d till the 5th minutes and in psycho-emotional test from the 3d till 7th minutes.

Statistical Methods

Due to the abnormality of the value distribution of oscillation power of haemodynamic indicators, their medians, the limits of 25 and 75 percentile were found; the average values and their errors for BP indicators distributed normally were determined. The reliability of differences between values in different OMC phases was estimated by means of Wilcoxon Paired Comparison and Student's t-test. The relationship between indicators was calculated by the nonparametric Spearman correlation coefficient (Glantz 2012).

Results

BP is known to be an important homeostatic indicator of an organism. Therefore, its changes in different OMC were analyzed in the prone position at rest, at tilt test and with psycho-emotional loading (Fig. 2). In the prone position at rest, BP_m levels increased in phases II and III compared with phase I: the differences between phases I and II were 2.53 ± 0.99 mmHg ($P < 0.05$), between I and III – 2.76 ± 1.24 mmHg ($P < 0.05$). At tilt test, BP_m increased in phases I and II,

the changes were not significant statistically in phase III. Herewith, the difference of BP_m was 0.78 ± 0.97 mmHg in phase I-II and 1.55 ± 0.87 mmHg in phase I-III.

BP_m was leveled in phase III, compared with phase I, with psycho-emotional loading ($P < 0.05$). Difference value of this BP_m was 3.33 ± 1.44 mmHg ($p > 0.05$) and 2.74 ± 1.16 mmHg, respectively. Thus, BP response to such loading is characterized by definite features and, in all the phases, there is its increase in phase II and, especially, in phase III of OMC compared with phase I.

The indicators of haemodynamic Mayer waves in women under different conditions are presented in Table 1. In the prone position at rest, oscillation power in the range of LF changed reliably in phase II (t-R-R) and in phase III (BSV) concerning phase I. Changing body position to a vertical one, the reactivity of t-R-R oscillation power was 27.6 % [- 35%; 71.8%] in this frequency range and differs significantly compared to phases I and II: - 1.4 [-35.6; 60.8] % and -21.7 [-59.2; 29.7] % respectively.

The amplitude of maximum peak of t-R-R and BSV waves also changed in different OMC phases. Thus, in the prone position at rest in women, there was significant ($P < 0.05$) decrease of t-R-R oscillation density in phase III compared with phases I and II, and the increase of BSV oscillation density in phase II compared with phases I and III. With psycho-emotional loading, this indicator was the lowest in phase I of OMC ($147.4 [81; 273.4] \text{ mc}^2 \cdot \text{Hz}^{-1}$) compared with phases II and III – $178.7 [103.8; 506.6] \text{ mc}^2 \cdot \text{Hz}^{-1}$ and $207.2 [101.2; 408.7] \text{ mc}^2 \cdot \text{Hz}^{-1}$ respectively.

The amplitude of the maximum peak of cross-spectral power (maxLF) in the prone position at rest increased in phases II and III compared to phase I. At tilt test, the highest values were in phase I. Under the conditions of psycho-emotional loading, there was the greatest decrease of this indicator in phase II (-22.1%) and III (-40.8%) according to its background level of minor violations (0.4%) – in I.

Thus, in the prone position at rest, at tilt test and with psycho-emotional loading, there are differences mostly in the indicators of R-R and BSV interval duration oscillations and their synchronization in women in phases II and III compared with phase I.

Discussion

BP is known to increase, in this case, due to the reduction of peripheral vessels in the lower limbs (Mohrman and Heller 2002). The mechanism of compensatory reaction to tilt test is due to the changes in the activity of baroreceptors in response to BP changes, the inhibition of vagus effect and the increase of sympathetic one on heart and blood vessels (Brunt *et al.* 2013).

The obtained reliable growth of BP value in phase III if compared to phase II and, moreover, to phase I shows the increased tone of ANS sympathetic part and agrees with literature data (Princi *et al.* 2005). Some authors (Vollebregt *et al.* 2006) indicate the individual features of autonomic regulation in women and suppose the relative stability of autonomous regulation type and its genetic determinism. However, there are some contradictions. Thus, Japanese scientists (Yamamoto *et al.* 2003) observed the increase of LF value reflecting the effect of

both sympathetic and parasympathetic parts of ANS on BP level at both phase II and phase I.

Princi and co-authors (Princi *et al.* 2005) found opposite data, i.e. LF increase in phase I and its decrease in phase III. However, only 6 women were examined, and therefore, these data are insufficient for statistic processing. Lucini D. and co-authors (Lucini *et al.* 2002) observed BP increase in phase II. Herewith, the content of sex hormones did not change. HRV indicators did not change in any OMC phase. However, the correlation between estrogen content and HRV absolute peak was identified in phase II. The authors explain the obtained correlation with cardiotropic effect of sex hormones.

The regulation of body functional systems in the classic sense is based on the phenomenon of receptor apparatus sensitivity. Anokhin's works (Anokhin 1962) showed that it was receptors that played a key role in the regulation of functional systems as a component of biosystem. According to the author, the system has infinite opportunities to align adaptive effect due to the innate specific features of receptors and their relationship with "working body)"

The features of haemodynamic Mayer waves are found to reflect the level of spontaneous baroreflex sensitivity, which stipulated the stability of BP (Vallais *et al.* 2009). Therefore, the relationship between these indicators has been analyzed. Our results (Table 2) show the significant correlation between the power of Mayer waves and BP_m and BP_d mostly in phase 1 of OMC. The amplitude of maximum peak of BSV spectrogram in LF range is associated with the levels of BP_m та BP_d

to a greater extent. This fact confirms the possibility of participating Mayer waves in keeping the level of system pressure in women.

The classic definition of baroreflex sensitivity is based on an assessment of haemodynamic changes when epinephrine is injected (Chaswal M *et al.* 2015). However, recently, the level of spontaneous baroreflex sensitivity has been determined in the investigation of human beings. Nowadays, the problem of interaction between baroreflex and BP in women under hormone action (during menstrual cycle) has not been decided. Sato N. and co-authors (Sato *et al.* 1995) consider that spontaneous baroreflex sensitivity in women can disappear under the effect of sex hormones action. Moak P. and co-authors (Moak *et al.* 2009) estimated HRV and spontaneous baroreflex sensitivity during their study of the features of autonomous nervous system under the conditions of normal menstrual cycle, and found that sympathetic tone increased in phase II compared with phase I. Brooks V.L. and co-authors (Brooks *et al.* 2012) determined that higher spontaneous baroreflex sensitivity and higher concentration of norepinephrine in the plasma of women were observed during phase III compared with phase I. The problem of what mechanism is in the basis of increasing the activity of ANS sympathetic part in phase III, remains debatable.

Limitations of the research are the following. First, the measurements were performed on a fairly limited (in age, social background) contingent. Second, the examined women had normal, for this group of people, blood pressure and, therefore, to carry the results to the individuals with its disorders is very

problematic. However, the results may be useful for understanding the etiology of hypertensive states.

CONCLUSIONS

In ovulatory and luteal phases of the ovarian cycle of women, the average and diastolic blood pressure was higher compared with the follicular phase at rest, in prone position and under the psycho-emotional loading. There are differences in the indicators of BSV and R-R interval duration oscillations and their synchronization in ovulatory and luteal phases in women compared with follicular phase in the prone position at rest, at tilt test and with psycho-emotional loading. There is a reliable correlation between the power of Mayer waves and mean and diastolic pressure mostly in OMC phase I of women under all the conditions. The amplitude of maximum peak of BSV spectrogram in the range of 0.04-0.15 Hz is associated with BP_m and BP_d to the greatest extent.

Conflict of interest: No conflict of interest

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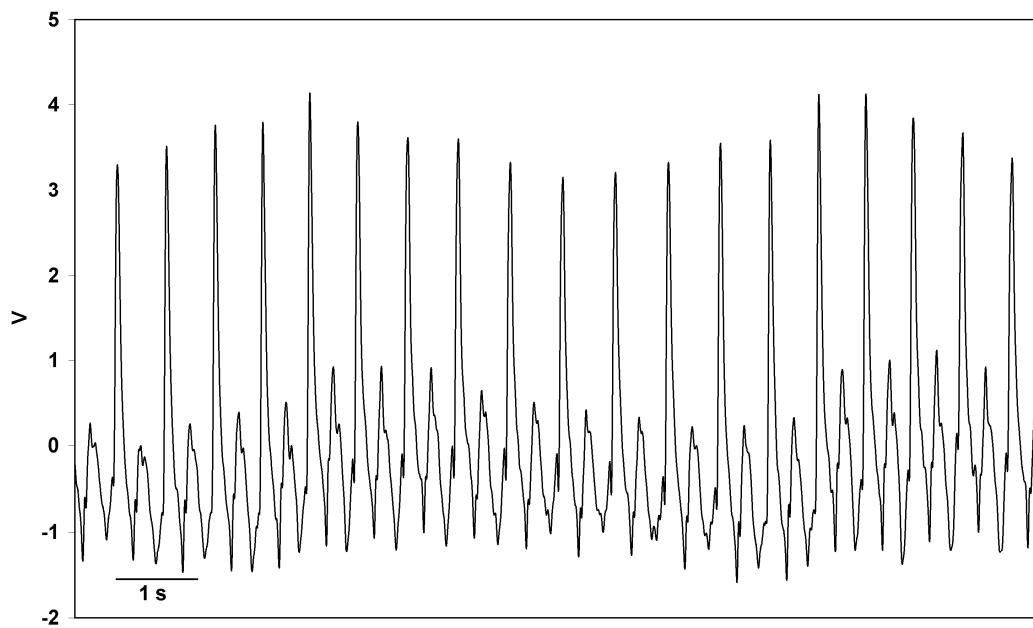


Fig. 1. Record fragment of differentiated impedance rheogram

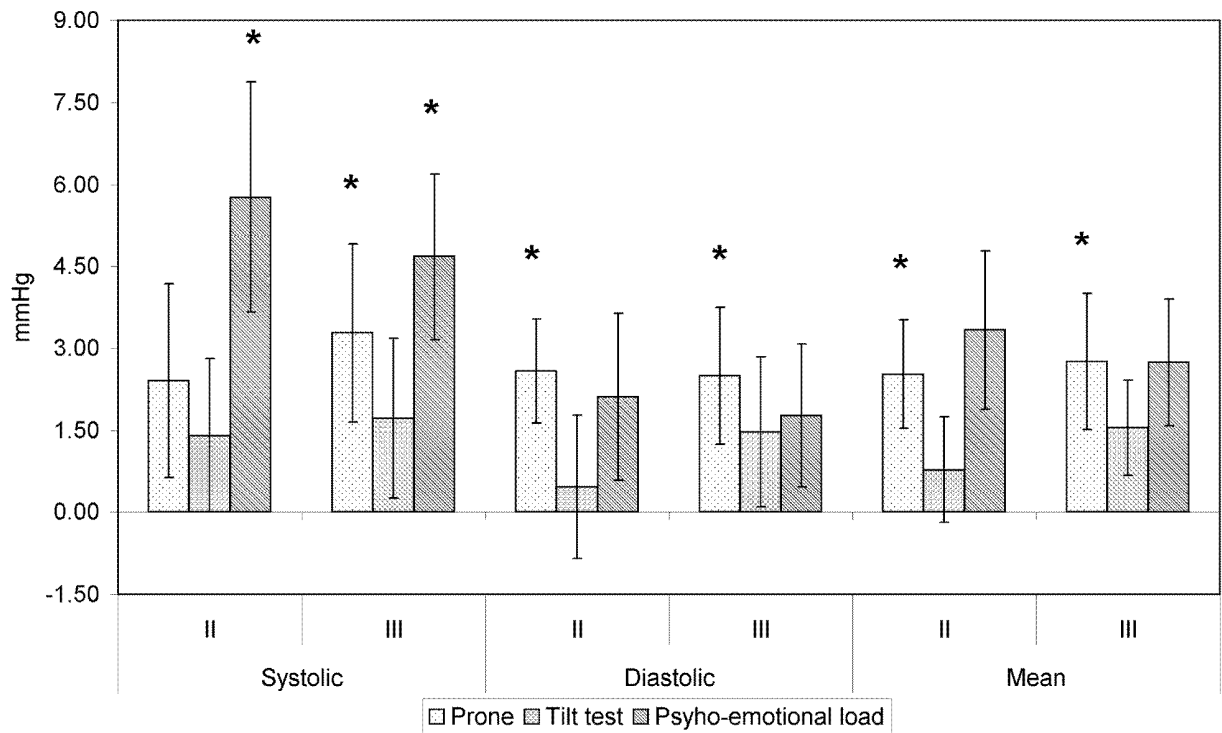


Fig. 2. Changes of systolic, diastolic and mean blood pressure in ovulatory (II) and luteal (III) phases of ovarian-menstrual cycle compared with follicular phase; * - $P < 0.05$ compared to follicular phase

Table 1. Indicators of Mayer Haemodynamics Waves in Women under Different Conditions (median, limits of 25 and 75 percentile)

Phase	Oscillation power in the range of 0.04-0.15 Hz		Amplitude of spectrogram maximum peak in the range of 0.04-0.15 Hz		Amplitude of maximum peak of cross-spectral power in the range of 0.04-0.15 Hz, mc·ml
	R-R interval duration, mc ²	stroke volume, ml ²	R-R interval duration, mc ² ·Hz ⁻¹	stroke volume, ml ² ·Hz ⁻¹	
Prone position					
I	612 [266; 832]	5.2 [2.2; 7.4]	14548 [6727; 23151]	279 [166; 737]	211 [114; 431]
II	670 [273; 974]*	6.1 [3.4; 7.2]	15979 [8686; 23902]	354 [135; 649]*	289 [145; 753] *
III	598 [241; 869]	4.9 [3.1; 8.1]*	11736 [5763; 24334]*#	292 [141; 528] [#]	258 [134; 445] * [#]
Tilt Test					
I	523 [276; 771]	2.9 [1.9; 5.1]	12137 [7560; 23689]	326 [130; 462]	296 [111; 426]
II	459 [276; 689]*	3.2 [1.9; 4.4]	14331 [9427; 17804]*	326 [139; 549]	286 [140; 364] *

III	553 [399; 867]	3.1 [1.6; 6.1]	13725 [10153; 17875]	254 [129; 628] [#]	266 [128; 401] [#]
Psycho-emotional loading					
I	492 [300; 1047]	2.0 [1.1; 4.3]	12299 [8192; 23955]	147 [81; 273]	206 [133; 318]
II	518 [341; 852]	3.4 [1.8; 5.7]	12981 [9027; 21818]	179 [104; 507]	294 [133; 446]
III	425 [#] [285; 605]	2.9 [1.6; 5.1]	10873 [6787; 14965] [#]	207 * [101; 409]	230 [#] [138; 378]

Note: * - $P < 0.05$ compared with indicators in phase I; # - $P < 0.05$ between indicators in phases II and III

Table 2. Correlation of Mayer Waves Features and Arterial Pressure Indicators in Women in Different Phases of Ovarian-Menstrual Cycle

Pressure Indicators	Oscillation Power in the range of 0.04-0.15 Hz						Amplitude of spectrogram maximum peak in the range of 0.04-0.15 Hz					
	R-R interval duration			stroke volume			R-R interval duration			stroke volume		
	I	II	III	I	II	III	I	II	III	I	II	III
	Prone position											
Systolic	0.01	-0.13	-0.10	-0.14	0.00	0.11	-0.03	-0.14	-0.10	-0.33	-0.16	-0.45
Diastolic	-0.31	-0.26	-0.05	-0.40	-0.36	0.29	-0.35	-0.17	-0.01	-0.56	-0.62	-0.38
Mean	-0.10	-0.24	-0.01	-0.27	-0.22	0.23	-0.15	-0.18	0.04	-0.46	-0.49	-0.46
Tilt Test												
Systolic	-0.14	0.01	-0.10	0.50	0.22	-0.06	-0.06	0.08	-0.12	-0.19	-0.31	-0.43
Diastolic	-0.48	-0.25	-0.28	-0.23	0.12	0.29	-0.40	-0.14	-0.41	-0.64	-0.34	-0.38
Mean	-0.39	-0.10	-0.24	0.19	0.17	0.27	-0.29	-0.02	-0.33	-0.49	-0.36	-0.47
Psycho-emotional loading												
Systolic	0.14	-0.28	-0.20	0.25	0.18	-0.08	0.09	-0.24	-0.14	0.161	0.008	-0.197
Diastolic	-0.13	-0.47	-0.26	-0.02	-0.27	-0.09	-0.07	-0.48	-0.34	0.057	-0.509	-0.033
Mean	0.05	-0.33	-0.36	0.17	0.04	-0.19	0.047	-0.32	-0.38	0.216	-0.212	-0.414