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Original Research Article

A comparative study of parasympathetic function tests during different phases of menstrual cycle in young healthy females

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ABSTRACT

Background: The hormonal fluctuations that occur during normal menstrual cycle has profound influence on autonomic functions. This influence on autonomic nervous system may affect cardiovagal control. The aim of the study is to find out the variation of Parasympathetic function tests during different phases of menstrual cycle in young healthy females.
Methods: The present study was carried out on 50 healthy female subjects with normal menstrual cycles between the ages of 18 to 25 years. Various non-invasive parasympathetic function tests during different phases of menstrual cycle were performed that include Resting heart rate (RHR), Heart rate variation during deep breathing (E:I Ratio), Heart rate response to standing (30:15 Ratio), Heart rate response to Valsalva maneuver (Valsalva Ratio). The results were analysed using ANOVA and student's paired-t tests.
Results: During the menstrual cycle, we found varied heart rate response with higher values towards the luteal phase, when compared to the follicular phase and the menstrual phase. There was a statistically significant difference in the heart rate parameters like resting heart rate, 30:15 ratio, valsalva ratio and E:I ratio during the three phases of menstrual cycle.
Conclusions: The study concludes that there was statistically significant heart rate variability during three phases of the menstrual cycle, as observed by the increased sympathetic discharge in the luteal phase compared to the increased parasympathetic discharge in the follicular phase. The results of our study have emphasized the complexity of the relationship between ovarian steroids and various hemodynamic regulatory systems.

Keywords: Heart rate, Menstrual cycle, Parasympathetic function tests

INTRODUCTION

The menstrual cycle apart from being a cycle of monthly periods involving endometrial and cervical changes, also associated with many physical, psychological and behavioural changes. This biological rhythmicity of the menstrual cycle is created by the interplay among hypothalamic, hypophyseal and ovarian hormones.[1]

The menstrual cycle is governed by well-coordinated variations in the levels of ovarian estrogen and progesterone which also produces varying responses in different tissues and organs.[2] Cyclic fluctuations in the plasma level of these hormones contribute to the expression of the menstrual cycle. Physiologically, estrogen is primarily a hormone of follicular phase and progesterone is primarily a hormone of luteal phase. But in the menstrual phase there occurs sudden drop in estrogen and progesterone levels.

The presence of estrogen receptors in the heart, vascular smooth muscle and autonomic brain centres-nucleus tractus solitarius and ventrolateral-medulla, suggest a possible combined involvement of autonomic nervous system and ovarian hormones in the regulation of cardiovascular system.[3]

The autonomic nerves have a pivotal role in the regulation of the cardiovascular system. Certain autonomic changes have been reported during premenstrual phase. It is likely that the varying levels of ovarian hormones in the normal menstrual cycle may be responsible for such changes in autonomic functions.[4]

Only a few studies, with rather conflicting results, have focused on the influence of menstrual cycle on cardiac autonomic modulation in Indian context. The aim of the present study is to examine parasympathetic response to physical stressors like deep breathing, postural change and valsalva maneuver on ECG, during follicular, luteal and menstrual phases of the menstrual cycle in young healthy females.

METHODS

The present cross-sectional study was carried out in the Department of Physiology, M.G.M. Medical College, Indore (M.P.). A total of 50 young healthy female medical students with normal menstrual cycle in the age group of 18-25 years were selected for study. A brief explanation to subjects regarding the procedure was given and written informed consent was taken. The ethical clearance was obtained from the institutional ethical committee. Only those participants were taken into study that fulfilled our inclusion criteria's.

Inclusion criteria

Female subjects of 18-25 yr age group, giving consent for participation in the study.

Exclusion criteria

- Subjects not giving consent for participation.
- History of alcohol intake.
- History of smoking, tobacco consumption.
- History of hypertension or any other clinical signs of cardiovascular diseases.
- Subjects receiving drugs known to affect autonomic function, for example: Adrenergic drugs, Adrenergic blocking drugs, Cholinergic agents, Diuretics, Antihypertensive drugs etc.
- Females with irregular menstrual cycle.

A thorough history with special attention to the menstrual history was taken. Subjects were instructed to visit the department during each phase of menstrual cycle. 1-5th day, 9-12th day and 19-25th day were selected to represent the menstrual, follicular and luteal phases respectively. Physical parameters like age, height and weight were noted. Electrocardiogram recordings were carried out in Lead II. All tests were carried out in the morning.

The following Parasympathetic function tests were performed:

Resting heart rate

The subject was asked to rest in supine position for 15 mins. After fixing the leads, the subject was asked to lie down quietly for 3 mins and at the end of 3 mins HR was recorded. The HR was counted with the following calculation:

HR/min= 1500/Distance between two consecutive R-R intervals in mm

Heart rate variation during deep breathing

The subject was asked to lie down comfortably and was asked to take deep breaths slowly in and out, approximately at 6 breaths per minute i.e. 5 seconds inspiration and 5 seconds expiration. The maximum and minimum R-R intervals during each respiration cycle were recorded.

E:I Ratio = Mean of maximum RR intervals during deep expiration/Mean of minimum RR intervals during deep inspiration

Heart rate response to immediate standing

The subject was asked to lie down comfortably for 10 mins and then was asked to stand up. On standing, the HR increases until it reaches a maximum at approx 15th beat, after which it slows down to stable state at approx 30th beat.

30:15 Ratio = Longest RR interval occurring about 30th beat after standing/Shortest RR interval occurring about 15th beat after standing

Heart rate response to valsalva maneuver

The subject was asked to sit. The nostrils were closed by nose clip and asked to blow by doing forceful expiration into the rubber tube of a mercury sphygmomanometer, raise the mercury column to 40 mm Hg and maintain that level for at least 15 seconds. The heart rate was recorded continuously during the whole procedure.

Valsalva Ratio = Maximum RR interval after strain/Shortest RR interval during strain

Statistical analysis

In the present study, results were expressed as Mean ± SD. All statistical analysis was done by using SPSS software version 20. ANOVA test used to find out significant variation across the different phases and student's paired-t test was carried out to study significance of variations between different phases. P Value < 0.05 is taken as significant.

RESULTS

This study was carried out in the Department of Physiology, M.G.M. Medical College and M.Y. Hospital, Indore (M.P.). A total of 50 female medical students without any co-morbidity, in the age group of 18-25 years were studied for a group of parasympathetic function tests and the following observations were drawn from the study.

The mean of anthropometric parameters of subjects were described in Table 1. The mean±SD of age in females was 19.32±1.150 yrs and the mean±SD of BMI in females was 20.33±2.993 kg/m^2.

Table 1: Mean ± SD of the anthropometric parameters.

Variables	Mean±SD
Age (yrs)	19.32±1.150
BMI (kg/m^2)	20.33±2.993

The mean of all the parameters of Parasympathetic function tests during different phases of menstrual cycle were described in Table 2.

Table 2: Comparison of parasympathetic function tests during different phases of menstrual cycle.

Parameters	Menstrual phase*	Follicular phase*	Luteal Phase*	P-value**
Resting heart rate	77.58±4.375	78.3±4.441	79.06±4.414	0.000
E:I ratio	1.32±0.069	1.31±0.062	1.36±0.072	0.000
30:15 ratio	1.17±0.053	1.15±0.052	1.16±0.033	0.013
Valsalva ratio	1.50±0.056	1.49±0.065	1.52±0.049	0.004

*Mean±SD **by ANOVA

The value of mean±SD of Resting Heart Rate was highest in luteal phase, as shown in Figure 1.

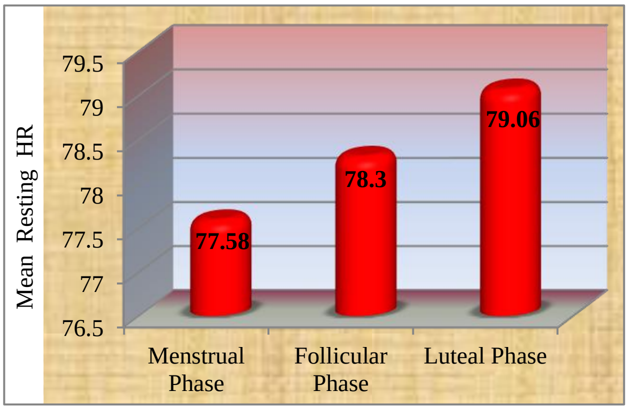

Figure 1: Comparison of resting heart rate during different phases of menstrual cycle.

The value of mean±SD of E:I Ratio was highest in luteal phase, as shown in Figure 2. The value of mean±SD of 30:15 Ratio was highest in menstrual phase, as shown in Figure 3.The value of mean±SD of valsalva Ratio was highest in luteal phase, as shown in Figure 4.

The data obtained was statistically analysed by repeated measures of ANOVA test which shows that there is statistically significant difference in the all the parameters of Parasympathetic function tests during different phases of menstrual cycle in females.

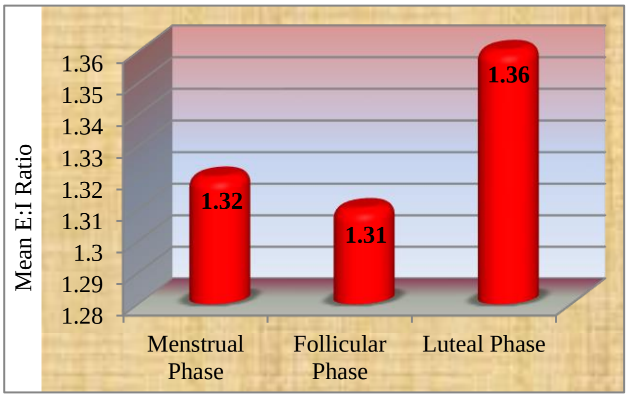

Figure 2: Comparison of E:I ratio during different phases of menstrual cycle.

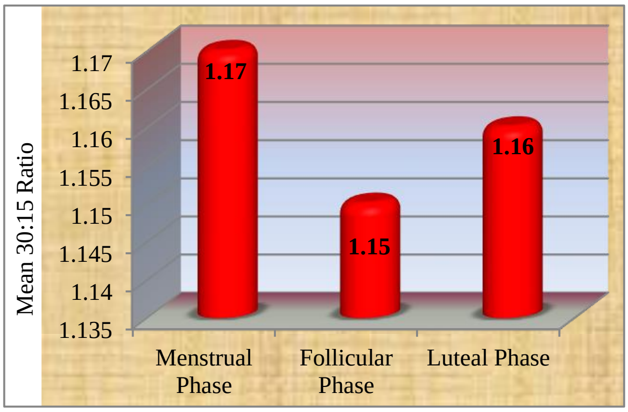

Figure 3: Comparison of 30:15 ratio during different phases of menstrual cycle.

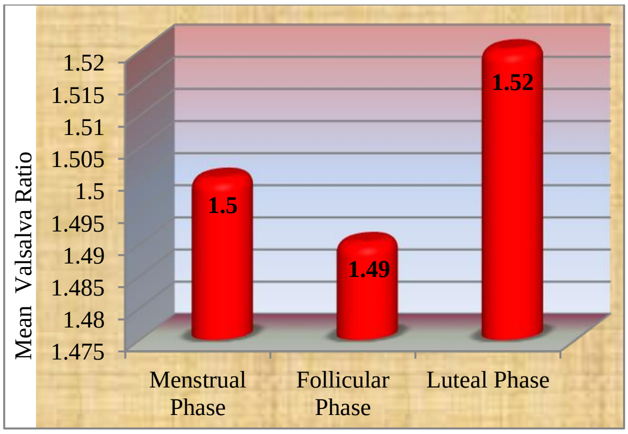

Figure 4: Comparison of valsalva ratio during different phases of menstrual cycle.

In Table 3, Student's paired-t test was used to compare the 2 phases of menstrual cycle at a time, e.g.: menstrual phase (MP) v/s follicular phase (FP), menstrual phase (MP) v/s luteal phase (LP) and follicular phase (FP) v/s luteal phase (LP).

Table 3: Comparison of parasympathetic function tests between different phases of menstrual cycle (p-value)*.

Parameters	Menstrual v/s follicular phase	Menstrual v/s luteal phase	Follicular v/s luteal phase
Resting heart rate	0.000	0.000	0.000
E:I ratio	0.069	0.000	0.000
30:15 ratio	0.006	0.121	0.127
Valsalva ratio	0.205	0.040	0.001

There was a statistically significant difference of RHR between MP v/s FP, MP v/s LP and FP v/s LP.

The E-I ratio difference between MP v/s FP of menstrual cycle in females is not statistically significant but statistically significant between MP v/s LP and FP v/s LP.

The 30:15 ratio difference between MP v/s FP of menstrual cycle in females is statistically significant but not statistically significant between MP v/s LP and FP v/s LP.

The valsalva ratio difference between MP v/s FP of menstrual cycle in females is not statistically significant but statistically significant between MP v/s LP and FP v/s LP.

DISCUSSION

In our study, there was a statistically significant difference in resting heart rate between all the three phases of the menstrual cycle: menstrual and follicular phases, follicular and luteal phases and luteal and menstrual phases.

This study result was also similar with other studies; A higher resting heart rate was observed in the luteal phase than in the follicular phase.[5] The heart rate variability was significantly higher in the luteal phase compared to the follicular phase, suggesting increased sympathetic activity in the luteal phase; the alteration in the balance of ovarian hormones might be responsible for these changes in the cardiac autonomic innervations.[6] The plasma norepinephrine levels were significantly higher in the mid-luteal phase than in the early follicular phase; therefore the hormonal fluctuations that occur during the normal menstrual cycle may alter sympathetic outflow.[7] But our result was not similar with the studies of Mehta V et al and Parlewar RK et al.[4,8]

Thus, it may be possible to conclude that the higher resting levels of circulating plasma norepinephrine and the higher sympathetic discharge in the late luteal phase is responsible for increased heart rate variability towards the luteal phase.

In E:I Ratio, there was a statistically significant difference between menstrual and luteal phases and follicular and luteal phases, but has not shown statistically significant difference between menstrual and follicular phases. Our result was also similar with the study of Kavitha C et al but the result was not similar with the studies of Mehta V et al, and Parlewar RK et al.[4,8,9] Normally there occurs a fluctuation of heart rate that is synchronous with the respiratory cycle. The heart rate increases slightly during inspiration and decreases on expiration. This sinus arrhythmia is a normal phenomenon and is primarily due to fluctuations in parasympathetic output to the heart. During inspiration, impulses in the vagi from the stretch receptors in the lungs inhibit the cardio inhibitory area in the medulla oblongata. The tonic vagal discharge that keeps the heart rate slow decreases and the heart rate rises.[10] Therefore, E:I Ratio reflects the parasympathetic activity during different phases of the menstrual cycle.

In 30:15 Ratio, there was a statistically significant difference between menstrual and follicular phases but has not shown any statistically significant difference between menstrual and luteal phases and follicular and luteal phases. Our results were similar with the study of Parlewar RK et al, Nilekar AN et al, Kavitha C et al but the result was not similar with the study of Mehta V et al.[4,8,9,11]

30:15 ratio is a biphasic response mediated by the afferent inputs from muscle, vagus nerve and the baroreceptor reflex arc. Changing from lying position to standing produces an integrated reflex response of the cardiovascular system, which includes alteration in the heart rate and blood pressure. There is a transient fall in blood pressure on standing with stimulation of the carotid baroreceptors and consequent reflex tachycardia and peripheral vasoconstriction. In normal subject, there is immediate reduction of R-R interval which is maximal around 15th beat on standing followed by relative increase of R-R interval around 30th beat after standing.[12] 30:15 ratio predominantly reflects the parasympathetic activity.[4] This immediate difference in heart rate on standing could be due to withdrawal of vagal tone.

In Valsalva Ratio, there was a statistically significant difference between menstrual and luteal phases and follicular and luteal phases but has not shown statistically significant difference between menstrual and follicular phases. Our results were similar with the study of Parlewar RK et al, Nilekar AN et al, Fuenmayor AJ et al, but the result was not similar with the studies of Choudhury R et al.[8,11,13,14]

Valsalva maneuver is forced expiration against closed glottis. The blood pressure rises at the onset of straining because the increase in intrathoracic pressure is added to the pressure of the blood in the aorta. It then falls because the high intrathoracic pressure compresses the veins decreasing venous return and cardiac output. The decrease in arterial pressure and pulse pressure inhibit the baroreceptors, causing tachycardia and rise in peripheral resistance. O'Brien and O'Hare suggested that the Valsalva maneuver elicit a complex scale of hemodynamic events that result in the activation of both sympathetic and parasympathetic neurons.[15] Fuenmayor AJ et al studied the cardiac autonomic nervous system balance variation during two phases of menstruation.[13] The Valsalva maneuver was performed to test the autonomic function and they concluded that the autonomic nervous system balance changes significantly during the luteinizing phase of the cycle in normal women. Based on the correlation of the various studies mentioned it can be concluded that the Valsalva ratio is a parameter, which reflects balance between both parasympathetic and sympathetic, show significant results in luteal phase. The present study also shows a similar rise in the valsalva ratio during the luteal phase indicating the sympathetic nerve activities in this phase and correlates well with other studies. It is likely that an exaggerated response to hormonal changes may be responsible for significant results.

In the present study, changes were observed in most of the parameters of parasympathetic function tests, which may be due to fluctuation of hormones in different phases of menstrual cycle. But there were certain limitations in carrying out this present study due to lack of required advanced equipments and proper ANS lab setup for carrying out our research work.

CONCLUSION

From the result of our study, it can be concluded that there is heart rate variability during various phases of the menstrual cycle in young healthy females as observed by the increased sympathetic discharge in the luteal phase as compared to the follicular phase and increased parasympathetic discharge in the follicular phase as compared to the luteal phase. This lower parasympathetic activity or higher sympathetic activity during the luteal phase of the menstrual cycle may be correlated with higher estrogen and progesterone levels, which may be responsible for premenstrual stress. Also, further study is required to correlate ANS functions with hormonal fluctuation in menstrual cycle by investigating the hormonal levels during various phases of menstrual cycle.

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