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Original Research Article

A Comparative Study of Cardiovascular Autonomic Function Tests during Different Phases of Menstrual Cycle

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ABSTRACT

The hormonal fluctuations that occur during the normal menstrual cycle may alter the autonomic functions. In the present study, an attempt was made to study cardiovascular autonomic functions during different phases of menstrual cycle and to correlate the changes if any to hormonal influences. Select cardiovascular sympathetic and parasympathetic autonomic function tests were conducted on 50 normal healthy young unmarried female subjects in the age group of 20 to 25 years who had normal regular menstrual cycles. The tests were conducted during menstrual phase, proliferative phase and secretory phase of the menstrual cycle using electrocardiograph and mercury sphygmomanometer. The results were statistically analysed by applying paired "t" test. Our findings indicate a higher sympathetic activity and a higher basal heart rate in secretory phase as compared to other phases. Parasympathetic activity on the other hand did not show statistically significant differences. This higher sympathetic activity may be correlated with higher oestrogen & progesterone levels during the secretory phase of the menstrual cycle. The results of our study have emphasized the complexity of the relationship between ovarian steroids & various hemodynamic regulatory systems.

Key words: menstrual cycle, autonomic function tests, sympathetic activity, oestrogen, progesterone.

INTRODUCTION

Rhythmic activities are abundant in biologic systems and the impact of these rhythms on humans is widely recognized. One such rhythm is the human menstrual cycle. [(1)] This is a feature which is unique to the female gender of humans and other higher apes. [(2)] 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. [(3)] Evidences also show that various behavioural and other changes in women also occur during the menstrual cycle. Exaggerated response to hormonal changes may be responsible for different physical and psychological ramifications occurring during menstrual cycle [(4)] though other factors may also be involved.

Some studies have reported that there are certain autonomic changes during

the menstrual cycle. The varying levels of ovarian hormones in the normal menstrual cycle may be responsible for such changes in autonomic functions. The autonomic nervous system balance and the left ventricular diastolic functions suffer significant changes during the secretory phase of menstrual cycle in normal women. [5] The menstrual cycle may influence sympathetic control of blood pressure and therefore white coat hypertension. [6]

But the studies conducted on autonomic functions during various phases of menstrual cycle are few and also provide little information about the impact of hormonal changes that occur during the menstrual cycle on autonomic functions. Hence, the present study was conducted to throw more light on autonomic changes during different phases of menstrual cycle and also to explore the relationship between changes if any and the hormonal fluctuations that occur during the menstrual cycle.

MATERIALS AND METHODS

This study was conducted on 50 healthy young unmarried female subjects having regular menstrual cycles in the age group of 20-25 years after obtaining informed consent, and the study was carried out in the physiology department, KIMS, Hubli. This study was cleared by the ethics committee of the institute.

Source of data:

Subjects:

Unmarried young female subjects having regular menstrual cycles in the age group of 20-25 years were selected after employing the following inclusion and exclusion criteria.

Inclusion criteria:

1. Subjects should belong to the specified age range (20-25 years).
2. They should have regular ovulatory menstrual cycles of 27 to 30 days as established by history, for at least the past 6 months.
3. Body mass index should be within the normal range (18.5-24.9kg/m^2).

Exclusion criteria:

1. Female subjects below 20 years and above 25 years.
2. Subjects having irregular menstrual cycle.
3. Subjects having anovulatory cycles.
4. Subjects taking any medication or hormonal preparations that could alter the menstrual hormonal milieu.
5. Subjects having any physical illness or endocrinological disorders.
6. Smokers, alcoholics or those with history of substance abuse.
7. Athletes and those involved in excessive physical activity.

Method of collection of data

The subjects were from Nursing College, KIMS, Hubli. They were briefed about study protocol and informed consent was obtained from them. A thorough history with special attention to the menstrual history was taken. A complete general physical examination was done. Height & weight of the subjects were also recorded using standard methodologies. Subjects were instructed to visit the department during each phase of menstrual cycle. 1-5th day, 9-12th day and 19-22nd day were selected to represent the menstrual, proliferative and secretory phases respectively. Phases were corroborated with the period of ovulation, as judged from daily basal oral temperature of subjects throughout the cycle. Subjects were received warmly in the laboratory and sufficient time allowed for subjects to get accustomed to the lab.

The following tests were performed:

A. Sympathetic function tests:

a. Blood pressure response to immediate standing.

b. Blood pressure response to sustained hand-grip exercise.

B. Parasympathetic function tests:

a. Heart- rate response to valsalva manoeuvre. (Valsalva ratio)
b. Heart rate variation during deep breathing.
c. Heart- rate response to immediate standing. (30:15 ratio)

C. Basal heart rate

All the above parameters were recorded during the menstrual (1 to 5th day), proliferative (9 to 12th day) and secretory (19 to 22ndday) phases of the menstrual cycle. The ECG machine cardiart 108T, J & A, 14901 was used for calculating the heart rate and mercury sphygmomanometer for recording the blood pressure.

Blood pressure response to immediate standing was calculated by taking the difference between systolic blood pressure on lying down & systolic blood pressure on immediate standing.

Blood pressure response to sustained hand grip was calculated by recording blood pressure at the beginning & at the end of the procedure, where in the subject is asked to maintain the Hand-Grip(isometric contraction) at 30% of the maximum voluntary contraction for 5 minutes.

The valsalva ratio was calculated by taking longest R-R interval after the manoeuvre/shortest R-R interval during the manoeuvre.

Heart rate variation during deep breathing was calculated by measuring maximum & minimum R-R interval during expiration & inspiration respectively, expressed as beats per minute & then the difference between maximum & minimum heart rate was calculated.

30:15 ratio was calculated by taking the R-R interval between 30th-31st beat/the R-R interval between 15th -16th beat.

Statistical Analysis

The present study was statistically analysed using paired‘t’ test. Mean, standard error of mean, t values and p values were calculated to get the results of the study.

RESULTS

The present study showed the following findings. The sympathetic function tests showed significant ($P<0.01$) differences between the three phases (Table 1 & 2). On the other hand, parasympathetic function tests did not show significant ($P>0.05$) differences between the three phases. Basal heart rate showed significant difference between menstrual phase & secretory phase, between proliferative phase & secretory phase, but not between menstrual phase & proliferative phase

Table 1. Comparison of sympathetic & parasympathetic function tests & basal heart rate during different phases of menstrual cycle.

Phase	BPS	BPH	VR	HRB	HRS	BHR
I	6.72±0.22	17.12±0.14	1.33±0.08	19.55±0.47	1.32±0.1	81.84±6.35
II	5.65± 0.25	17.04±0.15	1.32±0.07	20.6±0.49	1.3±0.11	81.56±7.24
III	3.96± 0.25	16.8±0.15	1.31±0.07	19.94±0.48	1.28±0.13	88.08±6.18

Data expressed as Mean ± SEM (n=50)

(Phase-I - Menstrual Phase. Phase-II - Proliferative phase. Phase-III - Secretory phase. BPS-Blood pressure response to immediate standing, BPH-Blood pressure response to sustained handgrip. VR-Valsalva ratio. HRB- Heart rate response to deep breathing. HRS-Heart rate response to immediate standing. BHR-Basal heart rate)

Table 2. Table showing the results of sympathetic & parasympathetic function tests & basal heart rate during different phases of menstrual cycle.

Phase	BPS		BPH		VR	
	t-value	p-value	t-value	p-value	t-value	p-value
I & II	0.906	0.369 *	1.23	0.728 *	0.00	1.00*
II& III	9.25	0.00 **	1.1	0.278 *	0.544	0.589 *
III& I	10.88	0.00 **	2.54	0.088 *	0.563	0.576 *

* Not significant ** Highly significant

Phase	HRB		HRS		BHR	
	t-value	p-value	t-value	p-value	t-value	p-value
I &II	1.6	0.116 *	0.725	0.472 *	1.89	0.65 *
II& III	1.03	0.306 *	1.04	0.304*	6.38	0.00**
III& I	0.72	0.475 *	1.605	0.115*	6.77	0.00**

* Not significant ** Highly significant

(Phase-I - Menstrual Phase. Phase-II - Proliferative phase. Phase-III - Secretory phase. BPS-Blood pressure response to immediate standing, BPH-Blood pressure response to sustained handgrip. VR-Valsalva ratio. HRB- Heart rate response to deep breathing. HRS-Heart rate response to immediate standing. BHR-Basal heart rate)

DISCUSSION

The high incidence of ischemic heart disease after menopause suggests a close association between ovarian hormone levels & the vulnerabilities in cardiovascular system. [(7)] In addition there are several lines of evidence connecting symptoms & illnesses such as edema, idiopathic orthostatic intolerance, syncope, mood & psychiatric illness to the hormonal alterations occurring during the menstrual cycle. [(8)]

Women become irritable, tense or depressed in the premenstrual week although intellectual impairment has not been demonstrated. [(9)] It is quite likely that some changes in the autonomic functions of the individual may also be responsible for some of the symptoms produced, though endorphins have been held responsible for behavioural changes. [(4)]

Emerging data regarding variations in plasma volume, cardio vascular homeostasis & sympathetic regulation have increased the interest in the effects of female gonadal hormones. [(8)] It is now evident that both estrogen & progesterone have marked effects on cardiovascular system. [(10)]

In the present study, blood pressure response to immediate standing (one of the sympathetic function tests) is significant between menstrual phase & secretory phase, and between proliferative phase & secretory phase (table 2). The normal response i.e. less fall in systolic blood pressure to immediate standing was seen in secretory phase as compared to other phases. Similar observations as regards to sympathetic autonomic function tests were also seen in the study conducted by Veena Mehta & A.S Chakrabarty. [(4)]

In contrast, study conducted by Dunne FP et al showed that blood pressure was higher at the onset of menstruation than at most other phases of the cycle and was lower during the days 17-26 of the cycle. [(11)]

In our study, the normal response to immediate standing seen during secretory phase could be due to higher sympathetic activity. This higher sympathetic activity takes care of the fall in the systolic blood pressure. A study conducted by Girdler et al found greater stroke volume responses during the secretory phase. [(12)] The borderline responses seen in the proliferative & menstrual phases may be due to lesser sympathetic activity

The Blood pressure response to sustained handgrip exercise test brought normal responses in all the subjects during different phases of menstrual cycle. Similar results have been obtained in study conducted by Veena Mehta & A.S Chakrabarty.[4] In contrast, the study conducted by Mc Fetridge showed lower diastolic blood pressure during the secretory phase.[6] The diastolic blood pressure depends upon peripheral resistance, which in turn depends on diameter of the blood vessel.

Oestrogen concentration is high in proliferative & secretory phases. Oestrogen enhances the basal release of the potent vasodilating substance nitric oxide (NO). [13] But at the same time, higher resting levels of circulating plasma norepinephrine (a potent vasoconstrictor substance) have been reported during the secretory phase of the menstrual cycle, when both oestrogen & progesterone concentrations are elevated. [14]

Thus in the secretory phase, the opposing actions of NO & norepinephrine on the blood vessel may result in the blood vessel diameter not being affected & hence diastolic blood pressure might not have changed & so blood pressure response to sustained hand grip exercise test might be normal in the secretory phase in our study.

In menstrual phase, the concentration of hormones oestrogen & progesterone is low & hence the concentrations of NO & norepinephrine may be low & therefore blood vessel diameter may not be affected & hence the diastolic blood pressure might have not been affected even in the menstrual phase in our study. However, we could not explain the normal diastolic blood pressure in proliferative phase in our study.

In the present study, parasympathetic autonomic function tests showed normal responses during all the phases. Similar results were obtained in the study conducted by Veena Mehta & A.S Chakrabarty. [4] A study conducted by Hirshoren et al reported that estrogen levels can cause a decline in the sympathetic tone with an increased vagal tone. [8] Increased vagal tone means better functioning of parasympathetic system. This could be the reason for getting normal Parasympathetic autonomic function tests in our subjects. The increased sympathetic activity is usually checked by the parasympathetic nervous system.

In the present study, basal heart rate is increased in secretory phase as compared to menstrual phase & proliferative phase. Studies conducted by Hirshoren et al. [8] found similar results. However, there are conflicting results in studies by De souza et al [15] & Pechere-Bertschi et al. [16]

Also the study conducted by AS Leicht et al demonstrated that the normal cyclic variations in endogenous sex hormone levels during the menstrual cycle were not significantly associated with changes in cardiac autonomic control as measured by heart rate variability (HRV). [17]

In our study, higher basal heart rate during secretory phase may be due to higher sympathetic activity in that phase. Sympathetic nervous system has been postulated to respond to stress differently during different phases of menstrual cycle. [6] Similar view is also observed by Yildirir et al [18] & also by Minson CT et al. [10] Regulation of autonomic tone is modified during menstrual cycle. The alteration in the balance of ovarian hormones might be responsible for these changes in the cardiac autonomic innervations. [18] Study by Mc Fetridge found greater increase in heart rate & stroke volume in response to menstrual stress during the secretory phase than during the proliferative phase. [6]

This finding is also consistent with study conducted by Sato N et al in which the results showed that the sympathetic nervous activities are predominant in the secretory

phase as compared with proliferative phase. [19] Similarly, the results of the study by Princi.T et al also showed a correlation between female sex hormones concentrations & some HRV parameters with higher heart rate variability during the secretory phase. [20]

Sympathetic nervous system activity is reflected by plasma concentrations of epinephrine & norepinephrine. [6] In the study conducted by Minson CT et al plasma norepinephrine concentrations were significantly higher in the mid secretory phase. [10] Based on this finding we can say that sympathetic activity is high in secretory phase.

Heart rate may also be higher in secretory phase due to higher levels of progesterone in that phase, which has thermogenic action. [21] Therefore we can also conclude that higher heart rate in secretory phase may also be due to the actions of progesterone.

CONCLUSION

1. The present study showed that there is higher sympathetic activity during the secretory phase of the menstrual cycle.
2. This higher sympathetic activity may be correlated with higher oestrogen & progesterone levels during the secretory phase of the menstrual cycle.
3. The data emerging from our study emphasize the complexity of the relationship between ovarian steroids & various hemodynamic regulatory systems.
4. Further investigations are required to explore the possible biomechanisms underlying our findings.

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