Article

Sympathetic Nerve Function Status in Follicular and Late Luteal Phases of Menstrual Cycle in Healthy Young Women

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Abstract

Background: Autonomic nerve function status may be changed during follicular and late luteal phases of menstrual cycle due to fluctuations of serum estrogen and progesterone level. **Objective**: To observe the sympathetic nerve function status during follicular and late luteal phases of menstrual cycle and their relationships with serum estrogen and progesterone in healthy young womens. **Methods**: This cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College, Dhaka from 1st January 2009 to 31st December 2009.A total number of thirty (30) apparently healthy unmarried women with age ranged from 20-25 years were investigated. Two simple autonomic nerve function tests, like fall of systolic blood pressure (SBP) on standing and rise of diastolic blood pressure (DBP) during handgrip were done to assess sympathetic activity. Serum estrogen and progesterone levels were also measured by AxSYM method. All these tests were performed in both follicular and late luteal phases of menstrual cycle. Data were analysed by paired student's 't' test and Pearson's correlation coefficient test as applicable. **Results**: Mean resting heart rate was significantly ($p<0.01$) increased in late luteal phase than that of follicular phase. Mean resting systolic blood pressure was significantly ($p<0.01$) increased and resting diastolic blood pressure was non-significantly increased in late luteal phase than those of follicular phase. Again, significantly ($p<0.05$) increased value of fall of systolic blood pressure after standing from lying and non-significant increased value of rise in diastolic blood pressure after sustained handgrip were observed in late luteal phase. The mean value of serum estrogen was non-significantly and serum progesterone was significantly ($p<0.001$) increased in late luteal phase than those of follicular phase. **Conclusion**: From this study it can be concluded that sympathetic activity is increased in late luteal phase of menstrual cycle. In addition, increased sympathetic activity during late luteal phase might be the cause of premenstrual syndrome (PMS) in some women.

Key words: Sympathetic nerve functions, progesterone.

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Introduction

A normal menstrual cycle is characterized by the regular rise and fall of estrogen and progesterone from the ovary [1]. Regular menstrual cycle is an index of women's normal reproductive health, occurs in follicular phase and luteal phase [2]. Autonomic nerve function system which is responsible for the homeostatic control of numerous bodily function, changes during follicular phase and luteal phases of menstrual cycle [3]. Some women in childbearing age may experiences some physical, psychological and behavioural symptoms which occur in the late luteal phase of menstrual cycle termed as premenstrual syndrome (PMS) and in

severe case termed as premenstrual dysphoric disorder (PMDD)[4]. However, altered functioning autonomic nervous system in late luteal phase may be responsible for this PMS or in severe case PMDD in eumenorrhic women[5].

Five simple non-invasive cardiovascular reflex tests have been considered to evaluate the status of cardiovascular autonomic nerve control[6]. According to their study, fall of systolic blood pressure (SBP) after standing from lying and rise of diastolic blood pressure (DBP) during sustained handgrip are the two (2) indices of sympathetic nerve function.

In an investigation on sympathetic nerve function status on healthy young women found that, resting heart rate and both resting systolic and diastolic blood pressure had increased significantly in luteal phase than those of follicular phase [7]. Whereas, some other researchers reported that both the resting systolic and diastolic blood pressure were increased at the onset of menstruation than other phases of the cycle [8].It is assumed that significantly increased sympathetic activity may occur mainly in women with PMS or PMDD or even in women without any PMS [5].

Some investigators observed slightly higher baseline mean arterial pressure during mid-luteal phase than that of early follicular phase. They also observed increased mean arterial pressure during handgrip exercise than baseline level in both early follicular and mid luteal phases[9]. Whereas other researchers observed that, the response to handgrip test showed slightly increased blood pressure in the follicular phase compared with the luteal phase[10].

Recently, some research worker studied BP response to sustained handgrip and fall in BP after standing during three phases of menstrual cycle and found almost similar values during all the three phases of menstrual cycle[11].

Though nearly half of the population of our country are female and they are engaged in different type of important productive activity but they are very much neglected. So their health care is very important to get birth of healthy population and their efficient work. To the best of our knowledge very few study has been done on sympathetic nerve function status in healthy young women in Bangladesh. Therefore, the present study was taken to observe the sympathetic nerve function status during different phases of menstrual cycle in healthy young Bangladeshi women. The result of this study would help to create awareness among the healthy young women about autonomic nerve function alteration during different phases of menstrual cycle to improve their quality of life and also the physicians may take appropriate measure for prevention of complications.

Methods

The present cross-sectional study was carried out in the Department of Physiology, Sir Salimullah Medical College, Dhaka, between January to December 2009. In this study, a total number of 30 apparently healthy unmarried women age ranged from 20-25 years with regular menstrual cycle were studied in both follicular and late luteal phases of menstrual cycle. All the subjects were selected from the medical students of SSMC belonged to middle socioeconomic status. Subjects with diabetes mellitus, hypertension, cardiac diseases, chronic obstructive lung disease, history of neurological problem, chronic renal failure,using prescribed medicine, having any acute or chronic disease were excluded from this study. By conventional method ,two sympathetic nerve function tests of all the subjects were studied in phase A that is in follicular phase treated as control value and in phase B that is in late luteal phase (within 7 days prior to next menstruation) treated as study value.

The purpose and procedure of the study were explained to each subject. Written informed consent was taken from all the participants. Study protocol was approved by ethical committee of Sir Salimullah Medical College, Dhaka. Detailed medical and family history was recorded in a

prefixed questionnaire. Height and weight of the subjects were recorded and BMI was calculated. Under aseptic precaution 5 ml of venous blood was collected and serum was prepared for estimation of serum estrogen and progesterone level by AxSYM method [12]. Then the sympathetic nerve function was assessed by two non-invasive cardiovascular reflex tests, BP response to sustained handgrip (Isometric exercise test) and BP response to standing (Orthostatic test) by using sphygmomanometer and an inflated calf. Before the tests, all the subjects took rest in supine position for 15 minutes. Resting heart rate and resting systolic and diastolic blood pressure of all subjects were recorded.

Statistical analysis of data was done by using SPSS program version-15. All the data were expressed as mean ± SD (standard deviation). Data were analyzed by paired student's 't' test and Pearson's correlation coefficient test as applicable.

Results :

Demographic data of the subjects are expressed in Table I.

Table I: Age, height, weight and BMI in study subjects (n=30)

Variables	Values
Age (in year)	21.57 ± 1.30 (20-25)
Height (in cm)	154.23 ± 4.89 (145-160)
Weight (in kg)	49.13 ± 2.11 (46-54)
BMI (kg/m^2)	20.68 ± 0.99 (18.99-22.77)

Data are expressed as mean ± SD. Figures in parentheses indicate ranges.

n= Total number of subjects

The mean resting heart rate was significantly ($p<0.01$) increased in phase B than that of phase A .The mean value of systolic blood pressure in phase B was significantly ($p<0.05$) increased when compared to that of phase A and the mean value of diastolic blood pressure was non-significantly increased in phase B in comparison to that of phase A (Table –II).

Table II: Resting heart rate and blood pressure of study subjects in both phases of menstrual cycle (n=30)

Variables	Phase		p value
	Phase A	Phase B	
Resting heart rate (beats/min)	72.20 ± 4.96 (64-80)	73.73 ± 3.87 (66-84)	0.007**
Resting blood pressure: Systolic (mm of Hg)	109.97 ± 6.52 (100-120)	111.93 ± 4.99 (100-120)	0.027*
Resting blood pressure: Diastolic (mm of Hg)	67.67 ± 5.37 (60-80)	68.40 ± 5.34 (60-80)	0.125^{ns}

Data are expressed as mean ± SD. Figures in parentheses indicate ranges.

Statistical analysis was done by paired t test.

Phase A = Follicular phase (Control group)

Phase B = Late luteal phase (Study group)

* = Significant at $p<0.05$

**= Significant at $p<0.01$

ns = Not significant

n= Total number of subjects

Fall in systolic blood pressure after standing was significantly ($p<0.05$) increased in phase B than that of phase A (Table III) .

The rise in diastolic blood pressure after sustained handgrip was increased in phase B than that of phase A but that was non-significant (Table IV).

Table III: Blood pressure response to standing (fall in systolic blood pressure) in both phases of menstrual cycle (n=30)

Systolic Blood pressure(mm of Hg)	Phase		p value
	Phase A	Phase B	
Lying	109.97 ± 6.52 (100-120)	111.93 ± 4.99 (100-120)	0.027*
After standing	103.50 ± 6.72 (90-115)	105.00 ± 5.05 (95-115)	0.082^{ns}
Fall of SBP after standing from lying	6.47 ± 1.80 (5-10)	6.93 ± 1.68 (5-10)	0.020*

Data are expressed as mean ± SD. Figures in parentheses indicate ranges.
Statistical analysis was done by paired t test.
Phase A = Follicular phase (Control group)
Phase B = Late luteal phase (Study group)
* = Significant at $p<0.05$
ns = Not significant
n= Total number of subjects

Table IV: Blood pressure response to sustained handgrip (rise in DBP) of study subjects in both phases of menstrual cycle (n=30)

Diastolic Blood pressure(mm of Hg)	Phase		p value
	Phase A	Phase B	
Before handgrip	67.67 ± 5.37 (60-80)	68.40 ± 5.34 (60-80)	0.125^{ns}
After handgrip	85.27 ± 6.22 (70-98)	86.50 ± 5.34 (76-98)	0.052^{ns}
Rise in DBP after handgrip	17.60 ± 2.88 (10-21)	18.10 ± 2.29 (10-21)	0.122^{ns}

Data are expressed as mean ± SD. Figures in parentheses indicate ranges.
Statistical analysis was done by paired t test.
Phase A = Follicular phase (Control group)
Phase B = Late luteal phase (Study group)
ns = Not significant
n= Total number of subjects
DBP = Diastolic blood pressure

Table V: Serum estrogen and progesterone levels of study subjects in both phases of menstrual cycle (n=30)

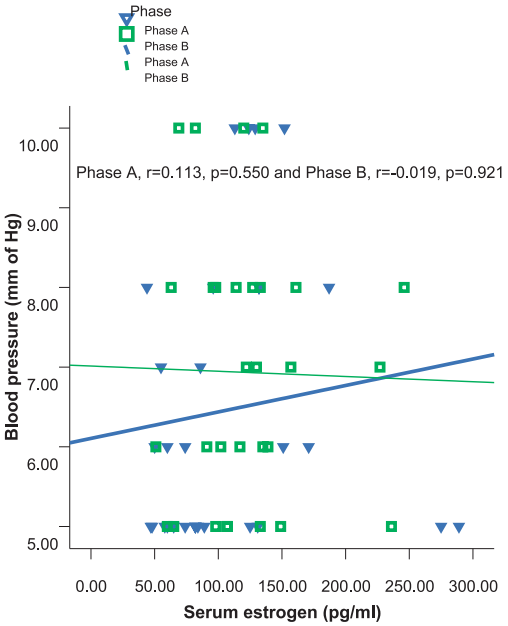
Variables	Phase		p value
	Phase A	Phase B	
Serum estrogen	108.83 ± 61.33	122.33 ± 48.27	0.323 ns
(pgm/dl)	(44-289)	(51-246)	
Serum progesterone	0.90 ± 0.34	13.49 ± 6.69	0.001***
(ng/dl)	(0.50-2.09)	(6.00-32.68)	

Data are expressed as mean ± SD. Figures in parentheses indicate ranges.
Statistical analysis was done by paired t test.
Phase A =Follicular phase (Control group)
Phase B = Late luteal phase (Study group)
***=Significant at p <0.001
ns = Not significant
n= Total number of subjects

The mean value of estrogen was increased in phase B than that of in phase A . But it was not statistically significant. The mean progesterone level in phase B was significantly (p<0.001) increased than that of phase A (Table V) .

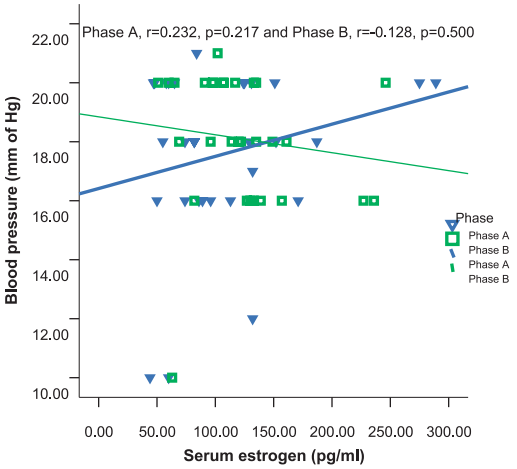
Again, fall in systolic blood pressure after standing and rise in diastolic blood pressure after sustained handgrip both were positively correlated with serum estrogen level in phase A but negatively correlated in phase B. They were not statistically significant (Figure 1 and 2).

Furthermore, fall in systolic blood pressure after standing were positively correlated with serum progesterone level in phase A and phase B . But all the values were statistically non-significant. Moreover, the rise in diastolic blood pressure after sustained handgrip was negatively correlated with serum progesterone level in phase A and in phase B. This relationship was statistically significant (p<0.05) (Figure 3 and 4).



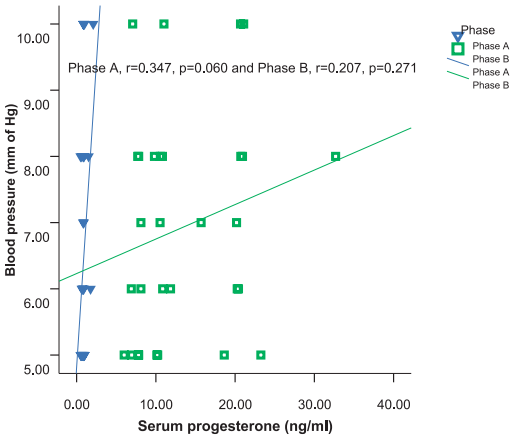
Statistical analysis was done by Pearson's correlation coefficient(r) test
Phase A =Follicular phase (Control)
Phase B = Late luteal phase (Study)

Figure 1: Correlation of serum estrogen level with fall in systolic blood pressure in both phases of menstrual cycle (n=30)



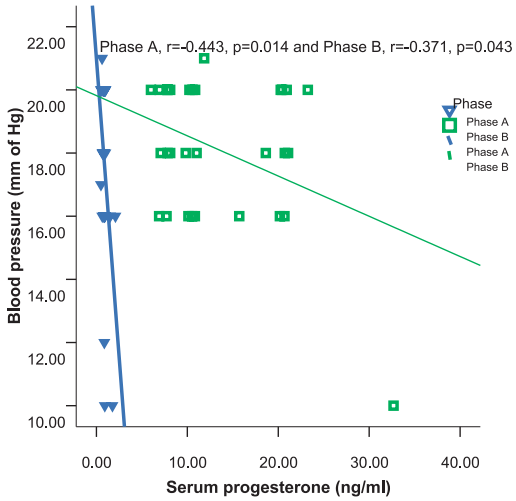
Statistical analysis was done by Pearson's correlation coefficient(r) test
Phase A =Follicular phase (Control)
Phase B = Late luteal phase (Study)

Figure 2: Correlation of serum estrogen level with rise in diastolic blood pressure in both phases of menstrual cycle (n=30)



Statistical analysis was done by Pearson's correlation coefficient(r) test
Phase A =Follicular phase (Control)
Phase B = Late luteal phase (Study)

Figure 3: Correlation of serum progesterone level with blood pressure response to standing (fall in SBP) in both phases of menstrual cycle (n=30)



Statistical analysis was done by Pearson's correlation coefficient(r) test
Phase A =Follicular phase (Control)
Phase B = Late luteal phase (Study)
*=Significant at p<0.05
ns= Not significant

Figure 4: Correlation of serum progesterone level with blood pressure response to sustained handgrip (rise in DBP) in both phases of menstrual cycle (n=30)

Discussion

In the present study, the observed significantly (p<0.05) increased resting heart rate in late luteal phase than that of follicular phase is similar to the observations made by other investigators [7,13] . Again, resting systolic and diastolic blood pressure was increased in late luteal phase than those of follicular phase were consistent with some researchers[14,15] .

In this study, significantly (p<0.05) increased fall in systolic blood pressure after standing from lying position and non-significant rise in diastolic blood pressure during sustained handgrip in late luteal phase in comparison to follicular phase indicate sympathetic hyperactivity in healthy young women. Similar results were observed by some other investigators but they used spectral analysis of HRV[16,17].

Again, serum estrogen level was non-significantly and serum progesterone level was significantly ($p<0.001$) increased in late luteal phase than those of follicular phase. Similar observations were also made by some other research workers[3,18].

Serum estrogen was positively correlated with fall in systolic blood pressure and rise in diastolic blood pressure during follicular phase but negatively correlated with fall in systolic blood pressure and rise in diastolic blood pressure during late luteal phase of menstrual cycle. All these correlations were statistically non-significant.

Moreover, serum progesterone showed non-significant positive correlation with fall in systolic blood pressure in late luteal phase of menstrual cycle also support that increased sympathetic activity occurred in late luteal phase of menstrual cycle.

There are some postulated mechanisms suggested by various investigators of different countries which may imply the possible mechanisms regarding this increased sympathetic activity during late luteal phase of menstrual cycle in this study.

In follicular phase, sympathetic activity was decreased may be due to increased level of oestrogen and low level of progesterone. In this phase, estrogen increases density as well as the function of presynaptic $á_2$ adrenoreceptors, thereby resulting in significant decrease in nor-epinephrine induced responses[19]. Estrogen stimulates the opening of calcium activated potassium channels by nitric oxide[20]. Estrogen also stimulates opening of calcium activated potassium channels by cyclic guanosine monophosphate dependent pathway[21]. Thus estrogen relaxes vascular smooth muscle and promoting vasodilatation. Again, estradiol might be associated with increase in acetylcholine concentration. These findings suggested that, estrogen has facilitating effect on cardio-vagal function[22].

In luteal phase, sympathetic activity was greater might be due to higher progesterone level in this phase[23]. It has been suggested that, increased level of progesterone during luteal phase inhibit the influence of estrogen on cardio-vagal activity[13, 24]. Resting systolic blood pressure increased significantly during luteal phase as progesterone might have hypertensive effect[11].

Some other investigators suggested that progesterone may increase cardiac excitability by its opposing effects on estrogen. They also suggested that estradiol increases the number and sensitivity of progesterone receptor, thus increasing action of progesterone hormone occurs during luteal phase[1].

As level of progesterone is significantly higher in luteal phase, causes rise in both systolic and diastolic blood pressure[7] .Again, increased level of progesterone causes decreased release of endothelium derived nitric oxide[25].

In addition, increased sympathetic activity during late luteal phase might be the cause of PMS as supported by presence of some symptoms like back pain, lethargy, depression etc. In this study those were also observed by some other investigators [5, 18].

Conclusion

From the result of the study, it can be concluded that sympathetic activity was increased in late luteal phase of menstrual cycle which may be due to significantly increased level of serum progesterone in this phase. In addition, increased sympathetic activity during late luteal phase might be the cause of premenstrual syndrome (PMS) in some women.

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