Article

Relationship Between Parasympathetic Nerve Function and Ovarian Hormones During Different Phases of Ovarian Cycle In Healthy Young Women

Latifa Afrin Dill Naher[1], Noorzahan Begum[2], Sultana Ferdousi[3]

Abstract

Background: Women having regular ovarian cycle often experience premenstrual syndrome which may be associated with alterations of autonomic nerve function due to fluctuation of ovarian hormones during different phases of ovarian cycle**. Objective:** To observe the parasympathetic nerve function status and their relationships with ovarian hormones during different phases of ovarian cycle in healthy young women. **Methods:** This cross sectional study was carried out in the department of Physiology at BSMMU, Dhaka in 2007 on 30 eumenorrhogic healthy females aged 20 to 30 years. Serum estrogen and progesterone were measured by MEIA method and parasympathetic nerve functions were assessed by valsalva, deep breathing test and orthostatic test during follicular and luteal phases of ovarian cycle. Data were analyzed by paired student 't' test, and Pearson's Correlation coefficient test where applicable. **Results**: Mean resting HR,SBP,DBP and all measures of parasympathetic nerve function were similar in all phases of ovarian cycle. With serum estrogen level, deep breathing showed significant ($p<0.05$) positive correlation in follicular and luteal phase and valsalva showed significant positive correlation during luteal phase. **Conclusion**: The results this study suggest that estrogen has got positive influence on parasympathetic nerve function which support cardioprotective role of estrogen in premenopausal females.

Key words: Premenopausal women, estrogen, parasympathetic nerve function, follicular phase, luteal phase.

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For Authors Affiliation, see end of text.

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Introduction

Women in their reproductive age, often experience premenstrual syndrome like abdominal bloating, weight gain, headache, fatigue, irritability, mood change, depression, tension etc. These symptoms usually subside within few days after the onset of menstruation[1]. This syndrome may be associated with the hormonal changes during luteal phase of ovarian cycle reported by studies[2]. Internal environment of our body is largely controlled by the autonomic nervous system. Alteration of autonomic nerve function may be attributed to fluctuation of estrogen and progesterone in different phases of ovarian cycle[3]. Studies on experimental animal showed that estrogen has effect on the modulation of the cardiovascular autonomic functions as it has facilitatory influence on glumatergic neurotransmission, which is essential for

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modulation of central baroreflex mechanism [4]. Some researcher observed increased parasympathetic activity during luteal phase[3] but others observed this increased activity in follicular phase of ovarian cycle [5,6]. However, some researchers observed increased sympathetic activity during luteal phase [6,7,8].

Some investigators observed positive influence of high level of progesterone on the GABA mediated baroreflex sympatho-inhibition within Rostral Ventro Lateral Medulla [9, 10]. Again, in high concentration it has been shown to decrease sympathetic baroreflex sensitivity [11] Premenopausal women are the bulk of female population. To the best of our knowledge very few research have been done regarding the parasymapthetic nerve function status in relation to endogenous estrogen and progesterone level in different phases of ovarian cycle of these women. Therefore the present study was conducted to see the parasympathetic nerve function status and their relationships with serum estrogen and progesterone level in this group of women.

Methods

This cross sectional study was performed in the department of physiology at BSMMU, Dhaka from January to December 2007 on 30 eumenorrheic healthy females aged 20 to 30 years. After selection of the subjects the objectives of the study were explained in details. All procedures for ethical clearance were followed and a written informed consent was taken from each subjects. The protocol of the study was approved by the ethical committee of the Department of Physiology, BSMMU.

Detailed family history, medical history, menstrual histories were taken. Subjects were asked about their date of onset of ovarian cycle. Then they were asked to attend in the Department of Physiology of BSMMU as per following schedule :Follicular phase: from 9th to 14th day of ovarian cycle, Luteal phase: from 19th to 23rd day of ovarian cycle.

BMI of all subjects were calculated during follicular and luteal phases of ovarian cycle. Basal heart rate, blood pressures were measured. Serum estrogen and progesterone were measured by MEIA method during follicular and luteal phases of ovarian cycle.

In addition parasympathetic nerve function of all subjects was assessed in both phases of ovarian cycle by performing three cardiovascular reflex test namely heart rate response to valsalva manuever, heart rate response to deep breathing and heart rate response to standing.

Data were analyzed by paired student's 't' test and Pearson's Correlation coefficient test where applicable.

Results

Mean age ±SD of the subjects was 24.30±3.88. Mean BMI, W: H ratio and resting HR and BP were similar in both phases of ovarian cycle. The mean estrogen was higher in follicular phase compared to luteal phase but it was not significant ($p>0.05$). However, the mean progesterone was significantly higher ($p<0.001$) in luteal phase than follicular phase (Table I)

Table I: Serum estrogen and progesterone levels in premenopausal women in different phases of ovarian cycle.(n= 30**)**

Groups	A2	A3	P value
Estrogen	155.36±69.03	138.20±56.73	0.204 ^{ns}
(pg/ml)	(67.00-305.00)	(56.00-259.00)	
Progesterone	0.85±0.60	11.12±3.92	
(ng/ml)	(0.28-2.26)	(3.36-17.67)	0.000***

Data are shown as mean ±SD. Figures in Parentheses indicate ranges.
Unpaired 't' test was performed for comparison.ns =$p>0.05$ *** = $p<0.001$
A2= Follicular phase A3 = Luteal phase

All measures of parasympathetic nerve function were similar in both phases of ovarian cycle[12]. Correlation analysis showed that valsalva ratio and deep breathing were positively correlated with serum estrogen level during both follicular and luteal phases. It was significant ($p<0.05$) for deep breathing during both luteal and follicular phases but for valsalva ratio it was significant ($p<0.05$)in luteal phase only (Figure 1 & Figure 2).

Heart rate response to standing were negatively correlated with serum estrogen level during both phases but it was not significant ($p>0.05$) (Figure 3).

The relationships of all the parasympathetic nerve function parameters with serum progesterone level were non significant ($p>0.05$)(Table II).

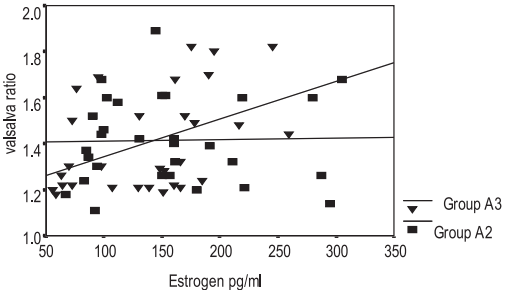

Figure 1: Correlation of serum estrogen level with valsalva ratio in follicular and luteal phases(n=30)Statistical analysis was done by Pearson correlation coefficient(r) test. Group A2= follicular phase Group A3= luteal phase * =$p<0.05$, ns =not significant

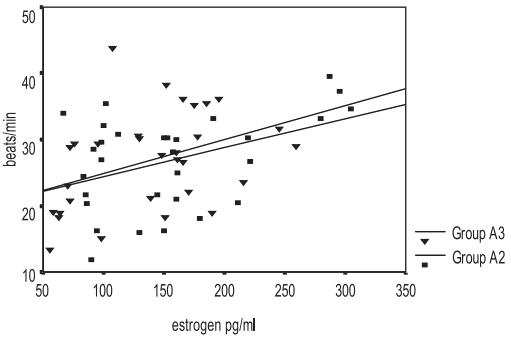

Figure 2: Correlation of serum estrogen level with heart rate response to deep breathing in follicular and luteal phases(n=30)Statistical analysis was done by Pearson correlation-coefficient(r) test * =$p<0.05$

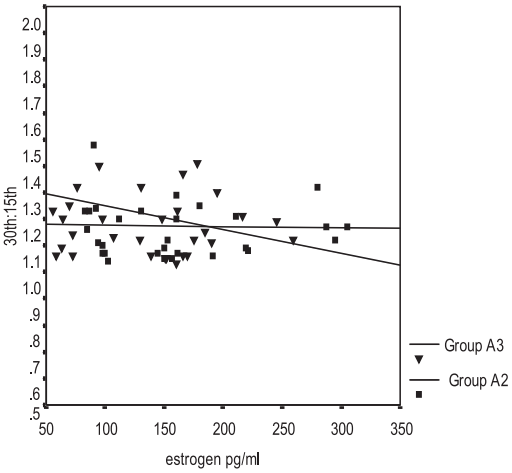

Figure 3: Correlation of serum estrogen level with heart rate response to standing in follicular and luteal phases(n=30) Statistical analysis was done by Pearson correlation-coefficient(r) test ns =$p>0.05$

Table II: Relationship of serum progesterone level with parasympathetic nerve function parameters in different groups (n=60)

Parameters	A2		A3	
	r	p	r	p
valsalva ratio	-0.239	0.203 ns	0.185	0.327ns
deep breathing	0.065	0.733 ns	0.191	0.313ns
30th:15th	0.360	0.051 ns	-0.086	0.653ns

Group A2= Follicular phase Group A3= Luteal phase ns = Not significant

Discussion

Premenstrual symptoms usually occur during luteal phase of premenopausal women, which subsides after menstruation[1]. It may have some relationships with changes in autonomic nerve function due to fluctuation of ovarian hormones during ovarian cycle in this group of women [3]. In thus study, menstrual history showed that none of the subjects were experiencing premenstrual symptoms.

In this study, serum estrogen level was higher in follicular phase than that of luteal phase but the difference was not statistically significant. Several researchers have reported similar findings [5,12].

Again, significantly higher serum progesterone level observed in luteal phase than follicular phase is in consistent to that of some authors[5,7,13].

In this study no significant differences were observed in resting heart rate and blood pressures, which indicate no apparent change in autonomic nerve function during three phases of ovarian cycle.

In this study deep breathing test showed significant positive correlation with serum estrogen level during both follicular and luteal phases of ovarian cycle. Valsalva ratio showed significant positive correlation with serum estrogen level only during luteal phase.

Anthony, David and Graham[14] found significant correlation of estrogen with parasympathetic nerve function during follicular phase. However, Matsumoto et al. [15] observed that these relationships were non significant during both follicular and luteal phases who do not have premenstrual symptoms. But the they demonstrated higher sympathetic nerve activity and lower parasympathetic nerve activity during luteal phase in symptomatic women[15].

In this study no significant relationships of parasympathetic nerve function parameters with progesterone level were observed..

The role of both estrogen and progesterone on the modulation of the parasympathetic nerve function has not yet been established. However, there are some postulated mechanisms suggested by various investigators of different countries, which may imply the probable mechanisms of these hormones on the regulation of parasympathetic nerve functions.

Several investigators have demonstrated that estrogen has regulatory influences on parasympathetic nerve functions [4,16,17]**.** It has been suggested that estrogen acts on central neural pathway of baroreceptor reflex arc and facilitates the baroreflex sensitivity as well as the activity. The exact central mechanisms involved in the baroreflex enhancement by estrogen have yet to be established. However, some investigators suggested that estrogen has facilitatory roles on glutamatergic neuro-transmission in nucleus tractus solitarius (NTS) and thereby modulate the central baroreflexes [4]. This enhancement of baroreceptor sensitivity is usually followed by increase in vagal tone[16]. Some investigators observed that estrogen has direct effect on vascular smooth muscle to cause vasodilatation [17].

The effect of progesterone on autonomic nerve function is still not clear. Some investigators suggested that progesterone in high concentration potentiate the GABA mediated baroreflex sympatho-inhibition within RVLM [9,10]. Again, some investigators have suggested that progesterone may cause vasodilatation by releasing NO from endothelium [18,19].

In this study, all the parameters of parasympathetic nerve function were similar during both phases of ovarian cycle[12] which indicate negligible phasic variation in parasympathetic nerve function, which may be related to the fact that all the subjects of our study were not suffering from any form of premenstrual symptoms

The significant positive correlation of estrogen with different parameters of parasympathetic

nerve function highlights the role of estrogen on the modulation of parasympathetic nerve function. But no significant relationships with progesterone level was found though the progesterone level was high in luteal phase than follicular phase. The exact mechanism of these relationships could not be elucidated from this type of study further study on premenopausal women having premenstrual syndrome may give more conclusive findings.

Conclusion

The present study concludes no phasic variation of parasympathetic nerve function despite the fluctuation of ovarian hormone levels during both phases of ovarian cycle. Estrogen has got positive influence on parasympathetic nerve function that support cardio protective role of estrogen in premenopausal women.

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Author Affiliations

1. *Latifa Afrin Dill Naher, Associate Professor of Physiology, Prime Medical College, Pirjabad, badarganj Road, Rangpur. Email: afrin_latifa 2007@yahoo.com.

2. Noorzahan Begum, Professor,Department of Physiology, Bangabandhu Seikh Mujib Medical University (BSMMU), Shahbag, Dhaka-1000, Bangladesh.

3. Sultana Ferdousi, Associate Professor, Department of Physiology, Bangabandhu Seikh Mujib Medical University (BSMMU), Shahbag, Dhaka- 1000, Bangladesh.

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