

Cyclical alteration in heart rate variability among young eumenorrhic women

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Abstract

Introduction: The female sex hormones are known to have a cardioprotective role in premenopausal women compared to postmenopausal women.^{1,2,5} The key hormone estrogen and progesterone shows a cyclical variation along the different phases of menstrual cycle. Parasympathetic activity via vagus is known to improve the cardiac function compared to sympathetic activity.³ Heart rate variability (HRV) is one of the sensitive and non-invasive method to record the cardiac autonomic activity.⁴ Thus we chose this study to assess how the female sex hormones affect autonomic activity on the heart during the phases of menstrual cycle. **Aim:** To assess the effect of cyclical alteration in female sex hormones on cardiac autonomic activity by HRV.

Materials and Methods: After getting institutional ethics committee clearance, short term HRV (5 minutes) was recorded in fifty young female volunteers aged between 20-30 years within normal range of BMI and regular menstrual cycle in supine posture after 10 minutes rest using PHYSIO PAC PP4 Medicaid system Chandigarh in the autonomic function lab, Department of Physiology, Sri Venkateshwaraa Medical College Hospital and Research Center, Ariyur, Pondicherry. Statistical analysis was done using SPSS 17 version.

Results: The sympathetic parameters like (low frequency domain) LF nu, LF/HF ratio was significantly increased in the premenstrual phase. The parasympathetic parameters like (high frequency domain) HF nu, TP (total power) were significantly increased in the proliferative phase of the menstrual cycle.

Conclusion: Thus the cardioprotective role of female sex hormones in premenopausal women was more pronounced in the proliferative phase of menstrual cycle.

Keywords: Heart rate variability, Cardioprotective, Premenstrual phase, Proliferative phase.

Introduction

Epidemiological studies showed that the risk of coronary heart disease is much lower in the premenopausal women compared to age matched men.⁵ This suggests that the female sex hormones in the premenopausal women contribute to their cardio protective role compared to postmenopausal women.⁶ Cyclical alteration in female sex hormones along the menstrual cycle affect the cardiac autonomic reactivity through hypothalamo-pituitary adrenal activity and sympatho-adrenomedullary system.⁷ Effect of female sex hormones on cardiac autonomic activity can be assessed with the help of HRV. HRV is the non-invasive tool to measure the autonomic activity in humans.⁴ Power spectral analysis is a sensitive index to assess the autonomic activity in the normal menstruating females during different phases of menstrual cycle. Vagal innervation influence the HF component in correspondence with sinus rhythm. The LF component varies with oscillations in blood pressure, influenced by both the divisions of Autonomic Nervous System (ANS).⁸ The equilibrium between both the divisions of ANS can be assessed by LF/HF ratio.⁸

Aim

To assess the effect of cyclical alteration in female sex hormones on cardiac autonomic activity by HRV.

Objectives

1. To record the 5 mins HRV during proliferative phase
2. To record the 5 mins HRV during premenstrual phase
3. To compare 5 mins HRV during both the phases

Materials and Methods

After getting institutional ethics committee clearance, written consent was obtained from all fifty healthy eumenorrhic women volunteers with regular menstrual cycle aging between 20-30 years with normal BMI (18- 24 kg/m²). This observational study was carried out in the Department of Physiology Sri Venkateshwaraa Medical College Hospital and Research Centre, Puducherry. Females with menstrual abnormalities, or any other medical illness prone to affect HRV were excluded from the study.

General examination and history collection were done for all subjects. Last menstrual period (LMP) and menstrual history were collected. After 10 minutes rest

ECG analysis was done by using PHYSIOPAC PP4 MEDICAID system Chandigarh in the Department of Physiology in supine position for 5 minutes. Limb leads were used to record ECG. Recordings were done in the morning between 9.00 am to 11.00 am in the autonomic function test lab during proliferative phase (6th-7th day) and premenstrual phase (24th- 25th day). The subjects were advised to avoid caffeine at least 2 hours before the

test and recording was done at least 2 hours after the meal.

Results

All the values were tabulated as Mean±SD. Statistical analysis was done using SPSS 17 version

Table 1: HRV (Frequency domain) in both the phases of menstrual cycle

Frequency domain parameters	Proliferative phase	Premenstrual phase	P value
LF nu	84.76±2.415	87.07±2.04	<0.0001*
HF nu	15.24±2.413	12.94±2.059	<0.0001*
LF/HF	5.711±1.005	6.977±1.675	<0.0001*
Total power(ms ²)	4441±2000	3437±1819	0.005*

*P< 0.05- statistically significant

LF- low frequency, HF- high frequency, LF/HF - ratio of LF and HF

TP- total power

In table: I - LF nu and LF/HF indicating the sympathetic activity has significantly increased in the premenstrual phase compared to the proliferative phase. The parasympathetic functions shown by HF nu and total power were significantly increased in the proliferative phase compared to premenstrual phase of the menstrual cycle.

These results were similar to the study done by Nozomi Sato et al with increased LF, and LF/HF in the premenstrual phase.⁷ Similarly Choudhury et al. has reported increased sympathetic activity in the luteal phase due to the combined effect of estrogen and progesterone which increases premenstrual stress.³

Discussion

Leicht et al. found that the sympathetic activity was higher during ovulatory and luteal phase compared to the menstrual phase.⁶ Increased vagal tone during proliferative phase could be one of the reasons for decreased sympathetic activity.⁹ In contrast Saeki et al. reported increased sympathetic activity in the premenstrual phase might be due to associated increase in LH, FSH and progesterone.¹⁰ Weisman et al reported sudden increase in the level of estrogen in women treated with ovulation induction for in-vitro fertilization showed increase in the vagal activity.¹¹

Some authors reported increased sympathetic activity only in females with premenstrual syndrome (PMS) in the late luteal phase compared to females without PMS.^{12,13} Similarly Baker et al. also reported decreased HF power in severe PMS subjects during sleep.¹⁴ Our results are similar to Sneha et al. where HRV is analysed among exercising and non- exercising women.¹⁵ Leicht et al. found a positive correlation between HRV and endogenous estrogen during ovulatory period. But they did not find any synchronistic changes in HRV with endogenous female sex hormones.⁶ Absolute measures of HRV and baroreflex

control of heart rate during normal menstrual cycle were correlated significantly with estradiol level in healthy females thus ovarian hormones might be the reason for altered cardiac autonomic function.¹⁶ Decreased HRV indicates increased risk of arrhythmic events and an increased mortality. This could be due to the environmental stressors, which bring about parasympathetic suppression and sympathetic over activation.¹⁷ Rosana et al reported that women with regular menstrual cycle and paroxysmal supraventricular tachycardia showed greater incidence of arrhythmia during luteal phase compared to follicular phase. Thus cardiovagal modulation has antiarrhythmic effect in proliferative phase which is consistent with our finding of increased parasympathetic function during the proliferative phase.¹⁸ Estrogen was known to increase the density and affinity of muscarinic receptors as studied by Rainbow et al.¹⁹ The sympathetic hormone Nor-epinephrine was found to be high during 21st-25th day of menstrual cycle along with higher estrogen and progesterone.^{20,21} Estrogen was known to modulate the neurotransmitter release presynaptically by secreting NO.²² Thus in this study vagal dominance in the proliferative phase (as shown by increased HF nu, TP) might be due to endogenous estrogen and increased sympathetic activity (as shown by increased LFnu, LF/HF ratio in premenstrual phase) might be due to increase in the progesterone, opposing the effect of estrogen.⁶ Hence HRV can be used to find the autonomic imbalance in the normal menstruating female subjects. With short term HRV, frequency domain parameters were found to be the better gauge of cardiac autonomic activity compared to time domain parameters which are better with long term HRV measured for 24 hours.²³ Thus we did not compare the time domain values in our study.

It was found that estrogen not only had a role of cardioprotection but also increased the working memory.²⁴ It also has a role over central nervous system

as shown by the studies on brain stem auditory evoked potential and visual evoked potential among females.²⁵

Conclusion

The HFnu indicating the parasympathetic activity was significantly increased in the proliferative phase of the menstrual cycle. This is mainly due to vagal dominance and release of NO by estrogen which in turn decreases the effect of sympathetic nervous system. Thus cardioprotective role of female sex hormone in premenopausal women is more pronounced in estrogen dominant proliferative phase compared to premenstrual phase.

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