Original Research Paper

International Physiology 6(2), May - August 2018

DOI: https://dx.doi.org/10.21088/ip.2347.1506.6218.21

Effects of Different Phases of Menstrual Cycle on Short Term HRV in Young Women

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Received on: May 17, 2018
Accepted on: June 09, 2018

Abstract

Introduction: Menstrual cycle is characterized by an intense activity of endogenous sex hormones. Autonomic nervous system (ANS) maintains the internal milieu of the body. Among the various organ systems that are influenced by the ANS, the cardiovascular system has a major role in the maintenance of homeostasis. Internal and external influences such as physical activity, food intake, pregnancy, menstruation are immediately balanced by specific adaptation mechanisms influenced by the ANS. Cyclical phases in menstrual cycle bring about changes in the stress levels which has a major influence on cardiovascular derangements which can be best studied by HRV. *Aim of the study:* To study the effects of different phases of menstrual cycle on short-term Heart rate variability in young adult women. *Materials and Methods:* 126 female students of age group 17-22 years have been included in the study from 2016-2017. A detailed questionnaire regarding their menstrual history was taken. After 5 minutes of supine rest, a five-minutes lead II ECG was recorded and digitized @ 256 Hz sampling rate and a vertical resolution of 10bits by NVQUIRE© software and two-channel digital polygraph hardware by INCO, Ambala. Throughout the procedure Taskforce recommendations for HRV was followed. *Results:* As expected, an increased sympathetic tone and decreased parasympathetic tone was found in the luteal phase when compared to the follicular phase, as shown by decreased RMSSD and HF indices and increased low-frequency (LF) values (p= 0.05). *Conclusion:* From the study, it can be concluded that exists a sympathovagal imbalance which is depicted by increased sympathetic activity in luteal phase than proliferative phase, and vice versa in the proliferative phase.

Keywords: Menstrual Phases; Sympatho-Vagal Imbalance; Parasympathetic Activity; HRV.

Introduction

Heart Rate Variability is a highly sensitive, non-invasive tool to measure the variations in beat to beat intervals or in the instantaneous heart rate (HR) [1,2]. Endogenous sex hormones and its levels in young females vary with different age groups, socioeconomic status, and lifestyle habits. In women, Heart Rate Variability (HRV) is influenced by many factors, including sex hormones, menstrual cycle, menopause, hormone replacement therapy, and with basic physical anthropometric differences like body mass index (BMI) & WHR [3]. In addition, the combined differences of age, BMI, and menstrual cycle in young women, showed that age was an essential predictor of HRV, followed by BMI and menstrual cycle [3]. Menstrual cycle has three phases: the menstrual phase, follicular phase, and the luteal phase. Two main hormones i.e. estrogen and progesterone plays a vital role in establishing a normal hormonal homeostatic milieu during the entire menstrual cycle [4]. The follicular phase is also called as the proliferative phase because endometrial growth is the primary outcome of proliferative phase and is mediated by increase in estrogens levels. The primary outcome of secretory phase is the maturation of the endometrium. Decreasing levels of estrogens halt endometrial

growth [3,4]. Through the influence of a rise in follicle stimulating hormone (FSH) during the first days of the cycle; a few ovarian follicles are stimulated [4]. The luteal phase is also called as the secretory phase. An important role is played by the corpus luteum, the solid body formed in an ovary after the egg has been released from the ovary into the fallopian tube which secretes progesterone. Peak progesterone production is noted in mid-luteal phase i.e one week after ovulation. In the luteal phase of menstrual cycle, premenstrual syndrome (PMS) also describes various ranges of emotional, behavioral, physical and mental changes which can alter the entire homeostatic milieu. These changes bring about a greater impact on designing the Hypothalamo-pituitary axis (HPO) [5]. Beat-to-beat variability in the heart's rhythm is mainly caused by the autonomic nervous system's modulation of intrinsic cardiac pacemakers [6]. Literature shows Sympathetic activity is significantly higher in the luteal phase than in the follicular phase. However, others have reported the menstrual cycle were not significantly associated with changes in autonomic nervous activity. Repeated cyclical blood loss in menstruation and variations in the estrogen and progesterone levels during menstrual cycle could affect the cardiac autonomic function [7]. There exists a cyclical variation of HRV along with menstrual cycle and many literature studies lack in substantiating the physiological role of endogenous sex hormones due to the influence of many plausible factors which can have an impact on Hypothalamo pituitary axis. These factors still remains to be clarified. So, this study was designed to assess whether any relationship exists between the short term HRV and different phases of menstrual cycle in young women. This study was designed to assess the changes in linear features of HRV during different phases of menstrual cycle in adolescent young normal female subjects .

Materials and Methods

A total of 126 healthy young female aged 17-22 years (with normal Menstrual Cycle of 30± 3 days, regular for at least 6 months prior to this study) studying MBBS in Aarupadai veedu medical college and hospital were selected for this study. The subjects are instructed to come to the electrophysiology department during each of three different phases. Day 1-5 during Menstrual phase (Phase-I), day 9 - 12 during the follicular phase (Phase- II) & day 19-21 during the luteal phase (Phase-III). The study was initiated after obtaining approval institute research and Ethics Committee.

Inclusion Criteria

Young, healthy female volunteers between 17-22 years.

Exclusion Criteria

Irregular menstrual cycles, preexisting cardiovascular diseases, Diabetes mellitus, Thyroid disorders, taking oral contraceptives

Thorough menstrual history was taken about menstrual regularity and total duration of cycle.

The examination was carried out at same time of the day to avoid diurnal variation.

Basal Parameters like Age, BMI, WHR, Resting Pulse Rate and blood Pressure were recorded according to the protocol provided, to select the healthy subject for study. After 5 minutes of supine rest a five-minute lead II ECG was recorded during three phases and digitized @ 256 Hz sampling rate and a vertical resolution of 10bits by NVQUIRE© software and two-channel digital polygraph hardware by INCO, Ambala. Throughout the procedure Taskforce recommendations on HRV is followed. Then offline measurements of RR tachogram across the phases done and analyzed using HRV analysis software version 1.1,biosignal analysis group, kuoppio, Finland.

Statistical Analysis

The data collected (Basal parameters, SBP, DBP, HRV parameters) were analyzed using IBM SPSS 20 and tested for normal distribution using Shapiro-Wilk test. Differences between the two phases (follicula and luteal) for all experimental parameters, including HRV indices, were determined by the Student's paired t-test. $p < 0.05$ was taken as statistically significant.

Table 1: Base-line values (Mean±SD) of different parameters in the subjects

Parameter	Females (N=126)
Age(years)	18.4±.90
BMI(Kg/m^2)	20.83±1.33
WHR(WC/HC)	.83±.01
Resting SBP(mmHg)	114.68±4.18
Resting DBP(mmHg)	75.16±3.83
Resting Pulse Rate (min.)	74.80±3.12

Table 2: Comparison of Time domain measures of HRV in the two phases (follicular and luteal) of menstrual cycle

Variables	Follicular phase(n=126)	Luteal phase(n=126)	P value
Mean HR	74.80±3.12	76.59 ±0.09	0.647
SDNN	41.09±0.02146	34.29±0.02836	0.0373
RMSSD	39.55±10.26	31.71±25.584	0.0387
NN50	127.55±67.97	105.18±88.95	0.0183
PNN50	31.36±18.82	25.75±19.33	0.0467
RRINDEX	0.20±0.08	0.17 ±0.034	0.0422
TINN	275.23±96.53	263.775±109.45	0.0258

Table 3: Comparison of Frequency domain (Non-parametric) measures of HRV in the two phases (follicular and luteal) of menstrual cycle

Variables	Follicular phase(n=126)	Luteal phase(n=126)	P value
LF (%)	27.5±12.5	35.12±17.58	0.0459
HF (%)	57.6±22.35	47.1625±28.093	0.034
VLF (%)	14.9±16.42	17.72±19.14	0.1874
LF:HF	0.478±0.24	0.825 ±0.6443	0.3271
LF nu	32.3±14.196	31.58 ±17.343	0.2279
HF nu	67.7±14.27	68.42±16.68	0.3047

p value of <0.05 is considered to be significant

Discussion

The first clinical study supporting this hypothesis has been reported by Sato et al. (1995) [8] who investigated the fluctuations of ANS activities during the follicular phase (day 7- 10 of last bleeding) and in luteal phase (3- 7 days prior to next bleeding) in 20 college students and reported increased LF nu and decreased HF nu in luteal phase and obviously LF/ HF ratio was significantly increased in luteal phase indicating predominant sympathetic activity during this phase [8,9]. In our present study, the time domain indices of HRV reflecting parasympathetic modulation like RMSSD and pNN50 are decreased in luteal phases of menstrual cycle when compared with follicular phase. Many literature searches in HRV depicts that there is a significant influence of endocrine sex hormones on maturation of autonomic nervous system. It remains to be established what sort of influence might induce the improvement in neural autonomic control at adolescence. Genetic morphology, hormonal status, and changes in physical activity are possible factors which influences on the menstrual cycle. The SDNN linearly decreases as a function of increased HR as it has been reported suggesting a greater incidence of arrhythmias in the luteal phase than in the follicular phase in women with regular menses [10,11]. Because sympathetic stimulation has an arrhythmic effect, these data support increased sympathetic activity in the luteal phase [12,13]. Our findings are similar to previous studies in which increased sympathetic activity in the luteal phase when compared to other phases and found a greater increase in parasympathetic activity in the follicular phase [14,15]. Inconsistent findings in many literature regarding the interaction between the menstrual cycle and HRV may be due to the differences in the sample size, age, method used to evaluate HRV and various phase studied [16]. It should also be noted that maturation of certain somatic nervous system functions also occurs at puberty. Taking the understanding that there are other contributory components which has an impact on HRV, we analyzed the frequency domain parameters.

By comparing the frequency domain indices, it was observed that a significant increase in LF% during luteal phase of menstrual cycle. The High frequency power (HF) which is a marker of vagal modulation has significantly decreased in our study population in luteal phase depicting the fall in vagal modulation of heart. This interesting finding can be attributed to the fluctuations in the levels of estrogen to progesterone ratio after ovulation which can alter the entire vasomotor milieu. Though not significant there was a slight increase in LF:HF ratio which warrants scientific explanation. Thus we conclude with maximum caution that in our study, young adolescent female population presented with overall lower heart rate variability expressed in terms of spectral components of HRVduring their different phases of menstrual cycle [12]. The rise in the sympathetic tone and modulation needs an established mechanism for its explanation in terms of endogenous sex hormonal roles in the blood vessels feeding the sensors, and its

altered dynamics in the sensor transducing mechanisms, permissive and inhibitory role of other hormonal mediators, altered integrator activity and external plausible psycho- social factors .The major limitation of this study was that serum endogenous sex hormone levels were not measured during the different cyclical phases. Thus, our findings could not be attributed to specific hormonal levels pertaining to the phases studied [15]. The possible existence and extent of inhibitory influences of pituitary and ovarian hormones on cardiac autonomic control can be well attributed by measuring their levels and correlation with HRV parameters. In view of the results obtained in the present age group, further studies should be conducted for at least four phases of menstrual cycle viz. early follicular, mid follicular, ovulatory and mid luteal phases and correlation should be determined by investigating the combined influence of age, BMI between the HRV indices and the sex hormones with a larger sample size.

Conclusion

In this study, the lower SDNN and RMSSD during the mid-luteal phase in comparison to the follicular phase could have resulted from enhanced sympathetic activity during the luteal phase. In reference to the same, there was significant higher parasympathetic modulation observed in follicular phase. These findings suggest that the variations in the hormonal status during follicular and luteal phases could contribute to the autonomic modulation of the heart which can be predicted by HRV.

Funding: No funding sources

Conflict of Interest: None declared

Ethical Approval: The study was approved by the institutional ethics committee.

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