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Original Article

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Heart Rate Variability & Behavioral Changes in Normal & Premenstural Syndrome Cases in Follicular and Late Leuteal Phase in Medical Students

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ABSTRACT

Background: Premenstrual syndrome (PMS) shows a wide variety of cyclic and recurrent physical, emotional, and behavioral symptoms occurring during the late luteal phase of the menstrual cycle and abating shortly following the beginning of menses. The present study assesses whether the activity of the autonomic nervous system is altered during the menstrual cycle of women with different degrees of premenstrual symptomatology

Material & Methods: Twenty PMS cases with their mean age 20±1.5 with regular menstrual cycles participated in this study. The autonomic nervous system activity was noninvasively measured by HRV power spectral analysis & menstrual distress questionnaire was compared among normal controls & PMS cases.

Results: has shown significant change in VHF (P=0.00), VLF (P=0.02), Sympathetic vagal balance (P=0.05) in PMS cases as compared to control. Significant increase in VHF (P=0.03) & VLF (P=0.00) is seen in leuteal phase as compared to follicular phase in PMS cases. SDNN & RR interval was also compared it was found to be significantly decreased in leuteal phase of PMS cases as compared to controls.

Conclusion: we can say that there is sympathetic over activity in Late leuteal phase of menstrual cycle in females of age group 20-25.This sympathetic over activity hampers in day to day routines of the subjects as dysphoric symptoms are increased markedly during late luteal phase in PMS cases as compared to controls.

Key Words: *Premenstrual Syndrome (PMS), Heart rate variability*

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INTRODUCTION

A lot of studies have been done to see the autonomic changes during menstrual cycle this study was done as to observe the changes in medical students during Follicular and Late leuteal phase. Premenstrual syndrome (PMS) describes a range of emotional, behavioral, and physical symptoms that occur during the leuteal phase of the ovulatory menstrual cycle and abate following menstruation [1]. Premenstrual syndrome (PMS) is characterized by the cyclic nature of a collection of psychological, physiological, and/or behavioral symptoms appearing during the late leuteal phase of the menstrual cycle and usually disappearing shortly after the onset of menses [2, 3]. Both severe PMS and premenstrual dysphoric disorder are associated with significant functional impairment and impact quality of life [1]. Despite findings that the autonomic function is altered in people with psychosomatic symptoms such as depression anxiety or chronic fatigue, a paucity of information exists regarding the potential association of PMS and autonomic nervous system activity [4, 5]. Measurement of heart rate variability (HRV) is a widely used noninvasive technique to assess the influence of sympathetic and parasympathetic activity on the heart. Heart rate with low variability reflects reduced parasympathetic (vagal) activity and/or elevated sympathetic tone and is considered an important cardiovascular risk factor [5-10]. There are two types of HRV measurements: time domain variables and frequency domain variables. The RR interval is the time interval between two consecutive R-points of the QRS complex intervals. The standard deviation of normal RR intervals (SDNN) reflects total variability and carries the strongest prognostic information in heart disease [7]. The frequency domain variables are derived from power spectral analysis of long-term or short-term registrations and are used to distinguish between sympathetic and vagal predominance [11]. The power of the high frequency peak (HF) corresponds to the respiratory sinus arrythmia and reflects mainly the cardiac vagal function [7]. In the supine position, the vagal afferents and efferents are activated and the HF component is assumed to reflect parasympathetic activity only. The low frequency peak (LF) is influenced by baroreceptor mediated regulation of blood pressure and reflects both sympathetic and vagal activity [11-14]. The LF/HF ratio has been used to reflect the sympatho-vagal balance and in the standing up position, when the sympathetic system is activated by an orthostatic response, it is assumed to be mainly an estimate of the sympathetic tone [15, 16].

One study reported that women with PMS have a higher resting heart rate than controls in the late-luteal phase consistent with altered autonomic nervous system function, but others have failed to replicate this effect [17-19]. As far as we are aware, only two studies have measured HRV in women with PMS or PMDD. Landen et al evaluated HRV in women diagnosed with PMDD and in controls during the follicular and late-luteal phases of the menstrual cycle [20]. Accordingly, the present study evaluates resting autonomic nervous system activity by means of HRV power spectral analysis of eumenorrheic women with different degrees of premenstrual symptoms and there comparison with controls.

MATERIAL AND METHODS

Subjects: Twenty females in the age group of 20-25 yr with PMS and 20 normal controls with regular menstrual cycles participated in this study. The study protocol was approved in advance by the institutional ethical committee and was performed in accordance with the declaration of Helenski of world medical association. All subjects received an explanation of the nature and purpose of the study, gave their written informed consent for the study. Prior to obtaining any data from experiments, the subjects had medical examinations and interviews and completed a standardized health questionnaire regarding medical history, medical examinations, medications, current health condition, menstrual cycle (length of cycle, length of menstrual flow and regularity of cycle), premenstrual discomfort and lifestyle. All subjects self reported regular menstrual cycle for at least two cycles. None of the subjects had clinical history of diabetes mellitus, hypertension, cardiovascular disease, or any other endocrine or systemic disorders.

Experimental procedure

Subjects were examined on two separate occasions: once during the follicular phase (with in five days after completion of menstrual bleeding), and once during the late leuteal phase (with in seven days before the next menstruation). Cycle phase was determined by the onset of menstruation and oral temperature [16]. All measurements in the follicular and late leuteal phase for subjects were taken between 12:00 and 15:00. The room was temperature controlled at 25°C, quiet, and comfortable, with minimization of arousal stimuli. Height and body weight of each subject were measured to calculate body mass index (BMI) as body weight divided by height squared. After skin preparation, the subjects were fitted with ECG electrodes. They then rested for at least 10 minutes before the start of the experiment. After the resting period, the II lead ECG was continuously recorded for 15 minutes during supine rest. All subjects breathed in synchrony to a metronome at 15 beats·min-1 (0.25 Hz) to ensure that respiratory-linked variations in heart rate did not overlap with lower-frequency heart-rate fluctuations (below 0.15 Hz) from other sources. The ECG sampling of R-R interval variations were later analyzed via HRV power spectral analysis described above to evaluate autonomic nervous system activity during the menstrual cycle. Before the subjects completed ECG measurement, each filled out the Menstrual Distress Questionnaire (MDQ) which evaluated physical, emotional, and behavioral symptoms accompanying the menstrual cycle [21].

R-R interval power spectral analysis procedure.

Periodic components of HRV tend to aggregate within several frequency bands [11, 13 & 22]. The autonomic nervous system activity was thus no invasively measured by HRV power spectral analysis, which decomposes the series of sequential R-R intervals into a sum of sinusoidal functions of different amplitudes and frequencies by the fast Fourier transform algorithm (FFT). Biopac MP100 with acknowledge 3.9 software machine was used for recording HRV data. The technique of the analysis for the present investigation has been applied in basic physiological and clinical research fields, and its validity and reliability has been previously confirmed [16, 23 & 24-28]. The procedure of R-R interval power spectral analysis used in the present study has been described in great detail elsewhere [25, 26]. The digitized ECG signal was differentiated, and the resultant QRS spikes and the intervals of the impulses (R-Intervals) were stored sequentially on a hard disk for later analyses. Spectral powers were calculated for the following respective frequency band: Very low frequency(VLF) power (≤0.04Hz) & low frequency (LF) power (0.04-0.15Hz), an indicator of both sympathetic and parasympathetic nervous system activity; high frequency (HF) power (0.15-0.4Hz), which solely reflects parasympathetic nerve activity; and Symaptaho /Vagal balance(Ratio LF[ms^2]/HF[ms^2] representing overall ANS activity [23-26 & 28].

Statistics

The data obtained was analyzed using SPSS software (Version 17.0).Kolmogrov -smirnov test was used for checking the normality of data. Equality of variance was checked using Leven's test. Mann- whitney U Test was used for comparison of control with PMS. Wilcoxon signed rank test was used for comparison of Late Leutal phase with Folicular phase in PMS cases. P value less than 0.05 is taken as significant. Results are expressed as mean±S.D.

RESULTS

The mean values of age in control were 20±1.2 &PMS were 20±1.5. Normality of data was checked using Kolmogrov -smirnov test VLF, LF, Sympathetic vagal balance are normally distributed HF &VHF were not.

Levene's test for equality of variance has shown that in controls VLF has F, 0.008 and p=0.930, LF has F, 6.723 & p=0.018 and sympathetic vagal balance has F, 13.158 & p=0.002) while in PMS VLF has F, 0.954 & p=0.342 LF has F, 9.253& p=0.007, sympathetic vagal balance has F, 10.691 & p=0.004.

Our data has shown significant decrease in HF& VHF in leuteal phase as compared to follicular phase (P=0.03).VLF is significantly increased (P=0.02) & VHF is significantly decreased in PMS cases as compared to controls (P=0.00), Sympathetic–vagal balance in PMS is slightly increased (P=0.05) as shown in table-1.

Table-2 shows comparison of Late leuteal phase with follicular phase in PMS cases with significant changes in HF (P=0.03), VHF (P=0.03) & VLF (P=0.00) among two groups.

Table -3 shows time domain variables i.e. RR interval & SDNN mean in PMS & Controls in follicular & Late leuteal phase. Significant decrease (P<0.05) in RR interval & SDNN mean is seen in PMS cases as compared to controls in both follicular & leuteal phases.

Figure 1: shows power spectral density in normal subjects.
Figure 2: shows power spectral density in PMS cases.
Figure 3: Shows comparing the frequency of symptoms number of subjects reported in controls and PMS cases.

Table 1: Comparison of control and Pre menstrual syndrome cases

Parameter	Control n=20	PMS n=20	P value
HF(Hz)	1.27±1.63	1.15±1.45	0.16
LF(Hz)	2.00±0.50	2.06±0.55	0.18
VHF(Hz)	0.79±1.00	0.50±0.56	0.00*
VLF(Hz)	4.25±1.00	5.87±1.03	0.02*
Sympathetic vagal Balance	3.00±0.00.45	3.45±0.36	0.05*

*Significant

Table 2: Comparison of Follicular phase and Late Leuteal phase in Premenstural syndrome cases

Parameter	Follicular phase n=20	Late Leuteal phase n=20	P value
HF(Hz)	1.90±2.17	1.73±1.93	0.03*
LF(Hz)	0.79±1.00	2.81±1.58	0.95
VHF(Hz)	1.30±1.24	0.74±0.74	0.03*
VLF(Hz)	4.63±1.27	5.67±1.47	0.00*
Sympathetic vagal Balance	1.15±1.45	2.82±1.24	0.22

*Significant

Table 3: Comparison of RR interval & SDNN mean in PMS & Controls in follicular & Late leuteal phase

	Follicular Phase n=20		Late Leuteal Phase n=20	
	Control	PMS	Control	PMS
RR(ms)	736.2±62.4	694.6±48.3*	723.3±53.4	663.8±32.5*
SDNN(ms)	132.5±21.3	118±26.4	112.4±23.6	96.3±16.4*

Significant*

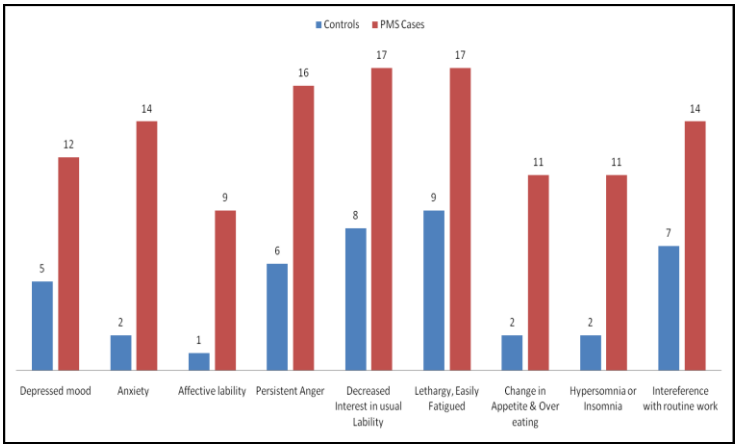

Figure 3: Frequency of Symptoms in Controls & Premenstrual cases

DISCUSSION

Previous studies have demonstrated that the autonomic regulation of the heart in normal women fluctuates during the menstrual cycle, HRV being lower in the leuteal phase than in the follicular phase [29, 30]. In the present study, this phenomenon was discernible in the control group, stressing the importance of taking menstrual cycle phase into account when interpreting HRV in menstruating women. The most prevalent symptoms include: irritability, mood labiality, depression, anxiety, impulsivity, feelings of "loss of control," fatigue, decreased concentration, abdominal bloating, fluid retention, breast swelling, and general aches [2, 3, 14 & 29]. HRV measurements are increasingly used in applications ranging from basic investigations and central regulation of autonomic state to studies of fundamental links between psychological processes and physiological functions and evaluations of cognitive development and clinical risk [9]. According to Kim et al. as an ancillary study of the Women's Health Initiative Observational Study, women with symptoms of depression had significant reductions in HRV and higher heart rate, suggestive of increased sympathetic tone [32]. Recent study with this method has revealed that patients with climacteric disorders possessed altered sympathovagal balance [28]. It should be mentioned that the widely fluctuated R-R interval and the corresponding power spectrum in the Control group were frequently observed in healthy individuals in previous research [23, 25-27]. In the PMS group, however, Total power and HF power were significantly decreased in the late luteal phase from the follicular phase. As to the PMS group suffering more severe negative emotional symptoms, heart-rate fluctuations as well as all components of the power spectrum were markedly more reduced regardless of the menstrual cycle. These findings demonstrated that power spectral analysis of HRV not only can evaluate the activities of both branches of the autonomic nervous system but also have potential capacity to scrutinize an intricate relationship between psycho-behavioral and physiological processes. In addition, age is an important factor influencing autonomic nervous system activity that's why we have kept narrow band of mean ages of the subjects [28, 33]. This study, however, indicates that parasympathetic nervous system activity decreased in the symptomatic late luteal phase compared to the follicular phase in women who experienced a substantial increase (> 20%) in diverse, but not unbearable, psychosomatic symptoms premenstrually. The study also suggests that physiological function in both branches of the autonomic nervous system might be more depressed during the entire menstrual cycle when premenstrual symptoms become more severe as seen in women suffering from PMDD. Kondo et al. measured the coefficient of variation of R-R interval during the menstrual cycle and demonstrated that the parasympathetic nerve activity was lower in the late luteal phase than in the follicular phase in women with PMS [34]. Recent clinical studies have revealed that women with PMS had elevated norepinephrine and total peripheral resistance at rest and during mental stressors compared with control subjects [35, 29]. These phenomena occurred in both the follicular and luteal phases. Recent research by Landen et al. with time and frequency domain of HRV measurement has shown an interesting finding, which suggests that women with PMDD have reduced vagal tone compared to controls and that this difference is more apparent in the non-symptomatic follicular phase [36]. We have also compared time domain variables, which in this study reveals RR interval and SDNN is significant lower in PMS cases as compared to controls and hence adds further support to the notion that reduced HRV is a feature shared by a number of related psychiatric disorders that are characterized by symptoms such as depressed mood, tension, and/or irritability and anger. The study of B grrishma et al has also shown decreased HRV & increase in DBP in leuteal phase [37]. The results are consistent with the Meta analysis study of Katja M. Schmalenberger eta al which indicates the presence of CVA fluctuations across the menstrual cycle. Menstrual Distress Questionnaire (MDQ) which evaluated physical, emotional, and behavioral symptoms accompanying the menstrual cycle has also shown increased distressing symptoms in PMS cases as compared to controls [38].

In conclusion we can say there is increased sympathetic activity in Late leuteal phase of menstrual Cycle in females of age group 20-25. This study also shows sympaththetic over activity in Pre menstrual syndrome cases in Late leuteal phase as compared to normal controls and in Follicular phase of PMS cases. The Symptoms of distress also increases which affects day to day activity in Premenstural syndrome cases.

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