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Research Article

INFLUENCE OF PRE MENSTRUAL SYNDROME ON AUTONOMIC FUNCTIONS OF HEART IN YOUNG ADULT FEMALES – A CROSS-SECTIONAL STUDY

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ABSTRACT

Objective: The aim of the study was to analyze the role of autonomic activity by heart rate variability (HRV) during different phases of menstrual cycle in subject with premenstrual syndrome (PMS).

Methods: This cross-sectional study was conducted in SRM medical college hospital and research center for 6 months (November 2017 to April 2018). Sixty young female subjects with regular menstrual history aged between 18 and 25 years of age were recruited in this study after obtaining ethical committee clearance. The subjects were categorized into mild and moderate PMS according to Premenstrual Syndrome Scale. This study includes 30 subjects in each category. HRV was done by Physiopac, the "Medicaid" system during the various phases of the menstrual cycle. Statistical analysis was done by t-test (paired and independent sample test).

Results: The mean heart rate (<0.005), low frequency (LF) power normalized unit (n.u) (<0.001), and LF high frequency (HF) ratio (<0.001) were significantly increased in the luteal phase whereas the mean RR interval (<0.008), standard deviation of normal to the normal (<0.05), RMSSD (<0.037), HF power n.u (0.054), and total power (<0.055) were significantly reduced in the luteal phase of moderate PMS when compared to the luteal phase of mild PMS.

Conclusion: Disturbances in the balance of autonomic function in the late luteal phase might be responsible for the psychological and somatic changes in women with PMS.

Keywords: Heart rate variability, Time domain parameter, Frequency domain parameter, Follicular phase, Luteal phase.

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INTRODUCTION

Premenstrual syndrome (PMS) is a common clinical problem experienced by majority of females in their reproductive life [1]. It includes extensive range of cyclic and recurrent physical, emotional, and behavioral symptoms that befall in the second half of the menstrual cycle and decline immediately after the beginning of menses [2-4]. Being a psychophysiological stress induced disorder; the underlying mechanism of PMS is multifactorial in origin. It might affect diverse neuropsychophysiological systems and remains unclear. It was proposed that alterations in the autonomic function especially in the second half of the menstrual cycle could be the prime reason behind this entity. Exploring heart-rate variability (HRV) could be the useful tool to provide a comprehensive quantitative and qualitative assessment of the autonomic nervous system [5,6]. HRV is a measure of the autonomic activity of heart which exhibits physiological changes throughout the menstrual cycle [7]. Earlier researchers have shown that decreased high frequency (HF) power is associated with decreased vagal activity and an increased low frequency (LF)/HF ratio was noticed in the mid-luteal phase [8,9]. It was established that the HF component of HRV was more in follicular phase and LF component was found to be increased on the ovulatory and luteal phases [10]. Till date, only very few studies reported the role of autonomic activity during menstrual cycle and none of the study measured the autonomic activity in mild and moderate category of PMS. Hence, this study was aimed to examine the activity of the autonomic nervous system in women with PMS.

METHODS

Sixty young female subjects between 18 and 25 years of age, having history of regular menstrual cycle, were included for this cross-sectional and observational study. This study was conducted in SRM Medical College Hospital and Research centre, Kattankulathur, for a period of 6 months after the approval of the Institutional Ethical Committee Number-658/IRC. Informed consent was obtained from all the participants. Females with an irregular menstrual cycle, pregnant, smokers, systemic problems such as diabetes mellitus, psychiatric illness, already diagnosed PMS with treatment, obesity, and on any medications with oral contraceptive pills and endocrine disorder were barred from the study.

Sample size calculation

Studies showed that the prevalence of PMS in India was 14.3% [11].

$N = Z^2pq/d^2$

Where
Z = 1.96 (for 95% confidence interval)
p = 0.143
Q = 1 − p (1 − 0.143) = 0.857
e = 0.1 (allowable error of 10%)
N = 1.96 × 1.96 × 0.143 × 0.857/0.1 × 0.1
N = 47

Hence, minimum sample size was 47 but in this study, 60 subjects were recruited.

In every case selected, demographic profiles such as age and personal data like height in meters and weights in kg were measured and calculated the body mass index (BMI) of the subject. The baseline

reading of BMI was categorized as underweight (<18.5), normal (18.5–24.99), overweight (25–29.99), and obese (30+) [12]. At that time, menstrual history was taken including nature and days of menstrual flow, regularity, and total duration of the cycle. After the menstrual history, the standardized form of premenstrual syndrome scale questionnaires (PMSS) [13] was used to analyze the description of symptoms in different phases of a menstrual cycle. This questionnaire is self-explanatory and can be filled by the subject themselves. The questionnaire has depiction of symptoms classified into three categories, namely, physiological symptoms (16 items), psychological symptoms (12 items), and behavioral symptoms (12), each of which was scored relating to different phases of a menstrual cycle. Hence, the questionnaire provided score based on 40 items related to PMS. Each item has five options ranging from 1 to 5 rating scale with the scores of, 1 – Never, 2 – Rarely, 3 – Sometimes, 4 – Very often, and 5 – Always and the total score was 200. Based on the total score, the premenstrual symptoms were categorized in to five levels, 1–40: No symptoms, 41–80: Mild symptoms, 81–120: Moderate symptoms, 121–160: Severe and 161–200: Very Severe. In this study based on the above score, we classified the subject as mild and moderate PMS. The cardiac autonomic status of mild and moderate PMS subjects was examined by recording the short-term HRV for 5 min. The examination was carried out at the same time of the day (9.30 am to 11.30 am) to avoid diurnal variation with a maintained room temperature of about 24°C–25°C. Participants were inculcated to avoid breakfast and caffeinated products for 4 h and from vigorous exercise and alcohol for 48 h earlier the tests. Each subject was examined on two phases of the menstrual cycle, on the 10th day (follicular phase) and the 21st day of (luteal phase) to avoid experimental bias.

After cleaning the skin, the ECG electrode was fitted on the corresponding limbs subsequently making the subject take a rest at least 10 min before commencing the experiment. As per the task force recommendation, the standard procedure was followed to acquire the lead II ECG at the sampling rate of 500/s for 5 min with the breath rate of 12–16/min at rest in a supine position using eight – channels Physiopac (updated), "Medicaid" system [14]. After excluding the artifacts, the RR waves were extracted and transferred to Kubios software to get the parameters such as time and frequency domain. The frequency-domain was obtained by analyzing the HRV- RR tachogarm by spectral power through fast Fourier transformation. It includes LF power (LF – 0.04–0.15 Hz), an indicator of both the autonomic nervous system (Sympathetic and parasympathetic nervous system); HF power (HF – 0.15–0.4 Hz), an indicator of parasympathetic activity; Relative power of LF normalized unit (n.u), and HF n.u which solely reflects the sympathetic and parasympathetic activity, respectively; total power (TP) (0.03–0.5 Hz) representing the overall activity of HRV and the LF/HF ratio indicates the sympathovagal balance. The time-domain parameter includes the mean RR interval, standard deviation of normal to the normal interval (SDNN) indicates the overall HRV; the square root of the mean of the sum of the squares of the difference between adjacent NN intervals (RMSSD) reflects solely the vagal tone [15].

Statistical analysis

This study data were analyzed using SPSS software (SPSS 20.0 for Windows, IBM Co). The continuous variable was analyzed by Student's paired t-test to get the mean difference between the same group (paired variables) either in the follicular and luteal phase of mild PMS or follicular and luteal phase of moderate PMS whereas the Student's independent t-test was used to compare the mean between different group (Mild and moderate PMS of follicular and mild and moderate PMS of luteal phase). The p-value was lower than 0.05 which was considered a significant.

RESULTS

Fig. 1 showed that there was no significant difference in age since the sample was taken from homogenous group of young adult females. There was no significant difference in BMI between groups. Mild group had 21.92 and moderate group had 21.55 as BMI. The mean PMSS

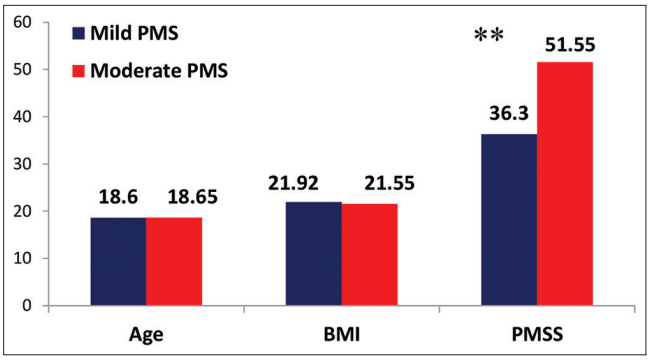

Fig. 1: Comparison of demographic and MDQ score between mild and moderate PMS in young adult by independent Student's – "t" test. **Statistically significant, PMSS: Premenstrual syndrome scale, PMS: Premenstrual syndrome, BMI: Body mass index

score for mild PMS was 36.3 whereas the moderate PMS was 51.55. It showed a highly significant difference between mild and moderate subjects. Table 1 describes the comparison of autonomic status between the follicular and luteal phases of mild PMS and we did not find any significant differences between the phases in mild PMS. Table 2 shows the comparison of autonomic status between the follicular and luteal phases of moderate PMS. We have noticed that the mean heart rate (0.003**) and LF power n.u (0.001***) was significantly increased in the luteal phase among the individuals with moderate PMS. Contrastingly, HF power n.u (0.001***) is reduced in the luteal phase. Table 3 illustrates a comparison of HRV among subjects with mild and moderate PMS in the follicular phase. HF power ms^2 (0.049*) and TP ms^2 (0.05*) showed decreased mean in the follicular phase of moderate PMS and it is found to be statistically significant. Table 4 describes the comparison of autonomic status between mild and moderate PMS of luteal phase. The time-domain parameters of mean RR interval, (0.008**), SDNN (0.05*), and RMSSD (0.005***) were significantly lower in the luteal phase of moderate PMS. The frequency-domain parameters of HF power ms^2 (0.000***), HF power n.u, (0.05*), and TP ms^2 (0.055*) were significantly lower in the luteal phase of moderate PMS whereas the LF power n.u (0.000***) and LF/HF ratio (0.001***) were significantly higher in the luteal phase of moderate PMS when compared to the luteal phase of mild.

DISCUSSION

PMS comprises myriad non-specific physical, emotional, behavioral, and cognitive symptoms that occur in the days before menstruation [16]. The symptoms regarding the severity and frequency experienced by different women subject to wide variability. The clinical signs are usually stable within each woman but may also fluctuate between her menstrual cycles. HRV measurements are used all over the world to study the autonomic functions [5].

In this study, it is observed that the HRV among women experiencing PMS in various phases of menstrual cycle. Heart rate was higher in luteal phase when compared with follicular phase in both the groups (mild and moderate). This result is in accordance with the study done by de Zambotti *et al*. [17]. Significant reductions in SDNN and RMSSD in the moderate PMS of luteal phase when match up with the mild PMS of luteal phase which indicate the reduction in overall HRV and cardiovagal drive in the luteal phase, respectively. This result was supported by the study done by Grrishma *et al*. [18].

Substantially, we have found that the frequency domain parameter of TP ms^2 was significantly reduced in the both phases of moderate PMS when compared with mild PMS group of follicular and luteal phases. It showed that the overall HRV was reduced in both phases of the menstrual cycle in the moderate group. Landén and Eriksson also found a similar reduction of TP in the late luteal phase of premenstrual dysphoric disorder [19]. We reported that individuals with moderate

Table 1: Comparison of autonomic status between follicular and luteal phase of mild pre-menstrual syndrome in young adult by Student's paired t-test

Parameter	Mild pre-menstrual syndrome (n=30), mean±SD		Mean difference	t	Significant
	Follicular phase	Luteal phase			
Mean RR interval	808.01±106.94	784.06±107.23	24.11	1.424	0.171 (NS)
SDNN	53.96±40.12	41.29±27.83	12.66	1.746	0.097 (NS)
Mean heart rate	75.86±09.21	77.87±09.87	−1.983	−1.226	0.235 (NS)
RMSSD	67.53±57.95	50.11±41.40	17.42	1.712	103 (NS)
LF power ms^2	988.80±1152.71	696.50±883.56	292.3	1.275	0.218 (NS)
HF power ms^2	3056.6±4673.75	1704.4±3105	1352.2	1.925	0.069 (NS)
LF power n.u	36.38±16.67	40.93±17.81	−4.55	1.265	0.221 (NS)
HF power n.u	63.33±16.63	58.62±17.91	4.7	1.324	0.201 (NS)
Total power ms^2	4144.6±5829.12	2501.14±3928.62	1643.8	1.826	0.084 (NS)
LF/HF ratio	0.7073±0.555	0.908±0.7309	−0.2013	−1.506	0.149 (NS)

*p<0.05 – is considered significant and ***p<0.001 – is considered highly significant statistically.[1] NS: Not significant, SDNN: Standard deviation of normal to the normal interval, RMMSD: Root mean square of successive difference between normal heart beats, LF: Low frequency, HF: High frequency, n.u: Normalized unit, SD: Standard deviation, RR Interval: Time interval between the consecutive heart beats

Table 2: Comparison of autonomic status between follicular and luteal phase of moderate pre-menstrual syndrome in young adult by student's paired t-test

Parameter	Moderate pre-menstrual syndrome (n=30), mean±SD		Mean difference	t	Significant
	Follicular phase	Luteal phase			
Mean RR interval	756.04±74.22	696.13±91.52	59.91	3.199	0.005**
SDNN	34.10±23.74	27.46±12.61	6.63	1.228	0.235 (ns)
Mean heart rate	80.18±8.22	87.84±11.03	−7.65	−3.395	0.003**
RMSSD	39.76±34.33	28.16±18.47	11.59	1.413	0.174 (NS)
LF power ms^2	458.50±515.08	363.15±347.25	95.35	0.725	0.477 (NS)
HF power ms^2	807.15±1613.36	309.45±461.72	497.7	1.431	0.169 (NS)
LF power n.u	46.49±20.19	61.36±12.88	−14.87	−4.157	0.001***
HF power n.u	52.89±19.83	38.12±12.45	14.77	4.158	0.001***
Total power ms^2	1350.13±2139.1	725.15±824.6	624.8	1.331	0.199 (NS)
LF/HF ratio	1.0354±0.83101	1.9005±0.969	−0.865	0.7223	0***

*p<0.05, ***p<0.001 statistically significant.[1] NS: Not significant, SDNN: Standard deviation of normal to the normal interval, RMMSD: Root mean square of successive difference between normal Heart beats, LF: Low frequency, HF: High frequency, SD: Standard deviation RR Interval: Time interval between the consecutive heart beats

Table 3: Comparison of autonomic status between mild and moderate pre-menstrual syndrome of follicular phase in young adult by independent Student's t-test

Parameter	Follicular phase (n=30), mean±SD		t	Significant
	Mild pre-menstrual syndrome	Moderate pre-menstrual syndrome		
Mean RR interval	808.01±106.94	756.04±74.22	1.791	0.081 (NS)
SDNN	53.96±40.12	34.10±23.74	1.905	0.064 (NS)
Mean heart rate	75.86±09.21	80.18±8.22	−1.556	0.128 (NS)
RMSSD	67.53±57.95	39.76±34.33	1.844	0.073 (NS)
LF power ms^2	988.80±1152.71	458.50±515.08	1.878	0.068 (NS)
HF power ms^2	3056.6±4673.75	807.15±1613.36	−1.514	0.138 (NS)
LF power n.u	36.38±16.67	46.49±20.19	−1.726	0.092 (NS)
HF power n.u	63.33±16.63	52.89±19.83	2.035	0.049*
Total power ms^2	4144.6±5829.12	1350.13±2139.1	2.013	0.051*
LF/HF ratio	0.7073±0.555	1.0354±0.83101	−1.468	0.150 (ns)

*p<0.05, ***p<0.001- statistically significant.[1] NS: Not significant, SDNN: Standard deviation of normal to the normal interval, RMMSD: Root mean square of successive difference between normal heart beats, LF: Low frequency, HF: High frequency, SD: Standard deviation, RR Interval: Time interval between the consecutive heart beats

PMS had decreased absolute and relative HF power (ms^2 and normalized unit) in both follicular and luteal phase when compared with mild PMS group individuals and HF power ms^2 showed statistically significant in luteal phase whereas HF nu showed significant in both follicular and luteal phase. This indicates the reduction in vagal tone in both phases in the moderate PMS group. Baker *et al*. and Kondo *et al*. also reported that HF power ms^2 and normalized unit were reduced in the late-luteal phase compared with the mid-follicular phase in severe PMS group but not in controls [20,21]. This study showed that the LH nu and LF – HF ratio was increased in the luteal phase of moderate PMS in contrast to the mild PMS. This indicates the dominance of sympathetic activity and decreased vagal tone. Matsumoto *et al*. and Grrishma *et al*. also found a similar result [18,22]. Overall this study reflected that more menstrual distress symptoms (moderate PMS) showed reduced overall variability of the heart (in both the phase), and decreased cardiovagal drive (in both the phase), and increased sympathetic activity (in luteal phase).

Several mechanisms might be responsible for the dominance of sympathetic tone during luteal phase. In follicular phase, estrogen gradually increases which causes peak increase in FSH and LH, whereas progesterone remains low all over the cycle. Both estrogen and progesterone dominate the luteal cycle [23]. These might exert direct and indirect effect on cardiovascular system through these receptors [24]. As a net result, the severity of the PMS is associated

Table 4: Comparison of autonomic status between mild and moderate pre-menstrual syndrome of luteal phase in young adult by independent Student's t-test

Parameter	Luteal phase (n=30), mean±SD		t	Significant
	Mild pre-menstrual syndrome	Moderate pre-menstrual syndrome		
Mean RR interval	784.06±107.23	696.13±91.52	2.789	0.008***
SDNN	41.29±27.83	27.46±12.61	2.024	0.050*
Mean heart rate	77.87±09.87	87.84±11.03	−3.010	0.005***
RMSSD	50.11±41.40	28.16±18.47	2.165	0.037**
LF power ms^2	696.50±883.56	363.15±347.25	1.570	0.125 (NS)
HF power ms^2	1704.4±3105	309.45±461.72	−4.171	0
LF power n.u	40.93±17.81	61.36±12.88	−4.158	0
HF power n.u	58.62±17.91	38.12±12.45	1.987	0.054**
Total power ms^2	2501.14±3928.62	725.15±824.6	1.979	0.055**
LF/HF ratio	0.908±0.7309	1.9005±0.969	−3.652	0.001***

*p<0.05, ***p<0.001: Statistically significant. NS: Not significant, SDNN: Standard deviation of normal to the normal interval, RMMSD: Root mean square of successive difference between normal heart beats, LF: Low frequency, HF: High frequency, SD: Standard deviation, RR Interval: Time interval between the consecutive heart beats

with increase in sympathetic activity. On contrast, cardiovagal drive was decreased throughout in moderate PMS group.

Limitation

Small sample size from the homogenous group is the limitation of the study. Larger sample size will be taken in future studies to understand the role of other confounding factors.

CONCLUSION

The dominance of sympathetic system is noticed during luteal phase in women with PMS. This could be the probable explanation behind the psychosomatic changes experienced by those women. Women having PMS are advised to undergo stress reduction programs and non-pharmaceutical treatment such as yoga and meditation for symptomatic relief.

AUTHORS' CONTRIBUTIONS

Thilip Kumar Ganandurai and Arulraja S carried out the conception and design of this study, acquired the data and analysis part. Poornima Kumbakonam Nagarajan has drafted the article with intellectual content. Prabhavathi K has interpreted the data and Lakshmi ANR gave the final approval for publishing in the journal.

COMPETING INTERESTS

The author declared "no conflicts of interest."

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