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Original Article

Physiology Section

Effect of Different Phases of Menstrual Cycle on Heart Rate Variability (HRV)

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ABSTRACT

Background: Heart Rate Variability (HRV), which is a measure of the cardiac autonomic tone, displays physiological changes throughout the menstrual cycle. The functions of the ANS in various phases of the menstrual cycle were examined in some studies.

Aims and Objectives: The aim of our study was to observe the effect of menstrual cycle on cardiac autonomic function parameters in healthy females.

Materials and Methods: A cross-sectional (observational) study was conducted on 50 healthy females, in the age group of 18-25 years. Heart Rate Variability (HRV) was recorded by Physio Pac (PC-2004). The data consisted of Time Domain Analysis and Frequency Domain Analysis in menstrual, proliferative and secretory phase of menstrual cycle. Data collected was analysed statistically using student's pair t-test.

Results: The difference in mean heart rate, LF power%, LFnu and HFnu in menstrual and proliferative phase was found to be statistically significant. The difference in mean RR, Mean HR, RMSSD (the square root of the mean of the squares of the successive differences between adjacent NNs.), NN50 (the number of pairs of successive NNs that differ by more than 50 ms), pNN50 (the proportion of NN50 divided by total number of NNs.), VLF (very low frequency) power, LF (low frequency) power, LF power%, HF power %, LF/HF ratio, LFnu and HFnu was found to be statistically significant in proliferative and secretory phase. The difference in Mean RR, Mean HR, LFnu and HFnu was found to be statistically significant in secretory and menstrual phases.

Conclusion: From the study it can be concluded that sympathetic nervous activity in secretory phase is greater than in the proliferative phase, whereas parasympathetic nervous activity is predominant in proliferative phase.

Keywords: Autonomic nervous system, Heart rate, Low frequency, Menstrual cycle, Vagal activity

INTRODUCTION

The reproductive system of women, unlike that of men, shows regular cyclic changes that teleologically may be regarded as periodic preparations for fertilization and pregnancy [1]. The duration of cycle averages 28 days. It may be as short as 20 days or as long as 45 days in some women [2].

The menstrual cycle is actually two distinct cycles: the ovarian cycle and the endometrial cycle. The ovarian cycle is divided into follicular and luteal phases. In follicular phase estrogens gradually increase, causing FSH and LH to peak, whereas progesterone remains low throughout. The luteal phase is dominated by the actions of estrogen and progesterone [3].

The endometrial cycle is divided into a proliferative phase, a secretory phase, and menstruation. Endometrial growth is the primary outcome of proliferative phase and is mediated by increase in estrogens. The primary outcome of secretory phase is the maturation of the endometrium. Decreasing levels of estrogens halt endometrial lining growth [3]. If conception does not occur, the endometrial lining is replaced to prepare for the next cycle [3]. The ovarian hormones estrogen and progesterone decrease greatly and menstruation begins [2].

Analysis of heart rate variability (HRV) could be a useful tool to assess cardiac autonomic control [4]. HRV describes the variation between consecutive heart beats. The rhythm of the heart is controlled by SA node, which is modulated by both sympathetic and parasympathetic branches of autonomic nervous system [5].

The HRV is evaluated by two ways: time domain analysis and frequency domain analysis [6]. VLF, LF and HF power are usually measured in absolute values of power (milliseconds squared {ms^2}). LF and HF can be also measured in normalized units (nu) to emphasize the controlled and balanced behaviour of the two branches of the autonomic nervous system, as well as baro-reflex responsiveness to beat-to-beat variations in arterial blood pressure. Normalization of LF and HF power tends to minimize the effect of the changes in the total power on the values of these two components [7]. The variations in the functions of the Autonomic Nervous System (ANS) are linked with the hormonal fluctuation in the menstrual cycle. The functions of the ANS in various phases of the menstrual cycle were examined in some studies. Heart Rate Variability (HRV), which is a measure of the cardiac autonomic tonus, displays physiological changes throughout the menstrual cycle [8].

Vishrutha KV et al., concluded that the HF component of HRV was higher in follicular phase and LF component was found to be higher on the ovulatory and luteal phases. Their results suggested a parasympathetic predominance during follicular phase and sympathetic activity in the luteal phase [9].

The aim of our study is to find the association of HRV with different phases of menstrual cycle in healthy young women. This study will help healthy young women to have a better understanding about their autonomic nerve function changes during different phases of menstrual cycle and hence to improve their quality of life. It may also help physicians to take appropriate measures for prevention of complications related to coronary artery heart disease, stroke and blood pressure in postmenopausal women.

MATERIALS AND METHODS

A cross-sectional (observational) study was conducted on 50 non-obese regularly cycling females in the age group of 18-25 years, for the duration of 3 days in a month each. The subjects for study

were taken up among the students of Government Medical College, Patiala. Written consent was taken from all the enrolled subjects after explaining them the details of the study in their own language. Heart rate of each subject was recorded by ECG monitoring, in RR mode (beat to beat), for 5 minutes at rest, in supine position, using 'Physiopac hardware' by 'Medicaid'.

The subject selection was based on exclusive-inclusive criteria.

Inclusion criteria: Females aged between 18-25 years and eumennorheic i.e., having regular normal menstrual cycles of 26-34 days were included in the study.

Exclusion criteria: Females who were pregnant, had irregular menstrual cycles, menorrhagic, had any endocrine disorder or were on any medication during the study (including oral contraceptive pills) were excluded.

Study Design: In every case selected, thorough menstrual history was taken including nature and days of menstrual flow, regularity and total duration of cycle.

The examination was carried out at same time of the day to avoid diurnal variation. Each subject was examined on three separate occasions of the menstrual cycle, on second day (menstrual phase), tenth day (proliferative phase) and twenty first day (secretory phase).

Prerequisites: The subject was allowed to relax on a comfortable chair with the subject's back towards the recording machine.

Physiopac Control unit was connected with Computer systems through USB cable. Bio potential Junction boxes were connected with channel no. 1 available on the front panel of the Physiopac control unit. ECG disc electrodes were inserted in the sockets of Bio-potential junction boxes.

Placement of electrodes- ECG electrodes were placed on the subject. Electrodes were placed on RA (right arm), LA (left arm), LL (left leg), and RL (right leg).

HRV Analysis: After recording ECG clicked at transform button and selected HRV. Filled the required time to achieve the HRV data for that particular time. After the test was completed, clicked at stop button to stop the test.

STATISTICAL ANALYSIS

The data was analysed statistically. Student's paired t-test was used for the analysis. $p<0.05$ was considered to be statistically significant.

RESULTS

The present study tested the HRV of healthy young female subjects. Comparison of HRV parameters in three phases of menstrual cycle viz. Menstrual, Proliferative and Secretory phase. It was evident from the results that Mean RR, Mean HR, VLF power, LF power, LF power%, LF/HF and LFnu are higher in secretory phase as compared to other two phases.

Menstrual and Proliferative phase: The difference in mean heart rate was found to be statistically significant [Table/Fig-1]. The difference in LF power%, LFnu and HFnu was found to be statistically significant [Table/Fig-2].

Proliferative and Secretory phase: The difference in mean RR, Mean HR, RMSSD, NN50 and pNN50 was found to be statistically significant [Table/Fig-3]. The difference in VLF power, LF power, LF power%, HF power %, LF/HF ratio, LFnu and HFnu was found to be statistically significant [Table/Fig-4].

Secretory and Menstrual phase: The difference in Mean RR and Mean HR, was found to be statistically significant [Table/Fig-5]. The difference in LFnu and HFnu was found to be statistically significant [Table/Fig-6].

Parameters	Phase		p-value
	Menstrual	Proliferative	
	Mean ± SD	Mean ± SD	
Mean RR	0.75 ± 0.13	0.18 ± 0.15	0.05
SDNN	0.04 ± 0.02	0.04 ± 0.02	0.43
Mean HR	79.08 ± 8.84	73.87 ± 8.96	0.004
RMSSD	27.78 ± 19.84	31.87 ± 21.22	0.32
NN50	9.30 ± 6.85	11.14 ± 7.59	0.20
pNN50	6.46 ± 4.8	7.70 ± 5.37	0.22

[Table/Fig-1]: Comparison of time domain analysis inmenstrual and proliferative phase

Parameters	Phase		p-value
	Menstrual	Proliferative	
	Mean ± SD	Mean ± SD	
VLF (peak)	0.02 ± 0.008	0.02 ± 0.008	0.85
LF (peak)	0.07 ± 0.03	0.07 ± 0.03	0.56
HF (peak)	0.18 ± 0.02	0.17 ± 0.02	0.54
VLF (power)	5.96 ± 12.37	3.08 ± 5.97	0.14
LF (power)	22.36 ± 58.30	8.06 ±18.03	0.10
HF (power)	7.34 ± 20.55	10.5 ± 31.24	0.33
VLF (power%)	24.31± 14.43	26.23 ±16.30	0.53
LF (power%)	54.68 ±12.41	48.58 ± 14.96	0.02
HF (power%)	20.98 ± 8.66	25.19 ±12.50	0.05
LF/HF ratio	3.01 ± 1.35	2.47 ± 1.49	0.06
LFnu	72.41 ± 9.19	65.93 ±13.93	0.007
HFnu	27.59 ± 9.19	34.06 ±13.93	0.007

[Table/Fig-2]: Comparison of frequency domain analysis in menstrual and proliferative phase

Parameters	Phase		p-value
	Proliferative	Secretory	
	Mean ± SD	Mean ± SD	
Mean RR	0.18 ± 0.15	0.70 ± 0.073	p<0.001
SDNN	0.04 ± 0.02	0.03 ± 0.026	0.06
Mean HR	73.87 ± 8.96	86.31 ± 7.98	p<0.001
RMSSD	31.87 ± 21.22	23.27 ± 19.50	0.03
NN50	11.14 ± 7.59	6.98 ± 6.67	0.004
pNN50	7.70 ± 5.37	4.78 ± 4.69	0.004

[Table/Fig-3]: Comparison of time domain analysis in proliferative and secretory phase

Parameters	Phase		p-value
	Proliferative	Secretory	
	Mean ± SD	Mean ± SD	
VLF (peak)	0.02 ± 0.008	0.02 ± 0.007	0.24
LF (peak)	0.07 ± 0.03	0.07 ± 0.02	0.88
HF (peak)	0.17 ± 0.02	0.17 ± 0.032	0.87
VLF (power)	3.08 ± 5.97	11.18 ± 21.55	0.01
LF (power)	8.06 ± 18.03	31.3 ± 71.70	0.02
HF (power)	10.5 ± 31.24	4.24 ± 9.40	0.17
VLF (power %)	26.23 ±16.30	26.66 ± 13.52	0.88
LF (power%)	48.58 ±14.96	55.44 ±11.16	0.01
HF (power%)	25.19 ±12.50	17.86 ± 6.99	p<0.001
LF/HF ratio	2.47 ± 1.49	3.54 ±1.46	p<0.001
LFnu	65.93 ± 13.93	75.82 ± 7.57	p<0.001
HFnu	34.06 ± 13.93	24.18 ± 7.57	p<0.001

[Table/Fig-4]: Comparison of frequency domain analysis in proliferative and secretory phase

Parameters	Phase		p-value
	Secretory	Menstrual	
	Mean ±SD	Mean ±SD	
Mean RR	0.70 ±0.073	0.75 ±0.13	0.01
SDNN	0.03 ±0.026	0.04 ±0.02	0.28
Mean HR	86.31 ±7.98	79.08 ±8.84	p<0.001
RMSSD	23.27 ±19.50	27.78 ±19.84	0.25
NN50	6.98 ±6.67	9.30 ±6.85	0.08
pNN50	4.78 ±4.69	6.46 ±4.8	0.07

[Table/Fig-5]: Comparison of time domain analysis insecretory and menstrual phase

Parameters	Phase		p-value
	Secretory	Menstrual	
	Mean ±SD	Mean ±SD	
VLF (peak)	0.02 ±0.007	0.02 ±0.008	0.33
LF (peak)	0.07 ±0.02	0.07 ±0.03	0.45
HF (peak)	0.17 ±0.032	0.18 ±0.02	0.47
VLF (power)	11.18±21.55	5.96 ±12.37	0.14
LF (power)	31.3 ±71.70	22.36±58.30	0.49
HF(power)	4.24 ±9.40	7.34 ±20.55	0.55
VLF (power%)	26.66±13.52	24.31±14.43	0.40
LF (power %)	55.44±11.16	54.68±12.41	0.74
HF (power%)	17.86 ±6.99	20.98 ±8.66	0.05
LF/HF ratio	3.54 ±1.46	3.01 ±1.35	0.06
LFnu	75.82 ±7.57	72.41±9.19	0.04
HFnu	24.18 ±7.57	27.59 ±9.19	0.04

[Table/Fig-6]: Comparison of frequency domain analysis in secretory and menstrual phase

DISCUSSION

Our study suggests highest sympathetic outflow in the secretory phase, compared to the proliferative phase and increased parasympathetic outflow in the proliferative phase, compared to the secretory phase. These results are in contrast to the study of Teixeira et al., which suggests that the different phases of the Menstrual Cycle did not alter the Resting Heart Rate in healthy women independently of the use of oral contraceptive [10].

Values of Mean RR and Mean HR in the present study are in agreement with the values of Kavitha et al., and Christina et al., [11,12]. Values of RMSSD in the present study are in agreement with Mckinley et al., [13]. Values of NN50 in the present study are in agreement with Vishrutha et al., [9]. RMSSD, NN50 and pNN50, the measurements of short-term variation, estimate high frequency variations in heart rate and are highly correlated [14]. So, the proliferative phase was characterized by increased vagal activity and the secretory phase was characterized by increased sympathetic activity [15]. Values of pNN 50 in the present study are in contrast to Vallejo et al., [16]. But as RMSSD and pNN50 have similar behaviour, which are parasympathetic related parameters [16]. So our study is in agreement with Mckinley et al., [13]. The increased pNN50 in our study may be due to increased parasympathetic activity during proliferative phase.

As VLF band provides an additional indicator of sympathetic function, which is predominant in secretory phase. Our values of VLF power, VLF power%, LF power, LF power%, LFnu and HFnu are in agreement with Bai et al., and Vishrutha et al., [9,15]. Values of HF power and HF power % in the present study are in agreement with Mckinley et al., and Vishrutha et al., [9,13]. Values of LF /HF ratio in the present study are in agreement with Kavitha et al., [11] and Rani et al., [17]. This shows increased vagal activity (lower LF nu and LF/HF ratio, greater HF nu) during the proliferative phase as compared with other phases of the menstrual cycle [18] and that the secretory phase of the menstrual cycle was associated with an increase in LF component and a decrease in the HF component. This suggests sympathetic activity predominance in the secretory phase during the menstrual cycle [19]. Results of varoius studies are shown in tabulated form [Table/Fig-7].

Authors	Changes in parameters in secretory phase in comparison to other two phases
Kavitha et al., [11]	Mean RR↑, MeanHR↑, LF /HF ratio↑
Christina et al., [12]	Mean RR↑, MeanHR↑
Mckinley et al., [13]	RMSSD↓, pNN50↓, HF power↓ and HF power % ↓
Vishrutha et al., [9]	NN50↓, VLF power↑, VLF power % ↑, LF power↑, LF power% ↑, LFnu↑ and HFnu↓, HF power↓ and HF power %↓
Vallejo et al., [16]	pNN50 ↑
Bai et al., [15]	VLF power↑, VLF power %↑, LF power↑, LF power% ↑, LFnu↑ and HFnu ↓
Rani et al., [17]	LF /HF ratio↑

[Table/Fig-7]: Changes in the parameters of HRV in secretory phase in comparison to other two phases, as observed in other studies

Some studies demonstrated that similar to pregnancy, menstrual cycle is also associated with characteristic changes in the cardiovascular system. So, it may also help physicians to take appropriate measures for prevention of complications related to cardiovascular system in postmenopausal women.

LIMITATIONS

The limitation to our study is a relatively smaller sample size.

CONCLUSION

Thus, our study concluded that the differences in HRV parameters can be due to parasympathetic predominance during proliferative phase and sympathetic activity in the secretory phase. A difference of the balance of ovarian hormones may be responsible for these changes of autonomic functions during the menstrual cycle.

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