EFFECT OF VARIOUS PHASES OF MENSTRUAL CYCLE ON THE TIME DOMAIN INDICES OF HRV

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ABSTRACT : Introduction and Objectives: The menstrual cycle, characterized by sex hormone fluctuations, is a basic physiological factor that continuously affects body function in premenopausal women. The extent to whichHeart rate variability (HRV) is influenced by the menstrual cycle has been a subject of interest.HRV is a reliable tool for assessing the activities of autonomic nervous system. Significantly greater heart rate variability during the different phases of menstrual cycle has been reported in literature but there is variation in the sympathetic and parasympathetic influence on myocardium in the follicular phase and the luteal phase in different studies. The present study was undertaken to determine the time domainindices of HRV across the three phases of menstrual cycle in healthy young women. Material and Methods : The present study was a cross sectional type of study involving 50 female subjects. HRV was done using Medicaid Physiopac during each of the three phases of the menstrual cycle. Kubois software version 2.1 was used for HRV analysis. Statistical analysis was done using Anova and Paired T tests. Results : Time domain indiceswere higher during follicular phase and least during luetal phase as compared to other two phases of menstrual cycle and also the difference was statistically significant. Conclusion : Our findings indicate a higher sympathetic activity in luteal phase as compared to other two phases. Parasympathetic activity on the other hand was higher during follicular phase.

Abbreviations : HRV – Heart Rate Variability

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INTRODUCTION

Endogenous sex hormone levels continuously change during the menstrual cycle. While estrogen starts to increase halfway through the follicular phase to reach a peak just before ovulation, both estrogen and progesterone are elevated during the midluteal phase. Different hormonal environments during the follicular and luteal phases may have implications for cardiac autonomic function.[1]Certain autonomic changes have also been reported during these phases, though more so during the pre-menstrual phase. It is likely that an exaggerated response to hormonal changes may be responsible for variable physical and psychological symptoms.[2]

Heart rate variability (HRV) is a non-invasive tool for the assessment of cardiac autonomic control.[3] Power spectrum analysis of HRV can quantify the sympathovagal balance modulating the sinus node pacemaker.[4]Heart rate variability is generally assessed based on time-domain or frequency-domain analysis. Indices of time-domain analysis derive from either direct RR interval measurements or the differences between successive RR intervals.[5,6]Parameters of time-domain analysis include : RR – time interval between two successive heart beats, RMSSD - the square root of the mean squared differences of the successive NN intervals, NN50 - Number of intervals greater than 50 ms, pNN50 - Proportion of differences in consecutive NN interval, TINN - Triangular interpolation of RR intervals, all reflecting parasympathetic activity.

The aim of our study is to find the association of time domain indices of HRV with different phases of menstrual cycle in healthy young women. This study will help us to understand theinfluence of hormonal fluctuationsduring menstrual cycle on the cardiac autonomic activity. It may also help to take appropriate measures for the prevention of cardiac complications postmenopausal women.

MATERIALS AND METHODS

Thepresent study was a cross sectional type of study. The study was conducted at Grant Government Medical College, Mumbai in the Department of Physiology over a period of 6 months. 50 healthy female volunteers in the age group of 18 to 25 yrs and having regular menstrual cycle of 28 to 35 days for the past six months were selected as subjects. Subjects with history of menstrual disorders, smoking, alcoholism, diabetes or any other endocrinological disorder were excluded from the study. Pregnant females or those on oral contraceptive pills, hormonal replacement therapy, drugs that alter the cardiovascular functions and those who were athletes or involved in excessive physical activity were also excluded from the study.

Written informed consent was taken from all the enrolled subjects after explaining to them the details of the study.The detailed menstrual history with respect to the nature and days of menstrual flow, regularity and total duration of cycle was taken in each subject. Subjects were asked to avoid caffeinated beverages for at least 12 hours prior to the study and to avoid strenuous physical activity from the previous evening.The ECG recording was carried out at 10.00 a.m. in the morning. The recordings of ECG of all the subjects were done by the same person in order to avoid any inter-observer error. The subject was allowed to relax on a bed in supine position for 10 minutes and then ECG recording was done for 5 minutes in supine position using “Physiopac” by “Medicaid”. Data collected on Physiopac was analysed by Kubois software, Version 2.1.

ECG was recorded during following three phases:

1.Menstrual phase – 1st or 2nd day of menstrual cycle (Group I : n=50)

2.Follicular phase – 9th to 12th day of menstrual cycle (Group II : n=50)

3. Luteal phase – 19th to 21st day of menstrual cycle (Group III : n=50)

Data recorded was segregated into three groups according to the three phases of menstrual cycle and was analysed with one way ANOVA. Each of the groups was compared with the other two and analysed by paired ‘t’ test. P value <0.05 was considered to be statistically significant for both the tests.

RESULTS

The mean age of the subjects was 18.433 ± 0.626 years. The mean height and weight of the subjects were 153.066 ± 10.044 cm and 48.766 ± 7.214 kg respectively. The mean calculated BMI of the subjects was 21.189 ± 3.621 kg/m2.

Table 1 : HRV analysis using Kubois software, version 2.1 (mean ± S.D.)

Parameters	MP	FP	LP
Mean RR	795±89.2	818.1±59	684.64±50
RMSSD	24.974±1	31.55±15	15.494±6
NN50	2.92±2.7	3.26±2.1	1.92±2.3
pNN50	7.348±7	9.218±5	3.24±3
TINN	118.42±33	129±42	82.5±24

HR = Heart Rate, MP = menstrual phase

FP = Follicular phase, SP = secretory phase

Table 2 : Analysis of all three groups using one way ANOVA test

Parameters	F value	P value	Result
Mean RR	53.89	<0.00001	Statistically significant
RMSSD	23.36	<0.00001	
NN50	4.1	<0.01	
pNN50	14.1	<0.00001	
TINN	24.77	<0.00001	

P value <0.05 is statistically significant.

Table 3 : Analysis of groups in pairs using paired ‘t’test (P value)

Parameters	MP& FP	PP& LP	MP & LP
Mean RR	0.0627	<0.0001	<0.0001
RMSSD	0.0139	<0.0001	<0.0001
NN50	0.4646	0.0046	0.073
pNN50	0.1642	<0.0001	0.0013
TINN	0.1797	<0.0001	<0.0001

P value <0.05 is statistically significant.

DISCUSSION

Present study shows that the time domain indices i.e. Mean RR, RMSSD, NN50, pNN50 and TINN were higher during follicular phase as compared to other two phases of menstrual cycle and least during luetal phase as compared to other two phases of menstrual cycle (Table 1) and the difference was statistically significant (Table 2 & 3). This suggests highest sympathetic activity in the luteal phase as compared toother two phases of menstrual cycleand increased parasympathetic activity in the follicular phase as compared toother two phases of menstrual cycle.

Our study is in accordance with the study done by Brar T K et al who showed thattime domain indices were higher during proliferative phase and least during secretory phase as compared to other two phase of menstrual cycle 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.[7]

It is also in accordance with the study done by McKinley PS et al who showed that during follicular phase monitoring, women had significantly lower average HR (−2.33 bpm), and higher SDRR, rMSSD, high frequency (0.04–0.15 Hz) and low frequency (0.15–.40 Hz) RRV than during the luteal phase.[8]

The alteration in the balance of ovarian hormones might be responsible for these changes in the cardiac autonomic innervation.The higher sympathetic activity may be due to higher levels of progesterone in the luteal phase as was shown in the study done by Leicht et al.[9]Similarly higher parasympathetic activity during follicualr phase may be attributed to higher levels of oestrogen during follicular phase as shown by Leicht et al and by Weissman A et al.[9,10]

Thus our findings supports many previous studies showing cardioprotective effects of oestrogen such as study done by Chao HT et al[11] and Sudhir K et al.[12] According Chao HT et al, Short-term transdermal estrogen for 3 weeks could improve cardiac autonomic nervous modulation and climacteric symptoms, and might have some cardioprotective effect in postmenopausal women.[11]Also Sudhir K et al showed that estrogen supplementation in perimenopausal women selectively attenuates vasoconstrictor responses to norepinephrine and reduces total body norepinephrine spillover, which is an index of sympathetic neural activity.[12]

On the other hand Princi et al suggested increased parasympathetic activity and decreased sympathetic activity in the luteal phase compared with the follicular phase.[13]SimilarlyKondo M showed that changes in the Coefficient of variation of R-R interval during the menstrual cycle are negligible. The results of these tests did not vary significantly during the menstrual cycle.[14]

CONCLUSION

Thus present study concluded that time domain indices of HRV varies with the different phases of the menstrual cycle. It may be due to parasympathetic predominance during follicular phase and sympathetic predominance during luteal phase. This could be due to endogenous sex hormone fluctuations modulating autonomic activity.

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Conflict of Interest: None