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ORIGINAL RESEARCH

A study to compare and evaluate variation in electrocardiogram, heart rate variability and hypertension during different phases of menstrual cycle to determine the effect of ovarian hormones on cardiovascular function.

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ABSTRACT

Purpose: During menstrual cycle the fluctuating level of endogenous sex hormones have an impact on cardiac autonomic function and may also affect blood volume along with electrocardiographic pattern. The main purpose of the study was to compare and evaluate variation in electrocardiogram, heart rate variability and hypertension during different phases of menstrual cycle to determine the effect of ovarian hormones on cardiovascular function.

Methods: This was a cross sectional prospective study conducted in 145 healthy female student who had regular menstrual cycle of 30 ± 3 days and aged between 18 to 24 years after taking informed consent and institutional ethical clearance. In different phases of menstrual cycle [Menstrual Phase (day 1-5), Follicular Phase (day 5–14) and Luteal phase(day 15-28)] blood pressure, lead II electrocardiogram recordings were captured and by using PHYSIOPAC after connecting the limb leads of ECG in supine resting position with eyes closed HRV was assessed for 15min.

Results: On electro gram parameters a significant QT interval and RR interval were observed. Longer QT interval during follicular Phase and shorter QT interval during Luteal phase were recoded where as shorter RR interval observed during Menstrual Phase which were longer during luteal phase. During the three phases no significant variation in both systolic and diastolic blood pressure were noticed. An increase resting heart rate were noted during menstrual phase which was lower during luteal phase. A non-significant increase in LF nudomain and LF/HF ratio were noted during the luteal phase as compared to other phases. Compared to luteal phase, during the follicular Phase, in LF nudomain and LF/HF ratio a non-significant increase were observed.

Conclusion: In healthy young women with regular menstrual cycle sympathovagal balance were greatly influenced by endogenous sex hormones. Cardiacautonomic dysfunction and be resulted due to any type of hormonal imbalance which effect sympathovagal balance. The study also concluded even within range of fluctuations, ventricular action potentials were were greatly influenced by estrogen as QT and Q Tc intervals shows changed in healthy young adults.

Keywords: Electrocardiogram, blood Pressure, heart rate variability, menstrual phase, sympathovagal Balance.

INTRODUCTION

During the reproductive life of a female repetitive occurring phenomenon is menstrual cycle which includes patterned sequenceal changes in hormonal, functional and structural

changes[1]. It is not just a reproductury process but also involves in good health well being of an women. During menstrual cycle changes occur in the level of progesterone, oestrogen, LH and FSH is also having an effect insignificant clinical changes in cardiovascular system a part of vaginal and endometrial environment along with oocyte maturation[2].

Among reproductive women, throughout them ensuration cycle there is a cyclic variation of sex hormones occurs which causes physiological alteration in various system including effect in cardiovascular activity and also having reflection on electrocardiogram [3]. As women are more likely to developed cardiovascular disease as compare to men[4], during ovulation and menstruation this could be even higher[5]. Thus in women there were more chance for the occurrence of ventricular arrhythmias and with them enstrual cycle its incidence exhibits cyclical variation[6].

During menstrual cycle several research articles demonstrated its effects on heart and respiration and few studies also light into the effects on variation of symphatho-vagal activities[7-9]. Thus in healthy Indian females, to improve the quality of life, a better understanding of the cardio-vagal activity in very much needed. The main purpose of the study was to compare and evaluate variation in electrocardiogram, heart rate variability and hypertension during different phases of menstrual cycle to determine the effect of ovarian hormones on cardiovascular function.

METHODS

This was a cross sectional prospective study conducted in 145 healthy female student who had regular menstrual cycle of 30±3days and aged between 18 to 24years. The Experiment work was initiated after obtaining approval of the study protocol from the Institutional Ethics Committee and written informed from the subjects were taken at the begin this study. Subjects who were having pre existing cardiovascular disease, respiratory disease, any previous or current habits of alcoholism or smoking, any history of dysmenorrhoea or irregular menstrual cycle were excluded from the study as per preapproved study protocol.

In different phases of menstrual cycle [Menstrual Phase (day 1-5), Follicular Phase (day5–14) and Luteal phase (day 15-28)] blood pressure, lead II electrocardiogram recordings were captured and by using PHYSIOPAC after connecting the limb leads of ECG in supineresting position with eyes closed HRV was assessed for 15 min. At 1mV standardization with a paper speed of 25mm/sec with the help of Lead-II machine (BPL CARDIART 108T-DIGI) ECG was recorded.

By using SPSS Version 23, the collected data were analyzed and were represented asmean ± standard deviation. One way ANOVA were used to to test the difference among study parameters. For statistical significance post-hoc tests were performed. Statistical significance was set at $p<0.05$.

RESULTS

A total of 145 patients were initially enrolled for the study with mean age of 19.86±1.12years and mean weight of 54.71±7.54Kg. The BMI, WHR(WC/HC), SBP, DBP and PR Were 20.51±1.87Kg/m^2, 0.81±0.02, 112.49±3.73 mmHg, 4.96±4.16mmHg and 75.14±3.21per min. The average mean Duration of menstrual cycle were 28.69±1.45days. Demographic parameters of the study population were listed in table1.

Table1: Demographic parameters of the study population

Parameter	N=145
Age(years)	19.86±1.12
Weight(kg)	54.71±7.54
BMI(Kg/m^2)	20.51±1.87
WHR(WC/HC)	0.81±0.02

Resting SBP(mmHg)	112.49±3.73
Resting DBP(mmHg)	74.96±4.16
Resting Pulse Rate(min.)	75.14±3.21
Duration of menstrual cycle	28.69±1.45

On electro gram parameters a significant QT interval and RR interval were observed. Longer QT interval during follicular Phase and shorter QT interval during Luteal phase were recoded (p=0.001) where as shorter RR interval observed during Menstrual Phase which were longer during luteal phase (p=0.001). On electrocardiogram, during different phases of menstrual cycle, QRS complex amplitude, QRS complex duration, P-wave amplitude, T-wave amplitude, ST interval and PR interval, did not show any statistically significant change.

Table2: Comparison of ECG Parameters in Three different Phases (in females)

Variables	Menstrual Phase (I) (day1-5)	Follicular Phase (II) (day5–14)	Luteal phase (III) (day15-28)	P-value		
				I vs II	I vs III	II vs III
P-waveamplitude(mv)	0.21±.03	0.22±.04	0.22±.04	0.895	0.397	0.721
QRS-complexamplitude(mv)	0.87±0.21	0.92±0.23	0.99±.25	0.841	0.317	0.596
QRS-complexduration(sec.)	0.08±0.01	0.9±.02	0.10±.01	0.323	0.296	0.892
T-waveamplitude(mv)	0.23±.06	0.21±.05	0.20±.04	0.118	0.021	0.818
PR-Interval(sec.)	0.13±0.02	0.15±0.04	0.14±0.04	0.058	0.824	0.011
ST-Interval(sec.)	0.27±0.03	0.27±0.01	0.27±0.03	0.893	0.947	0.903
QT-Interval(sec.)	0.34±0.05	0.45±0.2	0.34±0.05	0.001	0.893	0.001
RR-Interval(sec.)	0.72±0.07	0.77±0.08	0.80±0.12	0.084	0.001	0.044
R(beats/min.)	86±9.21	82±9.67	77±9.94	0.152	0.000	0.011

Blood Pressure Comparison in Three different Phases in Female were listed in table 3.Systolic blood pressure (SBP) recorded in menstrual, follicular and luteal phase were documented as 108±8.42mmHg, 108±8.41mmHg and110±6.32mmHg respectively. Diastolic blood pressure (DBP) recorded in menstrual, follicular and luteal phase were documented as 69±8.87 mmHg, 69±9.41 mmHg and 72±7.66 mmHg. During the three phases no statistical significant variation in both systolic and diastolic blood pressure were noticed.

Table3: Blood Pressure Comparison in Three different Phases in Female.

Variable	Menstrual Phase (I) (day1-5)	Follicular Phase (II) (day5– 14)	Luteal phase (III) (day15-28)	P-value		
				I vs II	I vs III	II vs III
SBP (mmHg)	108±8.42	108±8.41	110±6.32	0.997	0.287	0.324
DBP (mmHg)	69±8.87	69±9.41	72±7.66	0.981	0.274	0.365

SBP=Systolic blood pressure, DBP=Diastolic blood pressure

Frequency domain HRV parameters LF nu domain, HF nu domain, and LF/HF ratio of the study population in different phases of menstrual cycle were listed in table 4. A non-significant increase in LF nudomain and LF/HF ratio were noted during the luteal phase as compared to other phases. Compared to luteal phase, during the follicular Phase, in LF nudomain and LF/HF ratio a non-significant increase were observed.

Table 4: Frequency domain HRV parameters LF nu domain, HF nu domain, and LF/HF ratio of the study population in different phases of menstrual cycle

	Menstrual	Follicular	Luteal	P-value		
Domain	**Phase (I)(day1-5)**	**Phase(II) (day5–14)**	**phase (III)(day15-28)**	**I vs II**	**I vs III**	**II vs III**
LFnu	85.19±1.64	85.22±1.71	85.74±1.68	0.987	0.271	0.254
HF nu	14.68±1.94	14.71±1.91	14.18±1.98	0.992	0.326	0.282
LF/HF	5.61±0.78	5.89±0.92	6.31±0.28	0.897	0.452	0.311

HRV: Heart rate variability, HF: High frequency, LF: Low frequency, nu: normalized units

DISCUSSION

In menstrual phase physiological variations were observed in endogenous hormones, thus in women's health an important role were played by these hormones. In some cases this hormonal variation is also took place due to use of exogenous hormones like hormone replacement therapy and oral contraceptives [10]. Different phases of the menstrual cycle also influenced by different factors such as muscle strength, anaerobic power, sports performance, flexibility, risk of injury and cardiovascular mechanisms [11]. In the present study author had examine variation in electrocardiogram, heart rate variability and hypertension during different phases of menstrual cycle to determine the effect of ovarian hormones on cardiovascular function.

Complex interactions essentially involving the uterus and the hypothalamo-hypophyseal ovarian axis were resulted in physiological changes occurs in during the course various stages of menstrual cycle[12]. This physiological changes all most in all are dependent and related to sensitive regulatory mechanisms and directly related to fluctuation in the hormone levels. In our present study longer QT interval during follicular Phase and shorter QT interval during Luteal phase were recoded where as shorter RR interval observed during Menstrual Phase which were longer during luteal phase. In line of the current findings, few older studies also reported shorter mean duration of QT interval compared to the other two phases [13,14]. In current study effect of estrogen on ventricular action potentials were demonstrated as the author noted prolonged QT interval in the phase-II (follicular phase). The same results also documented in few previous study where healthy young adults where within the range of fluctuations effects seen physiologically [15]. Even few researcher documented that may be due to increase in sodium levels in the serum effects on electrolytes balance which resulted as prolongation of QT interval and mainly because of reverse effects of estrogen[16].

Duringthethreephasesnosignificantvariationinbothsystolicanddiastolicbloodpressurewerenoticed.Similarfindingswerealsonotedinapreviousstudywheresympathetic activity in secretory phase were influenced by the fluctuation of sex hormone[17].

In current study, a non-significant increase in LF nu domain and LF/ HF ratio were noted during the luteal phase as compared to other phases. Compared to luteal phase, during the follicular Phase, in LF nu domain and LF/ HF ratio a non-significant increase were observed. Cardio-vagal activity of estrogen directly inhibit effect of progesterone for which in the luteal phase increased sympathetic activity [18-20]. An increased sympathetic and parasympathetic activity was also demonstrated in few older study likewise the current documentation[21-23].

LIMITATIONS

There were few limitation of the study. Sample size and menstrual cycle hormone estimation was the major one.

CONCLUSION

In healthy young women with regular menstrual cycle sympathovagal balance were greatly influenced by endogenous sex hormones. Cardiac autonomic dysfunction and be resulted due to any type of hormonal imbalance which effect sympathovagal balance. The study also concluded even within range of fluctuations, ventricular action potentials were were greatly influenced by estrogen as QT and QTc intervals shows changed in healthy young adults.

REFERENCES

1. Kim.Barret, Susan.Barman, Scott.Boitano, Heddwen. Brooks. Ganong's Review of Medical Physiology, Edn 26,TataMcGraw-Hill publishers; 2019;392.
2. Harlow SD, Campbell OM. Epidemiology of menstrual disorders in developing countries: a systematic review. BJOG. 2004 Jan;111(1):6-16. doi: 10.1111/j.1471-0528.2004.00012.x.PMID:14687045.
3. Thiyagarajan DK, Basit H, Jeanmonod R. Physiology, Menstrual Cycle. [Updated 2021Oct 30]. In:StatPearls[Internet]. Treasure Island(FL): Stat Pearls Publishing; 2022Jan-. Available from:https://www.ncbi.nlm.nih.gov/books/NBK500020/
4. Mosca L, Barrett-ConnorE, WengerNK. Sex/gender differences in cardiovascular disease prevention: what a difference a decade makes. Circulation. 2011 Nov8; 124(19):2145-54.doi:10.1161/ CIRCULATIONAHA. 110.968792. PMID:22064958; PMCID: PMC3362050.
5. RodriguezI, KilbornMJ, LiuXK, PezzulloJC, WoosleyRL. Drug-induced QT prolongation in women during the menstrual cycle. JAMA.2001Mar14;285(10):1322-6.doi:10.1001/jama.285.10.1322.PMID:11255387.
6. RosanoGM, LeonardoF, SarrelPM, BealeCM, DeLucaF, CollinsP. Cyclical variation in paroxysmal supraventricular tachycardia in women. Lancet. 1996 Mar 23;347(9004):786-8.doi:10.1016/s0140-6736(96)90867-3.PMID:8622333.
7. Stoney CM, Owens JF, Matthews KA, Davis MC, Caggiula A. Influences of the normal menstrual cycle on physiologic functioning during behavioral stress. Psychophysiology. 1990Mar;27(2):125-35.doi:10.1111/j.1469-8986.1990.tb00364.x.PMID:2247544.
8. Weidner G, Helmig L. Cardiovascular stress reactivity and mood during the menstrual cycle. Women Health.1990;16(3-4):5-21.doi:10.1300/J013v16n03_02.PMID:2267809.
9. MehtaV, ChakrabartyAS. Autonomic functions during different phases of menstrual cycle. Indian J Physiol Pharmacol. 1993Jan;37(1):56-8.PMID:8449546.
10. GreerJP, FoersterJ, LukensJN(Eds.). Wintrobe's Clinical Hematology, 11thedn. Philadelphia, PA: Lippincott Williams & Wilkins, 2003. NLMID:101610272.
11. Brar TK, Singh KD, Kumar A. Effect of Different Phases of Menstrual Cycle on Heart Rate Variability (HRV). J Clin Diagn Res. 2015 Oct;9(10):CC01-4. doi: 10.7860/ JCDR/2015/13795.6592. Epub2015Oct1.PMID:26557512; PMCID:PMC4625231.
12. Holesh JE, Bass AN, Lord M. Physiology, Ovulation. [Updated 2021 May 9]. In: Stat Pearls[Internet]. Treasure Island(FL): Stat Pearls Publishing;2022Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441996
13. HulotJS, DémolisJL, RivièreR, StrabachS, Christin-MaitreS, Funck-BrentanoC. Influence of endogenous oestrogens on QT interval duration. EurHeartJ.2003Sep;24(18):1663-7.doi:10.1016/s0195-668x(03)00436-6.PMID:14499229.
14. PostemaPG, WildeAA. The measurement of the QT interval. Curr Cardiol Rev.

2014Aug;10(3):287-94. doi:10.2174/ 1573403x10666140514103612. PMID:24827793; PMCID:PMC4040880.

15. Balayssac-Siransy E, Ouattara S, Adoubi A, Kouamé C, Hauhouot-Attoungbré ML,Dah C, Bogui P. Influence of high ovarian hormones on QT interval duration in young African women. PhysiolRep.2014Mar20;2(3):e00263. doi:10.1002/ phy2.263. PMID:24760517; PMCID:PMC4002243.
16. SatoN, MiyakeS, AkatsuJ, KumashiroM. Power spectral analysis of heart rate variability in healthy young women during the normal menstrual cycle. PsychosomMed.1995Jul-Aug;57(4):331-5.doi:10.1097/00006842-199507000-00004.PMID:7480562.
17. Tsai PS, Yucha CB, Sheffield D, Yang M. Effects of daily activities on ambulatory blood pressure during menstrual cycle in normotensive women. Appl Psychophysiol Biofeedback. 2003Mar;28(1):25-36.doi:10.1023/a:1022364832488.PMID:12737094.
18. CarrMC. The emergence of the metabolic syndrome with men opause. J Clin Endocrinol Metab. 2003Jun; 88(6):2404-11. doi:10.1210/jc.2003-030242.PMID:12788835.
19. YazarŞ, Yazıcı M. Impact of Menstrual Cycle on Cardiac Autonomic Function Assessed by Heart Rate Variability and Heart Rate Recovery. Med Princ Pract.2016;25(4):374-7. doi: 10.1159/000444322. Epub 2016 Feb 1. PMID: 26828607; PMCID:PMC5588411.
20. Tanaka M, Sato M, Umehara S, Nishikawa T. Influence of menstrual cycle onbaroreflex control of heart rate: comparison with male volunteers. Am J Physiol Regul Integr Comp Physiol. 2003 Nov;285(5):R1091-7. doi: 10.1152/ajpregu. 00162.2003. Epub2003Jul24. PMID:12881201.
21. BaiX, LiJ, ZhouL, LiX. Influence of the menstrual cycle on non linear properties of heart rate variability in young women. Am J Physiol Heart Circ Physiol. 2009 Aug; 297(2):H765-74. doi: 10.1152/ajpheart.01283.2008. Epub 2009 May22. PMID:19465541.
22. KayaH, SünerA, KöroğluS, AkçayA, TürkbeylerİH, KöleoğluM. Heart rate variability in familial Mediterranean fever patients. EurJ Rheumatol. 2014Jun;1(2):58-61. doi:10.5152/eurjrheumatol.2014.013.Epub2014Jun1.PMID:27708876;PMCID:PMC5042279.
23. Leicht AS, Hirning DA, Allen GD. Heart rate variability and endogenous sex hormonesduring the menstrual cycle in young women. Exp Physiol. 2003 May;88(3):441-6. doi:10.1113/eph8802535.PMID:12719769.