ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Association between the different phases of menstrual cycle and time domain analysis of Heart Rate Variability in young adult and older adult in Indian Women's.

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ABSTRACT

The menstrual cycle is associated with corresponding significant changes in multiple neurohumoral homeostatic mechanisms regulating the cardiovascular system. Heart rate variability [HRV] has proved to be a more sensitive tool for the detection of autonomic balance than mean heart rate [HR]. HRV refers to the beat-to-beat alterations in heart rate. Hence, the present study was undertaken to assess the HRV in different phases of menstrual cycle in young adult and older adult women's. The present study was conducted after the institutional ethical clearance. About 90 subjects were recruited and are divided into 2 groups as young adult and older adult subjects. The influence of menstrual cycle on the HRV was investigated in 3different phases and compared between young adults and older adult women. The HRV evaluation was done in the time domain in accordance to the task force. Analysis of HRV in the time domain was done using the software Version1.1, AIIMS, New-Delhi. The data obtained was analyzed using student's't' test followed by Mann Whitney-U test and $P< 0.05$ was considered the level of significance. The mean value of SDANN in Group-1 showed non significantly higher values in the follicular phase whereas, when the SDANN values among the phases of menstrual cycle in the Group-2, there was no significant difference, but the values were high for luteal phase. Time domain analysis of these two groups in Luteal phase showed that SDANN of Group-2 was significantly higher [$p<0.05$] than Group-1 during normal breathing. This study concludes a slow and steady decline in autonomic modulation with age, which may have a close interaction with hormonal activity.

Keywords: HRV, SDANN, Menstrual phase, Follicular phase, Luteal phase

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ISSN: 0975-8585

INTRODUCTION

The cyclical changes that occur in female reproductive system are commonly termed as menstrual cycle. Menstruation is only one manifestation of the ovarian cycle which is itself associated with more than 200 physical, psychological and behavioral changes [1]. The menstrual cycle is an integral part of a major portion of a woman s life. The reproductive system of a female, unlike that of a male, shows regular cyclic changes that teleologically may be regarded as periodic preparation for fertilization and pregnancy [2]. Ovarian hormones alterations along the menstrual cycle are associated with corresponding significant changes in multiple neurohumoral homeostatic mechanisms regulating the cardiovascular system [3].

The heart is an organ under the influence of the autonomic nervous system for the maintenance of homeostasis, and, in this respect, one of its main characteristics is the constant modification of its rate on beat-to-beat basis [4]. Heart rate variability [HRV] has proved to be a more sensitive tool for the detection of autonomic balance than mean heart rate [HR]. HRV refers to the beat-to-beat alterations in heart rate. HRV is the natural rise and fall of heart rate in response to breathing, blood pressure, hormones and emotions [5]. It is seen as reflective and predictive of general health and overall physiological wellness. HRV is one of the promising markers of autonomic activity. It was demonstrated that the heart rate fluctuated with considerable irregularity in normal healthy individual whereas patients with cardiovascular diseases who were expected to have impaired regulatory systems had reduced and less irregular variability; and also beat to beat observation of heart rate or heart beat intervals have shown variability between beats even at the physiological steady state.

Goldberger speculated that HRV in normal healthy individuals was intrinsic to cardiovascular regulatory systems HRV represents one of the most promising such markers [6]. The clinical relevance of HRV was first appreciated in 1965 when Hon and Lee noted that foetal distress was preceded by alterations in inter beat intervals before any appreciable change occurred in heart rate itself. In 1981, Akselorod et al introduced power spectral analysis of heart rate fluctuations to quantitatively evaluate beat-to-beat cardiovascular control [7]. Variations in the heart rate are dependent on the activities of the Sino-atrial node, the natural pacemaker of the heart by the sympathetic and parasympathetic branches of the autonomic nervous system. The degree of balance between sympathetic and vagal nerve activity determine HRV.

Lee.P.Y.et.al hypothesized that normal variations in autonomic balance during menstrual cycle, which likely evolved as adaptation for reproduction, many contribute to catamanial variations in diseases independent of hormonal variations [8]. These autonomic modulations also affect the cardiac activity and can be best evaluated by heart rate variability. The human heart beat in a healthy individual is neither absolutely regular nor completely random. It varies as interplay between many factors including physical and mental stress, exercise, respiration, thermoregulation, blood pressure regulation, actions of rennin angiotensin system, circadian rhythm and other unknown complex mechanisms [9]. This subtle fluctuation in sinus rhythm is known as heart rate variability. Heart rate variability provides an

insight to comprehend autonomic modulation of the heart [10]. Since possible significance of fluctuations in heart rate was realized, heart rate variability has become a popular method for the studies of physiological mechanisms responsible for the control of heart rate fluctuations, autonomic neuropathy, heart transplantation, congestive heart failure, myocardial infarction and the other cardiac and non cardiac diseases [11]. HRV being a non invasive technique is now being adopted to evaluate various cardiac diseases. In order to rule out the natural variations if any in HRV due to menstrual effect in assessing various cardiac diseases by using HRV measurement.

The variations in heart rate may be evaluated by a number of methods. Perhaps the simplest to perform are the time domain measures. In these methods, either the heart rate at any point in time or the intervals between successive normal complexes are determined. In a continuous ECG record, each QRS complex is detected, and the so-called normal-to-normal [NN] intervals [that is, all intervals between adjacent QRS complexes resulting from sinus node depolarization] or the instantaneous heart rate is determined. Simple time domain variables that can be calculated include the mean NN interval, the mean heart rate, the difference between the longest and shortest NN interval, the difference between night and day heart rate, and so forth. Other time domain measurements that can be used are variations in instantaneous heart rate secondary to respiration, tilt, Valsalva maneuver, or phenylephrine infusion. These differences can be described as either differences in heart rate or cycle length.
Studies by various researchers have demonstrated that like in pregnancy, menstrual cycle is also associated with characteristic changes in cardiovascular system. But, the association of heart rate variability with different phases of menstrual cycle was less documented. Therefore the present study was undertaken to assess the HRV in different phases of menstrual cycle in young adult and older adult women's.

MATERIALS AND METHODS

The present work was carried out at Kasturba Medical College, Bejai, Mangalore after getting the institutional ethical clearance. 45 female students studying their MBBS course, who are below 25 years of age and 45 women above the age of 25 years were recruited for the study after an informed consent.

A detailed clinical history of these subjects was taken. Relevant past history, family history, any drug history, personal history like smoking, alcoholism occupational history etc, were also taken. General physical examination, vital signs, complete systemic examination was done.

The influence of menstrual cycle on the HRV was investigated in 3different phases and compared between young adults and older adult women. The HRV evaluation was done in the time domain in accordance to the task force [12].

A high quality ECG recording was taken under standardized condition to minimize artifacts. The ECG signal is first analogally recorded & then digitally converted. Analysis of this in

the time domain was done using Version1.1, AIIMS, New-Delhi software. Recording was done in the morning between 10:00 to 11:00 AM in a cool room temperature of 20 to 28 degree Celsius after breakfast. They were requested to come in a relaxed condition & quiet mood. The room was darkened & without acoustic disturbance. They were instructed to be relaxed and to breathe spontaneously at their own rate the procedure was explained to the subject. After a resting period, the subjects ECG was recorded in the supine position during normal breathing for 5 min .

The recruited subjects were divided into 2 groups as,

Group 1: Subjects with age between 18-25 yrs [45 females] and
Group 2: Subjects with age between 25-45 yrs [45 females].

The recordings were taken in both groups during the 3 phases of menstrual cycle namely, Menstrual phase [M] – 1st to 5th day of bleeding, Follicular phase [F]-6th day to14th day of menstrual cycle, Luteal phase [L] - 15th day to 28th day or the next menstrual bleeding.

The data obtained was analyzed for statistical significance using student's't' test followed by Mann Whitney-U test. P< 0.05 was considered the level of significance. ctions initiate complex events within the endometrium

RESULTS

In this study 90 female subjects between age group of 18 to 45 yrs were participated. They were divided in to two groups as Group-1, with 45 subjects who were less than 25 years of age and The Group-2, with 45 subjects who were between 25-45 years of age. ECG of these people was taken in normal conditions. The HRV of these people under different conditions were compared with different parameters and results were as follows.

In time domain method, the HRV i.e., standard deviation of adjacent normal to normal beat [SDANN], in menstrual phase were compared among each phase of the menstrual cycle. Though the mean value of SDANN in Group-1 showed higher values in the follicular phase, the results did not show any significant differences [Table 1, Fig 1]. Similarly when the SDANN values were compared among the phases of menstrual cycle in the Group-2, there was no significant difference, but the values were high for Luteal phase [Table 2, Fig 2].

Table 1: SDANN in different phases of menstrual cycle in Group- 1 with n =45.

PHASES	MEAN	STD.DEVIATION
MENSTRUAL	16.13	9.14
FOLLICULAR	20.17	9.36
LUTEAL	16.54	7.35

ISSN: 0975-8585

Fig. 1: SDANN in different Phases of Menstrual cycle in Group-1 with n =45.

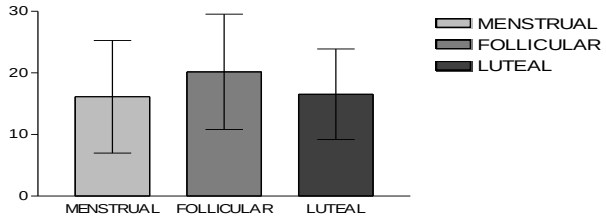
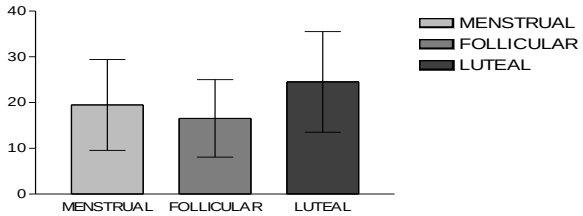


Table 2: SDANN in different phases of menstrual cycle in Group-2 with n =45.

PHASES	MEAN	STD.DEVIATION
MENSTRUAL	19.49	9.93
FOLLICULAR	16.54	8.47
LUTEAL	24.52*	11.01

Fig 2: SDANN in different phases of menstrual cycle in Group-2 with n =45.



In time domain method, the SDANN, in menstrual phase were compared among the two experimental groups viz; Group-1 & Group-2[Fig. 3]. The mean value of SDANN in Group-1was 16.13±9.14 and Group-2 was 19.49±9.93 in normal breathing. The Group-2 showed higher HRV than Group-1 which is not significant. In follicular phase when compared, the mean value of SDANN in Group-1 was 20.17±9.36 and Group-2 was 16.54±8.47 in normal breathing. The Group-1 showed higher HRV than Group-2 which is not significant. Time domain analysis of these two groups in Luteal phase showed that SDANN of Group-2 was significantly higher than Group-1 [$p<0.05$] with values 24.52±11.01 and 16.54±7.35 respectively during normal breathing.

DISCUSSION

In the female reproductive physiology, the maturation of the female gamete, the egg occurs in the ovary. Its release from the ovary- ovulation is cyclical. These cycles in humans is called menstrual cycle [13].

In terms of ovarian functions the menstrual cycle is divided into 2 phases namely the follicular phase and the luteal phase. This is followed by menstruation which is the most obvious event of a menstrual cycle. The hormonal interaction between the ovaries, hypothalamus and anterior pituitary gland produce the cyclical changes in the ovary.

The menstrual cycle is characterized by phases with the cyclical changes of female hormones. There is an increase in estrogens. They are mainly produced by the granulosa cells of the ovarian follicles, the corpus luteum and the placenta in pregnancy .There is also important hormone progesterone which is secreted in the secretary phase of the menstrual cycle by the corpus lustrum. Under the influence of progesterone and estrogen the endometrium increases secretary activity. The overall effects of estrogen and progesterone in Luteal phase was protective, adaptive and probably related to body preparation to a would be pregnancy [14].The general presence of functional sex steroid hormone receptors in the cardiovascular system is well established, their expression in both heart and blood vessels have been recognized for decades [15-18].

Gender differences in vascular regulation may result from differences in sex hormones. Estrogen stimulates the release of NO from the endothelium by increasing NO synthase activity. Estrogen is also associated with lower levels of endothelin and decreased sensitivity to the vasoconstrictive effects of peptide [19]. The presence of estrogen receptors in the heart, vascular smooth muscle and autonomic brain centres [20], suggest a possible involvement in the regulation of cardiovascular system. In the follicular phase, estrogen causes an up-regulation in the cardiovascular or myometrial adrenoreceptor [3].

The heart rate variability is a useful indicator to assess the modulating effect of ANS on CVS activity. This study was an attempt to evaluate the relative role of the components of ANS during different phases of menstrual cycle. In this study, the HRV didn't vary much in the time domain analysis in different phases of menstrual cycle in both the groups except for the Luteal phase whereas, Group-2 showed significantly high [$p<0.05$] value.

A high concentration of progesterone, estrogen and or other hormones may influence ANS during Luteal phase. In this study, it was seen that HRV was significant in the luteal phase when Group-1 and Group-2 were compared, than the other two phases. This shows hormonal fluctuation on the ANS is evident in the younger age group and, as the age advances it is stabilized. This result is in agreement with other findings [21, 22] which demonstrate that, the normal ageing is associated with a constant decline of cardio vagal modulation due to significant increase of parasympathetic activity which results in a decrease in HRV as the age advances in healthy adults. Thus this study concludes a slow and steady decline in autonomic modulation with age, which may have a close interaction with hormonal activity.

REFERENCES

[1] Hormonal changes during menstrual cycle. Wikipedia

[2] William F Ganong. Review of medical physiology. Lange medical publications 21 edition. 2003; 437.
[3] Nir Hirshoren et.al. The J Clin Endocrinol Metabol 2002; 87:4, 1569-1575
[4] Heart rate variability. Wikipedia.
[5] Anupama Bangra Kulur, Nagaraja Haleagrahara, Prabha Adhikary, Jeganathan P S. Arq Bras Cardiol. 92(6): 2009.
[6] Hughson Y, Yamamoto Y, Nakamura H, Sato M, Yamamoto. Ajpregu physiology.
[7] Akselrod S, Gordan D, Ubel FA, Shannon DC, Berger AC and Cohen R J. Science 213;4504: 220-222.
[8] Lee P Y, Bazar KA, Yun AJ. Med Hypotheses 2004; 63[1]:163-7.
[9] KatiraR, Narain VS, Puri VK. JAPI 1997; 45:49-51
[10] Stein PK, Kleiger RE. Ann Rev Med 1999; 50:249-461.
[11] Stys A, Stys T. Clin Cardiol 1998; 21:719-724.
[12] DiFrancesco D, Tromba C. J Physiol [Lond] 1988; 405:493-510.
[13] Vander's Human Physiology, In:Eric P, Widmaier, Hershel Raff, Kevin T Stang eds. N Y :Mc Graw Hill Pub Companies,2006:678.
[14] Tkachenko NM, Il'ina EM. Akush Ginekol [MOSK] Autonomic nervous system activity during the normal menstrual cycle 1994; [1]:35-8.
[15] Mendelsohn ME, Karas RH. Curr Opion Cardiol 1994; 9:619-626.
[16] Farhat MY, Lavigne MC, Ramwell PW. FASEB J 1996; 10:615-624.
[17] Mendelsohn ME, Karas RH. N Engl J Med 1999;340:1801-1811.
[18] Mendelsohn ME, Karas RH. Science 2005;308:1583-1587.
[19] Schwertz DW, Penckofer S. Heart Lung 2001;30:401-26.
[20] Virdis A, Ghiadoni L, Pinto S, Lombardo M, Petralgia F, Gennazzani A, Buralli S, Taddei S, Salvetti A. Circulation 2000; 101:2258-2263.
[21] Lipsitz LA, Goldberger. JAMA 1992; 267:1806-1809.
[22] Masaoka S, Lev-Ran A, Hill L R, Vakil G, Hon EH. Diabetes care 1985;8[1]64-68.