A STUDY OF PARASYMPATHETIC FUNCTION TEST DURING PRE AND POST MENSTRUAL PHASES OF MENSTRUAL CYCLE AMONG ADULT HEALTHY FEMALE

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Abstracts: **Background and objectives**: Menstrual cycle is the physiological phenomenon in adult healthy female in reproductive age. It is regulated by cyclical secretion of gonadal hormone mainly estrogen, progesterone, FSH, LH and GnRH during pre and postmenstrual period of menstrual cycle. This cyclical secretion of gonadal hormone not only causes changes in organs of reproductive system but also affect other systems of the body including Autonomic nervous system. Autonomic nervous system is the one of the important system that controls cardiovascular system along with other control mechanism. So if we observe changes in cardiac parasympathetic function test of female during pre and post menstrual phases of menstrual cycle, we can analyze effect of gonadal steroidal hormone on parasympathetic control of cardiovascular system. So we planned to study parasympathetic function test which is the part of cardiac autonomic function test during pre and post menstrual phases of menstrual cycle. **Aim:** Aim of this study was to determine whether fluctuation of reproductive hormone during premenstrual and post menstrual phases affecting cardiac parasympathetic function or not. **Objectives**: To do and compare parasympathetic function tests in pre and post menstrual phase. **Methods:** Study was carried out in 50 adult healthy female of 26-40 years age. Parasympathetic function tests were carried out by instrument Cardiac Autonomic Nervous System Analyzer (CANS) 504 in Department of Physiology, Government Medical Collage, Bhavnagar. Parasympathetic function tests were done using standard protocol and statistically analyzed. **Results**: Statistically significant difference was seen between premenstrual phase and postmenstrual phase in all parasympathetic function test parameters which includes HR variation to deep breathing, Immediate HR response from lying to standing or 30:15 ratio, Valsalva ratio except resting Heart Rate (HR). **Interpretation & conclusion**: According to this study parasympathetic dominance is seen in postmenstrual phase of menstrual cycle that may be due to increased level of estrogen during postmenstrual phase which increases baroreflex sensitivity, also having vasodilatory effect and increases Ach concentration.

Key Words: parasympathetic function test, menstrual cycle, premenstrual phase, postmenstrual phase.

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Introduction: The normal reproductive years of the female are characterized by monthly rhythmical changes in the rate of secretion of the female hormones and corresponding physical changes in the ovaries and other sexual organs. This rhythmical pattern is called the female sexual cycle or menstrual cycle.[1] Menstrual cycle mainly regulated by hypothalamus, pituitary and ovarian hormones by feedback loop that is called HPO axis. Female gonadal hormone estrogen and progesterone which have effect on reproductive organs also have effect mainly on ANS, CVS and CNS along with other body systems. Previous studies also suggested that after menopause female has more risk of cardiovascular morbidity and mortality than female in reproductive age that indicates cardioprotective role of oestrogen.[2]

The general presence of functional sex steroid hormone receptors in the cardiovascular system is well established and their expression in both heart and blood vessels have been recognized for decades.[3,4,5,6] The presence of estrogen receptors in the heart, vascular smooth muscle and autonomic brain centers suggest a possible involvement of estrogen in the regulation of cardiovascular system. Estrogen is also associated with lower levels of endothelin and decreased sensitivity to the vaso-constrictive effects of peptide. These suggested that

estrogen may have some role in controlling cardiovascular system via autonomic control. By analyzing parasympathetic function test which is the part of cardiac autonomic function test during pre and post menstrual phase of menstrual cycle, we can correlate effect of gonadal steroidal hormone with modulation of parasympathetic control of heart. So we plan to do and compare parasympathetic function test during pre and post menstrual phase of menstrual cycle.

Material and Methods: Prior permission was taken from Institutional Review Board (IRB) of Government Medical College, Bhavnagar. This study was carried out in Autonomic Function Lab in Department of Physiology, Government Medical College, Bhavnagar. The study group comprised of 50 young healthy female participants having regular menstrual cycles and age between 26-40years. They were selected after employing the following criteria.

A detailed clinical history with special attention to the menstrual history (length of cycle, amount of menstrual flow, and regularity of cycle) of each subject was taken. Relevant past history of any hormonal treatment, family history of diabetes, transplantation therapy and radiotherapy; personal history including smoking, alcoholism and occupation history was taken. A complete general physical examination as well as clinical examination was done. Height & weight of the subjects were recorded using standard methodologies. Subjects were instructed to visit the department during post menstrual phase (9-12th day) and premenstrual phase (19-22nd day) of menstrual cycle.

Selection criteria

Inclusion criteria:

1. Subjects should belong to the specified age range (26-40 years).
2. They should have regular menstrual cycles of 27 to 35 days as established by history, for at least the past 6 months.
3. Subject who gives written informed consent

Exclusion criteria:

1. Female subjects below 26years and above 40 years.
2. Subjects having irregular menstrual cycle.
3. Subjects taking any medication or hormonal preparations that could alter the menstrual hormonal milieu.
4. Subjects having any physical illness like diabetes, hypertension, TB, cardiac arrhythmia or any other endocrinological disorders.
5. Smokers, alcoholics or those with history of substance abuse.
6. Athletes and those involved in excessive physical activity.
7. Subjects having any disorder which can interfere with the autonomic responses

After they were informed about the procedures and objectives of the study, a written consent was taken as per standard protocol from all participants. All participants were advised to avoid eating and drinking (tea, coffee and alcohol) at least six hours prior to test as these may affect the results

Test preparation: After giving information about the procedure, each subject was advised to take rest for 15 minutes in a quiet room. After obtaining the clinical history and followed by physical examination; **Parasympathetic Function Test**s were carried out. The subjects were instructed to attend the study in a relaxed condition and in quiet mood. The room was darkened and without any acoustic disturbance.

List of Parasympathetic Function Tests **and Instrument to be used**

Parasympathetic function tests under the scope of this study had been carried out with CANS (Cardiac Autonomic Nervous System Analyzer) – 504.

Parasympathetic function test

1 Resting heart rate: Resting heart rate was observed over a period of one minute in all the patients by taking continuous ECG after a rest period of 15 minutes.

2. Heart rate variation during deep breathing: After taking resting heart rate, patients was instructed to take deep breaths at the rate of six breaths per minute with five seconds of inspiration and five seconds of expiration for one minute. During this process continuous ECG monitoring was done. Difference of HR during inspiration and expiration was calculated by ECG.

3**. Immediate heart rate response to standing or 30/15 ratio**

Patient was asked to stand up unaided and the starting point of standing is marked on the electrocardiogram. The shortest R-R interval was observed at or around 15th beat and longest R-R interval was observed at around 30th beat. So, 30/15 ratio was calculated by HR at 30th beat/HR at 15th beat

4. Heart- rate response to Valsalva manoeuvre or **Valsalva ratio:** To perform the Valsalva manoeuvre the subject was asked to sit and blow into the rubber tube of a mercury sphygmomanometer, raise the mercury column to 40 mm Hg and maintain that level for at least 30 seconds. Continuous ECG tracing was recorded during the whole procedure. The Valsalva ratio was calculated by taking longest R-R interval after the manoeuvre/shortest R-R interval during the manoeuvre.

Statistical Analysis: All data were represented as a Mean ± SD and statistical analysis was done by using unpaired t-test. We used graphpad instat statistical software (demo version) for data analysis.

Result: A total 50 healthy young female subjects having age between 26-40 years were recruited in this study.

Parasympathetic function test exhibited statistically significant difference between premenstrual and post menstrual phase. Table shows comparison of parasympathetic function test during postmenstrual and premenstrual phases of menstrual cycle.

Table: showing comparison of Parasympathetic function test during pr and post menstrual phases of menstrual cycle

Parasymp-athetic function test	Post menstrual phase (FP) Mean± SD	Pre - menstrual phase (LP) Mean± SD	Result p value
RESTING HEART RATE	80.54 ±8.6	83.71± 8.4	>0.05 (NS)
HR VARIATION DURING DEEP BREATHING	32.65 ± 3.5	28.52± 3.1	<0.001 (S)
30:15 RATIO (Lying/Standing ratio)	1.29± 0.3	0.98± 0.1	<0.001 (S)
VALSALVA RATIO	1.17± 0.05	1.20± 0.04	0.03(S)

SD – Standard deviation, FP- follicular phase, LP- luteal phase, NS- Not Significant, S- Significant

Discussion: Result in table shows that resting HR is less in postmenstrual period which has parasympathetic dominance. Also other result including deep breathing difference, 30:15 ratio and Valsalva ratio shows statistically significant difference between pre and post menstrual period of menstrual cycle. Study of Nirmala S. Anand and Shivprasad Goudar found statistically significant difference in E:I ratio, 30:15 ratio and also of Valsalva ratio that is also found in our study.[7] On other hand studies of Veena Mehta and AS Chakraborty; Rajeshwari L,Ganashree CP and Rajendra DH did not found statistically significant difference in parasympathetic function test during follicular and luteal phase of menstrual cycle.[8,9] Study of Shaily verma and prashant Khurasiya also did not found statistically significant difference in parasympathetic function test except Valsalva ratio which is significant statistically. Another same type of study done by Rama Chaudhary et al along with serum estrogen and progesterone shows statistically significant difference in resting HR and systolic BP, deep breathing difference.[10] They did not found statistically significant difference in 30:15 ratio and Valsalva ratio.

Above result can be explained on the basis that physiologically during post menstrual phase estrogen level is more compare to premenstrual period. Also progesterone is only secreted in premenstrual phase. Estrogen is a sympathoinhibitor and vagotonic while progesterone attenuates sympathetic baroreflex responses via a central mechanism.[11] so resting heart rate is more in premenstrual phase compare to post menstrual phase.

The 30:15 ratio is biphasic phenomenon mediated by the afferent from muscle, vagus nerve and the baroreceptor reflex arc. DJ Ewing showed that the initial heart rate response to standing is under vagal control with an immediate vagal withdrawal during standing from lying down position which increases the heart rate over the first 10-15 beats (tachycardia). This is followed by a vagal

reactivation that slows the heart and gives characteristic rebound bradycardia.[12] Estrogen increases baroreflex sensitivity. This effect will lead to increase in 30:15 ratio in post menstrual period than that of premenstrual period.

Heart rate variation to deep breathing shows statistically significant difference in pre menstrual and post menstrual phase. HR response to deep breathing is also mediated via vagus. During inspiration, impulses in the vagi from the stretch receptors in the lungs inhibit the cardio inhibitory area in the medulla oblongata. It decreases tonic vagal discharge that keeps the heart rate slow, so the heart rate increase during inspiration.[13] Therefore heart rate variation during deep breathing reflects the parasympathetic activity which is more during post menstrual phase of the menstrual cycle.

Valsalva manoeuvre is forced expiration against closed glottis. The blood pressure rises at the onset of straining because the increase in intrathoracic pressure is added to the pressure of the blood in the aorta. It then falls because the high intrathoracic pressure compresses the veins decreasing venous return and cardiac output. The decrease in arterial pressure and pulse pressure inhibit the baroreceptors, causing tachycardia and rise in peripheral resistance. Valsalva ratio shows balance between sympathetic and parasympathetic nervous system. In our study statistically significant difference is seen in Valsalva index due to increased parasympathetic activity in post menstrual period.

It has also been suggested that estradiol increases number and sensitivity of progesterone receptor thus increasing action of progesterone hormone during luteal phase. Also progesterone has inhibitory effect on cardiovagal baroreflex responses.[14] Because of these, even though in premenstrual period presence of estrogen and progesterone both, progesterone mainly affects cardiovascular autonomic function. While in post menstrual phase effect of estrogen is predominating as there is absence of progesterone in this phase.

Conclusion:

Parasympathetic function testing result of our study shows that progesterone increases sympathetic tone in premenstrual period while estrogen increases parasympathetic tone in postmenstrual phase of menstrual cycle. As cardiac autonomic function test is simple, non invasive method of knowing cardiac autonomic status we use this test. This result will be helpful for improving the health related problems present during menstrual cycle such as anxiety, depression in premenstrual phase in reproductive age group female.

Limitation of our study: We were taking small group and also we were not doing serum estrogen and progesterone level along with our test.

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