Evaluation of Sympathetic Function tests During Different Phases of Menstrual Cycle in Apparently Healthy Young Females - A Cross Sectional Study

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Abstract

Introduction: Menstrual cycle consists of three phases namely menstrual, follicular and luteal phase. It is reported that hormonal fluctuations during different phases may result in some autonomic function alterations. The objective of this study is to evaluate the sympathetic function tests during different phases of menstrual cycle in apparently healthy young females.

Methods: A descriptive cross-sectional study was conducted among 100 apparently healthy female students of medical, dental and nursing streams of Kathmandu Medical College for a year. Young girls in the age of 17 - 23 years with regular 28 days menstrual cycles for last six months was included in the study. The sympathetic function tests like blood pressure response to immediate standing, blood pressure response to sustained hand grip exercise and cold pressor test was done. Data was collected and statistical analysis was done. A P value of less than ≤ 0.05 was considered statistically significant.

Results: Resting systolic and diastolic blood pressure were increased in luteal phase (119.03 ± 7.04, 88.84 ± 5.88) compared to menstrual (112.07 ± 7.43, 70.44 ± 7.80) and follicular phase (112.91 ± 7.55, 73.36 ± 5.63) of the menstrual cycle. Fall in postural systolic blood pressure (blood pressure response to immediate standing) was statistically significant (P value < 0.05) between follicular (10.61 ± 7.39) and luteal phase (7.39 ± 6.82). Rise in systolic blood pressure in response to cold pressor test showed significant increase in the luteal phase (15.81 ± 7.84) compared to menstrual (12.18 ± 10.38) and follicular phase (11.76 ± 8.54). Blood pressure response to isometric handgrip exercise was statistically significant during the luteal phase compared to the menstrual and follicular phase.

Conclusions: The result of the present study concludes that the sympathetic function test responses were highest in the luteal phase of the menstrual

INTRODUCTION

The menstrual cycle's biological processes result from the coordination of hormones from the hypothalamus, pituitary gland, and ovaries.[1] The menstrual cycle consists of three phases: menstrual, follicular, and luteal. Changes in the functional parameters of various systems occur, likely influenced by hormonal fluctuations across these phases.[2] Variations in progesterone and estradiol levels throughout the menstrual cycle might influence the functioning of the autonomic nervous system.[3]

A series of non-invasive, standardized, and quantitative tests involving cardiovascular reflexes is commonly employed to evaluate sympathetic autonomic function. These tests include monitoring blood pressure changes during isometric handgrip exercise, the cold pressor test, and the orthostatic test.[4] Endogenous progesterone is known to cause an increase in blood pressure, while estrogen exerts a vasodilatory effect by enhancing the production of prostacyclin and nitric oxide.[5] This may explain the lower sympathetic activity observed during the proliferative phase compared to the secretory phase.

The aim of the present study is to study the sympathetic functions during the various phases of menstrual cycle in Nepalese females.

METHODS

This was a cross-sectional study conducted in the apparently healthy female students of medical, dental and nursing streams of Kathmandu Medical College Public Limited, Duwakot, Bhaktapur, Nepal between 1st January 2023 to 30th December 2023 after obtaining ethical approval from Institutional Review committee with reference number 23122022 / 03. The sample was selected from the study population using the purposive sampling technique. The sample size was calculated using the formula, assuming a confidence level of 95% (Z = 1.96), an estimated proportion of 50% (P = 0.5), and a margin of error (e) of 10%. Substituting these values, the required sample size was calculated as: $n = (1.96)^2 (0.5) (0.5) / (0.1)^2 = 96.04 \approx 100$. A sample size of 100 was considered adequate to provide reliable results while ensuring practicality and feasibility. Hundred young girls in the age of 17 - 23 years with regular 28 - day menstrual cycles for last six months were included in the study. Informed written consent was taken for the study. A thorough menstrual history was recorded to exclude any irregularities in the menstrual cycle. A proforma was used to collect details such as age, BMI, education stream,smoking and drinking habits. Height and weight was measured using a standard stadiometer and weighing scale, and body mass index (BMI) was calculated using Quetelet's formula (kg / m²). The cycle was calculated from the date of onset of the last menstrual period. Participants were assessed on the 1st to 5th day, 9th to 12th day, and 19th to 25th day to represent the menstrual, follicular, and luteal phases, respectively.[6] Subjects were instructed to visit the department during each phase of menstrual cycle at 9 to 11 am. The following tests were conducted to evaluate sympathetic functions:

a. Blood pressure response to immediate standing
b. Cold Pressor Test
c. Blood pressure response to sustained handgrip exercise

The subject was instructed to rest in the supine position for 10 minutes in a quiet room to alleviate anxiety, after which resting blood pressure was measured. The cold pressor test procedure was explained to the participants. Following the measurement of their resting blood pressure, they were instructed to immerse their left arm in ice - cold water (ranging from 2 to 4 °C) for a duration of one minute. During this time, blood pressure readings was taken from the right arm at the end of one minute, just before the hand is taken out of cold water. The blood pressure response to the cold pressor test was defined as the increase in systolic blood pressure (SBP) and diastolic blood pressure (DBP) from baseline levels. An increase of 15 - 20 mm Hg in SBP and ≥ 10 mm Hg in DBP was considered a normal response.[7] Baseline blood pressure was measured while the subjects were seated. They were then instructed to grasp a handgrip spring dynamometer with their right hand, ensuring a firm grip, and squeeze the handle with maximum effort for a few seconds. This procedure was repeated three times, with rest periods in between to avoid fatigue. The highest value among the three measurements was recorded as the maximal voluntary contraction (MVC). Subsequently, the participants performed isometric handgrip exercises at 30% of their MVC for two minutes. During this exercise, blood pressure was measured from the arm not involved in the activity at one minute after starting the handgrip and immediately before releasing it. The increase in diastolic blood pressure (DBP) just prior to releasing the handgrip was used as an indicator of the response to the handgrip exercise. A DBP increase of more than 15 mmHg was considered normal, 11 - 15 mm Hg was classified as borderline, and ≤ 10 mm Hg was deemed abnormal.[7] In the postural challenge test, the subject was instructed to lie down calmly for 10 minutes, during which baseline blood pressure was recorded. Subsequently, the subject was asked to stand up unaided within three seconds and remain still in the standing position for one minute. Blood pressure was measured immediately after standing. The difference in systolic blood pressure (SBP) between the supine and standing positions was calculated. A decrease in SBP of ≤ 10 mm Hg was considered normal, a drop of ≥ 30 mm Hg was classified as abnormal, and a reduction between 11 and 29 mmHg was regarded as borderline.[7] Data was collected and statistical analysis was done in Statistical Packages for Social Services version 22. All the data was expressed as mean ± SD and statistical analysis between groups was done using paired student's-t test. A $P \leq 0.05$ was considered statistically significant.

RESULTS

Table 1: Mean distribution of age and BMI among subjects

Variables	Mean distribution
Age (Years)	19.07 ± 1.40
BMI (kg / m²)	21.42 ± 1.46

A total of 100 female medical students were included in the present study. The mean age of the study population was 19.07 ± 1.40 years with mean body mass index of 21.42 ± 1.46 (Table 1).

Table 2: Sympathetic function tests during the menstrual phase and follicular phase of the menstrual cycle

Parameters (mm Hg)	Menstrual phase	Follicular phase	P value
Resting SBP	112.07 ± 7.43	112.91 ± 7.55	0.293
Resting DBP	70.44 ± 7.80	73.36 ± 5.63	0.002
Fall in Postural SBP	9.60 ± 7.28	10.61 ± 7.39	0.327
Rise in SBP Cold pressure test	12.18 ± 10.38	11.76 ± 8.54	0.732
Rise in DBP Cold pressure test	18.94 ± 8.43	16.09 ± 7.98	0.015
Rise in DBP in Handgrip	22.37 ± 11.08	17.74 ± 8.83	0.000

Table 3: Sympathetic function tests during the menstrual phase and luteal phase of the menstrual cycle

Parameters (mm Hg)	Menstrual phase	Luteal phase	P - value
Resting SBP	112.07 ± 7.43	119.03 ± 7.04	0.000
Resting DBP	70.44 ± 7.80	88.84 ± 5.88	0.000
Fall in postural SBP	9.60 ± 7.28	7.39 ± 6.82	0.017
Rise in SBP cold pressure test	12.18 ± 10.38	15.81 ± 7.84	0.004
Rise in DBP cold pressure test	18.94 ± 8.43	22.03 ± 4.88	0.002
Rise in DBP Handgrip	22.37 ± 11.08	25.08 ± 5.40	0.029

Table 4: Sympathetic function tests during the follicular phase and luteal phase of the menstrual cycle

Parameters (mm Hg)	Follicular phase	Luteal phase	P - value
Resting SBP	112.91 ± 7.55	119.03 ± 7.04	0.000
Resting DBP	73.36 ± 5.63	88.84 ± 5.88	0.000
Fall in postural SBP	10.61 ± 7.39	7.39 ± 6.82	0.001
Rise in SBP cold pressure test	11.76 ± 8.54	15.81 ± 7.84	0.001
Rise in DBP cold pressure test	16.09 ± 7.98	22.03 ± 4.88	0.000
Rise in DBP handgrip	17.74 ± 8.83	25.08 ± 5.40	0.000

Resting SBP and DBP were increased in luteal phase (119.03 ± 7.04, 88.84 ± 5.88) compared to menstrual (112.07 ± 7.43, 70.44 ± 7.80) and follicular phase (112.91 ± 7.55, 73.36 ± 5.63) (Tables 2, 3 and 4).

Fall in postural SBP(Blood pressure response to immediate standing) was statistically significant (P value < 0.05) between menstrual (9.60 ± 7.28) and luteal phase (7.39 ± 6.82), follicular (10.61 ± 7.39) and luteal phase (7.39 ± 6.82), but not significant (P value = 0.327) between menstrual and follicular phase (Tables 2, 3 and 4).

Rise in systolic blood pressurein response to cold pressor test was higher in the luteal phase (15.81 ± 7.84) compared to menstrual (12.18 ± 10.38) and follicular phase (11.76 ± 8.54) and the difference was statistically significant (P < 0.05). Rise in diastolic blood pressure was statistically higher in menstrual phase (29.16 ± 12.44) compared follicular phase (16.09 ± 7.98) and luteal phase (17.66 ± 8.06) (Tables 2 - 4) Blood pressure response to isometric handgrip exercise was statistically significant during the luteal phase (25.08 ± 5.40), compared to the menstrual phase (22.37 ± 11.08) and follicular phase (17.74 ± 8.83) (Tables 2 - 4).

DISCUSSION

In the present study, there was a statistically significant difference in systolic blood pressure between menstrual-luteal phase and follicular-luteal phase, with higher values in the luteal phase. Whereas there was a statistically significant difference in mean diastolic blood pressure between all the three phases of menstrual cycle as menstrual-follicular, menstrual-luteal and follicular-luteal phase, with higher values in the luteal phase and lower values in follicular phase. This finding is in accordance with the study of Garg R et al and Chakraborty A et al.[1,8] In a study done by Anuradha G et al, there was no significant difference in both systolic and diastolic blood pressure among different phases of the menstrual cycle suggesting due to less sample size.[9] The study done by Naher et al showed that systolic and diastolic blood pressure among the three phases were within normal range and there was no significant difference among the three phases of menstrual cycle indicating no altered sympathetic activity during these phases.[10] Another study carried out by McFetridge JA et al showed that resting DBP was lower during luteal phase and higher during follicular phase whereas SBP remained uniform across the menstrual cycle.[11] These differences may have been resulted as the studies have been done in different countries with different geographic regions and socioeconomic conditions. Decreased blood pressure during the follicular phase may result from the effects of estrogen, which promotes vasodilation by enhancing the release of prostacyclin and nitric oxide. Additionally, estrogen reduces the production of vasoconstrictors such as angiotensin II and endothelin.[6,12] Estrogen induces smooth muscle relaxation by activating calcium-dependent potassium channels through the nitric oxide and cyclic guanosine monophosphate (cGMP) pathway, leading to vasodilation.[13]

In our study, significant increase in the resting systolic blood pressure was observed in the luteal phase as compared to the menstrual phase which may be due to progesterone as it causes cardiac excitability by its opposing effects on estrogen.[6] Elevated progesterone levels reduce the release of nitric oxide from the endothelium, resulting in generalized vasoconstriction and an increase in blood pressure. Since progesterone levels are significantly higher during the luteal phase, this leads to a rise in both systolic and diastolic blood pressure.[14] There was a statistically significant difference in fall in postural systolic blood pressure between menstrual-luteal and follicular-luteal phase. Similar results were observed in study done by Kavitha C et aland Verma S et al.[15,6] However, a study conducted by Bir Hirshoren et al showed that orthostatic responses remain unaltered throughout the menstrual cycle.[16] When transitioning suddenly from a supine to a standing position, blood pools in the lower parts of the body, reducing venous return and cardiac output. As a result, systolic blood pressure, which depends on left ventricular ejection, decreases. This triggers the sino-aortic reflex, which acts within seconds to stabilize blood pressure.[6]

Our study showed that both systolic and diastolic blood pressure rise in response to cold pressor test was higher in the luteal phase as compared to menstrual and follicular phase and the differences were statistically significant. Similar results were observed in the study done by Garg R et al[1] and Kavitha C et al.[12] Increased sympathetic activity induced by cold water stress causes norepinephrine release and elevation of systolic and diastolic blood pressure in luteal phase.[17] Increase in the blood pressure might also be contributed by the release of endothelins, prostaglandins and angiotensin II.[18] During the follicular phase, elevated estrogen levels suppress the production of potent vasoconstrictors such as endothelins and angiotensin II. This suppression contributes to a lesser increase in blood pressure during the cold pressor test in the follicular phase.[16]

The rise in diastolic blood pressure in response to sustained handgrip was statistically significant between all the phases of menstrual cycle, with higher change in diastolic blood pressure in luteal phase. Our results were similar to the studies of Garg R et al and Chakraborty A et al.[1,8] In contrary, the study done by Christina KF et al showed no statistically significant difference between all the phases of menstrual cycle.[19] During isometric handgrip exercise, the concentration of metabolites such as lactic acid, hydrogen ions, bradykinin, and adenosine rises within the skeletal muscle interstitium. These metabolites are detected by nerve endings sensitive to chemical changes. Their presence enhances the activation of metaboreceptor afferent fibers, triggering a strong reflex that elevates sympathetic nervous system activity. This, in turn, causes vasoconstriction, contributing to an increase in blood pressure.[20] Our study did not take into account the estrogen and progesterone levels which were responsible for variation in sympathetic activity in follicular and luteal phases of the menstrual cycle. Further studies with hormonal assay are required to correlate the findings of the present study.

CONCLUSIONS

Our study concludes that the sympathetic function test responses were highest in the luteal phase of the menstrual cycle.

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and / or publication of this article.

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