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Comparison of Blood Pressure Variability in Different Phases of Menstrual Cycle in Apparently Healthy Females: A Cross Sectional Study

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ABSTRACT

Background: Hypertension is a leading cause of mortality and morbidity in today's world, wherein sedentary lifestyle and fast food dominate the youngsters and middle aged population. Also stress, increased screen time and lack of sleep hygiene are leading the population at risk of metabolic diseases such as diabetes and hypertension. Hormones also play a significant role in etiology of hypertension.
Materials and Methods: Our study was carried out in physiology department, King George's Medical University, Lucknow. This was a cross sectional observational study, including apparently healthy females in age group 18-35 years, having regular ovulatory cycles, and not undergoing any medication for chronic disease. We excluded pregnant and lactating females, those beyond the age criteria and patients of chronic diseases. Our study participants were initially trained to undergo ambulatory blood pressure monitoring, and twenty four hours ambulatory blood pressure monitoring was done in the peak of menstrual, proliferative and luteal phase, considering ovulation at day (x-14), where x is the last day of menstrual cycle.
Results: On comparing, systolic BP, mean in menstrual phase came out to be 103.79 with S.D 15.25, In proliferative phase it was 105.41, with S.D 7.33, in luteal phase it was 124.13, with S.D 10.60. ($p < 0.001$)
In diastolic BP, mean of 63.6 with S.D 15.75, in menstrual phase, 68.44 with S.D5.66 in proliferative phase and 76.32 with S.D 6.77, was observed. ($p < 0.001$).
Considering mean arterial pressure, in menstrual phase mean was 78.03, with SD 10.95, in proliferative phase 79.91 with S.D 6.34. In luteal phase, it was 89.58 with SD 5.49. ($p < 0.001$)
Comparison of pulse shows a gradual rise on transition from menstrual to proliferative phase, however the results did not reach a significant value.
Conclusion: our study shows that blood pressure tends to rise on transition from menstrual to proliferative and luteal phases, hence this should be taken into consideration while screening and diagnosing females as hypertensives.

Keywords: ABPM, mid luteal, menstrual, proliferative

INTRODUCTION

Blood pressure elevation is a known cause of mortality and morbidity in today's world. Common and proven causes being sedentary lifestyle, increasing stress, dietary modification, (1,2,3) and many others that are irrespective of genetic risk associated with hypertension. Studies show that there exists a correlation between genetically salt sensitive population and primary hypertension. (4) Etiology of hypertension includes innumerable physiological and pathological causation factors. There exists a clear multifactorial causation, which includes many factors to its credit, and there are researches still going on to find out other causes which may be associated with hypertension including genetic factors. (5) Variability is a feature of blood pressure which characterizes continuous and dynamic fluctuations which occur in blood pressure throughout a lifetime. This phenomenon is complex and can be evaluated in regards of time ranging from seconds to minutes to years. (6) Fluctuations in blood pressure may occur due to many emotional, physical and environmental factors, stress, high altitude, seasonal variation, postural elevation of blood pressure to name just a few. (6) Variability of blood pressure is vital to ensure balance between availability and demand of blood perfusion of different organs.

Blood pressure variability can be measured by tools such as automated machines which are timed to measure blood pressure at regular time intervals for a period varying from 24 hours to 72 hours and this may be done at half hourly intervals. Ambulatory blood pressure monitoring offers a very nice tool to measure variations in blood pressure and provides a wealth of data in regards to the diurnal, nocturnal, exercise and sleep variations in healthy as well as compromised subjects(7). Uses of this tool may include the diagnosis, assessment of control and efficacy of treatment of hypertension (7). The tool is also very good method to assess white coat hypertension and masked hypertension. (8,9) Unlike males, reproductive system of females exhibits regular cyclic changes that may be regarded as periodic preparation of the female for pregnancy and fertilization. In humans the most significant feature is periodic vaginal bleeding which occurs with shedding of uterine mucosae resulting into menstruation. On an average, it lasts for 28 days however the length of cycle may vary between 21 to 35 days, which is said to be normal. The menstrual cycle is expressed by Numbers starting with the first day of menstruation. The menstrual cycle may be divided into follicular / proliferative and luteal / secretary phase. Follicular phase begins from first day of menses and till ovulation, followed by ovulation under influence of Luteinizing hormone. Luteal phase is 14 days long. In this time, if fertilization occurs, it will result in pregnancy if not then there occurs progesterone withdrawal which results in menses. Average amount of blood loss in is about 30 ml. (10) There exists a relationship between psychosocial stress and menstrual cycle, abnormalities such as delayed ovulation and luteal phase defects. (11)

Studies show that there is strong evidence of increase in symptoms of psychosis, anxiety, stress, binge eating and alcohol use in luteal phase of menstrual cycle. (12) Blood pressure variability may also be a feature accompanying the hormonal variation that is responsible for cyclical ovarian and uterine changes

MATERIAL & METHOD

Study design: This cross-sectional observational study.

Study location: Department of Physiology, King George's Medical University, after obtaining ethical clearance.

Study duration: One year according to

guidelines of good Medical Research outlined in Helsinki declaration.

Study procedure: Volunteers were trained to undergo Ambulatory blood pressure monitoring for 24 hours continuously during all their activities, including sleep. Tool used in the study was ABPM machine from A and D Japan and was timed to record blood pressure every half hourly during daytime and hourly at night.

Inclusion criteria:

Females. The study included females in the age group of 18 to 35 years with regular ovulatory cycles, not undergoing any sort of medication. The subjects of a similar socio-economic group were included in the study.

Exclusion criteria:

Subjects beyond this age criteria, pregnant and lactating females. Those below 18 and above 35 years, those undergoing medication for thyroid, hypertension, PCOS, hypertensive, PCOS pregnant and lactating females and were all excluded from the study.

The study included 30 participants for whom ABPM was done on 3 occasions for 24 hours this was done at peak of menstrual proliferative and luteal phases considering ovulation at day x minus 14 where X is the last day of menstrual cycle.

Sample size: 30 participants, for whom ABPM was done on 3 occasions for 24 hours, this was done at peak of menstrual, proliferative and luteal phases considering ovulation at day

(x – 14) where X is the last day of menstrual cycle.

Study Design: Cross sectional study

Study Location: Department Of Physiology, King George's Medical University, Lucknow, Uttar Pradesh, India.

Sample size calculation: 30 Participants were enrolled in this study. The participant were selected on volunteer basis.

Inclusion Criteria:

1. Females in age group 18-35 yrs,
2. Having regular ovulatory cycles
3. Similar socio-economic groups,
4. Not undergoing on any medication

Exclusion Criteria:

1. <18 years, >35 years age
2. Patients of ovarian disorders, irregular/ anovulatory cycles
3. Pregnant females
4. Lactating females with irregular cycles
5. Having thyroid disorders, cardiovascular disorders

STATISTICAL ANALYSIS:

The collected data was analysed using IBM statistical passage statistical package for Social Sciences (SPSS) software version 24. The data was expressed in numbers, percentage or mean +/-+/-, standard deviation. Paired-, paired T test, was used to compare mean of two groups, while one way ANOVA was used to express data for more than two groups. For comparison. A p- value of 0.05 was considered as cut off for statistically significant Association.

RESULTS

The study was carried out on thirty, apparently healthy, voluntary participants during the peak of their menstrual, proliferative and luteal phase, by measuring their ambulatory blood pressure through automated machine at half hourly interval during daytime, and hourly at night. The study tries to find out a normal physiological phenomenon, the results of which are as follows.

Table no. 1: Shows Systolic blood pressure tends to rise on transition from menstrual to proliferative phase, but there is a sharp peak from proliferative to luteal phase.

	M Phase(n=30)		P Phase(n=30)		L Phase(n=30)		F	p-Value
	Mean	±SD	Mean	±SD	Mean	±SD		
SBP	103.79	15.25	105.41	7.33	124.13	10.60	28.16	<0.001

Table no. 1: comparison of systolic BP, in menstrual, proliferative and luteal phases

Table no. 2: diastolic blood pressure also rises from menstrual to proliferative phase, but there is a sharp rise in the mid luteal phase.

	M Phase(n=30)		P Phase(n=30)		L Phase(n=30)		F	p-Value
	Mean	±SD	Mean	±SD	Mean	±SD		
DBP	63.60	15.75	68.44	5.66	76.32	6.77	11.10	<0.001

Table no. 2: comparison table of diastolic BP in menstrual, proliferative and luteal phases.

Table no. 3: mean arterial pressure shows similar changes as systolic and diastolic blood pressure, there was rise from menstrual to proliferative phase, but a sharp increase in the mid luteal phase.

	M Phase(n=30)		P Phase(n=30)		L Phase(n=30)		F	p-Value
	Mean	±SD	Mean	±SD	Mean	±SD		
MAP	78.03	10.95	79.91	6.34	89.58	5.49	17.64	<0.001

Table no. 3: comparison table of mean arterial pressure in menstrual, proliferative and luteal phases.

Table no. 4: Comparison of mean changes in pulse did not arrive to a statistically significant value.

	M Phase(n=30)		P Phase(n=30)		L Phase(n=30)		F	p-Value
	Mean	±SD	Mean	±SD	Mean	±SD		
PUL	80.41	6.77	84.90	10.06	84.02	7.00	2.59	0.081

DISCUSSION

There are many researches available, which regard Ambulatory BP monitoring as a very good tool, to assess the changes in blood pressure at different times of the day, under the influence of many factors. (13,14). Blood pressure is also said to have a dip at night and rise in early morning which is said to be a natural phenomenon under the influence of hormones cortisol and melatonin. (15,16,17,18,19). Estrogen and progesterone also are suggested to play a role in blood pressure rise and fall. (20). Hormones seem to play a vital role in elevation of BP, due to direct effect on vasodilation, as suggested in studies done on peri - menopausal and postmenopausal women. (21) Also studies suggest that replacement of hormones can add to quality of life by maintaining body changes which occur after Menopause. Studies done in postmenopausal women suggest that correlation exists between follicle stimulating hormone and blood pressure variability also. In our study we could analyse, that there is a significant rise in blood pressure both systolic and diastolic, along with the rise in mean arterial pressure in the mid luteal phase however the difference in Pulse could not reach a significant value. On comparing menstrual with proliferative phase, there is a rise in blood pressure from menstrual to proliferative phase, however this is not as much as that exhibited by subjects in that luteal phase of the cycle. There were some strengths in our study, few of them being, that we included participants of similar socio economic groups, justifying similar stress levels, mental health and social conditions, hence we can say that the variations occurring may have more of physiological role than the existence of some underlying cause. Next we could manage to have very complaint subjects who despite of the

limitations and amount of this comfort while tying the BP cough for 24 hours have undergone the study for the required period which could have helped into gain approximately accurate data. Pre -menstrual syndrome encompasses clinically significant somatic and psychological manifestations during luteal phase of menstrual cycle leading to distress and functional impairment. These symptoms may disappear a few days after onset of menses. (23). Increased stress is said to have an adverse effect on severity of pre - menstrual syndrome. (24). Stress is also said to have been associated with rise in BP. One study, could also relate to this conclusion, as what we found was that there is a marked rise in BP in mid luteal phase, compared to other days of the menstrual cycle. We can also assess that the adverse symptoms of Pre - menstrual syndrome may be an aftereffect of the rise in BP in the mid luteal phase.

There are many researches available which regard Ambulatory BP monitoring as a very good tool to assess the changes in blood pressure at different times of the day and the influence of many factors. (13,14). Blood pressure is also said to have a dip at night and rise in early morning which is said to be a natural phenomenon under the influence of hormones cortisol and melatonin. (15,16,17,18,19). Estrogen and progesterone also as suggested to play a role in blood pressure rise and fall. (20). Hormones seem to play a vital role in elevation of BP due to direct effect on willow dilation as suggested in studies done on perimenopausal and postmenopausal women. (21).

Studies done in postmenopausal women suggest that correlation exist between follicles melting hormone and blood pressure variability also. (22). In our study we could analyse that there is a significant rise in blood pressure, both systolic and diastolic, along with the rise in mean arterial pressure in the mid luteal phase however the difference in Pulse could not reach a significant value., On comparing menstrual with proliferative phase there is a rise in blood pressure from menstrual to proliferative phase, however this is not as much as that exhibited by subjects in the luteal phase of the cycle. There were some strengths in our study, few of them being that we included participants of similar socio economic groups, justifying similar stress levels, mental health and social conditions. Hence we can say that the variations occurring may have more of physiological role than the existence of some underlying cause.

Next we could manage to have very complaint subjects, who despite of the limitations and amount of discomfort while tying the BP cough for 24 hours, have undergone the study for the required period which could have helped to gain approximately adequate data.

Premenstrual syndrome encompasses clinically significant somatic and psychological manifestations during luteal phase of menstrual cycle leading to distress and functional impairment. These symptoms may disappear a few days after onset of menses. (23). Increased stress is said to have an adverse effect on severity of the premenstrual syndrome. (24). Stress is also said to have been associated with rise in BP. One study could also relate to this conclusion as what we found was that there is a marked rise in BP, in luteal phase compared to other days of the menstrual cycle. We can also assess that the adverse symptoms of Premenstrual syndrome maybe an after effect of the rise in BP in the mid luteal phase.

Limitations of study

Tool used in our study is widely accepted and offers a wealth of data when it comes to evaluation of blood pressure at different occasions it is a wonderful tool as it can accurately assess circadian BP variability,

white coat and masked hypertension, has virtually no observer bias and can measure BP at all activities including sleep. Despite all these advantages there exist many drawbacks like the inability of the machine at primary setups due to high cost.

Cuff inflation is reported to have disturbed the sleep of participants, also even after proper instruction subjects could not comply tying the cuff continuously for 24 hours, they experienced variable levels of dis comfort as normal subjects, devoid of any symptomatic illness.

Tool used in our study is widely accepted, and offers a wealth of data when it comes to evaluation of blood pressure, at different occasions. It is a wonderful tool, as it can accurately assess circadian BP variability, white coat and masked hypertension, has virtually no observer bias and can measure BP at all activities including sleep. Despite all these advantages there exist many drawbacks like the inability of the machine at primary setups due to high cost, cuff inflation is reported to have disturbed the sleep of participants also, even after proper instruction subjects could not comply to tying the cuff continuously for 24 hours, they experienced variable levels of dis comfort, as normal subjects devoid of any symptomatic illness.

CONCLUSION

The present study shows that there is a significant rise in systolic, diastolic blood pressure and mean arterial pressure in the mid luteal phase, when compared to menstrual and proliferative phases of menstrual cycle. There, there was a slight rise in above parameters on transition from menstrual to proliferative phases, however it is not statistically significant.

Future perspectives

The study could show marked rise in BP in the luteal phase which may correlate to the dysphoric symptoms of Premenstrual syndrome. Also, it may suggest, that there is a physiological rise in BP after ovulation till the end of the mid luteal phase, after which it starts falling, thus suggestive in clinical practice to assess BP in all phases before arriving at a diagnosis of hypertension. Modifying lifestyle and diet may also help in regulating blood pressure and drug titration. However, however a study done including a large sample size may always promote more accurate results and a better understanding of the underlying mechanism.

Declaration by Authors

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