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Research Article

Blood Pressure Changes During the Normal Menstrual Cycle in Adolescent Females

Dixa B Thakrar, MBChB, MRCS*

University of Leicester, College of Medicine, Biological Sciences and Psychology, Maurice Shock Building, PO Box 138, University Road, Leicester, LE1 9HN , United Kingdom.

***Corresponding Author:** Dixa B Thakrar, MBChB, MRCS, University College Oxford, University of Oxford, High Street, Oxford, OX1 4BH, United Kingdom.*

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Abstract

Study Objective: The objective of this study was to investigate blood pressure (BP) changes during the menstrual cycle in adolescents.

Methods: Prospective primary data collection study. Systolic (SBP) and diastolic (DBP) pressures were measured from 22 female and 5 control male adolescents, daily for eight weeks. Readings taken on and after the onset of the first menstruation contributed to the primary analysis. Readings taken before this, in their previous cycle, were used to investigate consistency in trends observed in the primary analysis. BP was compared between different phases of the cycle.

Results: The primary analysis revealed that adjusted SBP was non-significantly higher in the luteal phase than follicular by 0.61mmHg (95%CI: -1.29to3.51; P=0.53). There was no statistical difference in DBP between the phases -0.07 (-1.62to1.48; P=0.93). In the previous cycle, however, SBP and DBP were higher during the follicular phase than the luteal (P=0.02 for both). This finding may be due to greater stress response, as these measurements were taken earlier in the experiment. Stress response is likely to affect the follicular phase more, as it is the first phase. This phenomenon was also observed in the male controls.

Conclusions: BP does not change during the menstrual cycle in adolescents. This has potential clinical implications. Physicians cannot attribute BP variations in adolescent females to their menstrual cycle and therefore may warrant further investigation. Another finding is that researchers investigating BP should consider a long familiarization period, between subjects and the experimental environment, to minimize stress response.

Keywords: Normal Menstrual Cycle; Adolescent Females; Blood Pressure (BP); Menstrual Cycle

Introduction

It has been suggested that pharmacological doses of the ovarian steroids, estrogen and progesterone, in oral contraceptives and hormone replacement therapies affect blood pressure (BP) due to their influences on vascular tone and salt and water balances.(1-4) However, the effects of natural ovarian steroids, which change during the menstrual cycle, on BP are unclear. A few studies have investigated changes in BP during the menstrual cycle. (1,3,5-11) However, these studies gave somewhat conflicting results and the majority were in adult females, 18 years and older. Thus, the present study investigates, prospectively, whether BP changes during the normal menstrual cycle in adolescent females.

Materials and Methods

Subjects and Procedure

The study included 22 postmenarchal, non-pregnant female students from grade 11 of the International School Basel, who volunteered to participate in the study. As this was an exploratory study, the population size was not necessarily specifically powered to detect changes. The week (Monday-Friday) prior to the commencement of the experimental stage was used to familiarize subjects with the BP measuring device to eliminate stress response or the white coat effect in the results. The experimental stage began the Monday after this. Each subject's systolic (SBP) and diastolic (DBP) pressures were measured everyday (Monday-Friday) for seven weeks using an automated upper arm sphygmomanometer, at a broadly consistent time of the day (± 20 minutes), unless the subject was absent from school. Single measurements were taken from the left arm after subjects had been silently sitting for five minutes, with their left arm resting on a table. In addition to these measurements, the first day of each menstruation was recorded. Subjects were requested not to consume alcohol, caffeine, smoke or undergo strenuous exercise in the hour preceding the measurement taking. All measurements were taken by the same observer.

Although each subject gave measurements for seven weeks and entered the experimental stage at different phases of her menstrual cycle, the primary analysis data comprised of the measurements taken during the first menstrual cycle that began within the experimental stage. The cycle beginning prior to the experimental stage, including the pre-experimental stage, were regarded as the previous cycle. Data of the previous cycle were analyzed to investigate consistency in any trends observed in the primary data analysis.

Information on smoking, alcohol and medication consumption, date of last menstruation and number of years of menstruation was collected using a self-administered questionnaire. Before beginning the experiment, all subjects gave their written informed consent, after the procedure was fully explained. The study was approved by the International School Basel and all procedures were in accordance with the ethical standards of the institution. The study also included five adolescent males for control purposes.

Determination of Cycle Phase

The day of the menstrual cycle was calculated from the date of the onset of the first and the second menstruation, within the experimental stage. To compare cycles between subjects, the cycle length was normalized to an ideal 28 days.(1) Therefore, each day of a subject's cycle was divided by the number of days of her actual cycle and then multiplied by 28. From this, the phases of the menstrual cycle were determined using different published methods, namely Greenberg *et al.*(1) and Moran *et al*.(5) Greenberg *et al.* split the menstrual cycle into the follicular phase (days 1-14) and luteal phase (days 15-28). In addition, to compare the effects of progesterone on BP, days 17-26, when the levels of progesterone are known to peak(1), was also used as a stage for comparison to the remaining days of the cycle, namely days 1-16, 27 and 28. Moran *et al*. divided the cycle into four phases: menstrual phase (days 1-3); follicular (days 4-12); ovulatory (days 13 -15) and luteal (days 16-28). Although the menstrual phase is part of the follicular, the authors looked at them separately. For the data collected prior to the first menstrual cycle, the day of the cycle was determined using the reported date of the previous onset of menstruation.

Statistical Analysis

As reported previously, the recorded BP values were analyzed using both the one-way (unadjusted)[5]and the two-way (adjusted)(1) analysis of variance methods. The two-way analysis, unlike the one-way, investigates the differences between the phases, controlling for the between-subject variation. In the present study, both analyses are presented. The analysis did not adjust for smoking, drinking, age or weight as it was the within subject variation that was relevant for the study and not any differences between subjects. Statistical significance was set at $P \leq 0.05$. Analyses were conducted using Statistical Analysis System (SAS).

Results

Twenty-two female students participated for seven weeks, of whom two were excluded because they reported oral contraceptive use (n = 20 analyzed). The mean age of the female subjects at the start of the experiment was 16.8 years (range 15.6-17.5 years), mean height was 1.66 m (1.52-1.75 m), mean body weight was 58.9 kg (47.0-85.0 kg) and mean body mass index was 21.3 kg/m^2 (17.5-27.8 kg/m^2).

The questionnaire identified one subject as a smoker and one as a regular drinker. All female subjects had been menstruating for at least 18 months and reported a mean menstrual cycle length of 31 days (21-45 days); however mean cycle length during the experiment was 28 days (15-49 days). On average, subjects were observed for 19 measurement days (10-35 days) before their first cycle when they started providing data for the primary analysis. No subjects reported taking medication that might affect BP.

Primary Analysis

First Cycle Table 1 summarizes mean BP for the first complete menstrual cycle at different phases. Mean SBP was higher during the luteal phase (114.14 mmHg) than the follicular (111.61 mmHg) (P=0.02). After controlling for subjects, the adjusted mean was 0.61 mmHg higher in the luteal phase than the follicular, which was not statistically significant (P=0.53).There were no significant differences in DBP, with the crude and adjusted mean differences between the luteal and follicular phases being 0.78 mmHg (P=0.40) and -0.07 mmHg (P=0.93), respectively.

Table 2 summarizes BP during the days of high progesterone levels (days 17-26) compared with the remaining days of the menstrual cycle. During days 17-26 of the menstrual cycle, mean SBP was higher than during the remaining days (113.76 mmHg vs. 112.02 mmHg). This difference did not reach statistical significance (P=0.16). Furthermore, the adjusted mean was 0.03 mmHg higher during days 17-26 (P=0.91). DBP was lower during the days when progesterone levels were high than the rest of the cycle, being 67.90 mmHg and 68.41 mmHg, respectively, with a crude mean difference of -0.50 mmHg (P=0.61). The adjusted mean difference, however, was greater with the average DPB being 1.32 mmHg lower during day 17-26 than the remaining days. This was of borderline statistical significance (P=0.11).

Table 1: Mean and mean differences [a] in blood pressure during luteal and follicular phases of the menstrual cycle.

Phase of Cycle	Systolic (mmHg)	Diastolic (mmHg)
	Mean (SE [b])	Mean (SE)
Follicular [c]	111.61(0.73)	68.06(0.63)
Luteal [d]	114.14(0.83)	68.83(0.63)
Unadj.[e] mean difference 95%CI P value	2.53 0.35,4.71 0.02	0.78 -1.00,2.56 0.40
Adj.[f] mean difference 95% CI P value	0.61 -1.29,3.51 0.53	-0.07 -1.62,1.48 0.93

[a]Difference is Luteal – follicular; [b] SE = standard error; [c] days 1-14; [d] days 14-28; [e] Unadj. = unadjusted; [f]Adj. = adjusted

Table 2: Mean and mean differences[a] in blood pressure during days of high progesterone levels and remaining days of the menstrual cycle.

Stage of Cycle	Systolic (mmHg)	Diastolic (mmHg)
	Mean(SE [b])	Mean(SE)
High progesterone days[c]	113.76(1.04)	67.90(0.72)
Remaining days[d]	112.02(0.67)	68.41(0.56)
Unadj.[e] mean difference 95% CI P value	1.75 -0.70,4.20 0.16	-0.50 -2.46,1.46 0.61
Adj.[f] mean difference 95% CI P value	0.03 -2.03,2.09 0.97	-1.32 -2.95,0.31 0.11

[a]Difference compares days 17-26 with all other remaining; [b] SE = standard error; [c] days 17-26; [d] days 1-16, 27 and 28; [e] Unadj. = unadjusted; [f] Adj. = adjusted

Table 3 displays the BP means according to the cycle divisions of Moran *et al.*(5) Crude values showed that the luteal phase had the highest and follicular the lowest SBP (114.74 vs. 110.75 mmHg).The overall unadjusted P value, testing the effect of phase on SBP was 0.05, however the adjusted P value was 0.41. Furthermore, none of the pairwise comparisons revealed any statistical difference between any two phases in this classification. There was no evidence of an overall effect of phase on DBP (adjusted P=0.62).

Table 3: Summary of blood pressure during the menstrual cycle according to four divisions of the cycle.

	Systolic (mmHg)		Diastolic (mmHg)	
Phase of Cycle	Unadj. mean (SE[a])	Adj. mean (SE)	Unadj. mean (SE)	Adj. mean (SE)
Menstrual[b]	112.45(1.86)	113.08(1.86)	68.69(1.51)	69.10 (1.01)
Follicular[c]	110.75(0.90)	110.91(0.80)	67.35(0.63)	67.78(0.57)
Ovulatory[d]	112.74(2.12)	112.51(1.59)	68.48(1.51)	68.88(1.13)
Luteal[e]	114.74(0.89)	112.45(0.86)	68.66(0.65)	68.22(0.61)
P value for phase (unadj.)	0.05		0.54	
P value for phase (adj.)	0.41		0.62	

Secondary Analysis: Previous Cycle

Eighteen of the twenty subjects provided some data from their previous cycle. These results were analyzed to investigate if similar trends would be observed as those in the primary analysis. The adjusted analyses revealed that during the luteal phase, both SBP and DBP were significantly lower than during the follicular phase (SBP by 2.63 mmHg (P=0.02) and DBP by 2.00 mmHg (P=0.02)).

Discussion

Blood pressure changes during the normal menstrual cycle in adolescent females are unknown. In this study, BP was investigated during the menstrual cycles of 20 adolescents. It was observed that BP does not change during the menstrual cycle in adolescents.

BP is an important biomarker of cardiovascular diseases. Any variability in BP can have potentially important clinical consequences. Understanding BP changes during the menstrual cycle could be useful for physicians trying to correctly diagnose high BP in adolescent females. Studies have shown that exogenous doses of ovarian steroids can affect BP. Therefore, it is important to understand any variability in BP that could occur naturally due to the hormone changes during the menstrual cycle. A few studies have investigated an association between blood pressure and the menstrual cycle. However, these have produced conflicting results and a paucity of data is available for females less than 18 years old. To our knowledge, this study is among the first to investigate females less than 18 years old.

The prospective studies, in adult women by, by Dunne *et al.* (6) and Kelleher *et al.* (3) revealed that SBP was highest at the onset set of menstruation when both natural estrogen and progesterone levels are low. However, only Dunne *et al.* found a similar increase with diastolic blood pressure DBP. In a retrospective analysis, Greenberg *et al.* found that SBP was significantly higher in the luteal phase, when there is a high concentration of progesterone.(1) However a second study, designed specifically to validate this finding, failed to find an association between SBP and the menstrual cycle. Moreover, they found that DBP was significantly lower in the luteal phase. Given that there is a correlation between DBP and SBP, the findings from the two studies are contradictory. Further studies by Hassan *et al.* (7) and Moran *et al.*(5) found decreases during the luteal phase in DBP and SBP, respectively.

Neither study found increases in both types of blood pressures, thus showing more inconsistencies. In addition, Moran *et al*. reported that SBP was significantly higher during the ovulatory phase, when the levels of estrogen increase, but progesterone levels are low. Williamson *et al*.[8], however, reported no significant changes in BP during the menstrual cycle. In two of the studies (mean ages 20 and 15 years) investigating changes in younger women, no changes in BP was found during the cycle. (9,11) However one study (mean age 19 years) found that BP was reduced in the luteal phase. (10)

These discrepancies could be attributed to many factors, for example number of subjects, number of full menstrual cycles, the regularity of BP monitoring, the determination of phase during the menstrual cycle, anovulatory cycles and the analytical methods. Another possibility could be the lead time used to familiarize both the observer and the subject with the measuring device. If this time is too short, stress response may affect the results and distort the true association between the menstrual cycle and BP.

The present study agrees with and contradicts some of the previous studies investigating BP and the menstrual cycle. During the days when progesterone peaked, the mean DBP was lower than other days. This finding agrees with the prospective study of Greenberg *et al*. However, the present result was only of borderline significance. Consistent with Greenberg *et al*., the present study did not reveal any other trends. Moran *et al*. revealed that SBP was significantly higher during the ovulatory phase, compared with the other phases. This finding however, is difficult to interpret as it seems that only a one-way analysis of variance was conducted. Therefore, their finding could be explained by between-subject variation. The present study however, found a non-significant increase in the ovulatory phase compared to the follicular phase. Kelleher *et al*. and Dunne *et al*. demonstrated a significant increase in SBP during the menstrual phases. The present study also observed a non-significant increase for both SBP and DBP during the menstrual phase.

The analysis was repeated in the previous cycle. Unlike the main analysis, this cycle revealed an association between BP and the menstrual cycle. It showed that BP was significantly lower in the luteal phase than the follicular. This finding may be an artifact of the data and not due to the hypertensive or antihypertensive actions of the endogenous ovarian steroids. Subjects entered the experiment during their previous cycle. However, for within subject analysis, each subject must have data in both the follicular and luteal phases for analysis. Therefore, in chronology, as the follicular phase precedes the luteal, the follicular phase measurements were taken earlier on during the experimental stage. During this earlier stage of the experiment, both the observer and subject were still familiarizing themselves with the experiment environment, which may have increased stress response. This could explain higher values in the follicular phase and lower values later on in the cycle.

This phenomenon was confirmed by the five males. Comparing BP during the first 14 days of the experiment with those during the subsequent 14 days, revealed that SBP was 3.45 mmHg higher in the first 14 days (P=0.02) than the next. This analysis was repeated but defined for the first 14 days after each male had been observed for 28 days. Here, SBP was 1.16 mmHg lower during the first 14 days than the subsequent 14 days. The pattern was weaker for DBP. Thus, the data suggests that BP measurements taken earlier on in the experiment have a tendency to be higher than those taken later on in the experiment. This could explain the observations in the previous cycle. This bias is minimized in the primary analysis as females had already been observed for an average of 19 days in the experiment before their first menstruation when they started providing data for the analysis.

The strengths and limitations of this study warrant consideration. All females were in the same grade, of similar age, socioeconomic status and reported no medical concerns. Therefore, the study population was likely to be homogeneous regarding BP changes. Furthermore, measurements were taken every school day at approximately the same time, minimizing any daily variations and by the same researcher thus eliminating inter-observer variation. Another advantage was that this study had two menstrual cycles and thus trends could be compared.

The study weaknesses include lack of hormonal measurements to more accurately determine the phase. Thus there is a possibility that the phases were misclassified. However, using two different classifications, both revealing no association, strengthens the conclusions. Other weaknesses include is that only single BP measurements were taken and that the study only had 20 subjects. As measurements were taken each week day for seven weeks and the primary analysis was a within person analysis, it is unlikely that repeated measurements would have changed the findings. Nevertheless, the study would have benefitted from a larger cohort.

Conclusions

Blood pressure does not change during the menstrual cycle in adolescents. The study results, once validated, have implications for clinical practice. A physician observing high blood pressure in an adolescent female cannot attribute the change to her phase of the menstrual cycle. Thus would have to take further action. An offshoot of the study is that any study investigating blood pressure over a period of time should incorporate a sufficiently long familiarization period to avoid stress related increases.

What is known already?

- Oestrogens and progesterones may affect vascular tone and hence blood pressure
- Oestrogens and progesterones vary during the menstrual cycle in females
- Varying evidence exists whether menstrual fluctuations of oestrogens and progesterones affect blood pressure in adult women and adolescents

What this study adds?

- Blood pressure does not change during the menstrual cycle in adolescent females
- A physician observing high blood pressure in an adolescent female cannot attribute the change to her phase of the menstrual cycle
- Blood pressure studies should incorporate a familiarization period to avoid stress related increases

Conflict of Interest

The author declares no conflict of interest.

References

1. Greenberg G, Imeson JD, Thompson SG, Meade TW. Blood pressure and the menstrual cycle. Br J Obstet Gynaecol 1985 Oct;92(10):1010-1014.
2. Karjalainen A. Effect of estrogen replacement therapy on metabolic risk factors for cardiovascular diseases in hysterectomized postmenopausal women. 2003; Available at: http://herkules.oulu.fi/isbn9514272404/isbn9514272404.pdf. Accessed Sep 1, 2011.
3. Kelleher C, Joyce C, Kelly G, Ferriss JB. Blood pressure alters during the normal menstrual cycle. Br J Obstet Gynaecol 1986 May;93(5):523-526.
4. Sarrel PM. The differential effects of oestrogens and progestins on vascular tone. Hum Reprod Update 1999 May-Jun;5(3):205-209.
5. Moran VH, Leathard HL, Coley J. Cardiovascular functioning during the menstrual cycle. Clin Physiol 2000 Nov;20(6):496-504.
6. Dunne FP, Barry DG, Ferriss JB, Grealy G, Murphy D. Changes in blood pressure during the normal menstrual cycle. Clin Sci (Lond) 1991 Oct;81(4):515-518.
7. Hassan AA, Carter G, Tooke JE. Postural vasoconstriction in women during the normal menstrual cycle. Clin Sci (Lond) 1990 Jan;78(1):39-47.
8. Williamson PM, Buddle ML, Brown MA, Whitworth JA. Ambulatory blood pressure monitoring (ABPM) in the normal menstrual cycle and in women using oral contraceptives. Comparison with conventional blood pressure measurement. Am J Hypertens 1996 Oct;9(10 Pt 1):953-958.
9. Hartwich D, Aldred S, Fisher JP. Influence of menstrual cycle phase on muscle metaboreflex control of cardiac baroreflex sensitivity, heart rate and blood pressure in humans. Exp Physiol 2013 Jan;98(1):220-232.

10. Adkisson EJ, Casey DP, Beck DT, Gurovich AN, Martin JS, Braith RW. Central, peripheral and resistance arterial reactivity: fluctuates during the phases of the menstrual cycle. Exp Biol Med (Maywood) 2010 Jan;235(1):111-118.

11. Driziene Z, Jakutiene E, Stakisaitis D, Pundziene B, Sveikata A. Characteristics of gender-related circadian arterial blood pressure in healthy adolescents. Medicina (Kaunas) 2008;44(10):768-774.

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