Changes in blood pressure during the normal menstrual cycle

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SUMMARY

1. Changes in blood pressure during the normal menstrual cycle are not well documented, and previous studies have given conflicting results.

2. Thirty normotensive women and ten mildly hypertensive women measured their blood pressure at home each morning for 6 weeks, under standardized conditions, using a UA-751 semi-automatic sphygmomanometer. All had normal menstrual cycles and subjects entered the study at different phases of the cycle.

3. Blood pressure was higher at the onset of menstruation than at most other phases of the cycle (systolic blood pressure, \( P < 0.05 \); diastolic blood pressure, \( P < 0.001 \)). Adjusted diastolic blood pressure was higher in the follicular than in the luteal phase (mean difference 1.23 mmHg, \( P < 0.001 \)). Similarly, blood pressure was lower during days 17-26 than during the remainder of the cycle (adjusted mean difference in systolic blood pressure -0.65 mmHg, \( P = 0.07 \); adjusted mean difference in diastolic blood pressure -1.19 mmHg, \( P < 0.001 \)).

4. Similar patterns were seen in normotensive and hypertensive subjects, and changes in plasma 17\(\beta\)-oestradiol and progesterone concentrations were also similar in the two groups.

Key words: blood pressure, hypertension, menstrual cycle, 17\(\beta\)-oestradiol, progesterone.

Abbreviation: BMI, body mass index.

INTRODUCTION

Changes in blood pressure during the normal menstrual cycle are not well documented, and available reports are conflicting. In a cross-sectional study, Greenberg et al. [1] found higher systolic blood pressure at days 17–26 of the cycle than in other phases. In contrast, in a smaller prospective study by the same group [1], when 33 women were seen three times weekly for 8 weeks, diastolic blood pressures were significantly lower at days 17–26 than in other phases, whereas systolic blood pressures were the same. In a similar prospective study of 18 women, Kelleher et al. [2] reported a significant increase in systolic blood pressure in the week before menstruation. A rise in systolic blood pressure at mid-cycle has also been described [3]. In a recent report, systolic blood pressure was similar at menstruation (days 1–2), in the late follicular phase (days 12–15) and in the luteal phase (days 21–26), whereas diastolic blood pressure was significantly lower in the luteal phase [4].

The development of reliable semi-automatic sphygmomanometers for home blood pressure measurement [5, 6] allows repeated monitoring without the presence of an observer, and facilitates frequent blood pressure measurements during the normal menstrual cycle. We report the findings in 30 normotensive women and 10 mildly hypertensive women, who measured their blood pressure at home each morning, under standardized conditions, for 6 weeks.

METHODS

Subjects

The study involved 30 healthy normotensive women recruited from hospital staff, and ten women who had been referred by their general practitioners because of mild hypertension. All had regular menstrual cycles lasting 26–34 days. Ages ranged from 20 to 44 years (mean 29.7 years), and body mass index (BMI) ranged from 19.4 to 32.0 kg/m\(^2\) (mean 23.6 kg/m\(^2\)). Blood pressure was <140/90 mmHg in all normotensive subjects before the study, but general practitioner readings averaged >160/95 mmHg in all women referred because of raised blood pressure. All had regular hours of employment and no shift workers were included. At the initial visit, before the study, a full medical history and examination were undertaken. No subject was taking any medication known to alter blood pressure and none was taking or had taken oral contraceptives in the previous 6
months. Nine women smoked and 33 drank alcohol in moderation. All subjects gave their written informed consent.

Protocol

Subjects entered the study systematically at different stages of their menstrual cycles, days 1–7, days 8–14, days 15–21 and days 22–28, with adjustment for cycle-lengths between 26 and 34 days. The stage of the cycle on entry was calculated from the date of onset of the previous menstrual period. Each woman was studied for 6 weeks, during which time at least one full menstrual cycle was completed.

Each subject was supplied with a UA-751 semi-automatic sphygmomanometer [5, 6] and a Hanson 120 kg step-on weighing scales, and was instructed on the use of each. Each UA-751 device was tested before use against a recently serviced random-zero sphygmomanometer, using the cross-over design of Sloan et al. [7], and was found to be accurate as reported previously [5, 6]. Subjects were tested for proper use of the semi-automatic sphygmomanometer before the study.

On each morning of the study, the subject recorded two consecutive blood pressure measurements before getting out of bed and the average was calculated. The measurement arm was supported on the bed and arm circumference was less than 33 cm in all subjects. Body weight was measured after voiding.

Each subject was reviewed on four separate occasions during the study, when blood was drawn for measurement of plasma 17β-oestradiol and progesterone concentrations. Blood was drawn on days 7, 14, 21 and 28 after the onset of menstruation, in a 28-day cycle. These days were calculated from the date of onset of menstruation, in a 28-day cycle. These days were calculated from the date of onset of menstruation, in a 28-day cycle. These days were calculated from the date of onset of menstruation, in a 28-day cycle. These days were calculated from the date of onset of menstruation, in a 28-day cycle.

Statistical analysis

The data were specifically analysed to test the findings of Greenberg et al. [1], Kelleher et al. [2] and Hassan et al. [4]. We used the following scheme to label the days of the cycle: the day of onset of menstruation was labelled day 0, the 14 days before menstruation were labelled days –1 to –14, and the 14 days after menstruation were labelled days 1–14, following the system of Kelleher et al. [2].

The principal analytic tool used was two-way analysis of variance, with subjects and time intervals as the factors; weight was used as a co-variate, with a separate regression coefficient fitted for each subject. In the analysis, the effect for the time interval containing the day of menstruation (day 0) was constrained to be zero. In this way, the effects for the other time intervals may be interpreted as mean differences relative to the interval containing day 0, and adjusted for weight differences and the fact that subjects did not all have the same number of readings in each time interval. For the latter reason, the mere reporting of the average blood pressures for each time interval would not accurately reflect true underlying changes.

We also report errors for the mean difference and the P value from the t-test of the hypothesis that the mean difference is zero. When more than two time intervals are involved, the P value for the overall F-test of the hypothesis that all the mean differences are zero is reported. When comparing the pattern of blood pressure variation between groups, we used the F-test for the interaction between group and time interval [8].

RESULTS

The menstrual cycle was divided into seven time intervals, days –14 to –11, –10 to –6, –5 to –2, –1 to 1, 2–5, 6–10 and 11–14, and the adjusted mean difference and P value between each interval and the days –1 to 1 interval were calculated. This allowed comparison with the findings of Kelleher et al. [2]. Morning systolic blood pressure was higher at the onset of menstruation than in other phases of the cycle (Table 1). Morning diastolic blood pressure was also higher at the onset of menstruation than during the luteal phase of the cycle (Table 1). For both systolic and diastolic blood pressure, there was evidence against the hypothesis of constant mean blood pressure through the cycle (systolic blood pressure, P<0.05; diastolic blood pressure, P<0.001). The so, having adjusted for subject, cycle and weight effects, was 6.7 for systolic blood pressure and 6.2 for diastolic blood pressure. 6.7 for systolic blood pressure and 6.2 for diastolic blood pressure.

Table 1. Adjusted mean differences in blood pressure from the onset of menstruation (days –1 to +1) in 40 subjects

<table>
<thead>
<tr>
<th>Days</th>
<th>Systolic blood pressure</th>
<th>Diastolic blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>−14 to −11</td>
<td>−0.98 ± 0.51 (P=0.055)</td>
<td>+0.09 ± 0.72 (P=0.91)</td>
</tr>
<tr>
<td>−10 to −6</td>
<td>−1.86 ± 0.65 (P=0.004)</td>
<td>−1.02 ± 0.60 (P=0.091)</td>
</tr>
<tr>
<td>−5 to −2</td>
<td>−1.42 ± 0.67 (P=0.034)</td>
<td>−1.80 ± 0.62 (P=0.004)</td>
</tr>
<tr>
<td>−1 to 1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2–5</td>
<td>−1.72 ± 0.68 (P=0.012)</td>
<td>−0.56 ± 0.63 (P=0.38)</td>
</tr>
<tr>
<td>6–10</td>
<td>−0.53 ± 0.64 (P=0.41)</td>
<td>+1.06 ± 0.58 (P=0.076)</td>
</tr>
<tr>
<td>10–14</td>
<td>−1.40 ± 0.67 (P=0.037)</td>
<td>+0.03 ± 0.62 (P=0.96)</td>
</tr>
</tbody>
</table>
Blood pressure and the menstrual cycle

Findings of Greenberg indicate considerable residual variation, in addition to the significant cycle effects discovered.

The data were also analysed for comparison with the findings of Greenberg et al. [1]. Overall systolic and diastolic blood pressures were higher in the follicular phase (days 0-14) than in the luteal phase (days 14-28); the adjusted mean difference was 0.22 mmHg for systolic blood pressure (not significant) and 1.23 mmHg for diastolic blood pressure ($P<0.001$). Days 17-26 (days 12 to 3 as described above) were also compared with all other days of the cycle. Both systolic and diastolic blood pressures were lower at this stage; the adjusted mean difference was 0.65 mmHg for systolic blood pressure ($P=0.07$) and 1.19 mmHg for diastolic blood pressure ($P<0.001$).

When compared with the analysis of Hassan et al. [4], systolic blood pressure was significantly lower in the late follicular phase (days 10-14) compared with levels at the onset of menstruation; diastolic blood pressures were similar (Table 1). Systolic and diastolic blood pressures were each significantly lower in the late luteal phase (days 10-14) compared with levels at the onset of menstruation (Table 1).

**Normotensive women compared with hypertensive women**

The 30 normotensive subjects and the ten mildly hypertensive women were also compared. The former were younger (mean ages 27.9 and 35.0 years, respectively, $P<0.005$) and slightly less heavy (mean BMI 23.1 and 25.2 kg/m², respectively, not significant). Mean blood pressure ($\pm$SEM) at the initial visit was 119/76±2/1 mmHg and 153/101±5/3 mmHg, respectively.

Changes in morning blood pressure were generally similar in normotensive and hypertensive women (Table 2). Systolic blood pressures were higher at the onset of menstruation than at most other times in the cycle in each group, whereas diastolic blood pressures were also generally lower in the luteal phase than at the onset of menstruation. Overall, the changes were somewhat more marked in the hypertensive group, but the differences did not reach statistical significance. There was evidence against the hypothesis of constant mean pressure throughout the cycle in the normotensive group (systolic blood pressure, $P=0.053$; diastolic blood pressure, $P<0.001$). This evidence did not reach statistical significance in the hypertensive group. In the normotensive group the so, having adjusted for subject, cycle and weight effects, was 6.2 for systolic blood pressure and 6.0 for diastolic blood pressure, whereas in the hypertensive group the values were 8.3 for systolic blood pressure and 7.0 for diastolic blood pressure.

Diastolic blood pressure was significantly higher in the follicular phase than in the luteal phase (normotensive women, adjusted mean difference 1.13 mmHg, $P<0.005$; hypertensive women, adjusted mean difference 1.53 mmHg, $P<0.05$). Diastolic blood pressure was significantly lower at days 12 to 3 than at other phases of the cycle (normotensive women 1.06 mmHg, $P<0.005$; hypertensive women 1.58 mmHg, $P<0.05$). The changes were greater in the hypertensive group, but again the differences did not reach statistical significance.

**Plasma 17β-oestradiol and progesterone concentrations**

Plasma 17β-oestradiol and progesterone levels were similar in normotensive and hypertensive women. Plasma 17β-oestradiol concentrations ($\pm$SEM) on days 7, 14, 21 and 28 were respectively 215±31, 553±80, 382±30 and 196±28 pmol/l in normotensive women, and 132±25, 469±79, 340±77 and 161±53 in hypertensive women. Plasma progesterone concentrations ($\pm$SEM) on days 7, 14, 21 and 28 were 1.2±0.1, 5.5±1.3, 27.4±2.7 and 9.9±3.1 nmol/l, respectively, in normotensive women, and 1.1±0.4, 5.3±2.9, 28.3±4.1 and 15.0±7.3 nmol/l, respectively, in hypertensive women.

**DISCUSSION**

This study clarifies and expands previous and apparently contradictory reports of blood pressure levels during the normal menstrual cycle. We confirm that morning diastolic blood pressure is lower in the luteal phase than at other times during the cycle [1, 4] and have demonstrated that there is also a decrease in morning systolic blood pressure. There is a significant increase in morning systolic blood pressure [2] and also in morning diastolic

<table>
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<th>Diastolic blood pressure</th>
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<tr>
<td></td>
<td>Normotensive subjects</td>
<td>Hypertensive subjects</td>
</tr>
<tr>
<td>11-14</td>
<td>-1.46±0.70 ($P=0.038$)</td>
<td>-1.12±1.70 ($P=0.51$)</td>
</tr>
<tr>
<td>6-10</td>
<td>+0.01±0.68 ($P=0.99$)</td>
<td>-2.42±1.62 ($P=0.167$)</td>
</tr>
<tr>
<td>2-5</td>
<td>-1.41±0.72 ($P=0.049$)</td>
<td>-2.69±1.70 ($P=0.115$)</td>
</tr>
<tr>
<td>-1 to 1</td>
<td>0</td>
<td>-1.0</td>
</tr>
<tr>
<td>-5 to -2</td>
<td>-1.19±0.71 ($P=0.090$)</td>
<td>-2.12±1.67 ($P=0.205$)</td>
</tr>
<tr>
<td>-10 to -6</td>
<td>-1.46±0.69 ($P=0.034$)</td>
<td>-3.11±1.61 ($P=0.054$)</td>
</tr>
<tr>
<td>-14 to -11</td>
<td>-0.72±0.83 ($P=0.39$)</td>
<td>-1.79±1.87 ($P=0.34$)</td>
</tr>
</tbody>
</table>

Values are means ±SEM. Days before the onset of menstruation are dated −14 to −2, days after are dated 2-14.
blood pressure at about the time of onset of menstruation. We did not confirm that systolic blood pressure is increased in the luteal phase [1] and found no evidence of an increase in systolic blood pressure at mid-cycle [3].

Changes in blood pressure through the menstrual cycle were seen in both normotensive and hypertensive women. The changes were somewhat more marked in the latter group, but differences between the groups did not reach statistical significance. It is possible that blood pressure variations through the menstrual cycle may be greater in those subjects with hypertension than in those without, but further study is required to confirm this possibility.

The changes in blood pressure during the menstrual cycle cannot, at present, be fully explained. Although exogenous progestagens may cause an increase in blood pressure [9], there is evidence that natural progesterone may have a blood-pressure-lowering effect [10]. The lower blood pressure levels in the luteal phase occur when progesterone levels are high, and it is at least possible that endogenous progesterone may cause a small decrease in blood pressure. The rise in blood pressure at the onset of menstruation is probably not related to pre-menstrual salt and water retention [11] and, in the present study, the changes in blood pressure reported were corrected for any changes in body weight. When the data were analysed without correcting for body weight changes, the findings were similar. Physical or psychological stress might also contribute to a blood pressure increase at this time [12]. The present data do not allow firm conclusions, however, and the possibilities discussed remain speculative.

The UA-751 semi-automatic sphygmomanometer is convenient and easy to use, and is both accurate and consistent [5, 6]. Semi-automated sphygmomanometers allow repeated blood pressure measurements to be taken at home more frequently than is usually feasible when recorded by an observer using a standard sphygmomanometer. Such instruments also help to reduce or eliminate the 'white-coat effect' on blood pressure [13, 14], and to eliminate observer bias and digit preference.

We conclude that morning blood pressure alters during the normal menstrual cycle, being higher at the onset of menstruation and lower on days 17–26, when compared with the remainder of the cycle. This variation in blood pressure occurs in both normotensive and hypertensive women.

REFERENCES