Changes in Sodium and Uric Acid Concentrations in Plasma during the Menstrual Cycle

Michael Mira,1 Peter M. Stewart,2 Val Gebski,3 Derek Llewellyn-Jones,1 and Suzanne F. Abraham1

Hormonal changes during the menstrual cycle are well documented (1–3). However, changes in other biochemical variables have not been studied. We find that in the luteal phase of the menstrual cycle the concentrations of sodium and uric acid are significantly lower. The changes may be of significance for the determination of the normal reference interval.

Additional Keyphrases: variation, source of ovulation, reference interval

Hormonal changes during the menstrual cycle are well documented (1–3). However, changes in other biochemical variables have not been studied.

It is possible that changes in hormone concentrations during the menstrual cycle may influence the concentrations in plasma of commonly measured analytes and hence necessitate small but significant alterations to the normal reference interval for these analytes in women.

During that part of the cycle between ovulation and the onset of menstruation (the luteal phase), the concentration of progesterone is high. Progesterone reportedly has a natriuretic effect (4) and the increase in progesterone after ovulation is thought to be followed by a compensatory rise in aldosterone concentration (5).

Many women report retention of fluid during the premenstrual days, especially noting breast swelling and abdominal "bloating" (6). However, there is no clear evidence of a change in weight related to the menstrual cycle (7, 8).

After the menopause the concentration of uric acid in plasma increases (9). This is believed to result from the decrease in sex-steroid concentration, similar to that which occurs at the time of onset of menstruation.

We aimed to determine whether the changes in hormone concentrations during the menstrual cycle are reflected in changes in concentration of other analytes, specifically sodium, potassium, chloride, creatinine, urea, uric acid, and albumin, during the luteal phase and the follicular phase.

Materials and Methods

Subjects. Subjects were apparently healthy women, ages 25 to 40 years. None had a history of any significant past illness (including premenstrual tension) or recent acute illness. All refrained from taking any medication (including dietary supplements such as vitamins) for at least a month before the study.

Subjects were all menstruating regularly (cycle length between 25 and 35 days) and none was using hormonal methods of contraception.

Blood collection. Blood from a large antecubital vein was collected with a 19-gauge needle after the subject had been seated for 30 min. Tourniquet time was less than 2 min, and only one venipuncture was attempted.

We collected the blood samples on predicted cycle day 23 and on predicted cycle day 5 of the following cycle (i.e., 10 days between sampling), at the same time of day. Urine was collected over the expected time of ovulation in both cycles and assayed for lutropin. This allowed us to estimate the time of ovulation, ensuring that all sampling was done in the appropriate phase of the cycle and enabling us to correct the cycle length to 28 days.

Assays. Sodium, potassium, chloride, creatinine, urea, uric acid, and albumin were assayed by continuous-flow analysis (SMAC, Technicon).

Progesterone was determined with an \(^{125}\text{I}\) radioimmunoassay kit (Farmos Diagnostica).

Urinary lutropin was measured with a double-antibody liquid-phase radioimmunoassay kit (Diagnostic Products Corp.).

Data Analysis. After transforming the data logarithmically, we compared differences between luteal- and follicular-phase values by use of paired \(t\)-tests. To determine correlations, if any, between the biochemical variables and the day of sampling, we used Pearson's correlation coefficient.

Results

We studied 22 subjects, two of whom were excluded from the analysis because each had one anovulatory cycle during the study. The mean age of the 20 women remaining was 30 (SD 5) years.

All samples were collected between day 18 and day 25 in the luteal phase, and between day 4 and day 10 in the follicular phase (cycle length corrected to 28 days, counting the first day of menstruation as day 1).

Table 1 shows our results. The only significant differences we found were for the mean concentrations of sodium and uric acid in plasma, which were lower in the luteal phase than the follicular phase.

We observed no correlations between the changes in the biochemical measurements and the day in the luteal phase on which the sample was collected, the day in the follicular phase on which the sample was collected, the time interval

\[\text{Table 1. Values for Some Commonly Measured Analytes in Plasma during the Luteal and Follicular Phase}\]

<table>
<thead>
<tr>
<th>Analytes</th>
<th>Luteal</th>
<th>SD</th>
<th>Follicular</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>62.8</td>
<td>10.0</td>
<td>62.7</td>
<td>10.0</td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>140.8</td>
<td>1.9</td>
<td>142.5*</td>
<td>2.1</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.0</td>
<td>0.36</td>
<td>3.8</td>
<td>0.29</td>
</tr>
<tr>
<td>Chloride, mmol/L</td>
<td>106</td>
<td>2.0</td>
<td>105</td>
<td>2.4</td>
</tr>
<tr>
<td>Creatinine, (\mu)mol/L</td>
<td>70</td>
<td>10.0</td>
<td>72</td>
<td>10.0</td>
</tr>
<tr>
<td>Urea, mmol/L</td>
<td>4.7</td>
<td>1.15</td>
<td>4.9</td>
<td>1.74</td>
</tr>
<tr>
<td>Uric acid, mmol/L</td>
<td>0.255</td>
<td>0.054</td>
<td>0.286*</td>
<td>0.050</td>
</tr>
<tr>
<td>Albumin, g/L</td>
<td>47</td>
<td>3.2</td>
<td>47</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*Significantly \((p < 0.001)\) different from concentration during luteal phase.
between samplings, the luteal-phase concentration of progesterone, or change in body weight (if any) between the luteal and the follicular phase.

Discussion

Variation in sodium or uric acid concentrations in plasma during the menstrual cycle has not previously been described.

The fact that the change in plasma sodium is not associated with changes in weight or in concentrations of creatinine, urea, or albumin suggests that total body water and intravascular volume remain constant. Thus it appears that sodium is lost in excess of water in the period after ovulation.

Changes in progesterone concentrations are not correlated with the changes in plasma sodium during menstruation, suggesting that this hormone does not account for the change between the follicular and the luteal phase. Possible causes for this change in sodium concentration include the increased concentrations of antidiuretic hormone in the luteal phase (10), or of other steroid hormones or metabolites that were not measured in this study. This change in plasma sodium supports the claim of many women that they suffer changes in fluid balance in the premenstrual days.

The change in uric acid concentration parallels that seen after menopause. During the luteal phase the concentration of ovarian steroids in the circulation is high and the uric acid concentration is low, whereas in the follicular phase the reverse is true. Again, we saw no correlation between the concentration of progesterone in plasma during the luteal phase and the change in uric acid.

These changes in uric acid and sodium in plasma may have significance in terms of the normal reference interval, especially for sodium, which is controlled within narrow limits. The mean change reported here for sodium is equivalent to 20% of our laboratory reference range.

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References