A New Method for Predicting and Confirming Ovulation

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A new method for predicting and confirming ovulation

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Evaluation of a method for predicting and confirming ovulation by measurement of vaginal and salivary electrical resistance (VER and SER) was the purpose of this study. Eighteen menstrual cycles from 13 subjects were analyzed. A clearly defined nadir in VER at day 0, the day of the luteinizing hormone (LH) peak, followed by pronounced increase the following day was observed. A peak in SER was consistently observed 5 to 6 days before day 0. The correlation coefficient (r) between the cycle day of the SER peak and cycle day of the LH peak was 0.94. After the peak in SER, values were low for several days but increased 1 to 2 days before the LH peak. Results indicate that monitoring of SER and VER may provide the basis for a simple method for predicting and confirming ovulation. Fertil Steril 44:200, 1985

A simple and reliable method for predicting and confirming ovulation would be desirable both for the management of infertility and for increasing the reliability of natural family planning (NFP) as a method of birth control. Serial hormone assays, such as the midcycle assay for luteinizing hormone (LH) surge or serial pelvic sonograms, are expensive and inconvenient. More importantly, even if these could be conducted with ease, they do not provide enough prediction of ovulation to be useful in NFP.

The changes in mucus during the preovulatory phase of the menstrual cycle follow a characteristic trend. These changes are used by followers of the symptothermal method of NFP for birth control and by clinicians in the management of infertility. However, a significant drawback of the method is that the technique for self-evaluation of mucus is subjective; intensive training is required before the user becomes competent.

The changes in mucus volume and its ionic content in response to estrogen can be monitored objectively with a suitably designed instrument. This is the basis for one of the sensors of the fertility monitor evaluated in this study. This commercially developed instrument uses a second sensor to monitor the changes in ionic concentration of saliva. Sodium, calcium, and potassium concentrations of saliva have been previously reported to change during the menstrual cycle.

The objective of this study was to evaluate the potential usefulness of the CUE Fertility Monitor (Zetek, Inc., Aurora, CO) system as a method of predicting and confirming ovulation. Specifically, the study was designed to determine if changes in vaginal electrical resistance (VER) and salivary electrical resistance (SER) during the menstrual cycle could be related to the time of the LH surge.
which has a known relation to the time of ovulation.

MATERIALS AND METHODS

SUBJECTS

Data for this study were from 18 menstrual cycles in 13 subjects. Ten subjects were candidates for artificial insemination at either the University of Colorado Health Sciences Center or Rose Medical Center, whereas others were volunteers. All subjects had normal ovulatory cycles and were not on clomiphene citrate or any other form of medication. Because the objective was to generate preliminary information, it was believed that data from spontaneously ovulating subjects would be desirable.

EXPERIMENTAL MEASUREMENTS

The instrument evaluated in this study (the CUE Fertility Monitor) measured the electrical resistance of vaginal mucus (VER) and saliva (SER). The instrument is a battery-operated device with a digital readout that indicated the measured resistance at the sensors. A constant, alternating current source was used to minimize polarization effects at the electrodes. Calibration of the device was in arbitrary units; a tenfold difference in VER and SER prevented a direct ohmic readout in the instrument because it was designed to be simple to use. The units of the instrument were, however, directly proportional to resistance in ohms. The conductive electrodes of the sensors were stainless steel.

Each subject was provided with a CUE unit and instructed on its correct use, which included the proper placement of the vaginal probe. To obtain a VER reading, the subject would lie on her back and insert the vaginal probe so that it was in contact with the posterior fornix of the vagina. The digital reading was recorded on the data sheet. Because preliminary work indicated that the sequelae of intercourse would affect the VER readings, subjects were requested to obtain VER measurements during the late afternoon or to ensure that about 6 to 10 hours had elapsed from the time of intercourse.

Oral readings were taken soon after the patients awakened in the morning, before eating, drinking, smoking, etc., but without any restriction on movement. To obtain an SER reading, the subject placed the oral probe on the surface of her tongue, after swallowing excess saliva, and recorded the digital reading. Because sodium in saliva has been found to have a circadian rhythm, SER readings were required to be taken at approximately the same time each morning. Electrolytes in saliva are also affected by its flow rate; therefore, SER measurements were obtained upon awakening, before any stimulation of the salivary glands.

Subjects recorded daily the date, day of cycle, basal body temperature (BBT), SER, VER, menses, and occasions of coitus. Other symptoms or variations in routine that were judged by the subject to be important were also recorded. Daily readings were obtained from subjects by telephone and a separate record maintained for each subject. This record was verified against the subject's own record sheet at the end of each cycle.

The subjects underwent several midcycle serum LH assays for determination of the day of their LH surge. These assays were timed according to their reported cycle length. The highest of the midcycle LH values was considered to be the LH peak. The assays for LH were done by a commercially available radioimmunoassay kit (Diagnostic Products Corporation, Los Angeles, CA), and were conducted at either the University of Colorado Health Sciences Center or at the Rose Medical Center, Denver, CO.

For analysis and summarization of the VER data, the cycle day of the LH peak was designated as day 0. For SER data, however, cycles were combined relative to the peak value observed on or after the fifth day from the beginning of the cycle. The cycle day of the SER peak was designated stage A, with other cycle days indicated by plus or minus as appropriate.

RESULTS

One of the subjects in the group had premature ovarian failure, and therefore her data were excluded from the pooled data set. Cycle day 0 was well defined by a progressive increase and decrease in LH concentration. Mean (± standard error of the mean [SEM]) LH concentrations (mIU/ml) on cycle days $-2, -1, 0$, and $+1$ were $16.3 (± 2.9), 34.2 (± 4.9), 87 (± 16.3),$ and $34.9 (± 9.3)$, respectively.

Mean (± SEM) BBT values by cycle day are given in Figure 1A. The postovulatory temperature shift is clearly visible. Changes in BBT dur-
The mean VER at day 0 (cycle day of LH peak) was compared with average VER values of certain other cycle days (Table 1). The VER at cycle day 0, with a value of 68.5, was significantly different from the mean VER for all other days and the mean values for days −2 and +1, but not from the mean value for day −1.

The first peak in SER values from each cycle, occurring on or after the fifth day of the menstrual cycle, was defined as stage A. The mean changes in SER during the preovulatory phase are shown in Figure 2. The preovulatory peak, stage A, is defined by a gradual increase in SER for several days and then a sharp decline after the peak value. The change in SER from stage A to A +1 was statistically significant (P < 0.05). The SER values were low for 3 days after stage A, at which time it was approximately 40 units lower than at stage A. Beginning on the third day after

**Table 1. Comparison of VER Mean on Day 0 with VER Mean on Certain Other Cycle Days**

<table>
<thead>
<tr>
<th>Cycle day</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>68.5 ± 6.2</td>
</tr>
<tr>
<td>−2</td>
<td>106.7 ± 15b</td>
</tr>
<tr>
<td>−1</td>
<td>83.0 ± 8.4c</td>
</tr>
<tr>
<td>+1</td>
<td>116.6 ± 11.3d</td>
</tr>
<tr>
<td>All cycle days excluding day 0</td>
<td>130.8 ± 4.0d</td>
</tr>
</tbody>
</table>

*Statistical significance was by t-test.

bP < 0.05.

Not significant.

cP < 0.001.

or 70%. After this rise, VER values remained elevated for the rest of the luteal phase.

Figure 2
Change in SER during the follicular phase of the cycle.
stage A, values increased for several days. The first increase in SER after the nadir, stage B, usually occurred 1 to 2 days before the LH peak. Of the LH peaks observed for the 17 cycles, 8 (47%) occurred on the fifth day (A + 5), 8 (47%) on the sixth day (A + 6), and 1 (5.8%) on the fourth day (A + 4) after stage A.

The relation between the cycle day of the occurrence of stage A and the cycle day of the LH peak is shown in Figure 3 in the form of a regression line. The correlation coefficient (r) of 0.94 indicates a strong relationship between the two variables. The regression coefficient of 0.98, together with an intercept of 5.54 indicates that, on the average, the predicted cycle day of the LH peak would be about 5 or 6 days after stage A. The regression coefficient of approximately 1 indicates that a change in the cycle day of stage A by a given number of days would be reflected by a change in cycle day of the LH peak by a similar amount.

The VER and SER trend of the anovulatory subject is shown in Figure 4, and is clearly atypical, when compared with the changes observed in ovulatory cycles.

**DISCUSSION**

The daily assay of serum LH at midcycle has been shown to be a reliable method of detecting the time of ovulation. In a majority of cycles, ovulation is expected to occur within 24 hours of the LH peak. Thus, it is to the day of the LH peak that all other measurements in this study have been related.

The changes in BBT (Fig. 1A) were very similar to previous findings. Mean (± SEM) BBT of 97.64 (± 0.028) °F during the follicular phase increased to 98.17 (± 0.24) °F during the luteal phase. A preovulatory dip in mean BBT was observed on day -3, and may have coincided with rising estrogen levels. A distinct change in mean BBT was not observed to coincide with the LH surge. The first significant rise in mean BBT was on the first day after the LH peak, the rise then continuing for 2 more days. Thus, these findings are consistent with previous observations that the BBT record, although it provides evidence of ovulation, does not provide the means for predicting it.

Mean changes in VER (Fig. 1B) indicate a clearly defined nadir on the day of the LH peak.
The VER mean at day 0 was significantly lower than the overall mean for all other days. Thus, the absolute value of VER, combined with the rapid decline from day -3 onwards, may be interpreted as a sign of imminent ovulation. However, because the VER nadir was not significantly lower than the value on the previous day, it may be difficult to identify day 0 on the basis of the absolute value of the VER. The most significant change in VER was on the day after the LH peak, when the mean VER was 48 units (70%) higher than on the previous day. Thus, this change may coincide with ovulation, which in most cases is assumed to occur within 24 hours of the LH peak.

Changes in VER may therefore not only indicate the onset of the ovulatory phase, but also pinpoint the day of its occurrence. In contrast to the BBT record, which confirms ovulation 2 to 3 days after its occurrence, VER change could be used for the short-term prediction of ovulation and also the early confirmation of it. In contrast, the VER trend of the anovulatory subject (Fig. 4A) is quite typical and consistent with insufficient estrogen production during the preovulatory phase.

The phenomenon of ferning described by several investigators for cervical mucus of both humans and nonhuman mammals is known to be maximized during the preovulatory estrogen peak. Ferning is due to formation of sodium chloride crystals in the presence of mucin. The proportion of sodium chloride in the dried component of mucus increases as ovulation approaches. Together with this increase in the NaCl content, a 10-fold to 12-fold increase in the volume, maximum spinnbarkeit, and lowest viscosity are also properties of mucus associated with the preovulatory estrogen peak. Although ferning, spinnbarkeit, and viscosity have been used as indices of approaching fertility, the subjective nature of their evaluation has been a disadvantage. The changes in VER observed in this study are primarily caused by changes in the ionic content of the mucus and its volume. Thus, VER measurement may provide a simple and practical method for evaluating changes in the cervical mucus for the detection of ovulation. Although the use of VER measurements for predicting ovulation in humans has not been previously reported, the technique has been successfully used in farm animals; several studies have shown the VER nadir to coincide with the LH peak in cows.

The changes in SER observed in this study (Fig. 2) followed a predictable pattern during the preovulatory phase. A peak SER value (stage A) was consistently seen 5 to 6 days before the cycle day of the LH surge. After stage A, SER remained low for 3 days but increased before ovulation. Sodium and calcium concentrations in submaxillary saliva were reported to decline to their lowest levels during the ovulatory period. Similar findings were reported for sodium in whole unstimulated saliva. These decreases in ionic content are consistent with our finding of increasing SER during the LH surge.

The most consistent feature of the SER data was, however, the timing of stage A relative to the cycle day of the LH peak. The strong relation between these variables (Fig. 3) is an indication that the cycle day of stage A could be used to predict the day of the LH peak and, therefore, ovulation. Even when stage A is identified after the decrease in SER on the following day, the SER record may enable the prediction of ovulation 5 to 6 days before its occurrence. The SER data from the anovulatory subject (Fig. 4B) are in contrast to the trend for ovulatory cycles, shown in Figure 2. Thus, the characteristic trend in SER after stage A, leading up to stage B and ovulation, is likely to lend additional confidence to the prospective user of the method. Although caution is indicated because of the relatively small sample size involved, the SER record may provide a method of predicting ovulation before the onset of the fertile phase of the menstrual cycle.

A possible physiologic rationale for the observed changes in sodium concentration, and therefore SER, may be related to the effect of estrogen on the renin-angiotensin system, as has been postulated. Estrogen is believed to stimulate the synthesis of angiotensinogen, which, by action of renin, is converted to angiotensin-I and subsequently to angiotensin-II. Angiotensin-II acts on the adrenal to increase the secretion of aldosterone. This is the suggested mechanism by which blood volume is increased during pregnancy and has also been implicated in the occurrence of reduced sodium levels observed in submaxillary saliva of pregnant women. Although estrogen levels during nonpregnancy are markedly lower than in pregnancy, the above pathway may be operative during the late follicular phase and especially at the preovulatory estrogen peak, resulting in increased aldosterone.
secretion. Increased aldosterone secretion results in lowered sodium concentration of both parotid and submaxillary saliva\textsuperscript{16} and is probably the cause of the preovulatory drop in salivary sodium\textsuperscript{6} and the resulting increase in SER that was observed at this time. In a previous study,\textsuperscript{17} a 3-day period of sodium retention was observed during the immediate preovulatory phase, which coincides with the increasing periovulatory SER values that were observed in this study. Preceding the sodium retention phase was a 3-day period of increased sodium excretion (higher sodium in urine and saliva), which corresponds with declining SER values after stage A (on days A1 to A3). Thus, the beginning of the 3-day preovulatory period of increased sodium excretion was observed 6 days before ovulation and is consistent with our observation of declining SER after stage A, 5 to 6 days before the cycle day of the LH peak. Because aldosterone promotes the resorption of sodium at the level of the kidneys and the salivary glands,\textsuperscript{16} the agreement between renal sodium excretion and observed SER trend is additional confirmation that the change in SER during the menstrual cycle is probably mediated by the action of estrogen on the renin-angiotensin system and thus on aldosterone secretion.

The results of this study indicate that SER may be used to obtain an indication of the beginning of the fertile phase of the cycle by predicting ovulation 5 to 6 days in advance, whereas VER enables a more short-term indication and later a confirmation of ovulation. Thus, the two methods may be combined to accurately define the fertile phase of the menstrual cycle. The method may result in a simple but reliable tool for the management of infertility and an aid to the practice of NFP.

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REFERENCES