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Variability in the Hormonally Estimated Fertile Phase of the Menstrual Cycle

Richard Fehring
Marquette University, richard.fehring@marquette.edu

Mary Schneider
Marquette University, mary.schneider@marquette.edu

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Richard J. Fehring
College of Nursing, Marquette University, Milwaukee, WI

Mary Schneider
College of Nursing, Marquette University, Milwaukee, WI

Abstract

The purpose of this study was to determine the variability in length of the fertile phase of the menstrual cycle with 140 participants who produced 1,060 cycles with an electronic hormonal fertility monitor. The length of the fertile phase, as defined by the first day with a threshold level of urinary E3G and ending with a second day above a threshold of LH, varied from <1to >7 days, with the most frequent length being 3 days.

Pregnancy from a single act of intercourse is close to zero outside of the day of ovulation or the 5 days preceding ovulation. These days with a probability of pregnancy have been referred to as the ''6-day fertile window'' (1). The probability of pregnancy

during the fertile window can decrease or increase because of other factors such as the presence or absence of cervical mucus and, in particular, increased age (2–5). What is not well known is whether and how much the length of the fertile window varies from cycle to cycle and from woman to woman.

Kuelers et al. (6) sought to determine the variability of the fertile window with 404 subfertile women who attended a fertility clinic and had menstrual cycle lengths from 25 to 35 days. For this study the first day of the fertile window was defined as the day of sexual intercourse resulting in the first normal sperm-to-mucus interaction as determined by a postcoital test or by the first laboratory analyzed sperm– mucus interaction. The end of the fertile window was the estimated day of ovulation as determined by ultrasound observation of the dominant follicle and resultant collapse. All women in the study had daily or every other day ultrasound exams for follicular dynamics at least 5 days before the estimated day of ovulation as well as cervical mucus aspirations.

The researchers discovered that the length of the fertile window varied from <1 day to >5 days, and the most frequent length was 3 days. They also found a strong relationship between length of the fertile window and the percentage of couples conceiving, with the longer length of the fertile window related to the quickest time to conception and an ongoing pregnancy. The researchers indicated that these findings disproved the maxim that the fertile window is a fixed 6-day period ending on the day of ovulation. They concluded the length of the fertile window varies considerably among subfertile couples, and is related to the time to pregnancy.

Although the Kueler et al. (6) study provided evidence for the variability of the length of the fertile window between couples with subfertility, further study is needed to verify these results among a population of women with normal fertility and to determine the variability of the 6-day fertile window between cycles in the same woman. The purpose of the current study was to determine the inter and intra variability of the length of the fertile window among women with normal fertility.

This was a retrospective analysis of a menstrual cycle data set produced by 165 healthy women participants from four clinical sites in three cities (i.e., Atlanta, Milwaukee, and St. Louis) who sought instructions on natural methods of fertility regulation. The participants had menstrual cycles within the range of 21–42 days, had not used hormonal contraceptives for the past 3 months, if postbreastfeeding, had experienced at least 3 menstrual cycles past weaning, and had no known fertility problems. The retrospective data analysis for this study received internal review board approval from the Marquette University Office of Research Compliance.

The 165 participants were taught how to monitor their fertility by observing and charting their daily externally observed cervical mucus observations and by use of a handheld electronic hormonal fertility monitor called the Clearblue Easy Fertility Monitor (CEFM; Unipath, Ltd, Bedford, England). The CEFM monitor was designed to read test strips with antibodies for estrogen and LH and provide the user with a daily reading of low, high, or peak fertility (7). The high reading of the monitor indicates a threshold level of urinary estrone-3-gluconuride (E3G), and the peak reading indicates a threshold level

of urinary LH. Product testing has shown the CPFM detected the LH surge in 169 of 171 cycles from 88 women, in agreement with a quantitative radioimmunoassay for LH (8).

The participants recorded their cervical mucus observations and information from the fertility monitor on a fertility chart. All data charts were sent to the investigators, and information from each chart was entered into a data set. The 165 participants produced 1,335 menstrual cycle data charts, of which 1,181 (88%) had usable and complete data.

For the purpose of this study the last day of the fertile window (and the estimated day of ovulation [EDO]) was the second peak day on the CEFM monitor. The Clearblue monitor automatically provides 2 peak days when the urinary threshold of LH is reached. The beginning of the fertile window was the day of the first high reading (i.e., threshold of E3G detected) on the monitor. The 15th version of the Statistical Package for Social Scientists was used to calculate descriptive statistics.

Menstrual Cycle Data Sets

Participants (of the original 165) were included only if they produced three or more menstrual cycles of data. Twenty five of the participants produced one to two cycles and were eliminated to reduce the data set to 1,142 cycles or 96.6% of the original 1,181. The data set was decreased further to include only those cycles with a CEFM identified peak, that is, an EDO. The final total number of cycles was 1,060 or 92.8% of the 1,142.

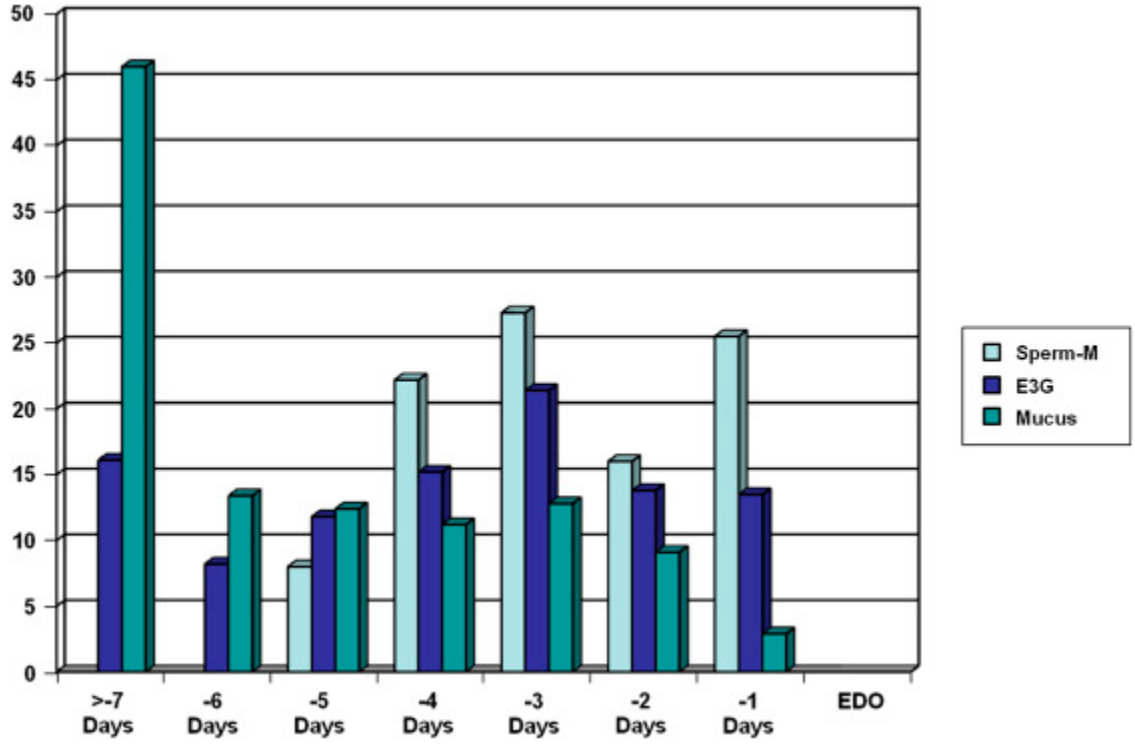
Demographics

The mean age of the 140 participants was 29.0 years (SD = 5.6; range 19–44), with a mean of 1.3 children (SD = 1.7; range 0–8). Each participant generated 3–13 cycles of data, with the mean being 5.2 cycles (SD = 3.2). The 1,060 menstrual cycles generated had a mean length of 28.97 days (SD = 3.35; range 21–50). Further information on these participants and menstrual cycle parameters can be found in an earlier study (9).

Intervariablility of the fertile window

Based on the E3G threshold as the beginning of the fertile window, the mean length of the fertile window was 5.1 days (SD = 2.59; median = 5 days). The estimated length of the fertile window varied from <1 to >7 days, with the most frequent length being 3 days. Frequencies of the number of days before the EDO were as follows: 1 day, N = 141 (13.5%); 2 days, N = 144 (13.8%); 3 days, N = 233 (21.4%); 4 days, N = 159 (15.2%); 5 days, N = 123 (11.8%); 6 days, N = 86 (8.2%), and ≥7 days, N = 168 (16.1%). See Figure 1 for percentages in comparison to the Kueler et al. (6) study results.

Figure 1. Percentage **c**omparison of the estimated length of the fertile phase of the menstrual cycle by sperm–mucus (sperm-m) interaction, threshold E3G, and self-observed cervical mucus in relation to the estimated day of ovulation (EDO).



Based on the beginning of high-rated (i.e., 3 to 4 on a 1–4 rating scale) externally observed cervical mucus and the monitor EDO, the mean length of the cervical mucus estimated length of the fertile window was 6.6 days (SD = 3.34; median = 6 days), but when the estimated length was based solely on cervical mucus, it was estimated to be 10.49 days (SD = 3.56; median = 9). In comparison to the CEFM estimated variability of the length of the fertile windows the high-rated cervical mucus estimate was as follows: 1 day, N = 30 (2.9%); 2 days, N = 40 (3.9%); 3 days, N = 93 (9.1%); 4 days N = 115 (11.2%); 5 days, N = 127 (12.4%); 6 days, N = 137 (13.4); and ≥7 days, N = 472 (46.0%). Again, see Figure 1 for comparisons.

Intravariability of the fertile window

The mean intradifference in length of the fertile window (based on the CEFM high readings) was 5.14 days (range. 0–16 days) (SD = 2.94). The frequencies of difference are as follows: 1 day, N = 9 (6.4%) 2 days, (N=0) (7.1%); 3 days, N = 18 (12.8%); 4 days, N = 28 (19.9%); 5 days, N = 21 (14.9%), 6 days, N = 19 (13.5%); R≥ days, N = 33 (23.43%).

Like the recent Kueler et al. (6) study among women with subfertility, this study found (intra and inter) variability in a length of the fertile phase of the menstrual cycle among women with normal fertility. Also like the Kueler et al. (6) study, we found that the most frequent length of the fertile if length of the fertile phase was 3 days when estimated by the first day of the E3G threshold. However, our results showed greater variability in length with a higher percentage of the lengths >5 days. The participants in

our study had a greater range of menstrual cycle lengths than the Kueler et al. (6) study. Another study showed that among 305 women in a randomized control trial of the CEFM to achieve pregnancy, the greatest percentage of ‘‘high’’ fertility days was 3 days before the first peak day of the monitor (10).

Physiologically it makes sense that the rate of follicular development would vary from cycle to cycle, that the rate of estrogen production from the developing follicles would vary, and that a small percentage of early growing follicles might stimulate higher levels of estrogen but not proceed to ovulation (11). Of further interest is that the variability in length as estimated by self-observation of cervical mucus was inconsistent with these findings in that there was an overestimation of the length and a kurtotic shift to the left from the estimated day of ovulation. Furthermore, the high-rated cervical mucus overestimated the actual length of the 6-day fertile phase on average by 4 days.

A limitation of this study is that the estimation of the fertile phase by use of the CEFM and the threshold of E3G and LH is not precise. There is a 2–3-day variability in the estimation of the actual day of ovulation. Based on a study that compared the actual day of ovulation by ultrasound with the peak day (LH surge) of the CEFM, ovulation occurred on the 2 peak days and the subsequent high day 98% of the time, but never before the peak on the monitor (12). Although not as accurate as ultrasound, Kueler et al. (6) and others have recommended that LH is a reasonable alternative to ultrasound to estimate the day of ovulation and the length of the fertile phase (6,13). Furthermore, the serum measured estrogen rise (serum estradiol) has been viewed by experts as the major physiologic determinant of the onset and duration of the fertile period (14). The rise of estradiol in plasma or a metabolite in urine has been suggested as an indicator to the start of the probable fertile phase (15). Other researchers have demonstrated that the CEFM levels of LH and E3G coincide well with the laboratory measurements in defining the potentially fertile period, and found that they follow the increasing concentrations of serum estradiol on the days before ovulation (12,16). They also found the mode warning of ovulation by the CEFM high was 6 days (range, 0–20 days) (12).

Implications of this study, as with the Kuelers et al. (6) study, is that the length of the fertile phase might be <6 days in many menstrual cycles. If so, then couples seeking to either achieve or avoid a pregnancy would benefit using indicators of fertility that can track the variable length of the fertile phase. Furthermore, Kuelers et al. (6) found that longer fertile phase length was associated with a higher probability of a conception and ongoing pregnancy. Use of the CEFM would be a very usable method to determine if length of the fertile window is predictive of conception and ongoing pregnancy. Ongoing studies are in progress to determine if length (i.e., early or late intercourse in the fertile phase) is predictive of conception (17).

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