Physiological signs of ovulation and fertility readily observable by women

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Introduction: Confirmation of ovulation can be difficult in clinical practice, as gold standard methods including serial transvaginal ultrasonography, serum luteinizing hormone (LH) measurements, or laparoscopic follicular observation are impractical. Numerous surrogate markers have been proposed and evaluated in relation to these gold standards that have more practical clinical applications.

Purpose: To review the evidence on physiological signs of ovulation timing and fertility in order to determine valid markers that can be easily identified by women.

Methods: A literature review of primary resources in Ovid Medline was undertaken to identify studies examining physiological signs as they relate to gold standard assessment of ovulation. Studies examining the efficacy/effectiveness of different types of natural family planning were excluded.

Results: The most commonly encountered physiological signs were urine LH, cervical mucus, and basal body temperature (BBT). Urine LH as assessed by home monitoring systems indicated ovulation 91 percent of the time during the 2 days of peak fertility on the monitor and 97 percent during the 2 peak days plus 1. Cervical mucus peak characteristics were identified 78 percent of the time ± 1 day, and 91 percent of the time ± 2 days of LH surge indicating ovulation. Further research supports the importance of cervical mucus in overall fertility, as conception rates were more closely related to mucus quality than to timing of intercourse related to ovulation. As a lone indicator of ovulation, BBT is at best a retrospective marker, and functions best in conjunction with other signs of ovulation. Additionally, salivary ferning, salivary and vaginal fluid electrical potential, finger–finger electrical potential, and differential skin temperature were postulated as possible indicators, but were not found to be temporally related to ovulation. The research on differential skin temperature is promising, but minimal thus far in number, and has not been evaluated as an adjunct to BBT as yet.

Conclusion: Home urinary LH monitors are becoming more widely available and less expensive giving women the potential to assess the ovulatory status of their cycle in real time. Cervical mucus observation is an effective and cost-efficient method, but requires some teaching to increase the confidence of users. In conjunction, LH monitors and cervical mucus can give the best indication of fertility and ovulation timing.

Keywords: ovulation, cervical mucus, luteinizing hormone, basal body temperature

INTRODUCTION

Ascertaining the ovulatory status of a woman's cycle has particular applications beyond the assessment of infertility. Evaluation of any combination of heavy, irregular, or painful bleeding can be aided by an awareness of ovulation. The gold

standards in determining ovulation are daily transvaginal ultrasonography and laparoscopic evaluation of the developing follicle until the point of rupture. This approach has obvious barriers to its use in the general population due to the invasive nature of the procedures. Conversely, using a basic physiological end point, "the

only positive confirmation of ovulation is the identification of an ovum in the female reproductive tract or the subsequent detection of a pregnancy" (Martinez et al. 1995). In between these two extremes "the prediction and detection of [ovulation's] occurrence [has] to be based on markers or indicators that lie at varying physiological distances from ovulation itself" (Martinez et al. 1995). The World Health Organization endeavored to discover the "temporal relationships between ovulation and defined changes in the concentration of plasma oestradiol-17B, luteinizing hormone, follicle-stimulating hormone and progesterone" (Anonymous 1985). This study, looking for a suitable chemical marker of ovulation, found that "both the rise and peak days and the day of the luteinising hormone (LH) peak were less significantly different" than other markers indicating ovulation. LH peak in the urine or serum is often used as a corollary indicator of ovulation when compared with other potential markers of ovulation. Many different physiological signs have been investigated for their accuracy and practicality in predicting ovulation.

METHODS

A literature review was undertaken looking for studies directly addressing the primary research question of which physiological signs easily identifiable by women are the best indicator of ovulation and fertility. Using the search strategy below, an initial 128 articles were identified. After reviewing the abstracts, the studies dealing specifically with method efficacy were discarded and those addressing the relation of physiological signs to ovulation were included in the review. This produced 24 suitable studies, whose references were then examined and an additional six studies were included.

Database: Ovid MEDLINE(R) <1946 to December Week 4 2011>

Search Strategy:

- 1 exp Ovulation Detection/ (927)
- 2 exp Ovulation Prediction/ (17)
- 3 exp Natural Family Planning Methods/ (426)
- 4 exp Family Planning Services/ (21 735)
- 5 fertility awareness.mp. (106)
- 6 1 or 2 or 3 or 4 or 5 (22 701)
- 7 exp Cervix Mucus/ (2767)
- 8 exp Body Temperature/ (69 471)
- 9 exp Luteinizing Hormone/du, ur [Diagnostic Use, Urine] (1233)
- 10 exp Ovulation/ph, ur [Physiology, Urine] (3249)
- 11 7 or 8 or 9 or 10 (76 280)
- 12 exp Fertility/ (29 498)
- 13 exp Contraception/ (20 791)
- 14 12 or 13 (48 330)
- 15 6 and 11 and 14 (219)
- 16 limit 15 to humans (167) & English (128)

MODERN HOME OVULATION MONITORS

Since 1982 "peak of LH was used as a reference point for ovulation and defined [...] Day 0," (Branch Collins and Collins 1982), setting a frame of reference for other hormone measures. By 1985, the "WHO study reported that ovulation occurred at a median time of 8 hours after the rise in plasma progesterone, 15 hours after the LH peak and 24 hours after the oestrogen peak" (Gross 1987). In search for a more practical measure for outpatient use Luciano et al. (1990) found that "assessment of the mid-cycle LH surge, either in serum or urine, is the most reliable predictor of ovulation."

This discovery opened the door for the development of home urinary hormone assays for the prediction of ovulation. Although, specific monitors vary in the

timing of urinary measurement, most rely on single daily readings. Modern monitors detect both estradiol indicating the onset of fertility and LH for ovulation. At that time, comparing the urinary LH surge with ultrasound findings as a direct reference for ovulation “was not useful ... because the size at which follicles rupture [varied] significantly” (Luciano et al. 1990), due to technical limitations that were later rectified. It is vital when “testing new family planning methods [...] for a systematic comparison between luteinising hormone expected date of ovulation and US-DO [ultrasound day of ovulation]” (Ecochard et al. 2001).

This approach by Ecochard et al. (2001) was important in discovering that “luteinising hormone-expected date of ovulation distribution is centred on the US-DO [and that ...] the average delay of luteinising hormone-expected date of ovulation with respect to US-DO was +0.46 days, which is significantly different from 0 (P, 0.01).” Recognizing that LH measures would always be imperfect they took “USDO ± 1 day to be a fair estimation of the day of ovulation, [and found that] luteinising hormone initial rise seemed to be more efficient than the luteinising hormone peak per se (77% vs. 67% of cycles)” (Ecochard et al. 2001).

Building upon that research, Behre et al. (2000) compared the urinary LH measurements taken with a Clearplan Fertility Monitor (CPFM) with serum hormone and transvaginal ultrasound. Similar to the above results, “ovulation was detected in 91.1% of cycles during the 2 days of CPFM peak fertility and 97.0% during the 2 peak days plus 1,” which was comparable to “ovulation [...] observed in 51.1% of cycles 1 day and in 43.2% of cycles 2 days after the surge in serum LH” (Behre et al. 2000). Interestingly, “ovulation never occurred before CPFM peak fertility or the serum LH surge day”

(Behre et al. 2000) further confirming the relative utility of the initial rise in LH as an ovulation predictor.

Interpreting the results for the purpose of guiding intercourse for conception is not as straightforward as picking the peak day of LH fertility on a monitor. Bigelow et al. (2004) found that cervical mucus “explained more of the variability in the day-specific probabilities of pregnancy than could be attributed to timing of intercourse relative to ovulation.” It is clear from these studies that LH monitoring is an excellent and practical surrogate marker for ultrasound or laproscopic evidence of ovulation.

CERVICAL MUCUS

The recent finding above from 2004 helps to confirm the utility of cervical mucus in the assessment of fertility, but does not touch on the prediction of ovulation related to this physiological sign. In the early 1950s, cervical mucus changes previously noticed by many gynecologists were examined for their application to the fertility of women. By the 1980s, it was widespread knowledge that “the peak mucus symptom is closely correlated with ovulation” (Gross 1987). As with other methods, quantifying the temporal relationship of peak mucus symptoms has changed with developments in gold standard technological advancements (transvaginal ultrasound). By 2001, “cervical mucus peak symptom was much closer to US-DO [ultrasound date of ovulation] or luteinising hormone-expected date of ovulation (USDO ± 1 day in nearly 75% of cycles compared with LH-expected date of ovulation ± 1 in nearly 70% of cycles)” (Ecochard et al. 2001), than BBT. Further quantification using a peak mucus scoring system “indicated that the peak in cervical mucus ratings was highest on the day of

the LH surge" (Fehring 2002), and that "ovulation occurred a mean of 0.9 days after the peak symptom, with a range of 3 days after to 2 days before" (Fehring 2002). The raw data in this study show that 78 percent of LH surges were within ± 1 day of peak mucus, and 91 percent within ± 2 days (Fehring 2002). Comparing an available LH urinary detection monitor with mucus found that the "average day for the peak of fertility by the [CPFM] and the self-observation of cervical mucus were very similar (i.e. day 16)" (Fehring, Raviele and Schneider 2004).

Although less specific an indicator for ovulation, changes in cervical fluid volume (CFV), regardless of fertile characteristics, revealed a "rise in CFV volume occurred between days -9 and -2 and a peak between days -4 and 0" (Flynn et al. 1988), with day 0 being the ultrasound day of ovulation. Knowledge of the fertile characteristics of cervical mucus has been taught, learned and applied by millions of women around the world for conception or pregnancy avoidance. "More ovulations (90%) were detected by the NFP instructor's inspection of vaginal CFV that was self-aspirated by women within G1 day from US-DO than by the women's observation of the same aspirated CFV samples (76%). This may show that a woman's CFV observation can improve further with training" (Alliende et al. 2005).

BASAL BODY TEMPERATURE

BBT changes have long been investigated as a potential indicator for detecting ovulation. The "biphasic nature of [the BBT] curve was first described in the 19th century" (Vollman 1977), which was mainly due to the rise in temperature related to increasing levels of progesterone immediately after ovulation. Daily basal measurements are taken orally before

rising from bed in the morning with a 2-decimal-place thermometer. Unfortunately, the results of work starting in the 1980s demonstrated that "none of the 4 BBT endpoints [(nadir, initial rise, dip and BBT coverline)] tested is precise enough to be a meaningful indicator of the "day of ovulation" in either research or clinical application" (Hilgers and Bailey 1980). Some proposed uses of BBT include "determining the premenstrual infertile period" (Gross 1987), and as a "retrospective method of indicating ovulation" (Barron and Fehring 2005). However, when compared with the gold standards, "body temperature measurements yielded a 30.4% correlation with the simultaneous ultrasonographic diagnosis of ovulation" (Guida et al. 1999), and "only 22.1% of the 77 cycles [...] determined by endocrine profiles to be ovulatory [...] demonstrated an interpretable shift" (Bauman 1981). Certainly, methods have been developed using BBT in combination with other signs of ovulation, cervical mucus as an example, and the "synopsis of the two cycle parameters [indicates] clinical ovulation, which corresponds within 1 day to the objective ovulation in 89% of the cycles" (Frank-Herrmann et al. 2005).

OTHER POTENTIAL INDICATORS OF OVULATION

Salivary ferning

Observation of salivary characteristic found that "in 88% of cycles there is a direct correlation between salivary ferning and the fertile phase" (Barbato, Pandolfi and Guida 1993) as well as a "connection between the ferning onset and mucus peak" (Barbato, Pandolfi and Guida 1993). Although peak fertile mucus has been proven to be a reliable indicator of ovulation, the relationship between salivary

ferning and peak mucus was that the onset of ferning was, on average, 6 days prior to peak mucus. This does suggest that salivary ferning is useful in identifying the onset of the fertile phase, but not for direct detection of ovulation according to available studies.

CUE fertility monitor

In the mid-1990s, a device designed to make “digital measurement of the electrical resistance of saliva and vaginal secretions” (Freundl et al. 1996) was developed and tested against gold standard indicators of ovulation. The relationship to ovulation was not always consistent; the “last day of fertility was shown in ten cycles 1–3 days after ovulation, in two cycles more than 3 days, and in three cycles at or before the day of ovulation” (Freundl et al. 1996). Further evaluation of “data from 21 menstrual cycles showed no statistical difference ($T=0.33$, $P=0.63$) between the CUE fertile period ... and the fertile period of the ovulation method” (Fehring 1996), but failed to show convincing evidence on changes more proximately related to time of ovulation. Confirming the utility of the CUE monitor for identifying fertility and infertility another study found “strong association [...] between the day of the CUE salivary peak and the day of the LH surge” (Moreno, Khan-Dawood and Goldzieher 1997), but, again, this was approximately 6 days prior to ovulation.

Finger electrical potential

A single study from 1978 “showed that in only five out of 104 cycles did the device show an isolated change at the time of ovulation. This device is not a reliable method either for prediction of or the detection of ovulation” (Poulson and

Carter 1978), and thus has not been examined since.

Skin temperature differential

Some limitations in BBT measurement are the many “factors that may affect the temperature readings [including] consumption of alcohol, having had a late night or disturbed night, oversleeping, holidays, travel, time zones, shift work, stress, illness, gynaecologic disorders, and medications” (Barron and Fehring 2005). In an attempt to “identify “dynamic” temperature points related to E2-induced vascularity and “static” temperature points reflecting the body’s core temperature” (Shah et al. 1984), a study was conducted using differential temperature points over the breasts of five healthy women. Although small in number the results “between a “dynamic” and “static” point, so located, provides advance information on ovulation timing independent of physiological disturbances and circadian and ambient temperature changes” (Shah et al. 1984). Unfortunately, no additional research was uncovered in this literature review to indicate the confirmation or integration of these findings with gold standard ovulation indicators or BBT methods of natural family planning.

CONCLUSION

Home urinary LH monitors have brought the capability of the laboratory in to the homes of average couples giving women the potential to assess the ovulatory status of their cycle in real time. Cervical mucus observation is an effective and cost-efficient method, but requires some teaching to increase the confidence of users. In conjunction, LH monitors and cervical mucus could give the best indication of

fertility and ovulation timing. Combining these two sources of information could improve optimal timing of intercourse for conception when both the peak mucus symptom and the LH surge coincide. Future research on a combination of the approach used by Bigelow et al., and Behre could lead to a more individualized understanding of peak fertility.

BBT shift should be used in conjunction with other signs of ovulation as confirmation if present, but not as a negative marker if absent. Modification of this sign using differential skin temperature measurement shows promise for rectifying the many possible disturbances in the accuracy of BBT.

Salivary ferning, electrical potential, and vaginal electrical potential have clear physiological change related to the onset of the fertile preovulatory period, but are not consistent or proximate enough to be markers of ovulation. Their main use at this point could be as additional markers for the fertile period in couples wishing to conceive or increase their confidence in using other signs such as cervical mucus.

Through this literature review it became clear that several markers of ovulation have more than 40 years of physiological data to support them. Clinicians need not shy away from an in-depth understanding of the physiology and its applications to the care of women, both in fertility and in infertility.

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BIOGRAPHICAL NOTE

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