

Natural Family Planning
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Natural Family Planning

Training in Fertility Awareness Based Methods Can be Helpful for Sub-fertile Couples Seeking Pregnancy

There is little evidence that the use of Fertility Awareness Based Methods (FABM) or Natural Family Planning (NFP) as a means to help focus intercourse during the estimated fertile phase of the menstrual cycles will improve pregnancy rates among sub-fertile couples. Researchers thus set out to determine the cumulative pregnancy rates among sub-fertile couples after they were taught a FABM of family planning.

A prospective observational cohort study was conducted by the researchers. It included 187 sub-fertile women (between the ages of 21–47) who were taught how to estimate the fertile phase of the menstrual cycle using a European FABM called *Sensiplan* (a Sympto-Thermal method that makes use of cervical mucus observations, basal body temperature readings, and a fertility algorithm). The women were asked to use the method for at least 8 months or until pregnancy.

The women participants were recruited from a local University based sub-fertility clinic and from advertisement in a local newspaper. The women participants and their male partners were recruited if they had been trying to achieve a pregnancy for at least one year. The study group had attempted to become pregnant for a mean of 3.5 years before the study began. Couples who experienced amenorrhea, known tubal occlusion and severe male factor were excluded from the study. Seven of the 187 women became pregnant before starting the study. Data from the seven women who had a spontaneous pregnancy before the study started were used to determine a comparative per cycle cumulative pregnancy rate of 21.6%. The participants were followed until natural pregnancy or until the last date of contact.

The researchers found a cumulative pregnancy rate among the 180 remaining sub-fertile couples was 38% (95% CI 27-49%; 58 pregnancies) after the FABM training and the eight months of use. They claimed that this rate is significantly higher than the estimated basic pregnancy rate of 21.6% in the seven untrained couples in the same cohort. For couples who had been seeking to become pregnant from 1-2 years prior to the study, the pregnancy rate increased to 56% after 8 months and for couples who had attempted to become pregnant for more than 2 years prior to the study had a cumulative pregnancy rate of 17%, $p < 0.01$). For the female participants above the age of 35, the cumulative pregnancy rate was 25%, $p = 0.06$. Both, increasing time to pregnancy and over the age of 35 significantly reduces the chances of conceiving naturally at some point. The researchers concluded that educating women with FABM to help them to self-identify their fertile window in the menstrual cycle seems to be a reasonable first-line therapy in the management of sub-fertility.

Comments

The reference group of only seven couples to establish a comparative pregnancy rate of couples not using FABM to focus intercourse is rather small. It would have been better to have a much larger cohort comparison. The best approach would be to have a random comparison. Until then, there will be skepticism that focused intercourse with FABM is any better in helping sub-fertile couples achieve pregnancy compared with just frequent random intercourse.

Frank-Herrmann, P., C. Jacobs, E. Jenetzky, C. Gnoth, C. Pyper, S. Baur, G. Freundl, M. Goeckenjan, and T. Strowitzki. 2017. **Natural conception rates in sub-fertile couples following fertility awareness training.** *Archives of Gynecology and Obstetrics* 295 (4): 1015-1024.

New Prediction Model of Natural Pregnancy for Sub-fertile Couples

Couples who wish to attain pregnancy and are unable to conceive after one year of trying with random intercourse are considered sub-fertile. About 30-60% of these couples with unexplained sub-fertility will conceive if they continue to try for another year. European standards indicate that couples who have unexplained sub-fertility should try for two years before seeking medical treatment. These are broad guidelines that apply to those couples who have primary and secondary sub-fertility. Seeking to have more precision to when sub-fertile couples should look for medical care, researchers from the Netherlands sought to develop a prediction model that can be used in a fertility workup and to provide couples with a predicted idea of their chances of pregnancy with natural intercourse and natural conception (van Eekelen, R., I. Scholten, R. I. Tjon-Kon-Fat 2017). The predictors in the model were female age, duration of sub-fertility, female sub-fertility being primary or secondary, sperm motility, and referral status.

The researchers used a cohort data set of 4,999 couples from 38 fertility clinics in the Netherlands that had no tubal occlusion, were not experiencing anovulation, and the male partner did not have a low sperm count. The outcome was the time to pregnancy that resulted in a live baby. They found of the 4,999 couples in the cohort, 1,053 (21%) women reached a natural conception that led to an ongoing pregnancy. Their prediction model estimated a 27% median probability of conceiving in the first year after the completion of the fertility workup. The percentage changed for couples not yet pregnant after half a year, one year, and one and a half years of expectant management. The median probability of conceiving over the next year was estimated at 20%, 15%, and 13%, respectively. The prediction ranges were sufficiently broad to aid in counselling couples for at least two years after their fertility workup. This dynamic prediction model allows reassessment of natural conception chances after various periods of unsuccessful expectant management. This gives valuable information to counsel couples with unexplained sub-fertility that are seen for a fertility workup. The dynamic prediction model needs to be validated in an external population.

Comments

This prediction model after further validation certainly could be a help for sub-fertile couples in discerning the need for medical treatments rather than just natural conception. It would be nice to also include in this prediction model as to whether couples are tracking their fertility with natural indicators of fertility. What could also be added are more specific parameters of the menstrual cycle, such as overall length, and length of the follicular and luteal phases—and most importantly indications of ovulation—ovulatory cycles.

van Eekelen, R., I. Scholten, R. I. Tjon-Kon-Fat, J. W. van der Steeg, P. Steures, P. Hompes, M. van Wely, F. van der Veen, B.W. Mol, M.J. Eijkemans, E. R. Te Velde ER, and N. van Geloven.

2017. **Natural conception: repeated predictions over time.** *Human Reproduction*, 32 (2): 346-353.

Effectiveness of an Online Natural Family Planning Program for Breastfeeding Women

Reviewed by Mary Lee Barron, PhD, APRN

A recent study is a very important addition to the care of women using Natural Family Planning (NFP) because breastfeeding and the breastfeeding transition to fertility are notoriously difficult for assessing fertile and non-fertile days. The researchers of the Marquette Method (with over a dozen studies since 2005) have previously published work on the 12-month pregnancy rate among breastfeeding and non-breastfeeding post-partum women who used an electronic hormonal fertility monitor (EHFM) to track fertility during the transition to fertility over 12 months of use and a special protocol. With the addition of the Marquette Method (MM) online system, four previous studies have been published examining the effectiveness of NFP among women with regular menstrual cycles, postpartum breastfeeding, peri-menopausal women, and women who desired to achieve pregnancy. The online MM postpartum breastfeeding protocol was modified to address the first six cycles postpartum and for the updated version of the EHFM.

The study is a longitudinal comparative cohort study of 816 women who were from all 50 U.S. A. states and five foreign countries. The women were primarily Caucasian (67.5%), Catholic (83.2%), well educated, married (for a mean of 5.57 years), and mother to about 3 children (mean of 2.97). Participants registered to use the Marquette Method online NFP system (<http://nfp.marquette.edu>) and indicated they were breastfeeding. The purposes of the study were two-fold: evaluate the effectiveness (i.e. correct use and total pregnancy rates) among women seeking to avoid pregnancy and to compare pregnancy rates among breastfeeding women who use the EHFM, cervical mucus monitoring (CMM), or both to assess their fertility status with breastfeeding.

Participants were instructed to avoid intercourse on high and peak estimated days of fertility and 3 full days past the last peak observation per MM protocol instructions. The period from birth to the return of menses is labeled as postpartum cycle 0. When menses return, women consider themselves fertile from Day 10 of the first menstrual cycle until 3 full days past the last peak of the monitor or last day of peak-rated cervical mucus. “The beginnings of the estimated first day of fertility for the next five menstrual cycles are tapered to begin on Days 9, 8, 7, and 6, respectively, and again to end three full days past the last peak reading. The tapering reflects the postpartum delay in the LH surge and day of ovulation that is experienced in the first six cycles postpartum.” Regular cycle instructions are followed once the woman has completed six cycles after cessation of breastfeeding.

Correct use pregnancy rates were based only on correct use menstrual cycles, and total pregnancy rates were based on correct use and incorrect or inconsistent use menstrual cycles and calculated over 12 menstrual cycles of use by survival analysis to produce survival rates (SR) and standard errors (*SE*; Kaplan-Meier). Researchers also calculated the differences in the frequency of total number of pregnancies among the three fertility indicator groups over 12 months of use by chi-square analysis with a probability of .05.

There were a total of 62 pregnancies among the 816 participants over 12 menstrual cycles of use, 36 in the first six menstrual cycles. The 12-cycle pregnancy rate was 14 per 100 users (SR = .86; SE = 0.019). Thirteen of these pregnancies were due to couples' conscious departure from the rules for avoiding pregnancy as indicated in their pregnancy evaluation form. Six of the unintended pregnancies occurred during the postpartum amenorrhea. Seven correct use unintended pregnancies over 12 cycles of use resulted in a 12-cycle correct use pregnancy rate of 3 per 100 users (SR = .97, SE = 0.009).

No significant differences occurred when comparing the EHFMM alone and EHFMM plus mucus observations in the correct use pregnancy rate [3 per 100 (SR = .97, SE = 0.009)] at 12 cycles of use for both subgroups. There were no correct use unintended pregnancies among the mucus-only participants ($n = 45$) at 12 cycles of use. However, there were significant differences in the method of determining fertility in the unintended pregnancy rate [EHFMM and the CMM-only group ($\chi^2 = 9.17, p = .002$) and between the EHFMM plus CMM and the CMM-only group ($\chi^2 = 11.89, p = .001$)]. Cervical mucus monitoring alone ($n=45$) resulted in a pregnancy rate of 81 at 12 cycles of use whereas EHFMM or EHFMM plus CMM resulted in a pregnancy rate of 16 and 12 respectively (per 100 users over 12 cycles of use). The high rate of unintended pregnancy associated with CMM may reflect the small sample size.

Comments

This is a very important study as postpartum breastfeeding is truly the most challenging time to counsel couples who are avoiding pregnancy with methods of NFP. The study reflects the reality of practice. This evidence demonstrates the MM online program and protocols are very effective in helping breastfeeding women and couples. Breastfeeding may lead to prolonged periods of abstinence because of the variability of fertility signs. Having the tools to promote accuracy in reading fertility signs is part of professional practice, but also, demonstrates sensitivity to not only the life-giving aspect but also the love-giving aspect of marriage.

Fehring, R. J., Schneider, M., and Bouchard, T. 2017. **Effectiveness of an Online Natural Family Planning Program for Breastfeeding women.** *Journal of Obstetrics Gynecologic & Neonatal Nursing* 46 (4): e129-137.

Primary Reason for Use of Creighton Model NFP is that it is Natural

Methods of Natural Family Planning (NFP) use biological indicators of fertility to help women to estimate the beginning, peak and end of the fertile phase of the menstrual cycle. With this knowledge women and couples can use these markers to help avoid, achieve, and/or monitor the menstrual cycle for health purposes. The Creighton Model (CrM) is a standardized system for educating women and couples primarily about the changes in cervical mucus in relation to other biomarkers such as menses to estimate the fertile and infertile phases of the menstrual cycle. With this information couples can discern whether they want to use those days to achieve or avoid a pregnancy. Currently, CrM researchers are conducting a prospective cohort study of CrM that is titled "Effectiveness, Intentions, and Behaviors Assessment" (CEIBA) to assess fertility motivations, intentions, fertility-related sexual behaviors, and their impact on effectiveness to avoid and to conceive among new users of the CrM. The current report of this

study involves the characteristics of couple users of CrM when they are first enrolled into a CrM educational program (Stanford and Porucznik 2017).

The couple participants for this study were obtained from 17 CrM educational programs in the USA and Canada. The couples were enrolled prospectively and at enrollment completed an extensive intake form that assessed their characteristics. The couple participants were new or returning users of the CrM. Couples who were trying to conceive or had a history of sub-fertility were excluded. The CrM instructors or CEIBA study staff enrolled and assessed 1,132 new couples but of these couples 429 (39%) couples were eligible and of these 305 women (71%) and 290 (95%) male partners were enrolled. The majority of the women participants were engaged (39%) or married (51%) most were college graduates (77%), white (80%), and listed as Catholic (80%).

The researchers found that the most common reasons that the women participants gave for learning the CrM was to use a natural method of family planning (91%), followed by moral/ethical/religious reasons (70%), the lack of side effects (71%), and knowledge of the menstrual cycle and fertility (62%). About 21% of the women participants intended to have a child within a year and 60% between one and three years and had a motivation score of doing so of 3.3 (range 1–4, with 4 being most positive). The reasons the men gave for using NFP were to use a natural method of family planning (76%), for moral/ethical or religious reasons (70%), for wife/partner's choice (62%) and lack of side effects (61%). Males also had a motivation score of 3.3. The authors concluded that when couples begin using NFP to avoid pregnancy they usually have high levels of motivation, desire, and intention for future childbearing. The CEIBA study researchers will be assessing, in future studies, whether couple's desires, intentions, and behaviors to achieve pregnancy will have an impact on pregnancy rates

Comments

Health professionals and others often assume that the major reason that couples use NFP is for religious reasons. This study and others, show that religion is often not the top reason for doing so. Future results of this study as to how couples' desires, intentions, and behaviors for achieving pregnancy affect unintended pregnancy rates will be of interest.

Stanford., J. B. and C. A. Porucznik. 2017. **Enrollment, Childbearing Motivations, and Intentions of Couples in the Creighton Model Effectiveness, Intentions, and Behaviors Assessment (CEIBA) Study.** *Frontiers in Medicine* 4 (article 147): 1-10.

Use of Natural Family Planning Perceived to Improve Marital Relationships

Previous survey studies that investigated the effect of using NFP on marital relationship have generally been with relatively small numbers of participants, with older methods of NFP (i.e., temperature only), and with single natural indicator methods (i.e., cervical mucus or temperature only). Previous studies, however, have provided evidence, that even though NFP methods require periodic abstinence users generally respond that use of NFP has been beneficial for their marital relationship. Researchers wished to conduct a study with a large respondent base from multiple countries and with couples that used a method of NFP that uses multiple natural

indicators of fertility, i.e., the Symptom-thermal method (STM) that uses temperature and mucus as key indicators to estimate the fertile time of the menstrual cycle Unseld, Rötzer, Weigl, Masel, and Manhart 2017). Specifically, they conducted a prospective multi-country study to describe the characteristics of STM users, understand their perceptions of NFP, and its perceived impact on relationships.

The researchers used an online survey that was sent to NFP users from two major NFP organizations in the U.S.A. (Couple to Couple League or CCL) and seven Europe countries (Institut für Natürliche Empfängnisregelung or INER). Of the 6,827 internet invitations (3,750 in the U.S.A. and 3,077 in Europe), 2,560 completed the questionnaire which yielded a response rate of 37.4% (32.4% in U.S.A. and 43.7% in Europe). The online questionnaire included questions on socioeconomic, health, gynecological, NFP, and sexual topics and was first developed in English and translated into the language of the seven European countries. The survey included a male and female form. The researcher found that 47% of the respondents had previously used contraceptives and that 95% of women and 55% of men said using NFP has helped them to know their body better, 64% of women and 74% of men felt NFP helped to improve their relationship, while <10% felt use of NFP had harmed their relationship. Most women (53%) and men (63%) also felt that NFP improved their sex life. Overall, 75% percent of women respondents and 73% of men said they were either "satisfied" or "very satisfied" with their frequency of sexual intercourse. The authors concluded that use of the STM was consistently viewed as being beneficial to couples' self-knowledge, their relationship, and satisfaction with frequency of sexual intercourse.

Comments

As with past studies that used convenience samples of NFP users the participants in this study were mostly married, well-educated, and financially secure. The response rate of only 37% and the miss match with almost three times more women responding [i.e., 77% ($n = 1,971$) were females and 23% ($n = 589$) were males] was problematic. Thus, generalizability of this study is difficult. However, the findings of this study are consistent with studies that used a similar questionnaire, and thus, the results adds to the evidence base of the influence of practicing NFP on marital dynamics.

Unseld, M., E. Rötzer, R. Weigl, E. K. Masel, and M. D. Manhart. 2017. **Use of Natural Family Planning (NFP) and Its Effect on Couple Relationships and Sexual Satisfaction: A Multi-Country Survey of NFP Users from US and Europe.** *Frontiers in Public Health* 5 (March 13): 42 (<https://doi.org/10.3389/fpubh.2017.00042>).

Brief Educational Program Improves Knowledge and Confidence in FABM among Third Year Medical Students

Past studies have shown that medical students receive little education in fertility awareness-based methods of family planning (FABM) and when they do, it is often from a negative context. Past studies also have shown that when FABM are presented by health professionals in a positive way that a significant percentage of women would be interested in using these methods for their own use (Stanford, Lemaire, and Thurman 1998). Furthermore,

physicians, and in particular, family medicine and obstetrician and gynecologist (OB-GYN) physicians are often the providers and advisors for family planning services. Therefore, clinical researchers set out to assess medical students' knowledge of FABMs, the students' confidence in applying FABM knowledge in patient practice, and to provide education on FABMs to improve knowledge and confidence (Danis, Kurz, and Covert 2017).

Two hundred seventy-seven third year medical students from in a mid-west private medical school in the United States were administered a ten item FABM questionnaire at the beginning of their OB-GYN rotation. The FABM assessment tool, developed by the clinical researchers, contained eight questions to assess knowledge of FABMs and two questions to assess confidence in applying that knowledge in a clinical situation. The medical students were then provided two lectures about FABMs and their application to clinical practice. A post-test with the same FABM assessment tool was administered at the end of the student's OB-GYN rotation.

Of the 277 students who completed the pretest assessment, 196 completed the posttest questionnaire. The researchers discovered that the medical student's knowledge of FABM knowledge improved from an initial test score of 38.99% to final test score of 53.57% ($p < 0.05$). The student's confidence in sharing FABM information with patients (0 = very uncomfortable; 5 = very comfortable) improved from 1.51 to 3.00 ($p < 0.05$). Confidence in applying knowledge of FABM in diagnosing and managing women's reproductive health (0 = not very confident and 5 = very confident) improved from 1.01 to 3.15 ($p < 0.05$). The researchers concluded that a brief, focused education can increase medical students' knowledge of and confidence with FABMs of family planning.

Comments

It was good that the authors were able to access a third-year class of medical students but it would be helpful to also replicate this study among other medical school, especially Catholic based programs. Furthermore, follow-up on these students as residents in relevant specialties and after when in practice to see the rate of retention of knowledge would be recommended.

Danis, P. G., S. A. Kurz, and M. Covert. 2017. **Medical Students' Knowledge of Fertility Awareness-Based Methods of Family Planning.** *Frontiers in Medicine* (June 1); <https://doi.org/10.3389/fmed.2017.00065>.

Stanford, J. B., J. C. Lemaire, and P. B. Thurman. 1998. **Women's interest in natural family planning.** *Journal of Family Practice* 46 (Jan.): 65-71.

Predicting Sex of Baby with use of Natural Methods of Family Planning – New Evidence

Having a baby boy over a baby girl is valued in many countries due to cultural and economic reasons. Couples might also have reasons for one sex over the other due to diseases associated with sex chromosomes. In some countries such as India and Korea, the ratio of baby boys over girls has become a demographic problem. Use of ultrasound imaging of the fetus or chromosomal analysis of the embryo and subsequent abortion when the “wrong” sex is detected

are immoral means in this process. However, and theoretically, there might be a moral method of helping couples to select the sex of their child.

There is a theory, and some anecdotal evidence, that use of Natural Family Planning and the targeting of intercourse before, on, or right after the Peak day of cervical mucus could enhance the ability of having a boy or girl. The theory is that the Y chromosome bearing sperm that result in a boy baby is more motile and shorter lived than the slower X bearing girl oriented sperm. The Y sperm would beat the girl sperm to the waiting ovum. Changes in cervical mucus can enhance the slower “girl” sperm if intercourse occurs before the Peak mucus sign. The rules for sex selection is to have intercourse on the days before the Peak mucus sign to enhance the chances of a girl baby and having intercourse on Peak or soon after will enhance a boy baby.

A study by pro-life and pro-family Billing Ovulation Method (BOM) promoters in Nigeria prospectively tested the proposed sex selection method among 99 volunteer couples who were taught the BOM and when to have intercourse for sex selection (McSweeney 2011). The volunteer participants agreed to declare their sex preference and provide a chart with the days of intercourse to researchers before the birth of the baby. Once the baby was born the sex was recorded – but only then. A group of BOM experts were shown the charts and intercourse patterns and from that were able to predict the sex of the pending baby. The BOM experts were blind to the identity of the couple and the desired sex. The researchers found that of the 99 couple volunteers, 94 gave birth to a child of their preferred sex – i.e., a 95% success rate – only 5 couples did not have a child of their desired sex. Furthermore, male selection success was 96.3% (i.e., 78 out of 80 pre-selected a male) and female was 88.9% correct (i.e., 16 out of 18 wanting a female child). There was only one user selection failure – i.e., the couple had an intercourse pattern for a boy and had wanted a girl. The authors concluded that with use of the Pre-Peak rules of intercourse for girl babies and Post-Peak for boy babies that couples using the BOM can predict the sex of their child with a high degree of confidence.

Although the findings of this study are fascinating, they are suspect based on studies that use more rigorous research methods. Previous studies on sex selection through the timing of intercourse were not as successful. For example, researchers conducted a study to determine if sex ratio was related to the timing of intercourse in relation to the day of ovulation, the estimated length of the follicular phase of the conception cycle, or by the planned or unplanned status of the pregnancies (Gray, Simpson, and Bitto 1998). This prospective study included as participants all women who became pregnant from while using NFP as taught in five centers located in Chile, Colombia, Italy and the United States. There were 947 singleton births during that time period, of which 477 were boys and 470 were girls. This yielded a sex ratio of 101.5 males per 100 females, which was not significantly different from the expected ratio of 105 males to 100 females as found in previous studies. The researchers also observed no association between the timing of intercourse and the sex ratio or evidence to show that intercourse around the time of ovulation results in predominance of female babies or later intercourse with male babies. Nor did they find any consistent association between follicular phase length or planning status of the pregnancy and the sex ratio.

Other researchers (Wilcox, Weinberg and Baird 1995) conducted a prospective study of 221 women who were planning a pregnancy and recorded daily urine samples for LH surge

detection and diaries of the time of intercourse. As in the Gray et al. study, the Wilcox, Weinberg, and Baird group did not find a sex ratio difference in association with the timing of intercourse but did find an excess of males in cycles with shorter follicular phases. Gray et al., stated that the differences might (but not probably) be due to the imprecision in the estimation of the day of ovulation through the mucus peak or shift in basal body temperature, the self-reporting of the actual day of intercourse, and the determination of which act of intercourse resulted in conception. They concluded that manipulating the time of intercourse in relation to the estimated day of ovulation or the length of the follicular phase cannot be used to preselect the sex of the baby.

A more recent study utilized a Bayesian statistical model to validate whether there is a significantly likelihood to have one sex or another based on follicular length and the timing of intercourse before or after the Peak day of cervical mucus (Scarpa 2016). They used an existing database of menstrual cycles from users of the BOM to test these associations. Results did not show an association of the follicular length on the sex of the baby. They did obtain a slightly larger non-significant probability of conceiving a female baby just after the mucus peak day. In another study, researchers proposed what they called a composite likelihood approach to analyze the relation between sex of the newborn and timing of the intercourse (Tiberi, Scarpa, and Sartori. 2017). They describe the “composite likelihood” as a pseudo likelihood modeling day-specific probabilities of conception and the sex of the newborn when a conception occurs. They applied this methodology to a large dataset from a European fecundity study. However, the results showed no significant dependence of the sex of the newborn on the time of intercourse. Furthermore, the results of the Scarpa (2016) seem to contradict the BOM theory in that they had a non-significant probability of conceiving a baby girl just after the peak day of mucus, which suggests having intercourse before the peak for having a baby girl.

Comments

Although there are questions about the validity of the findings from the African study on the use of the BOM and timing intercourse for selecting a baby girl or boy, there is a moral difference between that method and prenatal sex selection. The biggest difference is that prenatal sex selection involves the life of an existing human embryo or fetus, i.e., a developing human being. The intent of pre-natal sex selection is not just the curiosity about the sex of the developing baby, but rather (as evidence shows) that if it is not the desired sex then abortion is pursued. With the use of the Billings Ovulation Method of sex selection, the acts are done before there is any existing baby and there is no intent for abortion. Furthermore, the intent is not much different than what couples do naturally when they say that they are trying for a baby boy or girl. It would be great if the results of the Billings sex selection method by the timing of intercourse worked as well as it did as presented in the African study, since then it could be promoted in countries where a certain sex is desired. If used instead of prenatal sex selection, it could save many baby girls from being aborted around the world.

Gray, R., J. Simpson, and A. Bitto, et al. 1998. **Sex ratio associated with timing of insemination and length of the follicular phase in planned and unplanned pregnancies during use of natural family planning.** *Human Reproduction* 13: 1397-1400.

McSweeney, L. 2011. **Successful sex pre-selection using Natural Family Planning.** *African Journal of Reproductive Health* 15: 79-84.

Scarpa, B. 2016. **Bayesian Inference on Predictors of Sex of the Baby.** *Front Public Health* 24; 4: 102.

Tiberi, S., B. Scarpa, and N. Sartori. 2017. **A composite likelihood approach to predict the sex of the baby.** *Stat Methods Med Res* [Epub ahead of print].

Wilcox, A., C. Weinberg, and D. Baird. 1995. **Timing of sexual intercourse in relation to ovulation. Effects on probability of conception, survival of the pregnancy, and sex of the baby.** *New England Journal of Medicine* 333: 1517-1521.

MENSTRUAL CYCLE

Abnormal Menstrual Cycles are Reflected in Sport Related Head Injury

The hypothalamic-pituitary axis that regulates the menstrual cycle can be affected by many physical, hormonal, and behaviors situations. Brain injury as a direct assault on neurological function is a likely cause of interruptions in menstrual patterns by altering hypothalamic-pituitary-ovarian axis functions. Based on this notion, researchers sought to evaluate the association of brain injury (i.e., concussions) with menstrual cycle patterns in young women (Snook, Henry, Sanfilippo, Zeleznik, and Kontos 2017). Specifically, they conducted a prospective cohort study to compare abnormal menstrual patterns in adolescent and young women after a sport-related concussion with those after sport-related orthopedic non-head injuries.

Participants for their study were 129 adolescents and young adults aged 12 to 21 years and who presented within 30 days after a sport-related injury to a concussion or sports medicine clinic at a single academic center from October 2014, through January 2016. Inclusion criteria required participants to be at least 2 years post-menarche, to report regular menses in the previous year, and to report no use of hormonal contraception. Of the 129 participants 68 were diagnosed with a sport-related concussion and 61 with a non-head sport-related orthopedic injury. Participants were followed up for 120 days after injury and menstrual patterns were assessed using a weekly text message link to an online survey inquiring about bleeding episodes.

Abnormal menstrual patterns were defined as an intermenstrual interval of less than 21 days (short) or more than 35 days (long) or a bleeding duration of less than 3 days or more than 7 days. A total of 1,784 survey responses and 1,888 text messages were completed which yielded 487 menstrual patterns in 128 patients. Of the 68 patients who had a concussion, 16 (23.5%) experienced 2 or more abnormal menstrual patterns during the study period compared with 3 of 60 patients (5%) who had an orthopedic injury. They found that the risk of having 2 or more abnormal menstrual bleeding patterns after injury was significantly higher among patients with concussion than among those with an orthopedic injury (odds ratio, 5.85; 95% CI, 1.61-21.22). The authors concluded that young women may have an increased risk of developing abnormal menstrual patterns after a concussion. They suggested that monitoring menstrual patterns after concussion might be warranted in this population.

Comments

The authors also recommended further research to further elucidate the relationship between long-term consequences of concussion and the function of the hypothalamic-pituitary-ovarian axis. Note that if young women were taught how to monitor their menstrual cycle signs through fertility awareness methods perhaps using fertility monitoring apps that more information about how the menstrual cycle is affected by head injury (i.e., more than just frequency of menses-could be ascertained).

Snook, M. L., L. C. Henry, J. S. Sanfilippo, A. J. Zeleznik, A. P. Kontos. 2017. **Association of Concussion With Abnormal Menstrual Patterns in Adolescent and Young Women.** *Journal of the American Medical Association Pediatrics* [Epub ahead of print].

CONTRACEPTION

Women Often Prefer no Method of Contraception for Family Planning Needs

Over the past ten years newer methods of family planning have been developed with an emphasis placed on long acting reversible contraceptives (LARCs), i.e., the IUD and the hormonal implant. These methods of family planning also are the most effective in avoiding pregnancy. Family planning experts have a concern that more women are not using the more effective LARC methods of family planning (He, Dalton, Zochowski, and Hall 2017). They also are concerned that current family planning research has not adequately addressed women's preferences in family planning methods and, more importantly, to see if women's family planning experiences match their preferences.

Researchers conducted a cross-sectional survey study with women selected from the Women's Healthcare Experiences and Preferences Study. This study involved an Internet survey of 1,078 women aged 18-55 randomly sampled from a national probability panel. Survey items assessed women's preferences for contraceptive methods, match between methods preferred and used, and perceived reasons for mismatch. Of the 1,078 woman samples only 34% (n=363) responded and were at risk for pregnancy. Of these respondents, non-LARC hormonal methods were the most preferred method (34%), followed by no method (23%) and then LARCs at (18%). They also found that minority, married, and older women having higher rates of preferring less effective methods, compared to their counterparts ($p < .05$). Only 36% reported preference-use mismatch, with the majority preferring more effective methods than those they were using. The most common reasons for mismatch were cost and insurance cost (41%), lack of perceived/actual need (34%), and method-specific preference concerns (19%). The researchers concluded that they found substantial mismatch between preferred and usual methods, notably among women of lower socioeconomic status and women using less effective methods.

Comments

It is interesting that 23% preferred no method of family planning. It would be important to find out why. Usually, women want effective methods of family planning, but also a method that is easy to use and has no health risks. This study lacks statistical power and use of multiple testing that increases error rates. Another study found among 1,240 volunteer women from multiple family planning clinics throughout the United States that "no method at all" was rated

as the method that best met the 18 preferences for family planning methods with “using no method” having met 66% of the preferences (Jackson, Karasek, Dehlendorg and Foster 2016). Minority and racial participants were also more likely to rate as “extremely important,” methods that protect against sexual transmitted disease, having control over when and whether to use the method, and being able to become pregnant after stopping use of the method.

He, K., Dalton, V.K., Zochowski, M. K., and Hall, K. S. 2017. **Women's Contraceptive Preference-Use Mismatch.** *Journal of Women's Health* (Larchmt), 26 (6): 692-701.

Jackson, A.V., D. Karasek, C. Dehlendorg, and G. Foster. 2016. **Racial and ethnic differences in women's preferences for features of contraceptive methods.** *Contraception* 93 (5): 406-411.

UNDER THE MICROSCOPE:

New Technologic Aids for Methods of Natural Family Planning

There have been many technological advances since the first methods of Natural Family Planning (NFP) were developed in the late 1920s and early 1930s. Some of the less technological devices that have been used to aid the use of NFP include beads, charts, stamps, tables of dates, credit card size fixed day calendars, and fertility wheels. The technological advancements of micro-electronics, immunoassay technology, computers, cell phones and other hand-held devices, the internet and internet applications (apps) has ushered in new ways of monitoring fertility. This review is intended to illustrate and evaluate some of the newer available technology to aid in the use of NFP that have been discussed or researched in the scientific literature. NFP providers will be confronted with these devices since couples are already using them, have investigated them through the internet, and will be asking advice about using these devices for NFP purposes. Devices that are in development will also be discussed for possible future uses and needs.

Calendar Based Systems of NFP

A fixed calendar day method of NFP was developed and tested that involves use of a blanket rule type of Calendar-Rhythm along with a bead system to keep track of the days of the menstrual cycle. For example, one fixed day method developed and tested at Georgetown University and by the United States Center for Disease Control and Prevention called the collar method, is for a woman to consider herself fertile from days 9 through 19 of her menstrual cycle (Burkhart, de Mazariegos, and Salazar, et al., 1999). In order to see how useful this method might be, researchers from the Population Council in New York and Guatemala evaluated the regularity of menstrual cycles among 303 Guatemalan women of whom 96% were Mayan. The 303 Guatemalan/Mayan women yielded 880 cycles of useful data. Regularity was defined as having a cycle length in the range of 26 to 32 days for three consecutive cycles. Cycle lengths out of this range would not be effective in the use of a fix-day calendar system. Of the 808 cycles, 76% fell within the cycle length range of 26 to 32 days. More than half (54%) of the women participants did not have 3 consecutive regular cycles. The researchers estimated that from 11 to 28% of the cycles would have days within the 9-19 blanket which could be considered fertile days. The apparent irregularity of Mayan women's menstrual cycles seems to be influenced by a younger age and high incidence of breast-feeding among this population of

women. The researchers essentially found that the 9-19 method would not work with a sizable portion of the Mayan women. A follow-up effectiveness study of was tested with 301 couples (women between the ages of 18-39 years) living in the Guatemalan highlands (Burkhart, de Mazariegos, Salazar, and Lamprecht 2000). After 12 months of use, 32 couples were pregnant giving an 11% pregnancy rate. However, only 34% of these couples were sure that they did not have sexual relations during the fertile period. At 1, 3, and 12 months, 100% of the women reported satisfaction with the method. Only 5 of the men reported being dissatisfied due to the periodic abstinence.

Researchers from the Georgetown University Institute for Reproductive Health (IRH) reported on a multi-site effectiveness study of what they call the Standard Day Method (SDM) of family planning (Arevalo, Sinai, and Jennings 1999; Arevalo, Jennings, and Sinai, 2002). The SDM is essentially a modified form of Calendar Rhythm that has a fixed number of days of fertility for each cycle (i.e., days 8 to 19). The method is intended for women who have regular cycles between 26 and 32 days in length. The SDM uses a colored bead necklace system (called CycleBeads) that indicate the beginning (a red bead) of the cycle, followed by 6 brown beads of infertility, then 12 days of fixed fertility (white beads), and then 13 more days of infertility (with brown beads). The CycleBead system also has a dark brown bead for day 27 that indicates to the user that if they start their menses before that date they should contact their provider. If they reach the last bead (day 32) and still have not started their menses they were also asked to contact their provider. The marker beads help the user to know whether they fall into the 26-32 day cycle length to which this CycleBead system applies. The rules for the CycleBead system are simple: brown bead days are open for intercourse with very low probability of pregnancy; and white bead days mean that pregnancy can occur if a couple has intercourse.

The SDM was prospectively tested for its effectiveness in helping couples avoid pregnancy among 478 women from 5 different sites in three developing countries (the Philippines, Peru, and Guatemala). The participants were between 18-39 years old, had menstrual cycles between 26-32 days in length, and were willing to avoid intercourse for 12 consecutive days each cycle. Each study site had 5-10 trained health workers who instructed the participants in the SDM and who contacted them monthly for the length of the study. Participants were also asked to keep a calendar to record the beginning and end of their cycles, acts of intercourse, and any method other than SDM used to avoid pregnancy (e.g., condoms or withdrawal).

The 478 women generated 4,035 cycles of data of which 92% had correct method use (i.e., no intercourse on the white bead fertile days of 8-19), 5% of the cycles had intercourse with condoms or withdrawal during the fertile phase, and 3% had intercourse during the fertile phase. Only 43 of the 478 women became pregnant with use of the CycleBead system. Of these 43, 15 conceived when having intercourse outside of the method-defined fertile phase. Most (65%) of the pregnancies occurred in cycles in which the participant reported intercourse during the 8-19 day fertile phase. Using life table analysis, the Georgetown University researchers were able to calculate a 1- year pregnancy rate of 4.8 (95%; CI 2.33-7.11) with perfect use and a 1-year pregnancy rate of 12.0 (88%; CI 8.74-15.33) with typical use of the method (that involved all cycles and all pregnancies).

Comments

The authors concluded that this study demonstrated that the SDM with use of the CycleBead system was an effective method of family planning that is comparable to the male condom and significantly better than other barrier methods for pregnancy avoidance. They also concluded that this method is acceptable to couples in a wide range of settings and would be a valuable addition to reproductive health providers and other community services programs. A SDM fertility app for cell phones or other handheld devices has been developed for ease of use.

The SDM method would not work for a sizable portion of a reproductive age population due to postpartum breastfeeding status, irregular cycle lengths, women with polycystic ovarian syndrome, and peri-menopausal women. A combination of cervical mucus monitoring and a bead method was recently illustrated by Mulcaire-Jones, and others (2016) that might have more flexibility in that regard. However, this bead and mucus system has not been tested for its efficacy or for its satisfaction among a population of users.

There is an app for the SDM but it is only intended for women with menstrual cycle lengths of 26 through 32 days in length. Therefore, researchers set out to develop a simple fertility monitoring app called the Dynamic Optimal Timing or DOT app. This app only requires the woman to record the first day of her menses every menstrual cycle (Li, Heyer, Jennings, Smith and Dunson 2016). The app is based on day specific probabilities of pregnancy and length of the menstrual cycle. The monitor “learns” the cycle lengths and provides the user with a daily percentage of the probability of pregnancy. The app was developed by use of three available data sets of menstrual cycles from three past studies: the North Carolina study with N = 68 participants and 171 menstrual cycles of data; the Early Pregnancy Study with N = 221 participants and 696 cycles of data; and the World Health Organization study of the ovulation method with N = 706 participants and 8,118 cycles of data. Researchers estimated the theoretical unintended pregnancy rate using Bayesian analysis. The researchers found a theoretical cumulative unintended pregnancy rate of 4.4% over 13 cycles of use with correct use among women with menstrual cycle lengths between 20 and 40 days and a range of cycle length differences less than or equal to 9 days. The researchers felt that a limitation of use with DOT would be the need to have a fairly regular menstrual cycle length, and rule out use with women who have polycystic ovarian syndrome, thyroid disorders, etc., or during excessive stress or exercise. They also pointed out that perfect use would not be expected when used by a large population of women.

Comments

There are other large portions of reproductive age women that the DOT app would not be suitable for due to irregularity in menstrual cycle lengths. These take in postpartum breastfeeding women, peri-menopause women, early adolescents, and those women discontinuing post-hormonal contraception. A benefit or strength of this system of fertility monitoring is that it is easy to use and only requires entering the first day of the menstrual cycle. It remains to be seen how effective this system will work with a large actual population of women. At this time a large prospective study is being conducted in the United States to determine the effectiveness of this DOT app in helping women avoid pregnancy. Finally, the app was written for a secular audience. Due to this perspective, DOT acknowledges that some women will use a barrier method during the fertile time. This, of course, is unacceptable for Catholics.

Arevalo, M., I. Sinai, and V. Jennings. 1999. **A fixed formula to define the fertile window of the menstrual cycle as the basis of a simple method of Natural Family Planning.** *Contraception* 60: 357-60.

Arevalo, M., V. Jennings, and I. Sinai. 2002. **Efficacy of a new method of family planning: the Standard Day Method.** *Contraception* 65: 333-338.

Burkhart, M. C., L. de Mazariegos, and S. Salazar, et. al. 1999. **Incidence of Irregular Cycles Among Mayan Women Who Reported Having Regular cycles: Implications for Fertility Awareness Methods.** *Contraception* 59: 271-275.

Burkhart, M. C., L. de Mazariegos, S. Salazar, and V. Lamprecht. 2000. **Effectiveness of a Standard-Rule method of Calendar Rhythm among Mayan couples in Guatemala.** *International Family Planning Perspectives* 26: 131-136.

Li, D., L. Heyer, V. H. Jennings, C. A. Smith and D. B. Dunson. 2016. **Personalised estimation of a women's most fertile days.** *The European Journal of Contraception & Reproductive Health Care* 21 (4): 323-8.

Mulcaire-Jones G., R. J. Fehring., M. Bradshaw, K. Brower, G. Lubega, P. Lubega. 2016. **Couple Beads: An integrated method of natural family planning.** *Linacre Quarterly* 83 (1): 69-82.

Basal Body Temperature Devices

The measurement of basal body temperature (BBT) to track the upward shift in temperature that indicates that ovulation has occurred has been around since the 1930s. The Rev. Wilhelm Hillebrand, a Catholic parish priest, is credited as the first person to apply temperature as a method of NFP when he found that his parishioner couples were experiencing unintended pregnancies with use of the new calendar based system (Ober, 1971). He received an honorary doctorate for his work. In the early 1950s, Edward Keefe, MD developed a thermometer that measures temperature with more precision to enable a better differentiation of the temperature shift (1986). These glass and mercury thermometers are specific for use with BBT and are still available today.

In the 1980s and 1990s cheap microelectronics made available fast digital thermometers as an aid to using BBT NFP. During that same time period, electronic BBT monitors were developed that had small computers that to track the menstrual cycle and tell when in the cycle is the fertile time or not. The Bioself monitor is an example of such a monitor that has a built-in computer that tracks cycle length and temperature. The Bioself is based on BBT and calendar algorithms. The Bioself provides the user with a red light for fertility and a green light for infertility. The Babycomp (for achieving pregnancy) and the Ladycomp (for avoiding pregnancy) are similar devices that are only available in Europe. The L'Sophia is developed and marketed in Japan. They are available on limited bases in the USA. The monitor measures and tracks BBT.

German researchers were able to obtain the names of 648 women from Germany and Switzerland who purchased and used the Ladycomp fertility monitor (Fruendl, Frank-Hermann, and Godehardt, et al. 1998). These women were sent questionnaires on whether they were using these electronic devices to achieve or avoid pregnancy and whether the light on the day they had

intercourse was green, red or yellow (a green light indicates an infertile time, a red light indicates a fertile day, and a yellow indicates a potential fertile day). Of these 648 women, 597 used the device for contraceptive purposes (i.e., to avoid pregnancy) over a grand total of 10,275 months. Thirty-three of these women had an unintended pregnancy. Using life-table analysis, the researchers determined that there was a 5.3% unintended pregnancy rate after one year, 6.8% after two years of use and 8.3% after 3 years. The average length of the fertile period that the monitor identified was 14.3 days. Ninety percent of the Ladycomp users would recommend the monitor for their friends. Twenty-one of the 33 users with an unintended pregnancy would also do so. The Ladycomp is available but is a bit pricy at close to \$500.00.

Another computerized BBT device called the Cyclotest 2 which is still available and advertised on the internet and has been updated as micro-electronics have developed. A group of researchers from the Academic Teaching Hospital of the University of Dusseldorf, Germany tested the efficacy of the Cyclotest 2 Plus by comparing the fertile time in a woman's cycle as detected by the Cyclotest 2 Plus with the fertile time determined by the Sympto-Thermal Method (STM) of NFP (Freundl, Frank-Herman, and Bremme, 1998). Two hundred seven women used the device for 13 cycles, which yielded 4,430 cycles of comparison. In 120 women (58%) the beginning of the fertile time (FA) was on the same day for both methods, in 57 women (27.5%) there was a difference of 1-3 days, in 3 women the FA was four days later with the Cyclotest 2 Plus. The computer/thermometer detected the beginning of the fertile time 6 days later than the STM in only one woman. The end of the fertile time (FE) as detected by the Cyclotest 2 Plus, was on the same day as the STM with 127 women (61.4%), the FE was 1-2 days earlier than the STM day with 4 women, and with only 1 woman did the device show the FE 3 days earlier than the STM day. From this data, the researchers predicted that the device would detect a wrong FE in about 1 in 200 women and have a marked reduction in the fertile time in 2 out of 207 woman cycles. The authors concluded that the Cyclotest 2 Plus has a medium degree of reliability when used to avoid pregnancy and that there is a need for further studies to determine the actual efficacy of the device in helping couples avoid pregnancy.

Newer temperature measuring devices have recently been developed that offer continuous temperature measurement and are thought to be more accurate than a single temperature upon rising in the morning. One such device called the DuoFertility measures continuous temperature and movement by having the woman wear a sensor as an axillary patch. Researchers recently conducted a study to determine the accuracy of the device by comparing the continuous measure of body temperature with serial ultrasound of the developing follicle, i.e., the gold standard of detecting the day of ovulation and, in comparison to luteinizing hormone (LH) (Rollason, Outtrim, and Mathur, 2014). They evaluated this device with eight volunteer women that provided 35 menstrual cycles but only 18 cycles had complete data and were useful for the purpose of the study. The researchers found that in every cycle that ultrasound detected the day of ovulation the temperature monitor did so as well. The estimated day of ovulation by use of the DuoFertility was 100% plus or minus one day of the ultrasound detected day of ovulation. In 10 of the cycles the temperature monitor detected ovulation on the estimated day of ovulation and in 3 one day after. The researchers realized that as a pilot study it did not have an adequate number of participants or an adequate number of menstrual cycles of data.

Over the past several years a number of fertility monitoring applications (apps) for smart phones and other electronic devices have been developed to serve as a convenient device for

women who wish to track their menstrual cycles and their fertility. One such app called Natural Cycles was developed by Swedish researchers that included the ability to record (BBT) and results from luteinizing hormone (LH) urine test kits. The app has a built-in algorithm that calculates an estimated fertile window based on the first day of menses and the BBT recordings, and provides a red color for potential fertile days and green color for estimated infertile days. Researchers and developers of a new fertility monitoring application conducted a study to provide evidence for the accuracy of determining ovulation and the fertile window of the menstrual cycle with their fertility monitoring app (Scherwitzl, Hirschberg, and Scherwitzl 2015). They were able to obtain 317 women participants (mean age 30.1) who generated 1,501 cycles of data. They discovered that the average numbers of days from the subset of women who recorded LH results, was 1.9 from the positive LH test to the estimated day of ovulation indicated by the BBT shift. They also found that only 0.05% of the non-fertile green days were actually in the estimated fertile window. There were no pregnancies recorded with intercourse on the green days, one pregnancy was reported with intercourse on a red fertile day among the participants using this system to avoid pregnancy. The researchers concluded that this fertility application monitoring device was accurate and could be used as a birth control device.

The developers and researchers of the fertility app subsequently conducted and published a study to determine the effectiveness of the Natural Cycles app in helping women avoid pregnancy (Scherwitzl, Daielsson, Sellberg, and Sherwitzl 2016). The study was a retrospective analysis of data produced by 4,050 women who used the app for three months at a minimum, enter data for at least 20 days, and be at least 18 years old. The 4,050 women who purchased the app and agreed to the study produced 2085 women years of data. The participants had a total of 143 unintended pregnancies. These pregnancies and the 2,053 women years of use yielded a perfect use Pearl Index of pregnancy rate of 0.5 and 7.0 (per 100 woman years) for typical use. Survival analysis produced a typical use pregnancy rate of 7.5. The authors concluded that their app improved the effectiveness of using a fertility awareness-based method of family planning. They indicated that the app is effective in preventing unintended pregnancy when couples consistently used methods of protection on the estimated (red) fertile days.

Comments

Daily monitoring of the BBT is a useful but fuzzy indicator of fertility for women using it for the purposes of avoiding or achieving pregnancy. Use of BBT is of particular concern since the upward shift in body temperature is due to the rise in progesterone post ovulation and as result the indication of fertility is often too late to affect an act of intercourse that would lead to pregnancy. With regard to the DuoFertility BBT monitor, many women with infertility have irregular cycles and future studies to test the accuracy and usability of this temperature monitoring device will need to include more participants, especially with irregular cycles. Furthermore, among women who are postpartum and breastfeeding, these devices would not be likely to be of much use. Although continuous measure of body temperature might provide a more accurate measure of temperature it still would be susceptible to body temperature variability that makes use of BBT difficult, i.e., during stress, lack of sleep, exercise, alcohol, infections, etc. Furthermore, since the DuoFertility BBT shift in body temperature was either on the day of ovulation or the day after, those days most likely are already too late for achieving pregnancy. In addition, the authors promote a fertility awareness combined approach, that is, they allow use of barrier methods during the fertile time. This philosophy is promoted in the app

itself, the web site that advertises the app, and the blog connected to the Web site, and is not in accord with the intrinsic meaning of sexual intercourse.

Freundl, G., P. Frank-Hermann, and M. Bremme. 1998. **Results of an efficacy-finding study (EFS) with the computer-thermometer Cyclotest 2 plus containing 207 cycles.** *Advances in Contraception* 14: 201-207.

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Rollason, J. C. B., J. G. Outtrim, and R. S. Mathur. 2014. **A pilot study comparing the DuoFertility monitor with ultrasound in infertile women.** *International Journal of Women's Health* 16; 6: 657-62

Scherwitzl, E. B., A. L. Hirschberg, and R. Scherwitzl. 2015. **Identification and prediction of the fertile window using NaturalCycles.** *The European Journal of Contraception and Reproductive Health Care* 20 (5): 403-408.

Scherwitzl, E. B., K. G. Daielsson, J. A. Sellberg, and R. Sherwitzl. 2016. **Fertility awareness-based mobile application for contraception.** *The European Journal of Contraception & Reproductive Health Care* 21 (3): 234-241.

Salivary and Vaginal Electrical Resistance Fertility Monitors

A number of fertility devices have been tested to see if salivary or vaginal electrical resistance can provide the user with information to determine the beginning and end of the fertile window. One such device, called the OvaCue (formally called the Cue) fertility monitor are sold and marketed (both in magazines and on the Internet) in the U.S.A. as a device to achieve pregnancy only and for use with NFP. The OvaCue fertility monitor is a hand-held device that is designed to measure salivary and vaginal electrical resistance. The OvaCue monitor provides a predictive marker (a peak in salivary resistance readings) about 5-7 days before ovulation and a vaginal electrical resistance nadir followed by a rise in vaginal electrical resistance readings as a confirmation of ovulation. Because the CUE both predicts and confirms ovulation it can potentially be used as a method to avoid or achieve pregnancy, i.e., as a means of or an assistive device for NFP. The device is marketed and developed by Zetek Corp in Aurora, Colorado.

An independent assessment of the OvaCue monitor was made with an idea for its use in NFP (Moreno, Weitzman, Doody, Gibbons, Besch, Goldzieher 1988). Researchers recruited 11 regularly cycling women who monitored with BBT, urinary LH, the readings from the OvaCue monitor and serial pelvic ultrasound and produced 29 cycles of data. They found that peak salivary electrical resistance was able to predict ovulation on average 5.3 days in advance of the estimated day of ovulation. Nadirs in the electrical resistance of vaginal secretions occurred

within 2 days of ovulation in all but one patient. Variation in this interval from cycle-to-cycle was small as well. From this data the researchers proposed an algorithm for the use of these intervals in NFP and they felt that this device would help reduce the length of abstinence as compared with current methods of NFP. They also felt that the simplicity and objectivity of the device could result in greater general acceptance of NFP. An algorithm for use of the CUE device for Natural Family Planning, using abstinence for 9 days, not including menses, and alternate days avoiding coitus to measure vaginal mucus more accurately, was suggested.

Based on the first study researchers then compared the OvaCue method with the Ovulation Method (OM) in defining the fertile time of the menstrual cycle. In this study, ten experienced users of the OM monitored their cervical mucus, urinary LH and basal body temperature on a daily basis for two menstrual cycles. In addition, they were also monitored by pelvic ultrasound from day 9 of their cycle until follicular collapse was observed. The Texas study had 42 usable cycles of data and the researchers found a strong significant linear correlation between the peak in OvuCue salivary readings and the LH surge ($r = 0.82$, $p < 0.001$). The researchers also found a very strong correlation between the vaginal electrical resistance rise and the day of follicular collapse ($r = 0.98$, $p < 0.001$). Furthermore, they reported that the vaginal electrical resistance rise occurred 100% of the time within one day of the follicle collapse whereas, the peak in mucus occurred only 69% of the time within one day of follicle collapse. These results suggest that the OvuCue markers of predicting and confirming ovulation are accurate when compared with other standardized methods of determining the fertile period. The Baylor researchers concluded that a more precise beginning and end of the fertile phase were found with the OvuCue than with OM and with fewer days of required abstinence.

Fehring (1999) also studied the OvaCue and like the Moreno study found strong, significant linear correlations between the peak in OvaCue salivary readings and the LH surge ($r = 0.82$, $p < 0.001$ for Moreno and $r = 0.79$, $p < 0.0101$ for Fehring). The Fehring study also found a strong linear association between the vaginal electrical resistance nadir readings and the LH surge ($r = 0.84$, $p < 0.001$), whereas the Moreno et al., study found a very strong correlation between the vaginal electrical resistance rise and the day of follicular collapse ($r = 0.98$, $p < 0.001$).

Of interest is that Moreno et al. defined the theoretical fertile period as beginning at least three days before ovulation and until one day after (i.e., a five day theoretical fertile period). Based on this theoretical definition, they determined the actual fertile period in 39 of the 42 cycles in which follicular collapse was observed. The actual day of ovulation was defined as the day of follicle collapse preceded by an LH surge. Using these criteria, they determined that the OM method defined the beginning or end of fertility in four cycles out of 42 incorrectly and that the OvuCue method defined the beginning and end of the fertile period correctly in every cycle. Therefore, Moreno, et al. concluded that a more precise beginning and end of the fertile phase was determined with the OvaCue than with the OM and with fewer days of required abstinence.

However, an earlier prospective study of the reliability of the OvaCue Fertility Monitor to identify the fertile time of the menstrual cycle compared the readings of the device with the fertile time by ultrasound detection of the day of ovulation and by detection of the LH surge (Freundl, Bremme, Frank-Herrmann, Baur, Godehardt, and Sottong 1996). Researchers evaluated thirteen women who participated in the study. Sixteen cycles evaluated contained signals (i.e., salivary and vaginal electrical resistance) for the beginning and the end of the fertile

period. In two cycles OvaCue signals could not be found with the device. Using a computerized algorithm for evaluation of the CUE signals, the beginning of the fertile period was accurately detected in 14 cycles; in 2 cycles the signal was found less than five days prior to ovulation. The last day of fertility was identified correctly by the OvaCue Fertility Monitor in 10 cycles; in 6 it was incorrectly identified during the time when the woman was still fertile. The researchers suggested that the OvaCue Fertility Monitor utilizing the algorithm on which it currently is based cannot be recommended for natural family planning.

Another watch type device also was purported to measure fertility through electrical resistance and was popularized by a scene in the show “Sex in the City.” Researchers obtained federal funds to research the device—but no paper has been published at this time even though the research was completed in 2008 (Clinical Trial Identifier number: NCT00239603). An older device that also measured vaginal electrical resistance (called the Ovulon) was researched and researchers felt there was some potential for the device but it is not manufactured, marketed or sold in the United States (Fehring and Schlaff, 1998).

Comments

Moreno et al. concluded that the OvaCue method has potential for use in NFP. What Moreno, et al. had failed to take into consideration however, is the role that cervical mucus plays in the fertile period. Cervical mucus serves as a medium for the viability of sperm, so at least theoretically, even though the OM fertile period began or ended within the 5 days of defined fertility, if the couple was using the method to avoid pregnancy they would not become pregnant because the sperm could not survive beyond six days. If the couples were trying to achieve pregnancy, it would not serve any purpose to have had intercourse on a dry day within the defined period of fertility other than to strengthen conjugal relations. No mention was made in Moreno’s study of user satisfaction with the OvaCue monitor. Since it is an invasive device, it might not appeal to many women. There is also potential for spread of infection if the vaginal probe is not kept clean or shared among women. I commented in my 1996 study that further research needs to take place with the OvaCue method. That recommendation still stands. Furthermore, there never has been any study with the OvaCue to determine the efficacy or effectiveness of the monitor in helping women/couples to either avoid or achieve pregnancy.

Freundl, G., M. Bremme, P. Frank-Herrmann, S. Baur, E. Godehardt, and U. Sottong U. 1996. **The CUE Fertility Monitor compared to ultrasound and LH peak measurements for fertile time ovulation detection.** *Advances in Contraception* 12 (2): 111-121.

Fehring, R., and Schlaff, W. 1998. **Accuracy of the Ovulon fertility monitor to predict and detect ovulation.** *Journal of Nurse Midwifery* 43 (2): 117-120.

Fehring, R. 1996. **A comparison of the Ovulation Method with the CUE Ovulation Predictor in determining the fertile period.** *Journal of the American Academy of Nurse Practitioners* 8: 461-466.

Moreno J. E., G. A. Weitzman, M. C. Doody, W. E. Gibbons, P. Besch P, and J. W. Goldzieher. 1998. **Temporal relation of ovulation to salivary and vaginal electrical resistance patterns: implications for natural family planning.** *Contraception* 38 (4): 407-418.

Moreno, J. E., F. S. Khan-Dawood, and J. Goldsieber. 1997. **Natural Family Planning: Suitability of the CUE(TM) Method For Defining the Time of Ovulation.** *Contraception* 55: 233-237.

Accuracy of Miniature Microscopes to Monitor Salivary Ferning

Over the past twenty years there have been numerous miniature microscope type devices that were developed and marketed to observe changes in salivary ferning patterns that are purported to reflect the fertile window of the menstrual cycle. The changing patterns of salivary ferning are thought to reflect the changes in estrogen levels from a developing follicle much like what happens with the changes in the characteristics of cervical mucus. Women who use these microscope type devices, lick a small microscope lens, let the saliva dry and then view the ferning pattern with the miniature microscope. There are three general patterns, i.e., no ferning which indicates an infertile time, a mixed pattern with some ferning which indicates potential fertility or transitional fertility, and then peak fertility when there is a clear ferning pattern that takes up the whole field of view.

These microscopes are small enough to be placed in a purse and to be used in the privacy of an office, bathroom or home. The devices range in price from \$39 to \$75, are reusable and have a magnification of about 50-100X. Theoretically, the crystallization pattern of the mucus and saliva coincides with the female fertile period. The crystallization is due to NaCl that cyclically increases under the influence of estrogen.

Four studies have been published that have evaluated three of these miniature microscope fertility monitors. In 1993, Barbato, Pandolfi, and Guida (1993) reported a study in which they had 32 women participants use the PG/53 pocket microscope. Of the 32 women, 28 had interpretable salivary ferning patterns during the same period as other markers of fertility, i.e., basal body temperature rise and changes in the appearance of cervical mucus. Ferning lasted a mean of 6.2 days and began 1-2 days before the cervical mucus appearance and were an average of 7.2 days before the first day of the temperature shift. Guida, Barbato, and Bruno, et. al. (1993) also reported a study in which 10 women underwent serial ultrasound to determine the probable day of ovulation by the observation of follicular collapse. Of the ten women, six had maximum ferning the day of ovulation and four had maximum ferning two days before or after ovulation. These authors recommended that the PG/53 Fertility Monitor could be used in combination with other markers of fertility (e.g., BBT, cervical mucus) and that further research be conducted to improve the use of salivary ferning for family planning.

Fehring and Gaska (1998) published a study in which the Lady Free Biotester was compared with the self-observation of cervical-vaginal mucus and the self-detection of luteinizing hormone (LH) in the urine (see figure three). Twelve seasoned Creighton Model NFP teachers (with an average age of 36.7 years and who have used NFP for an average of 12 years) observed their cervical mucus on a daily basis, tested their urine for LH with the OvuQuick ovulation detection kits, and observed salivary and cervical mucus ferning patterns (with the Lady Free Biotester) for two menstrual cycles. The results showed that there was a very strong correlation between the LH surge in the urine and the peak in self-observed cervical-vaginal mucus ferning and salivary ferning. However, there was no definable beginning and end of the fertile time based on salivary ferning patterns. The authors were able to observe ferning throughout some of the cycles.

A new salivary ferning monitor miniature microscope type device was recently developed called the *Geratherm ovu* control device and researchers conducted a study to determine the accuracy of this device in estimating fertility by comparing the results of the *Geratherm* salivary ferning monitor (SFM) with a test strip that measures a threshold of luteinizing hormone (LH) in the urine (Günther, Bauer, and Hedderich, et al., 2015). The researchers were able to study 74 healthy women volunteers with a mean age of 24 years (range 20-35 years of age) with regular menstrual cycle lengths (25-35 days) from one medical clinic in a Department of Obstetrics and Gynecology at a University Hospital in Keil, Germany. The women were asked to use the SFM from day 5 until day 22 of their next menstrual cycle and to rate and record daily the viewed ferning pattern as not fertile, transitional, or fertile. They were also asked to use the EXACTO brand of a urinary LH test strip on the same days when using the SFM with concentrated urine. The researchers plotted out the correlation between the positive LH surge and the ferning levels with a line graph.

They found that the curve of fertility with the LH test and the peak of fertility with the SFM was almost parallel with the maximum day of fertility with use of the SFM on day 16 of the menstrual cycle and the LH test on day 17 of the menstrual cycle. The conformity between the two tests of fertility was 100% on day 5 through day 13, and 84% on day 14. At the 18th day there was 80% conformity and from day 19 through day 22 at 96% conformity. The researchers speculated the one-day difference in peak fertility between the LH surge and peak in ferning is because the LH surge would follow the rise and peak in estrogen levels from the developing follicle. The researchers concluded that since the SFM conformed well the LH tests, that it could be used by women for help in achieving pregnancy and also felt confident that the device could be an aid for contraceptive purposes.

Comments

As was discussed researchers in the 1990s and early 2000s compared salivary ferning to serial ultrasound of the developing follicle as the gold standard of estimating the day of ovulation and found salivary ferning did not conform to the peak in fertility and the estimated day of ovulation. They also found peak ferning at other times in the menstrual cycle and that the field of view from these devices did not match a more sophisticated standard microscope in which they could view peak ferning at one part of the field and no ferning at other parts.

This author would not recommend the use of the miniature microscope to monitor ferning patterns in saliva as a marker of fertility. The miniature microscope might have some use in differentiating cervical-vaginal mucus patterns, especially with women who have continuous mucus. Further research however, needs to be conducted to evaluate the use of these microscope fertility monitors with mucus ferning patterns. I would not recommend these devices as an aid with use in NFP methods. German and Italian researchers had the same conclusion in their evaluation of salivary ferning devices (Guida, Tommaselli, and Palomba, et al. 1999; Freundl, Godehardt, Kern, Frank-Hermann, Koubenec, and Gnoth 2003).

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Urinary Hormonal Monitoring

In 1990, Carl DeJarrsi, one of the developers of the hormonal birth control pill in the United States, predicted that in the future women would be able to monitor their own reproductive hormones in order to determine the fertile and infertile time of their menstrual cycles. He called this new method “Jet Age” Natural Family Planning. In the mid-1980s, the World Health Association (WHO) and others (Collins 1985) conducted studies with serum measure of reproductive hormones and recommended use of the key reproductive hormones to use in future urinary hormonal monitoring devices. The prediction of Karl Djerassi and the WHO study came through in the late 1990s with the introduction of a couple of monitors designed to measure reproductive hormones. There are some recent breakthroughs in home monitoring of reproductive hormones as well and some that have future potential.

Home monitoring of Luteinizing Hormone (LH)

The development of new biological and electronic technology now provides women with the ability to self-monitor female hormones that are secreted in the urine. These fertility monitors can provide an objective picture of fertility. The most readily available technologies are urinary LH test kits - sometimes called ovulation test kits. These kits provide the user the ability of detecting the urinary surge of LH about 24 hours before ovulation.

Detecting the LH surge in the urine is considered by experts to be a standard method and one of the best tests for indirectly self-predicting ovulation (Corson, Ghazi, and Kemmann, 1990; Anderson, 1993; Crosignani, 2000). Ovulation detection kits have been developed employing monoclonal antibody technology to detect the LH surge that occurs in the urine 12-24 hours before ovulation since the 1980s (Batzler 1987; Seibel 1986). The manufacturers of ovulation test kits claim greater than 90% accuracy in detecting the LH surge. However, the test kits miss the LH surge or do not detect the surge in about 10% of cycles. The LH surge in the urine may not give a long enough warning period before ovulation takes place in order to be used for avoiding pregnancy. Test kits need to be purchased for each menstrual cycle and thus will be a monthly expense. Recent studies have questioned the accuracy of using the LH surge due to different patterns of the LH profile that includes double peaks of LH and a plateau type pattern (Stanford, White, and Hatasaka 2002; Alliende 2013; Leiva, Bouchard, Abdullah and Ecochard 2017).

European researchers recently set out to determine the correlation of serum and urinary reproductive hormones in relation to the ultrasound determined estimated day of ovulation and to establish more modern standards of reproductive hormone variation among women with normal menstrual cycles (Roos, et al., 2015). The thinking is that these standard cycles and variations need to be established in order to be able to determine abnormal parameters and potential health problems. The study involved 51 women volunteers, recruited by word of mouth, who were between the ages of 18-40, were not on any hormonal form of contraception, and reported to have normal length menstrual cycles. Of the 51 volunteers, 40 (with a mean age of 29.5 years, range 18-37 years) met the study criteria and provided data from one full menstrual cycle. Each participant provided a daily first morning void urine sample and received daily transvaginal ultrasound once a follicle diameter of 16mm was detected. On days of ultrasound, serum samples were also taken. Urine and serum samples were tested for serum luteinizing hormone (LH), progesterone, estradiol, and urinary LH, pregnanediol-3-glucuronide (P3G) and estrone-3-glucuronide (E3G). Ultrasound was conducted by two physicians and results of the ultrasound were reviewed by experts to determine the estimated day of ovulation.

The 40 menstrual cycles of data generated by the participants had a median length of 27 days and a range of 22 to 37 days. The estimated day of ovulation had a median of day 15 and range of day 8 to day 26 of the menstrual cycle. The researchers found excellent correlations between serum and urine measures of the reproductive hormones, i.e., with urinary LH against serum LH (coefficient of correlation $r = 0.72$), Urinary E3G with serum E (coefficient of correlation $r = 0.51$), and urinary P3G with serum progesterone (coefficient of correlation $r = 0.81$). The rise in estrogen and LH always occurred before ovulation and the rise in progesterone from baseline always after ovulation. However, the serum and urinary peaks in estrogen and LH had more variability around the estimated day of ovulation. They concluded that the LH surge was an excellent predictor of ovulation, the rise in progesterone from baseline was a good consistent marker for confirming ovulation, and both LH and progesterone surges provided clear and sharp signals for detecting and confirming ovulation. They also indicated that this study confirmed or validated the use of hormonal endocrine monitoring for purposes of family planning, help in achieving pregnancy, and for detecting menstrual cycle abnormalities. This study as well as the study by (Guida, Tommaselli, and Palomba, et al. 1999) provides good evidence for the use of urinary LH tests for aiding women in using natural family planning, to either help confirm other markers of fertility.

High Tech Hormonal Monitoring

In the late 1990s, Unipath Ltd. (Bedford, England) introduced two new electronic fertility monitors to help women determine their window of fertility (May, 2001; Genuis and Bouchard 2010; Bouchard and Genuis 2011). The Persona fertility monitor was developed for women or couples wishing to avoid pregnancy and the Clearplan Easy Fertility Monitor (CPEFM) for couples choosing to achieve a pregnancy. The Persona monitor consists of a hand held electronic device and disposable test strips that were designed to detect urinary luteinizing hormone (LH) and a urinary metabolite of estrogen, i.e., estrone-3-gluconeride (E3G) from early morning urine samples. The monitor picks up a rising threshold level of urinary estrogen as the beginning of the fertile period and the urinary LH + 3 days surge as the end of the fertile period. The monitor displays a “green” light to indicate the infertile days and a “red” light to indicate fertile days.

The Persona also has a built-in calendar formula when the LH surge is missed in order to determine the end of the fertile phase for those cycles.

Researchers from Germany, Ireland, and the United Kingdom collaborated on a study to determine the effectiveness of a prototype of the Persona monitor (Bonnar, Flynn, and Freundl, et al, 1999). This study involved 710 volunteer women (median age 30 years, with regular menstrual cycles) that were asked to use the fertility monitor (without any formal training) for the purpose of avoiding pregnancy for a one-year period. At completion of the study, there were 67 method related pregnancies (i.e., a pregnancy resulted from having intercourse on a “green light” day, 92 user related pregnancies (intercourse on “red light” days,) and 3 unsure pregnancies, from 7,209 cycles of use. A 13-cycle life table analysis yielded a method pregnancy rate of 12.1 percent. After changing the algorithm to a more conservative formula the method related pregnancy rate dropped to 6.2 percent. The revised algorithm is currently used in the Persona, which is only sold in Europe and Canada. The authors calculated the method effectiveness based on the new algorithm for the Persona as 93.8 percent and concluded that personal hormone monitoring is simple to use and of value for women trying to avoid pregnancy. Of interest is that many women who use the Persona in Europe, use the monitor in reverse to achieve a pregnancy (Janssen and van Lunsen 2000).

The CPEFM was also designed to identify a woman’s fertile period by tracking the changing levels of estrone-3-glucuronide (E3G), the urinary metabolite of estradiol and by identifying the urinary surge of luteinizing hormone (LH) (Genuis and Bouchard 2010). The CPEFM however has a higher threshold level of detecting E3G levels than the Persona and thus has a shorter pre-LH phase and overall a shorter fertile phase to target the optimal days to achieve a pregnancy. The CPEFM was designed to read the result of antibody impregnated test sticks to identify changes in the hormone levels and provide the user with a reading of “low”, “high” and “peak” fertility. The “high” reading is triggered by the detection of rising levels of urinary E3G and the “peak” of fertility by the urinary surge of LH. At a minimum, the monitor will indicate at least one day of “high” fertility and two days of “peak” fertility. However, in a very few women the day of the estrogen rise coincides with the day of the LH surge. The user therefore goes straight from “low” to “peak”. In addition, some women may only see “low” and “high” signals, particularly if they miss tests or have an infertile and anovulatory cycle.

German researchers conducted a study to determine the accuracy of the CPEFM (Behre, Kuhlage, Gassner, et al., 2000). They monitored 53 women to detect daily serum levels of LH and estradiol and employed transvaginal ultrasound to ascertain the precise day of ovulation. The 53 women volunteers contributed 150 cycles of data with use of the CPEFM of which one cycle was determined to be anovulatory. Of the remaining 149 cycles, there were 135 cycles (90.6%) in which the CPEFM detected an LH surge, and there was an ultrasound confirmed ovulation. In those 135 cycles, ovulation occurred 97.0% of the time during a three-day period that included the two “peak” days plus the next day “high” on the CPEFM. There were no ultrasound-detected ovulations before the monitor “peak” days. They also found that in 92% of the cycles, the first “high” reading on the monitor reading coincided with the serum estradiol rise day. Another study with 30 healthy women volunteers showed that a Japanese-made version of the CPEFM provided up to 5 days of “high” fertility readings before the CPEFM Peak reading in 58.6% of the cycles (i.e., 17 out of 29 cycles). The researchers also found that the High reading

on the monitor was before a laboratory determine LH peak in 82.8% of the cycles (i.e., 24 of 29 cycles) (Tanabe, Susumu, and, et al., 2001). The authors of this study concluded that the device will allow couples to use the information to time intercourse for the best prospects of achieving pregnancy.

The CPEFM is currently sold and marketed in the United States only for women and couples who wish to achieve pregnancy. However, the information provided by the monitor could be used inversely for avoiding pregnancy as an off-product use. In greater than 70% of the cycles, the monitor will provide 5 or more days of “high” and “peak” fertility and in 85% 4 days or more. If a user avoids intercourse during the “high” and “peak” fertility days and at least 1-day after, there should be less than a 30% chance of pregnancy using the monitor alone. This is because sperm live 3 days in good cervical mucus and in rare cases up to 5 days and once a woman ovulates she is only fertile for 12-24 hours. So, at a minimum the fertility monitor alone provides the user with a 1-3 days warning before ovulation takes place.

To use the CPEFM monitor as a method to avoid pregnancy alone would require the use of another marker to help define the beginning of the fertile phase in those cycles that the monitor underestimates the actual beginning. Use of the CPEFM and cervical mucus monitoring together as a means to avoid pregnancy might be beneficial. Having two markers to estimate the beginning, peak and end of the fertile time could be thought as a double check. A recent European study that compared a double check method (cervical mucus and a calendar count) with a single check method found that the double check method was somewhat more effective in helping couples to avoid pregnancy (European Natural Family Planning Study Group, 1999). However, a down side is that this makes the method more complex and has the risk of uncorrelated signs of fertility, e.g., the peak in mucus and the peak in LH are not correlated. Teaching couples and women how to monitor the two signs of fertility and to interpret them makes the process a lot more complex. The complexity increases when the mucus signs are unclear and/or the CPEFM “peak” is not detected. The complexity of using both markers might also decrease the compliance with instructions and continuation of use. Users of the CPEFM and the Persona have found the ease of use as a single measure of fertility to be high (Severy, 2001). As indicated by Mary Lee Barron in this issue of *Current Medical Research*, researchers at Marquette now have conducted and published five efficacy/effectiveness studies among users of the Marquette Method of NFP with use of the CPEFM, a prospective study, a retrospective study, a cohort comparison study, and an extended use effectiveness study. Marquette researchers and others also have conducted effectiveness studies among special circumstances including among women with perimenopause, those trying to achieve pregnancy, and among postpartum breastfeeding women.

Swiss Precision Diagnostics (SPD) has an updated version of the CPEFM that has a touch screen mechanism, a calendar format for entering menstrual cycle data, and a memory and display from the past six menstrual cycles. The new monitor (now renamed as the Clearblue Easy Fertility Monitor), like the older form, continues to provide three levels of fertility, i.e., low, high, and peak, based upon urinary measure of estrogen and LH. Swiss Precision Diagnostics also recently released a digital urinary LH detection kit (Called the Clearblue Digital) that provides an objective indicator of a positive test (i.e., a smiley face emoticon) and does not require the user to compare a changing line with a reference line. SPD also released a

Clearblue Advanced Digital Fertility monitor that measures both a rise in estrogen (E3G) from baseline (indicated by a flashing smile emoticon) and an LH surge (indicated by a fixed smile emoticon).

All of the SPD fertility monitors are sold and marketed as devices to help couples to achieve pregnancy. The monitor does not have FDA approval for selling it for other purposes. These devices however, can be used personally for other purposes. Specifically, the CPEFM can be used as a device to monitor fertility and to determine the days of fertility and infertility, as an aid to fertility awareness. There is no reason that women and couples cannot use the monitor in a reverse manner or for health professionals to teach couples how to use the monitor as an aid to observe their fertility. This is similar to the way that health professionals have been using the basal body thermometer to help couples to identify the approximate time of ovulation to either achieve or avoid pregnancy. The CPEFM, is more accurate in doing so and directly measures the urinary metabolites of female reproductive hormones rather than the effects (e.g., the rise in body temperature) of the hormones.

Comments

The advantages of the Clearblue monitors are that they provide objective and very clear information about fertility - i.e., low, high and peak fertility. It has two of the best urinary assays to predict ovulation - urinary estrogen and LH. On average, it will provide about a 2-5 days warning before the actual day of ovulation. It is simple to use and understand. The disadvantage of the monitor, if using to avoid pregnancy, is that the 2-5 days warning period it provides is not long enough to avoid pregnancy and it does not tell anything about the status of cervical mucus. Furthermore, the monitor itself costs about \$175 and the test strips cost about \$18 – 20 dollars per month. These instructions are only to be used for those women who have cycles between 22 and 42 days in length.

The Brown Ovulation Monitor

The home use Ovarian Monitor has been in development for over 20 years primarily under the influence of Doctors James Brown (Australia) and Len Blackwell (New Zealand). The purpose of the ovarian monitor is to have a home use device that measures hormonal profiles of estrogen and progesterone throughout the menstrual cycle. The monitor utilizes a timed three-hour urine collection that is diluted to 150 ml. Samples of the urine are placed in pre-coated assay tubes and then read by the monitor. The monitor is based on homogenous enzyme immunoassay principles and is designed to measure estrone glucuronide (E1G) and pregnanediol glucuronide (PdG) levels. The monitor was tested previously in comparison to laboratory values and found to be accurate and reliable. Researchers now wish to determine the reliability of the monitor with home use by comparing home use results with those results obtained by experts in established reproductive centers.

Researchers from New Zealand, Australia, and Chile, undertook a study to determine the accuracy and reliability of the Ovarian Monitor in comparison to those found in a laboratory (Blackwell, Brown, Vigil, et al., 2003). Approximately 60 women volunteers with a mean age of 34 years, regular ovulatory cycles, who were current users of a method of NFP and who charted their fertile signs were asked to use the Ovarian Monitor for 6 cycles. These volunteer women

generated close to 360 cycles of data. The researchers then randomly selected 18-19 of these cycles in order to compare the results with Ovarian Monitor results at the three centers by experts and with the results from a World Health Organization reference laboratory in London.

The researchers essentially compared the initial E1G rise (which indicated the beginning of fertility), the peak levels of E1G (which indicated the peak in fertility and the approximate time of ovulation), and the PdG threshold level (which indicated or confirmed that ovulation occurred). The overall correlation between the Ovarian Monitor E1G results and the laboratory results utilizing radioimmunoassay methods (RIA) was 0.653 (range 0.581-0.949) and the overall correlation between the Ovarian Monitor and the laboratory PdG results was 0.842 (range 0.712 to 0.968). The Ovarian Monitor agreed with the laboratory in determining the day of the E1G rise in 50% of the cycles, but was delayed by up to 3 days in the other 50%. In contrast, the day of the peak in E1G and the PdG threshold by the monitor agreed very closely to the laboratory results. Overall, the correlation between the results from the monitor and the laboratory results were better than 0.84 in 80% of the cycles. The researchers concluded that the results of the monitor produced by women in the home setting were comparable to those produced by laboratory procedures. However, the researchers also indicated that the women volunteers needed close supervision to maintain quality control.

Comments

When the researchers asked the women volunteers if they would use the Ovarian Monitor as a means of NFP they answered that they would prefer to monitor their own symptoms. The average time to conduct the P1G test with the monitor is around 40 minutes and the PdG test about 15 minutes. The monitor also requires timed urines (over a minimum of three hours) and diluting the urine in a large jug. Furthermore, close supervision is required to maintain quality. Therefore, at this time the Ovarian Monitor is viewed as a research tool to improve current methods of NFP and as a possible alternative to more costly laboratory testing. The monitor costs about \$220 and each assay tube about 40 cents. I would also suggest that future research investigate the ease of use and satisfaction of use of the monitor in comparison with current methods of NFP. Daily three-hour urine collections and dilutions might not fit well with the lifestyle of many modern women. A newer version of the Ovarian Monitor is in development that would be more user friendly.

New and Developing Hormonal Fertility Monitoring

A recent study showed that the serum threshold of 5-7 $\mu\text{g/mL}$ of progesterone past the LH surge or cervical mucus peak confirms ovulation in close to 100% of ovulatory menstrual cycles (Ecohard, Leiva, and Bouchard et al., 2013). Based on the results of this study a simple home urine progesterone (P) dip test has been developed by Amy Berkley, PhD, that is designed to confirm ovulation when a threshold level of progesterone has been reached post a peak day of mucus or a positive LH test. Currently, the only way to self-confirm ovulation is to take daily first morning body temperatures and track a significant rise in the body temperature from baseline. This temperature method is time consuming and often inaccurate. Women who wish to confirm ovulation with a progesterone test currently need to have a physician order a serum test and have a laboratory measure the progesterone level—this approach expensive and time consuming. The P tests are now commercially available through MFB Fertility and many women are already using the P tests for various reasons. There are a number of independent ongoing

studies to confirm the accuracy of the new P test. The P test could be useful for women with PCOS, during the postpartum breastfeeding transition, for women who have very serious reasons to avoid pregnancy, and when the usual indicators for the end of the fertile phase are not conclusive. This urine P test recently received Food and Drug Administration approval and other brands of the P test are now available.

Two professors of biochemistry at the University of Wisconsin–Madison (Drs. Katie Brenner and Doug Weibel) have started a company call BluDiagnostics. They have received over one million dollars in start-up funds to develop a quick, saliva-based method for measuring progesterone and estrogen. They indicated that variations and ratios in estrogen and progesterone levels are closely related to ovulation and could be very helpful for conception timing. According to their web site information, BluDiagnostics aims to obtain Food and Drug Administration approval and reach the market by 2017. The device they have developed has a wet paper saliva test that connects to a cellphone app system through Bluetooth technology and provides the user with daily probabilities of fertility. Brenner and Weibel are also thinking beyond fertility and thinking how they can provide data that will contribute to women’s health.

Comments

The new urine P test designed has not yet been validated with independent published studies that compare the urine results with serum progesterone levels. Ideally, a study that compared the urine P test with ultrasound detected day of ovulation would provide the best evidence. As of this writing, BluDiagnostics has not released any salivary based hormonal products for fertility monitoring nor any published studies to validate the proposed monitoring device.

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