Natural Family Planning
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In this issue

Natural Family Planning

The Marquette Method is Effective for Avoiding Pregnancy during Perimenopause
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Fehring and Mu (2014) have published the first efficacy study of a Natural Family Planning (NFP) method used during perimenopause. Other NFP studies in the past have included older participants, but none have analyzed efficacy specifically in this reproductive category.

The study included 160 participants, 80 who were taught the Marquette Method (MM) of NFP in person and 80 who learned online. The age range was 40 to 54 years, but only 15 of these (9%) were over 45 years. The population was homogeneous, including mainly Caucasian (79%) Catholic (94%) couples. They analyzed subgroups that included 35 using only an electronic hormone fertility monitor (EHFM), 73 using mucus only, and 52 using both markers.

There was only one correct-use unintended pregnancy out of 79 participants who could be analyzed using correct-use cycles, giving a correct-use survival rate of 1.5 pregnancies per 100 users over 12 months of use. There were 5 unintended pregnancies with typical use (including incorrect or inconsistent use), 1 in the EHFM group (pregnancy rate 3/100 over 12 months of use), 2 in the mucus only group (pregnancy rate 4/100 over 12 months of use), and 2 in the group using both markers (pregnancy rate 6/100 over 12 months of use).

There were no pregnancies in women older than 44 years. Three of the 5 unintended pregnancies occurred in the first menstrual cycle postpartum. The authors reported that the menstrual cycles of the participants appeared to be ovulatory based on the ovulatory EHFM/mucus findings as well as follicular and luteal phase lengths.

Comments

Despite its small sample size, this is an important study for establishing the efficacy of a particular NFP method used during perimenopause. It is important to provide couples with efficacy data when discussing the use of NFP at a time when older couples are limiting their family size.

As the authors point out, it would be ideal to recruit older women participants (over age 45), a more diverse population, and if the sample size were adequate, a randomized comparison between mucus-only and monitor-only approaches of the MM. This would allow a more statistically robust comparison of the two methods to see if there are any differences in efficacy. With the current subgroup sizes, it is not possible to compare them in the current study. It should also be noted that the mucus-only approach used in this study also employs an algorithm that is a “back-up” to the mucus observations, and thus may not be directly comparable to other mucus-only methods of NFP.

The authors rightly highlight that the efficacy in this older group of participants likely has a lot to do with their higher motivation and overall lower fertility in these women. Conspicuously absent is an analysis of satisfaction which has been included in previous studies of the Marquette Method, and would have been helpful to know what these older women felt about the use of this method during perimenopause.

Besides the inclusion of satisfaction analysis, it would have also been helpful to have more details on the circumstances of the 5 pregnancies. It is important to know that there were none after age 44, and that 3 of 5 occurred in the first cycle after postpartum amenorrhea. On this latter point, this would suggest that the breastfeeding/postpartum transition remains a challenging time even in older women and that this is the main concern in these 3 women rather than the perimenopause per se. The one correct-use pregnancy should have been analyzed in detail to describe how these situations could be avoided in highly motivated women.

Finally, the authors comment that it would be helpful to have objective markers for the end of a woman's fertility when NFP would no longer be required. Future studies that analyze predictive markers like anti-Müllerian hormone and follicle stimulating hormone (i.e., AMH and FSH) should look at identifying the end of fertility and not just menopausal amenorrhea. This study is a welcome addition to the NFP literature showing its application to another challenging period in the menstrual cycle continuum.

Fehring, R., and Q. Mu. 2014. **Cohort efficacy study of Natural Family Planning among perimenopause age women**. *Journal of Obstetrics, Gynecology, and Neonatal Nursing* 43 (3): 351-358.

Sokkay, N., R. Mansouri, and J. Yoost, et al. 2013. **A multicenter survey of contraceptive knowledge among adolescents in North America.** *Journal of Pediatric and Adolescent Gynecology* 26: 274-276.

Contraception/Sterilization

Prior Contraceptive Use Increases Risk of Endometriosis Among Nulliparous Women

Endometriosis is a serious health problem among 5-10% of reproductive age women and is a disease that often results in pelvic pain and infertility. Although oral contraceptive pills (OCPs) are commonly used to treat endometriosis (i.e., treat the symptoms rather than the disease) there is mixed evidence regarding if prior use of OCPs actually influences the development of endometriosis. Therefore, researchers sought to determine whether prior use of OCPs increases or decreases the incidence of endometriosis among a cohort of young women (Tu, Du, Goldstein, Beaumont, Zhou, and Brown 2014).

Researchers were able to obtain and analyze data from the Australian Longitudinal Study on Women's Health (ALSWH) a twenty year study from 1996-2016. The study focused on the 18-23 year old cohort at baseline in 1996 and in the 2000, 2003, and 2006 surveys of this cohort. The goal was to assess whether there was self-reported use of OCPs prior to the first self-reported diagnosis of endometriosis. The primary outcome of the study was self-reported diagnosis of endometriosis and the independent variable was reported use of OCPs. They also were able to ascertain potential confounders of marital status, body mass index (BMI), education and depression.

The researchers found 514 subjects with a new diagnosis of endometriosis over the 10 year length of the study among 9,585 participants in the 18-23 year old cohort. They discovered that the risk of being diagnosed with endometriosis was 2.4 times higher among women with greater or equal to 5 years of OCPs use versus the never users of OCPs. Among the nulliparous participants, after controlling for confounders, they found that prior use of OCPs greater than 5 years of use was associated with a 2.3 fold increased risk of a diagnosis of endometriosis compared to those women who never used OCPs. Among parous women, however, they found that with greater than 5 years of use of OCPs there was a 59% reduction in the risk of being diagnosed with endometriosis compared with never users of OCPs. The researchers did not determine whether the endometriosis occurred before or after a pregnancy. The authors concluded that the prior use of OCPs did not provide a protective effect for developing endometriosis but rather found a significant association with prior use but not among parous women. The authors noted that a limitation of the study was relying on self-reporting of endometriosis and OCP use. They also mentioned that some of the increased rate of endometriosis might be due to younger women being treated in their early years with OCPs with symptoms like menstrual pain and not for contraceptive purposes.

Comments

The decreased risk of endometriosis with prior OCP use among the parous women might be due to the effects of pregnancy and postpartum breastfeeding, i.e., a natural reproductive state in which the menstrual cycle is suspended and not under hormonal fluctuation of estrogen and endometrial build up and under high levels of natural progesterone (Thylan 1996; Decherney 1992). It would have been nice to include pregnancy and breastfeeding as predictors of endometriosis.

Decherney, A. H. 1992. **Endometriosis: recurrence and retreatment.** *Clinical Therapy* 14: 766-772.

Thylan, S. 1996. **Breast-feeding and endometriosis.** *Journal of Paediatrics and Child Health***.** 32 (3): 271-272.

Tu, F. F., H. Du, G. P. Goldstein, J. L. Beaumont, Y. Zhou, and W. J. Brown. 2014. **The influence of prior oral contraceptive use on risk of endometriosis is conditional on parity.**

Fertility and Sterility 101 (6): 1697-1704.

Qualitative Study Concludes that Restrictive Sterilization Policies in Catholic Hospitals Place Women at Risk for Unintended and Undesired Pregnancies

Female sterilization is the second most frequent method of family planning in the United States and the most frequent among older (40-44) women of reproductive age (Mosher and Jones 2010). Furthermore, tubal sterilization is more frequent among minority (Black and Hispanic) and poor women. Despite this popularity within the general public, sterilization is contrary to Catholic teachings. In the *Ethical Religious Directives for Catholic Health Care Services* (ERDs), published by the United States Conference of Catholic Bishops, contraceptive sterilization is forbidden. Sterilization is forbidden because it separates the unitive and procreative aspects of the marital act while subjecting the patient to the risks of surgery when no pathology is present. Since Catholic health care settings and hospitals are growing in the United States, this barrier to female sterilization is a concern to those health care providers who do not share these ethical concerns.

As was recently reported by Henpenny (2013) the prohibition of sterilization in Catholic hospitals is not uniformly followed and administrators and bioethics committees often find what are called "workarounds" to those directives. The growing presence of Catholic health care systems, the prohibition of sterilization for family planning by the ERDs, and the uneven implementation of those directives precipitated researchers to determine obstetrician-gynecologists' beliefs and experiences with female sterilization (i.e., tubal ligation) in Catholic hospitals (Stulberg, Hoffman, Dahlquist, and Freedman 2014). Researchers were able to interview 31 obstetrician-gynecologists (ob-gyns) they obtained through a purposeful selection of 237 ob-gyns who agreed to be contacted for follow-up interviews from a previous study of 1154 ob-gyn participants. They also conducted a snowball type process to increase willing participants. The 31 ob-gyns in the study were 12 men and 19 women, only three were Catholic (7 were listed as "non-metaphysical connection") and most (n=19) felt that religion was not important or only fairly important in their lives. Of these participants, 27 had experienced working in a Catholic hospital system. The open-ended interviews focused on physicians' likes and dislikes of working in the Catholic hospital, the fit of their own personal values, and clinical issues such as the provisions of abortion, infertility treatments, and direct sterilization. The interviews were transcribed, coded, and content analyzed for main themes and subthemes.

Three main themes (and subthemes within each), were discerned through content analysis of interviews that were responses to being unable to provide direct sterilization in a Catholic hospital. Here we will review two of the themes.

Theme One: "Risk of harm to women." Subthemes: "Medical indication for sterilization" and "Unnecessary additional surgery." The Obstetrician-gynecologists participants felt that the

strict prohibition of sterilizations could place a patient at medical risk, as for example when a subsequent pregnancy could be a serious health problem and would need the further risk of another surgery for a tubal sterilization.

Theme Two: "When workarounds do not work." Sub-themes: "Partial workaround"; "Change in enforcement," and "Insurance or financial barriers." With regard to workarounds: respondents described some of the difficulty such as having a surgical room in the Catholic hospital dedicated for a short time a day for tubal ligations by non-hospital staff; or, when a new, more conservative bishop arrives in a diocese and changes the hospitals' liberal sterilization policy. Further barriers might be due to insurance policies of the woman seeking sterilization only being in force at the Catholic hospital and that these insurance restrictions posed greater barriers for low-income and minority patients.

The researchers concluded that ob-gyns working in Catholic hospitals often do not share the Catholic Church's beliefs on human life or accept the ERDs – especially on sterilization and other reproductive restrictions. They called for further quantitative research to validate their findings and questioned whether public funding should be provided to Catholic hospitals that restrict health care procedures like tubal sterilizations.

Comments

This study had some major limitations, primarily with the low number of participant ob-gyns and their seemingly biased responses. The researchers were only able to obtain less than 31 ob-gyns from a total of 237 who were willing to have a follow-up interview, i.e., about a 7% response. They had to ask participants to forward their request to other ob-gyns that they thought might participate. This methodology likely enriched the number of respondents who had a negative attitude toward restrictions on access to sterilizations. A challenge to the premise for the study would be to conduct a similar study on the attitudes of faithful Catholic ob-gyns who are practicing in a secular setting and their beliefs and experiences in dealing with unfettered access to sterilizations and any pressure they have felt to perform them.

The authors did not consider if the woman patient had a serious medical reason not to have another pregnancy or if there were better means to help prevent another pregnancy. Furthermore, the authors did not address why a heath professional would need to destroy a normal physiological system when the responsibility to avoid pregnancy was the patient's, and that they are required to do no harm. The woman in question could be offered a secure method of Natural Family Planning. So too, the husband (or partner or partners) of the given woman also have a responsibility for family planning in these serious situations.

Hapenny, S. 2013. **Divergent practices among Catholic hospitals in provision of direct sterilization.** *The Linacre Quarterly* 80 (1): 32-38.

W. D. Mosher and J. Jones. 2010. **Use of contraception in the United States: 1982-2008**. *Vital and Health Statistics Series* 23, no. 29: 1-771.

Stulberg, D. B., Y. Hoffman, I. H. Dahlquist, and L. R. Freedman. 2014. **Tubal ligation in Catholic hospitals: a qualitative study of ob-gyns' experiences.** *Contraception*. [E-publication ahead of print.]

Fertility/Infertility

Age of Mother at Last Birth in Multiple Populations Used to Determine End of Fertility

A question often asked Natural Family Planning (NFP) providers and those health care providers involved with family planning and women's healthcare is how to know when a woman is no longer fertile. This information is important for older women and couples wishing to have a child and for those couples who have decided that their family is complete. Researchers from the Netherlands wished to determine an age curve denoting when women are no longer able to biologically reproduce. To answer this question in today's modern societies is difficult because there are few, if any, large naturally fertile populations in which couples have not used contraception to limit family size. Furthermore, sterilization is often the response to managing the desire to limit family size.

To build an age curve as to when natural populations of fertile couples no longer are able to procreate, the authors were able to obtain six electronic data sets that included large naturally fertile populations that recorded marriage, ages, and births of the participants. The data sets were from populations in the 17^{th} – 19^{th} centuries and from France, Old Quebec, the Netherlands, Utah, and newer Quebec. From these six data sets they selected 58,051 first-time married women who remained with their spouse until age 50. They found that the median age of the last biological birth was pretty consistent among all data sets, i.e., from 41.8 years to 42.6 years. The chance that the age of last birth (ALB) occurred before age 20 years was also similar in these data sets, i.e., around 2% of the population. The ALB curve that they developed showed that age related infertility rises slowly until age 35 to 40 and then rises rapidly. The curve also showed that involuntary infertility was 12% at age 35, 20% at age 38, about 50% at age 41, and almost 90% at age 45 and close to 98% at 50. They also found that early marriage and age of first birth did not correlate with an early ALB nor did women with multiple births have an earlier ALB. The authors defended using older data to establish this ALB curve in that their curve was similar to more modern data curves from smaller populations of contemporary naturally fertile couples, like the Hutterite population. They also pointed out that their curve of age dependent decline of fertility is similar to data from couples using donor insemination.

The authors indicated that this curve could be used to counsel couples wishing to have children. Specifically, women aged 31-34 still have a very good chance of child birth but that childlessness will substantially increase after 35. They mentioned that couples in their early 30s should not wait long to have children. For couples in their late 30s, the advice was to try now, don't wait, and don't be pessimistic since you still have a chance to succeed. For couples in the

early 40s, they should try to conceive right away and that their chances are not hopeless. Significantly they mentioned that the hope that IVF will reverse the effects of age is mistaken.

Comments

Couples who use Natural Family Planning would be a good cohort of modern couples to determine age related chances of pregnancy and birth of a healthy child. To obtain such a large NFP user data set would require large national NFP providers to keep good data on couples until menopause.

In a related article, the American College of Obstetricians and Gynecologists' Committee on Gynecologic Practice and The Practice Committee of the American Society for Reproductive Medicine's opinion paper (2014) mentioned that the percentage of live births from IVF cycles for women older than 44 years was 1% and that the miscarriage rate for women older than 42 was 36.6%. They also recommended education and enhanced awareness of the effect of age on fertility, that women older than 35 should receive medical treatment after 6 months of failed attempts, and that couples older than 40 years receive immediate evaluation and treatment. I would recommend that these couples first learn NFP and use focused intercourse during the estimated fertile phase. Weight loss and other positive lifestyle changes to improve fertility would be recommended as well.

American Society for Reproductive Medicine (ASRM). 2014. **Female age-related fertility decline.** Committee Opinion No. 589. *Fertility and Sterility* 101 (3): 633-635.

Eijkemans, M. J., F. van Poppel, D. F. Habbema, K. R. Smith, H. Leridon, and E. R. te Velde. 2014. **Too old to have children? Lessons from natural fertility populations.** *Human Reproduction* 29 (6): 1304-1312.

Chronic Stress Found to Extend Time to Pregnancy

Determining factors that optimize natural fertility, especially low cost lifestyle factors, could be important means to help couples with delays in achieving pregnancy and a way to avoid referral to expensive endocrine analysis and (often immoral) infertility treatments. Acute and chronic stressors are factors that affect fertility and stress management modalities have potential for managing stress related infertility; however, the evidence for the effects of stress on fertility and time to pregnancy is sparse. Furthermore, there is a need for valid measures of both chronic and acute stress to be able to monitor stress throughout the menstrual cycle. To shed some light on this problem researchers designed a study to determine the effects of stress on time to pregnancy (TTP) and day specific probabilities of pregnancy during the fertile window over a 12 month time period (Lynch, Sundaram, Maisog, Sweeney, and Buck Louis 2014).

Researchers obtained 501 couples who agreed to participate in their study of which 100 (20%) were lost to the study due to lack of interest. The remaining 401 participants reported having menstrual cycle lengths between 21-42 days, had been trying to achieve pregnancy, and had been off contraception for less than or equal to 2 months, and had not been on hormonal birth control injections in the past year. Each woman was provided a fertility monitor that measured a urinary metabolite of estrogen and luteinizing hormone to determine the fertile phase. They were also asked to collect saliva as their first act in the morning on the day of enrollment into the study, and on the first day of their menstrual cycle. The saliva samples were laboratory analyzed for levels of cortisol and alpha-amylase as two biological markers of stress. They were also asked to respond to a perceived stress scale on a daily basis. The perceived stress scale levels were: 1) almost no stress, 2) relatively little stress, 3) a moderate amount of stress, and 4) a lot of stress. Of the 401 participants, 80% completed the study protocol.

The researchers discovered that 347 (87%) of the participants became pregnant and 54 (13%) were unable to achieve pregnancy within the time scope of the study. They also found that those women who had the highest tertile of salivary amylase had a 29% decreased odds of pregnancy (i.e., longer TTP with a fecundability odds ratio of 0.71; 95% CI = 0.51 – 1.00) compared with women in the two lowest tertiles. Whereas women in the middle tertile had a 7% decreased odds of pregnancy (i.e., a fecundability odds ratio of 0.93; 95% CI= 0.68 – 1.29) than those women in the lowest tertile. The women in the highest tertile of alpha-amylase also had a greater than 2 times the risk of infertility (i.e., a relative risk of 2.07; 95% CI = 1.04- 4.11) than those women in the lower two tertiles. They did not find any association of decreased fertility with levels of salivary cortisol or perceived stress. A limitation of the study is that the biomarkers of stress were only measured at enrollment and the first day of the first menstrual cycle and not throughout the study.

Comments

The researchers also reported that they did not see differences in the acts of intercourse during the fertile window between women who became pregnant and those that did not, nor among women with higher levels of alpha-amylase. These results indicate that the differences in results were not due to frequency of intercourse and decreased amounts of intercourse among higher stressed women. One mechanism of stress on the menstrual cycle that is often mentioned in NFP programs is that stress could suppress or delay ovulation. The researchers found no difference in the day of the LH surge and presumed ovulation between women with high and low alpha-amylase.

Lynch, C. D., R. Sundaram, J. M. Maisung, A. M. Sweeney, and G. M. Buck Louis. 2014. **Preconception stress increases the risk of infertility: results from a couple-based prospective cohort study – the LIFE study.** *Human Reproduction*, Advanced Access pp. 1-9.

Weight Loss and Exercise Intervention Found to be Helpful for Infertile Couples Wishing Pregnancy

Obesity is a known risk factor for infertility but evidence for weight loss as an intervention for treating infertility is mixed and lacking. Clinical researchers at Stanford University sought to determine if significant weight loss (i.e., at least 10% of current weight) improved conception and live birth rates among overweight women diagnosed with infertility (Kort, Winget, Kim, and Lathi 2014).

The Stanford researchers carried out a retrospective cohort clinical study of a weight loss intervention among over-weight infertile women. Overweight was defined as women with a body mass index (BMI) greater than 25 kg/m^2. Infertility was defined as failure to achieve a successful pregnancy after 12 months of trying with unprotected intercourse. They obtained participants as they were consecutively admitted to the practice of one reproductive endocrinologist at Stanford University Medical Center. All participants were provided a weight loss goal of 10% of their maximum weight and lifestyle changes that included a decreased calorie intake and exercise of 30 minutes a day for at least 5 days per week. The participants were followed with weekly telephone or e-mail contact and with monthly in-person office visits.

There were 63 patients enrolled in the study period but 11 were either lost to follow-up or did not meet the study criteria. The remaining 52 participants had a mean BMI of 33 kg/m^2 and of these, one-third were able to achieve a meaningful weight loss of at least 10% of their maximum BMI. The researchers found that those infertile women who had a greater than 10% weight loss had a conception rate of 88% compared with a 54% rate with those with less than a 10% weight loss ($p = .049$). The live birth rate was 71% among the greater than 10% weight loss women compared to 37% for the less than 10% weight loss women ($p = .04$). The researchers indicated the study limitations as including a retrospective design, a small study population, and no measure of the male partner infertility factors. The researchers concluded that weight loss was a modifiable lifestyle intervention and that overweight infertility patients be encouraged to lose weight to improve their reproductive and general health.

Comments

Another way to help improve infertility among over weight patients might be to add Natural Family Planning with the weight loss program and to help them have focused intercourse during the fertile phase of the menstrual cycle. A disheartening finding of the study is that only one third of the participants were unable to achieve a significant weight loss. Furthermore, some of the participants achieved pregnancy through inter-uterine insemination and in-vitro fertilization.

Kort, J. D., C. Winget, S. H. Kim, and R. B. Lathi. 2014. **A retrospective cohort study to evaluate the impact of meaningful weight loss on fertility outcomes in an overweight**

population with infertility. *Fertility and Sterility* 101 (5): 1400-1403.

Most (86%) Medical Treatments for Infertility in United States Are Morally Acceptable

Although millions of couples in the United States (US) have been treated for infertility there is no information on infertility treatment patterns over the past 3-4 decades. There is some evidence that the use of in vitro fertilization has steadily increased over the last few decades. The reason that there is a lack of data is because there are no established national registries to track that information. Due to this situation, researchers from the Harvard University School of Public Health sought to describe the infertility treatment patterns in the U.S. and to analyze the influence of financial, biological, and temporal factors, i.e., age, parity, and decade of treatment (Farland, Missmer, Rich-Edwards, Chavarro, Barbieri, and Grodstein 2014).

The Harvard researchers used data from the Nurse Health II cohort data set that began in 1987, and specifically the 10,036 female professional nurse participants that were surveyed since 1993 when questions were included that reported use of fertility treatments, i.e., from the 1993 – 2009 questionnaires. The fertility treatments that were included in the questionnaires were clomiphene and gonadotropin injections, either with or without intrauterine insemination (IUI) and IVF. The listed reasons for infertility were ovulatory disorders (46.9%), 20.7% spousal factors, 19.4% endometriosis, 8.6% cervical mucus factors, 12% tubal factors, and 19.1% other. Of note is that 9.9% reported menstrual cycle lengths longer than 40 days and 16.3% reported irregular menstrual cycles.

The researchers found the most common treatment was use of clomiphene without further medications or procedures, i.e., 73% reported use of clomiphene as the only treatment. However, 22.3% of the clomiphene users also subsequently used gonadotropin injections alone or as part of IUI/IVF, i.e., 11.2% used only gonadotropin injections, 6.5% used IUI, and 4.6% used IVF. The next most common treatment (11.2%) was gonadotropin treatments alone. Those women with health insurance and with higher incomes had a higher use of gonadotropin treatments. The use of a large sample of infertile female professional nurses marks a strength of the study. The limitations of the study include the fact that the data were self-reported and the bias of using primarily Caucasian professional nurses as participants (i.e., “Are professional nurses a good representation of reproductive age women in the United States?”). The authors felt that this study was the first to report infertility treatment patterns in the United States and the results could be used for public health planning.

Comments

Of interest was that IVF procedures were more prevalent among women with higher household incomes, women who lived in states that mandated insurance for infertility, and women under the age of 36. The good news (from a Catholic Church standpoint) is that (by far) most of the infertility treatments involved medications that enhanced fertility and did not

interfere with the conjugal act of intercourse or create human embryos in a petri dish. The authors felt a need for further studies to see if there are treatment disparities among racial subpopulations. This author would recommend further studies on the use of focused intercourse during the fertile phase of the menstrual cycle with use of a method of Natural Family Planning to track fertility and with lifestyle modification, like weight loss, diet, and stress management. A limitation of this study is that they did not use focused intercourse with use of natural fertility monitoring and lifestyle changes.

L. V. Farland, S. A. Missmer, J. Rich-Edwards, J.E. Chavarro, R. L. Barbieri, and F. Grodstein. 2014. **Use of fertility treatment modalities in a large United States cohort of professional women**. *Fertility and Sterility* 101(6): 1706-1710.

Menstrual Cycle

Luteal Phase Defects Found in 4.3-8.9% of Menstrual Cycles of Healthy Eumenorrheic Women

A short (post-ovulatory) luteal phase is thought to contribute to infertility and miscarriages due to poor ovulatory events, lack of a mature secretory endometrium, and/or too short of a receptive endometrium for implantation of embryonic life. Current means of diagnosing a luteal phase defect (LPD) is through determining the length of the post-ovulatory phase based on basal body temperature changes, peak in cervical mucus, and/or urine luteinizing hormone (LH) estimation of the day of ovulation, histological dating of the endometrium, and timed post-ovulatory serum progesterone levels. The accuracy of these diagnostic means and even the diagnostic category of LPD have been questioned, and part of the questioning is due to a lack of a valid and reliable diagnostic test. Researchers sought to determine the prevalence of (clinical and hormonal) LPD in healthy regularly menstruating women and their relationship to reproductive hormones (Schliep, Mumford, and Hammoud, et al., 2014). Clinical LPD was defined as a luteal phase equal to or less than 10 days and the hormonal LPD was defined as a suboptimal luteal phase serum progesterone of equal to or less than 5ng/mL.

This was a prospective cohort study of 259 women between the ages of 18-44 with reported regular length menstrual cycles (21-35 days in length) who were not on any hormonal contraception for the past 6 months and who resided in western New York state. Exclusion criteria included any infertility, infertility treatments or chronic gynecological health problems. The participants were followed for 1-2 menstrual cycles and had serum samples drawn at menstruation, at the mid and late follicular phase, at the LH/FSH surge, at the estimated day of ovulation and at the early, mid and late luteal phase. All participants were provided a handheld electronic fertility monitor that measured urinary levels of estrone-3-glucuronide (E3G) and LH to help time the hormonal serum testing of LH, follicle stimulating hormone (FSH), estrogen and progesterone.

Based on the criteria for LPD and 463 menstrual cycles that had apparent ovulation, they discovered there were 41 (8.9%) of cycles with clinical LPD, i.e., with a luteal phase equal to or less than 10 days, 39 (8.4%) cycles with hormonal deficiency with progesterone levels less than or equal to 5 ng/mL, and 20 cycles (4.3%) that met both the clinical and hormonal requirements for LPD. They also discovered that clinical LPD was associated with lower LH and FSH across all phases of the menstrual cycles and both clinical and hormonal LPD was associated with lower serum estrogen levels in the follicular and luteal phases. These results suggested to the authors that there might be different underlying mechanisms for clinical and hormonal LPD. They speculated that the best means (at this time) to identify LPD would be through the estimation of ovulation (through urine LH testing) and a well-timed serum progesterone test.

Comments

I also support the notion that a luteal phase serum progesterone levels alone lacks specificity for diagnosing a luteal phase defect and would also question its specificity with it being timed in association with the estimated day of ovulation since serum progesterone levels are pulsatile. I would also like to see more than 1-2 menstrual cycles of data, e.g. patterns of LPD across 12 cycles of data. Also, the criteria of a luteal phase of less than or equal to 10 days might not inhibit implantation of embryonic life since earlier studies have shown that implantation can happen as early as 4 days after ultrasound identification of ovulation. The authors do point out that due to expense they did not use the gold standard of estimating the day of ovulation through serial ultrasound measures of the dominant follicle. They also pointed out that the use of LH testing could have skewed the results as LH testing is not as precise as the use of serial ultrasound and because the hormonal monitor can miss the LH surge when it occurs in the afternoon or evening of the day of testing.

K. C. Schliep, S. L. Mumford, and A. O. Hammoud, et al., 2014. **Luteal phase deficiency in regularly menstruating women: prevalence and overlap in identification based on clinical and biochemical diagnostic criteria.** *Journal of Clinical Metabolism*. Early Release Online.

Under the Microscope

Validation of A Simplified Mucus Only Method of Natural Family Planning

One of the major complaints about Natural Family Planning methods (NFP), among consumers and providers of family planning services alike, is that NFP methods are often too complex to teach and learn (Arevalo 1997). Over the past ten to fifteen years, there have been efforts to develop and simplify NFP methods because of this complaint and need. At the same time, efforts among providers of contraception have been trying to reduce barriers to the provision and access to contraception (Trussell 2011). Some of the more recent efforts of NFP providers to simplify NFP methods is the Standards Days Method (or SDM) and the use of

Cyclebeads to teach NFP (Arévalo, Jennings, and Sinai, 2002), the two step method that just requires the use of two simple questions to assess fertility (Arevalo, Jennings, Nikula, and Sinai, 2004) and the simplified Marquette Method fertility algorithm and means of rating cervical mucus (Fehring 2005; Fehring, Schneider, Raviele and Barron, 2011; Fehring, Schneider, Raviele, and Barron, 2013). These efforts are noteworthy since they also involve extensive research as to the efficacy and satisfaction in helping couples to avoid pregnancy. A simplified method of NFP that is not effective would not be well accepted among couples seeking a secure method of family planning.

In order to develop a simple prospective fertility monitoring system for epidemiological purposes researchers from Utah developed a simple one page brochure explaining a method of tracking fertility based on cervical mucus observations (Porucznik, Cox, Schliep, and Stanford, 2014). The one page instructions with diagrams can be used as a hard copy of the instructions and/or viewed online. They piloted the system with 26 women who also used a blinded fertility monitor designed to measure the follicular estrogen rise and the peak in luteinizing hormone surge (LH) in daily urine samples. These women produced 26 menstrual cycles of data, and based upon a best quality of cervical mucus as a marker of ovulation, identified ovulation plus or minus three days of the fertility monitor LH surge in 24 of the 26 (92%) menstrual cycles. The authors mentioned that this was a small pilot study and that it was very limited in validating their simplified cervical mucus only method with the blinded electronic hormonal fertility monitor (EHFM).

Marquette University researchers and clinicians have developed a simplified NFP method that uses either an electronic hormonal fertility monitor (i.e., the same one used in the Porucznik et al., 2014 study) or cervical mucus monitoring. Both the monitor and the mucus observations use a Low, High, and Peak fertility rating. The monitor ratings are based on a High when there is a significant rise in estrone-3-glucoronide (E3G) and a Peak when it detects the LH surge. Mucus is rated Low with minimal non stretchy mucus, High with some stretch, and Peak with peak quality characteristics, i.e., perfuse, clear, stretchy, and slippery. The Marquette system also uses a simple Quick Start instruction (and pictures of the mucus levels) that can be accessed online – and that takes only five minutes to read before beginning to use the method. Because the Marquette researchers also studied the efficacy of this simplified method they developed a large data set of individuals who used both the EHFM and the simplified mucus rating data chart. This data set, therefore, has information that can lend further validation of a simplified mucus monitoring system. The purpose of this short review is to further validate a simple mucus only method of natural family planning by comparing the fertile phase as estimated by cervical mucus monitoring (CMM) with electronic hormonal fertility monitoring (EHFM).

Methods

The data for this study was prospectively collected among women seeking NFP services in a university based online NFP education and service program managed by advanced practice professional nurses. Before receiving access to the website the participants signed a consent

form for participation and the study received human subject approval through the Marquette University Office of Research compliance. The online website is encrypted through an external cloud server system and is accessed only through protected passwords. The personal information of the participants and their fertility charts can be accessed only by the professional nurse NFP teachers or a vetted graduate research assistant at Marquette University.

The Marquette University College of Nursing NFP website (http://nfp.marquette.edu) has free information on fertility, a downloadable user manual and charting system, protocols for special circumstances (e.g., use of NFP postpartum), and instructions for achieving and avoiding pregnancy. A unique aspect of the information section of the website is one page simple Quick Start Instructions that can be read in five minutes and allows the user to begin charting and using a NFP method right away. Women who register on the website are able to access an online electronic charting system, discussion forums, and have consultation from professional nurse NFP teachers, an obstetrician gynecologist with expertise in the use of NFP, and a bioethicist. The online charting system also notifies the user of possible health problems, including unusual bleeding, infertility, and cycle dynamics that are out of the norm. The Marquette online NFP system is offered in both the English and Spanish languages.

The online charting system has designated sections for recording the results of the EHFM or self-observed cervical-vaginal mucus. The charting system has pop-up windows that illustrate the three fertility levels provided by the fertility monitor or the cervical-vaginal mucus observations.

The estimated day of ovulation (EDO) was either determined by mucus Peak or the monitor Peak, i.e., the day of the menstrual cycle with the last Peak reading for either monitor or mucus. The length of the luteal phase was calculated from the day after either the last monitor or mucus Peak rating and ended the day before the next menses.

Information from the online menstrual cycle charts were accessed from the website by graduate student research assistants and entered into a statistical program data file (SPSS Version 21). Descriptive statistics were used to determine the percentage of the day of Peak mucus days (i.e., the mucus EDO) that fell plus or minus two days of the monitor EDO. Pearson correlations were calculated between the EDO of mucus and monitor and between the first High ratings of mucus and monitor. Paired t-tests were used to determine differences between the monitor and mucus determined EDO, the luteal phase length, the first recorded High day, the total number of High days per menstrual cycle, and the total estimated fertile phase, i.e., the total High and Peak rated days of fertility. Since there was a series of t-tests, to control for error rates, the Bonferroni correction average of .05/5 = .01 was the level of accepted significance.

Results

Correlation of High and Peak Mucus Days with Peak LH

There were 38 participants from the pilot study that charted both cervical mucus observations and fertility levels from the EHFM. They produced 329 usable charts of menstrual cycle data. Of these cycles, 255 had both a recorded Peak in mucus and Peak monitor recording, 50 (15.3%) of the 329 menstrual cycles had no Peak mucus recorded and 47 (14.5%) of the menstrual cycles had no monitor Peak recorded. The percentage of Peak mucus days that were within plus or minus 2 days of the monitor estimated day of ovulation (i.e., the day after the LH surge) was 245 or 96% of the cycles. The Pearson correlation statistic between the estimated day of ovulation (EDO) by CMM and EHFM estimates was $r = 0.96$ $p < .001$. The correlation between the first High reading between CMM and EHFM was $r = .47$, $p = < .001$, and the correlation of the total length of fertile days (Highs plus Peak readings) was $r = .31$, $p = < .001$.

Table 1: Estimation of parameters of the menstrual cycle

	Mucus Monitoring Mean (*SD*)	Hormonal Monitor Mean (*SD*)	*t*-test	*p* <
Day of EDO*	16.36 (3.99)	16.90 (3.69)	7.67	.001
Luteal Phase**	12.26 (2.28)	11.70 (1.94)	7.45	.001
First High Day***	11.47 (3.12)	13.06 (3.82)	7.57	.001
Total High Days	4.36 (2.55)	5.12 (4.34)	2.81	.005
Total Days of Fertility	8.80 (3.15)	8.40 (3.21)	1.82	.070

* EDO = the number of days of the menstrual cycle from the first day of menses up to and including the estimated day of ovulation (EDO), i.e., the Peak mucus day and day of the second Peak recording of the hormonal monitor. This is also the follicular phase length of the menstrual cycle.

** Luteal Phase = the number of days of the menstrual cycle counted from day after EDO as estimated by the Peak mucus or the monitor Peak and up to the day before the next menses, i.e., to the end of the menstrual cycle.

*** The day of the menstrual cycle when the first High rated mucus was recorded or the first High reading of the monitor was recorded.

Mucus (CMM) and Monitor (EHFM) Estimated Fertile Days of the Menstrual Cycle

As seen in Table 1 there were significant statistical differences in the estimation of the day of ovulation (i.e., the EDO) the length of the luteal phase, and the determination of the first High day by CMM with that of the EHFM as determined by serial paired *t*-tests. The total High days and total fertile days were statistically similar between CMM and EHFM monitoring.

Discussion

This small study demonstrated that a simple method to teach and rate cervical mucus observations for determining the fertile phase for use in NFP has been further validated by comparing with an EHFM that measure E3G and LH. Specifically, the Peak in cervical mucus as determined by this simplified method of NFP correlated very closely with the LH surge and Peak reading of an EHFM. The 96% correlation of plus or minus 2 days of the LH surge by the EHFM with the Peak in cervical mucus is close to the results that was found by the Parucznick et al. (2014) study (92%) with a smaller number of menstrual cycles. So too, the strong high positive statistical correlation between the Peak in cervical mucus and the urinary LH surge of 98% is similar to the findings of other studies (Fehring 2002).

Although the current study showed statistical differences in estimated parameters of the menstrual cycle as determined by CMM and EHFM, the differences might not have clinical relevance. The fact that the average mucus High day came before the EHFM High reading would not be a problem with NFP, in fact, the early mucus High would make the method a tad more conservative and maybe more secure. A concern would be that there might be excessive days of fertility and required abstinence; however, the length of the total days of fertility (i.e., the total of High and Peak days) is very similar between the two methods of estimating fertility.

An earlier study by this author compared the estimated fertile phase by cervical mucus monitoring with a more detailed mucus grading system (i.e., a 1-8 scale). This method of mucus ratings resulted in considerably more days of fertility compared with the EHFM (Fehring, Schneider, and Raviele 2004). The current simplified system of rating mucus as Low, High, and Peak seems to have eliminated extended estimated fertile phases when mucus is of a continuous or low grade nature.

A strength of this study is that it involved a fairly large data set of menstrual cycles that compared the CMM estimated days of fertility with an EHFM by the same woman with each menstrual cycle. The Parucznik et al. (2014) study only generated 39 cycles. A limitation is that the EHFM was not blinded to the users and thus could have influenced the rating of the cervical mucus.

Although this study provided evidence to validate the accuracy of the CMM estimate of the EDO and fertile phase of the menstrual cycle, the real clinical concern would be whether the simplified mucus method is effective in helping couples avoid (or achieve) pregnancy and provides confidence and satisfaction with the consumer. An earlier pilot study showed a correct

use of 98% and typical use of 90% in avoiding pregnancy among non-postpartum breastfeeding participants using either the EHFM, CMM, or both to estimate the fertile phase of the menstrual cycle. This study was too small to determine if there were differences among the CMM only participants and the EHFM participants or the participants who used both EHFM and CMM to estimate the fertile phase. An extended use study with a much large population of women (i.e., greater than 1,000 participants) will allow us to analyze sub groups and determine the effectiveness of the simplified CMM.

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