

Natural Family Planning

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Natural Family Planning

Knowledge of Effectiveness of Natural Family Planning and Contraceptive Methods Found to Be Poor

Central among the many issues that form a person's choice in family planning is the method effectiveness rate for pregnancy avoidance (typically, most people do not consider the difference between moral and immoral methods). Despite the fact that couples who have just reasons to avoid pregnancy want a secure method of family planning, they often base their decisions on false perceptions of efficacy per method. Due to this tendency, researchers at Washington University conducted a study to determine the knowledge of contraceptive effectiveness among a cohort of women from Saint Louis.¹ The women were enrolled in a project call Contraceptive CHOICE. The project had a larger, more global purpose—to promote the use of long acting reversible contraceptives (LARC), e.g., hormonal implants and intrauterine devices. Once in place in the woman's body, these contraceptive methods involve little behavioral action. They also have very high “perfect use” and “typical use” effectiveness rates.

The researchers enrolled a convenience sample of 5,090 women between the ages of 14-45 years who were willing to start a new reversible contraceptive method. Of these women, 4,144 (81%) completed a baseline contraceptive knowledge effectiveness questionnaire. The main question asked on contraceptive efficacy was: “What percentage (or number of women out of 100) do you think would get pregnant in a year using each method listed below? The available response categories were <1%, 1-5%, 6-10%, > 10%. The answers were judged based on the contraceptive effectiveness results determined by James Trussell (Princeton University) and widely published in journals and books on contraception.²

The researchers found that the perceived contraceptive effectiveness of sterilization, the IUD, and contraceptive implants were incorrect among 76%, 65%, and 55% of respondents, respectively. Most participants overestimated the effectiveness for condoms, the hormonal birth control pill, and Natural Family Planning (NFP). Only 50% identified the correct typical effectiveness rate of NFP and only 33% identified the effectiveness rate of condoms. The author recognized the limitations of the study indicating that the participants were selected by convenience (i.e., mostly poor and minority women) and were biased in that health professionals promoted use of LARC methods with this group of women. They concluded that there is a gap in knowledge about contraceptive methods and encouraged contraceptive counseling.

Comments

The researchers raise concern about deceptive advertising practices among manufacturers of hormonal birth control pills who often provide only perfect use pregnancy rates and neglect typical use rates. The researchers suggest that providing typical use effectiveness rates would be more honest for the consumer. This advice is also useful for those promoting NFP methods. NFP

promoters and teachers should provide both perfect use and typical use pregnancy rates in all educational materials as well as in instruction. In addition, NFP promoters and teachers should also provide comparative differences in the efficacy of the various methods of NFP when available. (RJF)

1. D. L. Eisenberg, G. M. Secura, et al, "Knowledge of Contraceptive Effectiveness," *American Journal of Obstetrics and Gynecology* 206 (2012): 1.e1-1.e9.
2. J. Trussell, "Contraceptive Failure in the United States," *Contraception* 83 (2011): 397-404.

Fertility

Forty-five Percent of Women Seeking Pregnancy Unable to Estimate a Day within the Fertile Window

The days of the fertile window within a woman's menstrual cycle are the day of ovulation and the five preceding days. The most fertile of those days are the 2-3 days before the day of ovulation. Couples wishing to achieve pregnancy most likely would increase the probability of pregnancy by targeting sexual intercourse on the most fertile days of the menstrual cycle. There is some evidence that women and couples often mistime intercourse in their attempts to achieve pregnancy. Infertility specialists and scientists connected to manufacturers of hormonal fertility monitors sought to gather evidence to confirm that this is the case.¹ The purpose of their study was to compare women's perceptions of the actual day of ovulation with a hormonally estimated day of ovulation.

The study involved 330 women between the age of 18-45 who were seeking pregnancy and were recruited via a Web site advertising the study. At the time of the study's registration, the volunteer women were asked their average menstrual cycle length, their longest and shortest menstrual cycle length, and the day they thought they had ovulated. The women were then provided with a hormonal fertility monitor that measured urinary metabolites of estrogen and luteinizing hormone (LH). They were also asked to collect daily urine samples and send them to the researchers for laboratory testing of the LH surge.

One-hundred-two women provided a prediction of their day of ovulation. Of these women, only 13 correctly predicted the day of ovulation but 57 women predicted the day of ovulation plus or minus two days of the actual day. The most common estimated days of ovulation were day 14 (35.5%) and day 15 (15.7%) of the menstrual cycle. A surprising finding is that only 55% were able to target a day within their actual fertile window. The researchers concluded that women seeking pregnancy might benefit from a prospective method to identify the fertile phase. The researchers also mentioned that if a broader more diverse population of

women were studied that the results would probably show an even greater lack of identification of the fertile phase.

Comments

The bias of this study is that the volunteer women were seeking pregnancy and might have greater knowledge of fertility than other women. It also should be pointed out that the participants in this study were not using NFP. Knowledge and use of simple NFP methods would greatly enhance their prediction of the fertile phase of the menstrual cycle. Although it makes sense that being able to predict and target the fertile phase will enhance the ability to achieve pregnancy there is little evidence to show that targeting the fertile phase is any more efficient than just having frequent intercourse. Furthermore, there are those who indicate that monitoring fertility for couples can be stressful. (RJF)

1. M. Zinaman, S. Johnson, J. Ellis, and W. Ledger, "Accuracy of Perception of Ovulation Day in Women Trying to Conceive," *Current Medical Research & Opinion* 28.5 (2012): 749–754.

Only 12.7% of Sub-fertile Women Seeking Pregnancy Able to Accurately Identify Fertile Window

In order to achieve pregnancy couples need to have intercourse during the fertile window of the menstrual cycle, i.e., the day of ovulation and the five days preceding. This intercourse pattern would be particularly important for sub-fertile couples desiring pregnancy. However, in order to have intercourse during the fertile window (other than through frequent intercourse), they need to have knowledge of fertility and be able to estimate the fertile window of the menstrual cycle and the most fertile days of this window. Researchers from Australia (Manash University, Victoria, Australia) set out to determine the fertility-awareness knowledge, attitudes, and practices of sub-fertile women who were seeking fertility assistance in a primary care setting.¹

The researchers used a cross sectional survey study of sub-fertile women. They were able to obtain sub-fertile women who entered two different assisted reproductive technology clinics in a major city of Australia. They administered a 17 item fertility awareness knowledge questionnaire to 282 women on admission to these two clinics and received 204 completed usable questionnaires (a response rate of 72.3%). Of these respondents, 200 had attended at least one primary care appointment for their fertility problems, 125 had attended two or more sessions with an infertility specialist, and 161 were diagnosed as being infertile. Seventy-seven of these respondents reported charting at least three menstrual cycles with either cervical mucus observations or basal body temperature (BBT) monitoring. The 17 item questionnaire had three main sections, socio-demographic, knowledge and practice of fertility awareness methods (i.e.,

calendar rhythm, cervical mucus monitoring and BBT), and attitudes about fertility knowledge and in particular gathering information about fertility.

The researchers discovered that although 68.2% believed that they had been timing intercourse during the fertile window, only 12.7% could accurately identify the fertile window. These 26 women (27.7%) were respondents that charted at least three menstrual cycles with both cervical mucus changes and BBT. They also found that 86.8% actively sought information about fertility and the internet was the number one source. They concluded that although most sub-fertile women attempt intercourse during the fertile phase of the menstrual cycle, few are able to identify that fertile window. They suggested that poor fertility knowledge contributed to sub-fertility and that fertility education by health professionals would help decrease the need for couples to seek assisted reproductive technology clinics.

Comments

Although timing intercourse during the estimated fertile phase makes physiological sense, there is little evidence that this approach is any more effective than just frequent intercourse. A deficit of the questionnaire is that there were no questions about the use of LH testing or use of hormonal fertility monitors to focus intercourse, i.e., modern objective and accurate methods to time intercourse during the most fertile days of the menstrual cycle. (RJF)

1. K. D. Hampton, D. Mazza, and J. M. Newton, "Fertility-Awareness Knowledge, Attitudes, and Practices of Women Seeking Fertility Assistance," *Journal of Advanced Nursing*, E-published ahead of print, 2012.

Infertility

Managing Infertility in a Canadian Family Practice

Study Reviewed for CMR by Paul Yong MD, PhD and Thomas Bouchard MD

Impaired fertility affects 5-15% of couples. Some causes can be corrected with good effectiveness (e.g. ovulation induction for anovulation), other causes can be corrected but with limited effectiveness (e.g. surgical treatment of minimal-mild endometriosis), while other causes cannot be corrected or are simply unknown (e.g. "unexplained" infertility) and are empirically treated with assisted reproductive technology (ART).¹

There is a critical need for studies that 1) identify currently unknown, novel causes of infertility; and 2) investigate novel "disease modifying" treatments which correct the underlying causes of infertility with good efficacy and low risk.

Tham, Schliep, and Stanford² described the experiences of a Canadian family practice in the utilization of a natural procreative technology³ (NPT) for treatment of infertility. As a general principle, NPT is “restorative” in that it seeks to restore normal reproductive physiology and anatomy in order to optimize spontaneous (natural) conception. In addition to routine infertility evaluation, NPT involves work-up for potentially novel causes of infertility, such as abnormalities in cervical mucus or serum progesterone/estradiol patterns throughout the menstrual cycle. In addition to routine infertility treatments (e.g. clomiphene or laparoscopic treatment of endometriosis), NPT also involves use of potentially novel disease modifying treatments, such as medications to improve cervical mucus and targeted hormone supplementation. NPT is based on the Creighton model of cervical mucus charting and utilizes fertility-focused intercourse (FFI) whereby intercourse is targeted to the fertile period.

The study by Tham et al was a retrospective cohort of 99 couples with infertility and another 9 couples with recurrent miscarriage.² The cohort was selected sequentially from a single family practice clinic in Canada, and included those referred by NPT teachers as well as self-referrals. The average age of women in the study was 35.4 years, the average duration of infertility was 3.2 years, and the proportion with no previous live birth was 80%. Thirty-three of the couples (31%) had previous ART, of which 9 couples (8%) had undergone in vitro fertilization (IVF).

On initial presentation, 40% of couples had unexplained infertility (i.e., causes unknown); after NPT assessment, only 1% of couples were felt to be still unexplained. Prior to NPT evaluation, the most common explanations for infertility were unexplained miscarriage (29%), endometriosis (13%), male factor infertility (13%), low luteal progesterone (7%), blocked fallopian tubes (5%), fibroids (4%), polycystic ovarian syndrome (3%) and limited cervical mucus (3%). After NPT evaluation, the most common explanations were hormonal alterations (e.g. low luteal progesterone (67%) and low follicular and luteal estrogen (50%) based on hormone profiles developed from serial serum hormone measurements timed to ovulation), endometriosis (14%), anovulation (14%), male factor infertility (12%), limited cervical mucus (9%), polycystic ovarian syndrome (6%) and blocked fallopian tubes (3%).

After NPT treatment, the crude proportion of conceptions at 12 months was 41.7 per 100 couples and at 24 months was 47.2 per 100 couples; for live births, the crude proportion at 12 months was 32.4 per 100 couples and at 24 months was 38.0 per 100 couples.

After adjustment by life table analysis, the proportion of conceptions at 12 months was 53.9 per 100 couples and at 24 months was 73.1 per 100 couples; for live births, the adjusted proportion at 12 months was 44.5 per 100 couples and at 24 months was 66.0 per 100 couples. There were no twin pregnancies, and 54% of live births were at term.

Comments

The study by Tham, Schliep, and Stanford,² similar to the previous NPT study from Stanford, Parnell, and Boyle,⁴ is an important step towards more restorative treatments for infertility that seek to optimize the rate of spontaneous (natural) conception. Future studies should include a (matched) control group undergoing expectant management or other infertility intervention, to determine if pregnancy and live birth rates are similar or higher with NPT.

A control group is important because couples with infertility can sometimes conceive even without any treatment. For example, Steures et al studied couples with unexplained infertility and intermediate prognosis (a predicted 30-40% probability of spontaneous pregnancy in the next 12 months), and randomized them to ART (specifically, intrauterine insemination and ovarian hyperstimulation) or to expectant management (no treatment).⁵ At 6 months, there was no difference in (ongoing) pregnancy rate or live birth rate between the two groups. In particular, in the group randomized to expectant management, who received no treatment, one-quarter achieved pregnancy in 6 months.

In the absence of a matched control group for comparison, the authors do cite a Canadian study that found a live birth rate of 14.3% at 12 months amongst infertile couples with no treatment.⁶ In comparison, Tham et al found a (crude) live birth rate of 32.4% at 12 months. However, as noted by the authors, comparing studies must be done cautiously as the cases in the two studies are not matched for prognostic factors such as age, duration of infertility and previous treatments, previous pregnancy/birth, tubal status, and semen analysis findings. The authors also cite a live birth rate of approximately 50% after 1 year for IVF. Any comparison with IVF (with or without intracytoplasmic sperm injection (ICSI)) is challenging as IVF (+/- ICSI) patients have particularly poor prognosis (e.g. bilateral tubal disease, abnormal semen parameters, failure of previous treatments).

It is notable that Tham et al found half of the live births in their study were delivered pre-term, compared to <14% of live births being delivered pre-term in the NPT study by Stanford et al,⁴ which warrants further investigation.

Based on these findings of Tham et al² and Stanford et al⁴, it is important that follow-up studies (with a control group, and ideally prospective and randomized) be carried out for NPT. At least one high-quality randomized trial will be required before NPT and similar treatments are likely to receive widespread acceptance. Such a randomized trial could involve subjects randomized to one arm involving NPT versus another arm involving expectant management or other infertility treatment.

NPT is multifactorial, which is one of its strengths; however, it is not clear what component of NPT is most efficacious: Is it the FFI, or medications that enhance cervical mucus, or hormone supplementation, or another NPT treatment – or a combination of the above – which has the most fertility benefit? Interestingly, NPT evaluation attributed anovulation, inadequate

cervical mucus, and hormonal disturbances (e.g. low luteal progesterone), in more instances than were noted prior to NPT evaluation, likely because these are specific targets of NPT protocols. Randomized studies should also focus on the individual components of NPT to determine which specific interventions are truly effective. For example, subjects could be randomized to one arm involving FFI alone versus another arm involving the full NPT approach. Alternatively, subjects could be randomized to one arm involving NPT without hormone supplementation versus another arm involving the full NPT approach.

Tham, Schliep, and Stanford are to be congratulated on their work, and we hope to see more studies of NPT and other restorative treatments for infertility in the future.

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 6. J. A. Collins, E. A. Burrows, and A. R. Wilan, "The Prognosis for Live Birth among Untreated Infertile Couples," *Fertility and Sterility* 64 (1995): 22-8.
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Abortion

Women's Education Level, Maternal Health Facilities, Abortion Legislation and Maternal Deaths: A Natural Experiment in Chile from 1957 to 2007

Study Reviewed for CMR by Dr. Rebecca Peck, MD, CCD

A new study, which demonstrated that abortion restrictions did *not* have any deleterious influence on maternal health in Chile (and actually showed *improved* maternal mortality outcomes after abortion was banned) is a very important study for many reasons. First, it is one of the most rigorous studies of its kind, and could have implications for future public health research. Second, it dispels widely-held beliefs by researchers that the availability of unrestricted abortion decreases maternal mortality ratios (MMRs). Third, the study examines MMRs in Chile both before *and* after abortion was made illegal, thus allowing for the examination of this “natural” experiment in closer detail. The primary author stated that “we can firmly conclude that there is no actual causal association between abortion restrictions and maternal mortality outcomes and this is one of the most important findings of this study.” Finally, a fourth strength of this study is that it used time series of MMR along with parallel time series of eight predictors year-by-year over the last fifty years (including years of education of reproductive age women, per capita income, total fertility rate, birth order, age of the mother at the first birth, clean water supply, sanitary sewer and childbirth delivery by skilled attendants). Thus, this is the first study allowing researchers to assess interaction and confounding effects of different variables and to separate the actual effects of simple statistical correlations.

Prior to this study's release, public health researchers assumed that expanded access to abortion improved public health outcomes for reproductive age women. A literature review of the Chilean mortality study cites only five studies that have analyzed the impact of abortion policy on MMRs.¹ Only two of these five studies appeared in peer-reviewed journals and had methodological shortcomings.^{3,4} Two of these studies identified countries where MMRs decreased after abortion was legalized and failed to take into account other possible confounding factors (like increased education level of the woman, increased sanitation and sewage, increased per capita income, and increased access to obstetrical care) which could also account for the lowered rates. The other study simply compared MMRs in countries where abortion is legal to MMRs in countries where abortion is restricted. The problem is that many of the countries where abortion is restricted are places like Africa and the Middle East and have high levels of poverty and decreased access to obstetrical care.²

The Chilean study used 50 years of official data from Chile's National Institute of Statistics (1957-2007) which is considered a very reliable data base, according to both the WHO and United Nations.⁵ The authors looked at factors likely to affect maternal mortality, such as years of education, per capita income, total fertility rate, birth order, clean water supply, sanitary sewers, and childbirth delivery by skilled attendants. They also analyzed the effect of historical

educational and maternal health policies, including legislation that has prohibited abortion in Chile since 1989, on maternal mortality. During the 50-year study period, the overall MMR (number of maternal deaths related to childbearing divided by the number of live births) declined by 93.8% from 270.7 to 18.2 deaths per 100,000 live births between 1957 and 2007. The authors used time series of MMRs along with parallel time series of the factors likely to affect MMRs (listed above) and used autoregressive models.

One of the most significant findings is that, contrary to the widely held beliefs, making abortion illegal in Chile did not result in an increase in maternal mortality. In fact after abortion was made illegal in 1989, the MMR continued to decrease from 41.3 to 12.7 per 100,000 live births (69.2% reduction). The variables affecting this decrease included the predictable factors of delivery by skilled attendants, better nutrition for pregnant women and their children, the availability of clean water, and sewage systems, but the most important factor and the one which increased the effect of all others was the educational level of the woman.

This study had very few limitations. The authors state that this study is a natural experiment based on time series and therefore did not allow them to establish causal relationships; however they incorporated robust segmented regression techniques to test their different hypotheses. In addition, there were different ICD 7 – 10 coding categories used during that 50 year period, and some earlier categories had to be combined together (i.e. spontaneous abortion deaths along with induced abortion deaths) before the ICD coding system grew to incorporate separate codes.

Comments

The Chilean study clearly indicates that the MMRs, which were decreasing before abortion was prohibited, continued to significantly decline. This provides very solid evidence that increases in the educational level of women and improvements in maternal-health facilities were responsible for the decline in the MMR, and access to abortion had little to do with the improved public health outcomes for the women. Moreover, this research supports some previous evidence that countries with restricted access to abortion (like Poland, Malta, Ireland, Nicaragua and El Salvador) have lowered MMRs.⁶ Attempts by organizations such as the Guttmacher Institute to debunk this study have largely failed, due to the study's methodologically rigorous and reliable public health data. Nations that prohibit abortion should not be bullied into legalizing the practice on the grounds that doing so is necessary for women's health. As the Chilean example shows, that is simply not true.⁷ (RP)

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Birth Outcomes after Induced Abortion: A Nationwide Register-Based Study of First Births in Finland

Study reviewed for CMR by Mary Keen MD

The observational study, "Birth Outcomes after Induced Abortion: A Nationwide Register-Based Study of First Births in Finland," by Gissler, Niinimaki and Hemminki,¹ is based on data collected in a nationwide register. This includes 300,858 first time mothers during 1996-2008, which was linked to the abortion register for the period 1983-2008. The abortion registry is based on obligatory notification from physicians.

European countries have collected data for years on the health of their citizens. Unlike the United States which does not have a uniform policy for collecting data on pregnancy outcomes for childbirth or abortion, Finland has been collecting extensive public health records for decades. This study was based on nationwide obligatory health registers and took into account the mothers' background characteristics, previous miscarriages and ectopic pregnancies.

The number of induced abortions correlated strongly with the risk of preterm birth, low birth weight, very low birth weight and perinatal death. Even one abortion increased the risk of very preterm birth by 25% from 3 per thousand to 4 per thousand. Three abortions led to an almost 4 fold increase, from 3 per thousand to 11 per thousand with the risk associated with 2 abortions falling in between at 6 per thousand or double that of a woman with no prior abortions.

This study confirms what has been found in many previous studies, that there is a positive association between induced abortion and the risk of preterm birth. Like other observational studies, it documents an association but not necessarily causality.

1. Klemetti, Gissler, Niinimaki and Hemminki, “Birth Outcomes after Induced Abortion: A Nationwide Register-Based Study of First Births in Finland,” *Human Reproduction* 0.0 (2012): 1-6.

Pregnancy

Short and Long Term Mortality Rates Associated with First Pregnancy Outcome: Population Register Based Study for Denmark 1980-2004

Study reviewed for CMR by Mary Keen MD

Western European nations have collected data for years on the health of their citizens. This study on short and long term mortality rates associated with first pregnancy outcome by Coleman and Reardon¹ makes use of this preexisting data from Denmark. Unlike the United States which does not have a uniform policy for collecting data on pregnancy and even short term outcomes, much less long term outcomes, Denmark has been collecting extensive public health records for decades.

The data assessed in this study is taken from the Danish health register. All Danish residents were assigned unique identification numbers (ID). These ID numbers were linked to pertinent medical records for the entire population of women born in Denmark between 1962 and 1991 and who were alive in 1980. A strength of this study is the fact that it had access to complete reproductive histories. Mortality rates associated with first pregnancy outcomes (delivery, miscarriage, abortion, and late abortion) were calculated. Odds ratios were also calculated for death rates based on reproductive outcomes.

Out of a total of 463,473 women who had their first pregnancy between 1980 and 2004, 2,238 died.

Unadjusted death rates per 100,000 cases occurring within each year of the first ten years following each pregnancy outcome demonstrated that *death rates associated with birth were lower than those associated with all three types of pregnancy loss in every year*. Compared to mortality rates of women who gave birth, *the mortality rates associated with early and late abortion was significantly higher*.

The greatest differences were observed in the first 180 days of the pregnancy outcome but the higher rates persisted for many years. An abortion prior to 12 weeks was associated with an 80% higher risk of death within the first year and 40% higher risk of death over 10 years

when compared to a first pregnancy ending in a live birth. A woman who had an abortion was *twice as likely to die within the first 180 days after an abortion* compared to a woman who delivered and a woman who had an abortion after 12 weeks was almost *4.5 times as likely to die* than a woman in comparison with a woman who delivered her baby.

Weaknesses of this study include the fact that all causes of death were analyzed together; it did not control for social-economic factors, marital status, psychological history, or other factors prior to first pregnancy and did not study the effects of subsequent pregnancy outcomes. None the less, this is an important study. Utilizing highly reliable data it documented that women who had early and late abortions had significantly higher mortality rates than women who delivered their infants.

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Under the Microscope

Fertility Awareness in Gynecology: Application to Family Planning and Endometriosis

Paul Yong MD, PhD and Thomas Bouchard MD

Background

Fertility awareness can be defined as the prospective self-monitoring of physiologic biomarkers that are correlated with the menstrual cycle and its serum hormone patterns, in particular for the identification of ovulation and the fertile window. Numerous studies have confirmed the correlation between the physiologic biomarkers (e.g. cervical mucus, basal body temperature, and urinary hormones) and the menstrual cycle, and the ability of women to prospectively self-monitor their biomarkers.¹⁻²⁶ For example, based on women's self-assessment of cervical mucus, a mucus score (calculated by assigning a higher score to more fertile components of cervical mucus in terms of color, consistency, change, and sensation) was correlated with serum patterns of estradiol and progesterone.²⁰

Fertility awareness has been formalized into several major models based on:

- a) cervical mucus (Billings ovulation method,^{27, 28} Creighton model,²⁰ TwoDay method²⁹)
- b) a combination of cervical mucus, basal body temperature, and calendar calculation (Sympto-Thermal Method),³⁰ and

- c) urinary hormone assessment (Marquette Model, which uses the Clearblue fertility monitor to measure urinary LH and estrone-3-glucuronide, in combination with a double-check by cervical mucus or calendar calculation)^{19, 31, 32}

Fertility awareness and family planning

Because of the correlation between the physiologic biomarkers and the hormonal patterns of the menstrual cycle, fertility awareness has the potential for application to gynecology and women's health. For example, fertility awareness has been applied to Natural Family Planning (NFP) for over 50 years.

The effectiveness of NFP methods to avoid pregnancy have improved over time,³³ with the most recent observational cohort studies showing good effectiveness rates. For example, the Billings Ovulation Method™ was found to have a total pregnancy rate of 1.0% at 1 year in a Chinese study of 688 women.³⁴ In a meta-analysis of five cohort studies (1876 women), the Creighton Model FertilityCare™ Method was found to have a pregnancy rate of 0.5% at 1 year for method-related pregnancies, and a pregnancy rate of 3.2% at 1 year for use-related pregnancies (e.g. due to error).³⁵ In Creighton Model cohort studies, some couples use the model for achieving pregnancy by having intercourse on a fertile day, and thus a total pregnancy rate cannot be calculated.²⁰ With the TwoDay Method, the pregnancy rate was 3.5% for correct use, with a 13.7% total pregnancy rate at 1 year in a cohort of 450 women.²⁹ For the Sympto-Thermal Method, a European cohort study of 900 women found a total pregnancy rate of 1.8% at 1 year.³⁰ Finally, for the Marquette Model, in a cohort of 204 women the pregnancy rate was 0.6% at 1 year for method-related pregnancies, with a total pregnancy rate of 10.6%.³⁶ For comparison, the pregnancy rate in the first year of typical use is 15% for the male condom, 8% for the birth control pill, and 0.2-0.8% for the IUD or tubal sterilization.³⁷

Fertility awareness for family planning has been hindered by the unsatisfactory results of two randomized controlled trials (RCT) of NFP published in the 1980s.^{38, 39} RCTs are the gold-standard of medical evidence, as their design limits bias and confounding variables. Grimes et al⁴⁰ performed a systematic review of these two randomized studies, in addition to a small randomized study of fertility awareness combined with the contraceptive sponge.⁴¹ Due to the studies' weaknesses and limitations, Grimes and his colleagues were unable to make a clear conclusion about the comparative efficacy of the fertility awareness based methods.⁴⁰ Hilgers has summarized some of the problems of these older studies, with particular concern about the quality of teaching of the NFP methods to the study subjects.⁴²

Given the good effectiveness rates of more recent observational cohort studies, there is an urgent need for a well-designed RCT of modern fertility awareness methods for family planning. Fehring and colleagues have recently completed a RCT of the Marquette Model of NFP, randomizing women to the Clearblue fertility monitor with a calendar calculation as a double check compared to a cervical mucus based method with the same calendar calculation. Interestingly, this RCT utilized online teaching methods.⁴³ The use of NFP in the general population is limited by the number of certified instructors and the need for intensive teaching; thus, the online approach of the Marquette Model has the potential for wider acceptability and accessibility. The results of this RCT have been accepted for publication: preliminary findings

for the Clearblue arm are 0 method-related pregnancies, with total pregnancy rate of 7, at 1 year.⁴⁴ These findings are comparable to the pregnancy rate of 8% for the birth control pill in the first year of typical use.³⁷

In summary, since the initial RCTs published in the 1980s, more recent observational and now randomized studies of NFP have demonstrated much better effectiveness rates.

Fertility awareness and endometriosis

Endometriosis affects one in ten reproductive aged women⁴⁵ and is responsible for \$22 billion and \$1.8 billion in total annual costs to the United States⁴⁶ and Canada,⁴⁷ respectively. Endometriosis is associated with infertility and pelvic pain, with strong clinical predictors of endometriosis being primary infertility, moderately-to-severely painful periods, and palpation of nodularity on pelvic exam.⁴⁸ Because endometriosis is a hormone dependent disease,⁴⁹ fertility awareness of menstrual cycle hormone patterns has potential clinical applications to endometriosis.

Empirically, fertility awareness could improve fertility in endometriosis through fertility focused intercourse (FFI). Since fertility awareness allows self-determination of ovulation and the fertile window, it theoretically should identify the optimal timing of intercourse for pregnancy.⁵⁰ We are aware of only one published study evaluating fertility-focused intercourse to achieve pregnancy in comparison to a control. Using the Clearblue monitor, Robinson et al⁵¹ showed a 22.7% pregnancy rate with monitor use (n = 305) vs. 14.4% with no monitor (n = 348) after 2 months in women trying to conceive, which was statistically significant even after controlling for other factors. The sample was from a general population of women attempting to conceive, and thus was likely to include both couples of normal fertility and subfertility and women with or without endometriosis. There have been other studies of FFI using fertility awareness,^{52, 53} but these studies lacked controls. Controls in studies of infertility are critical, since couples can conceive over time even with no intervention.⁵⁴ More evidence is needed to elucidate the role of FFI in the management of infertility in general and endometriosis infertility specifically.

The pathophysiology of infertility in endometriosis is not completely elucidated.⁵⁵ In advanced (moderate-severe) endometriosis, anatomic abnormalities can contribute to infertility. Other mechanisms, in particular for minimal-mild endometriosis, include potential adverse effects on follicular development, fertilization, and implantation. Because of the correlation between the physiologic biomarkers and menstrual cycle hormonal patterns, fertility awareness could also provide insight into the pathophysiology of infertility in endometriosis. Such applications of fertility awareness have been primarily done by practitioners of the Creighton model, the foundation of which was published in a series of articles in *Obstetrics and Gynecology*.^{1, 2, 5}

Using the Creighton model, Hilgers²⁰ found a lower mean mucus cycle score of 6.7 in 206 women with endometriosis and infertility, compared to mean score of 9.3 in 62 controls of normal fertility. The maximum possible mucus cycle score is 16.0. In addition, the frequency of limited mucus or dry cycles was 78% in a series of 152 women with endometriosis, compared to

a frequency of about 20% in the normal population.²⁰ This finding of decreased mucus cycle score and more frequent limited mucus or dry cycles in endometriosis adds another potential mechanism of infertility. Quality of cervical mucus (higher mucus cycle score) is not only associated with ovulation and the fertile window, but is itself a determinant of fertility; that is, the presence of good quality cervical mucus affects the probability of fertilization, regardless of the timing of intercourse relative to the day of ovulation.¹⁸ Therefore, decreased cervical mucus quality may play a causative role in some cases of endometriosis-associated infertility.

In addition, there have been several recent studies where a more “restorative” approach to infertility management has been promoted, with the goal of maximizing pregnancy rates in natural cycles. Such approaches tend to be multifactorial, and include FFI, treatment of poor quality cervical mucus (e.g. with vitamin B6, guaifenesin, amoxicillin, erythromycin, or clarithromycin), and/or the use of ovulation-inducing agents (e.g. clomiphene) or hormonal supplementation based on serial measurements of progesterone/estradiol timed to the cervical mucus peak.²⁰ Two studies utilized the approach of natural procreative technology (NPT) which is based on the Creighton model.^{56, 57} Stanford et al⁵⁶ found that one-quarter of infertile couples had endometriosis. In the entire population studied they found an adjusted proportion of conceptions at 12 months of 35.5 per 100 couples and at 24 months of 64.8 per 100 couples; and an adjusted proportion of live births at 12 months of 27.1 per 100 couples and at 24 months of 52.8 per 100 couples.⁵⁶ Fifteen percent of couples who conceived did so with FFI alone. In addition, it was interesting that one-third of the couples had previously attempted ART. In the study by Tham et al,⁵⁷ (reviewed in this issue of *Current Medical Research*), 14% of cases had endometriosis. In Tham’s entire population, they found an adjusted proportion of conceptions at 12 months of 54.9 per 100 couples and at 24 months of 73.1 per 100 couples; for live births, the adjusted proportion at 12 months was 44.5 per 100 couples and at 24 months was 66.0 per 100 couples.⁵⁷ Of note, one fourth of couples who conceived in this study did so with FFI alone. Clearly, a sub-analysis of the cases with endometriosis is required before any conclusions can be made for the management of infertility in endometriosis, but their initial results are encouraging.

A study using the Billings method found that of 207 couples with subfertility who used the method to achieve pregnancy (i.e. through FFI), 65% became pregnant.²³ Fourteen of the 37 couples who had previously used ART achieved pregnancy (38%). The proportion of the cases with endometriosis was not given.

A limitation of the above studies is that they lacked matched control groups. Such control groups are important as there can be a significant pregnancy rate with only expectant management, as has been shown in “unexplained” infertility.⁵⁸ A simulation study suggested that expectant management is almost as efficacious as ART in the long-term for unexplained infertility.⁵⁹ Furthermore, in the two NPT studies, there were no specific analyses to evaluate which of the treatments were most beneficial: whether it was the FFI, the cervical mucus enhancement, the clomiphene or hormone supplementation, or a combination of treatments (for further discussion, see the review of the Tham study in this issue). There is a definite need for a RCT of one or more of these treatments in the endometriosis infertility population.

Laparoscopic surgery for endometriosis also has benefit for fertility, as demonstrated in the randomized Endo-Can study⁶⁰ and follow-up Cochrane review.⁶¹ Surgical treatment of

endometriosis also has benefit for pain reduction in endometriosis.⁶² Creighton practitioners tend to be proponents of a more intensive surgical approach for endometriosis.²⁰ For example, Hilgers⁶³ recently showed a low rate of post-operative adhesions after endometriosis surgery by using aggressive use of adhesion barriers, laser or micro-electrosurgery instruments, fine low-reactive suture choice, and uterine suspension. Only 7% of women had laparoscopic surgery as part of their management in the study of Tham et al,⁵⁷ specialized laparoscopic surgery for endometriosis was not available in the study of Stanford et al,⁵⁶ and no comment was made about laparoscopic surgery in the study of Corkill and Marshall.²³ More research is required to delineate the role of laparoscopy in a multifactorial “restorative” approach to endometriosis-related infertility.

Conclusion

There is an urgent need for RCTs evaluating the application of fertility awareness to gynecology, such as in family planning and in endometriosis. It cannot be emphasized enough that physiological or observational studies are insufficient; RCTs are required to show that fertility awareness can improve “hard” outcomes such as pregnancy or live birth rates. These RCTs should ideally involve an arm with placebo or routine treatment. Medical utilization of fertility awareness represents a paradigm shift, and therefore rigorous RCTs are required before fertility awareness will be appropriately integrated into women’s reproductive health care.

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