Natural Family Planning

CMR

CURRENT MEDICAL RESEARCH

A SUPPLEMENT OF *NFP FORUM*

Vol. 17, Nos. 1 & 2, Winter/Spring 2006

NATURAL FAMILY PLANNING

Large European Data Base Indicates STM Effective Method of Family Planning

Since 1984, German researchers from the University of Dusseldorf and the University of Heidelberg have been developing and analyzing a data set of menstrual cycles collected from multiple European sites. This long-term menstrual cycle data base (of 32,788 prospectively collected menstrual cycles) was produced by 1,551 women who were taught and used the European Sympto-Thermal Method (STM). The European STM system follows a double check rule for the beginning and end of the estimated time of fertility (see Figure 1). The double check for the beginning of the fertile window includes the first detection of change in cervical vaginal fluid (CVF) plus the earliest shift in basal body temperature (BBT) from the previous 12 menstrual cycles minus 7 days. The end of the estimated fertile phase is the shift in BBT plus 3 days or the peak in CVF plus 3 days, which ever comes last (see Figure 1). From this data set they have provided results on effectiveness to avoid pregnancy, accuracy of biological indicators of fertility, and time to pregnancy data with use of the European double check STM.[1]

Effectiveness of European NFP methods to avoid pregnancy

In this study, the researchers reported a method-effectiveness (correct use) unintended pregnancy rate of 0.3% per annum (i.e., 18 unintended pregnancies from 396 users and 8,052 menstrual cycles of data over 12 months of use) and a 2.25% use-effectiveness (imperfect use) unintended pregnancy rate. They also report unintended pregnancy rates (per annum) with subsets of the European data set by: 1) abstinence only in the fertile window; 2) protected intercourse (i.e., with barriers) in the fertile phase; 3) unprotected intercourse in the fertile phase; 4) unprotected and protected intercourse; and 5) genital contact within the fertile window (see Table 1). Of significance is that both "protected intercourse during the fertile time" and "abstinence during the fertile time" have similar unintended pregnancy rates. As would be expected, intercourse during the fertile phase had the highest unintended pregnancy rate. However, none of these comparison pregnancy rates are based on randomized controlled trials.

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RESEARCH ON. . .

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Accuracy of biological indicators of fertility

In addition, by analyzing a data set of 62 menstrual cycles, the researchers reported the results of correlating the self-detected peak in cervical mucus and the BBT temp rise with the serial ultrasound (US-DO) and urinary LH surge estimates of the day of ovulation. They reported what they called "the synopsis" of the BBT rise and the cervical mucus peak to be + 1 day of the US-DO/LH surge in 89% of the 62 cycles. They concluded from this data that the "synopsis" of the peak in mucus with the BBT shift is the most accurate natural indicator of ovulation.

Data on achieving pregnancy

The researchers reported further results from a sub-data set of 346 women who began using the European STM from the first cycle of use to achieve a pregnancy. They found (based on cumulative probabilities of conception) that 81% of the STM users achieved a pregnancy within 6 months of use and 92% after 12 months of use. (To read about some of the controversy over these results, see this issue of CMR, "Efficacy of Fertility Focused Intercourse with NFP Questioned: Timed Intercourse with Ovulation is not recommended.")

Figure 1.

Determination of the fertile phase of the menstrual cycle by rules of the European Sympto-Thermal Double Check Method

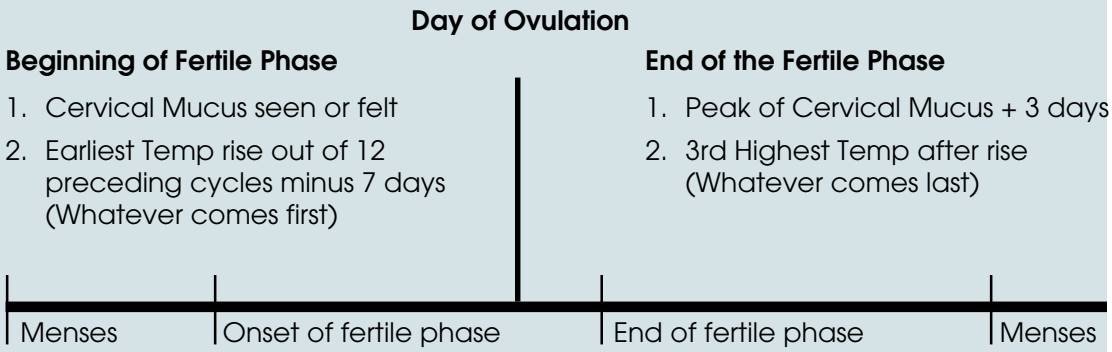

Table 1:

Unintended Pregnancy Rates per Annum based on Behavior during the estimated Fertile Window

Behavior	Cycles	Unintended pregnancy	% Rate
Abstinence only	8766	3	0.50
Intercourse with Barriers	2917	1	0.45
Unprotected intercourse	2364	17	8.96
Protected & Unprotected	882	3	4.33
Genital contact	841	4	4.54

Comments

This article was a good summation of the current and ongoing research of the European double check STM. The authors used the article to make comparisons (and provide evidence) of the European STM system in comparison with the Billings Ovulation Method (BOM). They essentially stated that the BOM method is not accurate or effective enough to be used by women in developed countries (e.g. Europe) were there is expectancy for high efficacy. They believe that the BOM is more appropriate for women in developing countries, especially since the method does not require any devices, i.e., a thermometer. Another

reason they provided for the BOM to be less effective than the STM is because pregnancy can occur by having intercourse on a dry day before the mucus peak (i.e., essentially on a dry day during the 6 day fertile phase of the menstrual cycle). The researchers continue to recommend a double check for the beginning and end of the fertile phase. They did not provide suggestions for other indicators to identify the beginning or end of the fertile phase. Based on this analysis, the use of urinary LH could be suggested as one of those indicators.

One aspect of the study is confusing. I am not sure how they obtained what they call a "synopsis" of the BBT shift with the peak in cervical mucus. The STM identifies the end of the fertile phase with the BBT shift plus three days or the peak in mucus plus three days - whatever occurs last. It is confusing in the article how they correlate the BBT shift with peak mucus to estimate the single day of ovulation. Furthermore, it was unclear how they estimated the day of ovulation by both LH and ultrasound if these two markers of ovulation did not agree with one another. (RJF)

1. Frank-Hermann, P., Gnoth, C., Baure, S., Strowitski, T., & Freundl, G. **Determination of the fertile window: reproductive competence of women - European cycle databases.** *Gynecology Endocrinology*, 2005; 20: 305-312.

Unintended Pregnancies Common with Fertility Awareness Based Methods of Family Planning

Randomized control trials (RCT) are considered by the medical and health professions as the gold standard for generating efficacy data for any type of medical, surgical, or behavioral intervention. RCT studies include randomly assigning participants to an intervention group and to either a control group that does not receive the intervention or a comparison group that receives another type of intervention or levels of the intervention. RCTs also involve determining (before conducting the study) how many participants are needed (i.e., sample size) to obtain statistically significant differences in the outcome variables (this is called power analysis). Ideally, methods to conceal from the researcher (called blind) and if possible from the participant (called double blind) what intervention the participants (i.e., subjects in an experiment) are assigned to is recommended for RCTs. Methodological concealing participants from behavioral interventions such as Natural Family Planning (NFP) methods would not be easy to do. Concealment is important to eliminate bias in producing and interpreting the results.

Researchers from Family Health International, Durham, North Carolina, recently conducted a review of all RCT studies that investigated the effectiveness of fertility awareness based or NFP methods to avoid pregnancy, methods that included Calendar Rhythm, Basal Body Temperature (BBT), ovulation or cervical mucus only methods, Sympto-Thermal or multiple indexed methods, and methods that utilized electronic fertility monitors.[1] The review report was essentially a reprint of the previously published Cochrane Database of Systematic Reviews of fertility awareness based (FAB) methods for family planning by the same authors.[2]

After conducting numerous electronic searches, reviewing the references of published studies, contacting authors of effectiveness studies, and contacting FAB/NFP organizations, they found only three RCT of FAB/NFP methods, one of which was a comparison of using the Today Sponge contraceptive in comparison with using the Sponge during the fertile time estimated by BBT and calendar calculations.[3]

The other two studies compared STM with OM but both studies had method problems,

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i.e., high drop out rates and encouraging participants that were not following the rules of the method to drop out of the study.[4,5] The studies did not include power analysis or any blinding procedures. Therefore, the authors of this review were only able to analyze the methodology problems of the three studies. The authors concluded that comparative efficacy of these methods remain unknown, unintended pregnancies with these methods are common, and continuation rates are low. Furthermore, they stated there is a high unintended pregnancy rate using FAB based on the re-analysis of the five country World Health Organization WHO study of the OM (i.e., an unintended pregnancy rate of 23% per annum).[6]

Comments

Of interest was the high drop out rate and the difficulty of recruiting participants for the two OM versus STM studies. The drop out rate comprised a major flaw of the studies in that it was difficult to enable relevant comparison of effectiveness.

One of the studies had the support of the Catholic hierarchy and utilized two public relations firms to recruit subjects from a city (Los Angeles) that has a very high population of Roman Catholics. Furthermore, the study included a very new (at that time) natural method of family planning, i.e., the Billing Ovulation Method. Essentially, this review points out the difficulty of conducting and the need for good RCTs of NFP methods. (RJF)

1. Grimes, D.A., Gallo, M.F., Grigorieva, V., Nanda, K., & Schulz, K.F. **Fertility awareness-based methods for contraception: systematic review of randomized controlled trials.** *Contraception,* 2005;72:85-90.
2. Grimes, D.A., Gallo, M.F., Grigorieva, V., Nanda, K., & Schulz, K.F. **Fertility awareness-based methods for contraception.** *Cochrane Database Systematic Review,* 2004 Oct 18;(4):CD004860. Review. PMID: 15495128
3. Kass-Annese, B., Kennedy, K.I., Forrest, K., Danzer, H., Reading, A., & Hughes, H. **A study of the vaginal contraceptive sponge used with and without the fertility awareness method.** *Contraception,* 1989;40:701-14.
4. Medina, J.E., Cifuentes, A., Abernathy, J.R., Spieler, J.M., & Wade, M.E. **Comparative evaluation of two methods of natural family planning in Columbia.** *American Journal of Obstetrics and Gynecology*, 1980;138:1142-7.
5. Wade, M.E., McCrthy, P., Braunstein, G.D., et al. **A randomized prospective study of the use-effectiveness of two methods of natural family planning.** *American Journal of Obstetrics and Gynecology,* 1981;141:368-76.
6. World Health Organization Task Force. **A prospective multicentre trial of the ovulation method of natural family planning: II. The effectiveness phase.** *Fertility and Sterility,* 1981;36:591-8.

Self Evaluation of Cervical-Vaginal Fluid Deemed Accurate Indicator of Ovulation

Researchers at a university-based NFP Center (Universidad de los Andes) in Santiago, Chile recently conducted a study to determine and compare the accuracy of various biological indicators of ovulation.[1] The biological indicators of ovulation they chose to evaluate were: 1) the self-observed peak day of cervical vaginal fluid (CVF) detected at the vulva, 2) the peak of self-aspirated cervical vaginal fluid with a specially designed vaginal syringe (the aspirated mucus was observed and graded by both the researchers and the participant), 3) the self-determined basal body temperature (BBT) shift, and 4) first morning urine samples tested by immunoassay for estrone (E1G) and pregnanediol glucuronide (PdG) enzyme ratios to estimate ovulation. The criterion or gold standard for the estimated day of ovulation was determined by serial ovarian transvaginal ultrasound scans (US-DO). Participants for this study were 15 multiparous women who had regular menstrual cycle

patterns and were using NFP methods. They produced 29 usable cycles of data.

The Chilean researchers reported their results by determining frequency and percentage of each natural indicator of ovulation that fell + 1-day of the US-DO and (-1 to +2 days) of the US-DO (See Table 2). As seen in Table 2, the researcher observed and graded CVF Peak was the most accurate (by percent) of the biological markers, however, the self-observed Peak in CVF reached equivalent accuracy (i.e., 97%) with the more liberal boundaries surrounding the US-DO. Surprisingly, the accuracy of the urine E1G/PdG ratio was lower than self rated CVF but not surprisingly was the lower accuracy of the self determined BBT shift.

Table 2:

Percentage of estimated days of ovulation in comparison with US-DO

Method	± 1-day of US-DO	-1 to +2 days of the US-DO
Self-observed Peak CVF	76%	97%
Syringe Aspirated CVF	76%	90%
Researcher Graded CVF	90%	97%
E1G/PdG Ratio	76%	86%
BBT shift	71%	79%

The researchers concluded self-observation of the CFV Peak is an accurate means of determining the day of ovulation. They also concluded that estimating ovulation by urine LH test kits and/or E1G/PdG ratios does not seem to be better. They did suggest (as an implication of the results for teaching NFP) that NFP instructors could ask the woman NFP client to collect mucus by vaginal syringe and then the NFP teacher could grade the samples provided. By this comparative process, the NFP teacher could aid the woman in interpreting the CVF and estimating her fertile window. This was recommended for women who have continuous or confusing mucus patterns.

Comments

Since the researchers did not compare urine LH test kits in this study I am not sure how they could conclude that self-observation of the CVF Peak is more or just as accurate an estimate of ovulation. Of interest is that they used the Brown Ovarian Monitor to determine E1G/PdG ratios. They did indicate that the monitor is not very user friendly i.e., they stated "all these aspects make the clinical determination of the fertile period end difficult with E1G/PdG ratio."

Although the results provided in the study compare with recent studies that utilized US-DO as the gold standard to evaluate the accuracy of natural indicators of ovulation, I am not sure how the information in this study advances knowledge and use of NFP. Furthermore, the researchers had a very small number of participants and only 29 menstrual cycles of data. A positive is that they did use US-DO as the gold standard to evaluate the other methods of estimating ovulation. The use of the vaginal syringe to help the woman client interpret the CVF does not seem to be user or teacher friendly. However, the results do contribute to the knowledge that self-observation of the CVF Peak is a fairly accurate measure of the day of ovulation. (RJF)

1. Alliende, M.E., Cabezon, C., Figueroa, H., & Kottmann, C. **Cervicovaginal fluid changes to detect ovulation accurately.** *Obstetrics and Gynecology,* 2005;193:71-75.

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Efficacy of Fertility Focused Intercourse with NFP Questioned: Timed Intercourse with Ovulation is Not Recommended

A recent letter (Snick) in the European journal *Human Reproduction* questioned the efficacy of using fertility focused intercourse as opposed to spontaneous intercourse to achieve a pregnancy.[1] The author questioned the results of two published studies of using NFP to achieve pregnancy, i.e., a small United States study that involved use of the Creighton Model to achieve pregnancy (N=50)[2] and a larger German based study (N=304) using the European Sympto-Thermal method of NFP.[3] The base of the critique was essentially that without a comparison group the authors cannot claim that fertility focused intercourse with NFP methods quickens the time to pregnancy. Furthermore, the author pointed out the two NFP studies excluded couples (and cycles) that did not have intercourse during the fertile time and couples with ovulatory problems and infertility, and included a high proportion of couples in upper social classes. The author provided data from a retrospective study on time to pregnancy which he conducted with 719 couples (from a general population) that were not instructed in timed intercourse. He found similar cumulative pregnancy rates to the German study, i.e., 40, 75, 98 and 97% at 1, 3, 6, and 12 months respectively. In addition, the author cited evidenced-based National Institute for Health and Clinical Evidence (NICE) Guidelines which do not recommend timed intercourse for infertility couples since this recommendation causes stress (for the couple).[4] The author ends by stating that NFP promoters "have a duty" to provide evidence for the efficacy of timed intercourse with use of NFP methods in well-designed clinical trials.

Fertility monitoring does not have negative impact on couples' relationship

In a related study, researchers from Family Health International and the University of Florida, conducted a study to determine the psychological impact of using technology to help couples achieve a pregnancy.[5] The technology is a palm size electronic fertility monitor (i.e., the Clearplan Easy Fertility Monitor, Unipath / Inverness Medical Innovations, Waltham, Massachusetts) that provides couples with a daily reading of their fertility level, i.e., low, high, or peak fertility. The monitor is designed to detect threshold levels of urinary metabolites of estrogen and luteinizing hormones. Fifty two couples, from Florida and North Carolina (of which the woman participant was experiencing regular length menstrual cycles and not on any hormonal medications) utilized the monitor for 4 consecutive cycles to achieve pregnancy and to focus intercourse on high and peak fertile days, as indicated by the monitor. The couples also were provided with a multiple item paper and pencil tool to measure dimensions of acceptability for their family planning method. Both the male and female participants completed the questionnaire at baseline and after each cycle of use.

Results indicated there was at least one act of intercourse during the estimated fertile phase in 96% of the menstrual cycles produced for the study. Acceptability of the monitor and having fertility focused intercourse was more favorable at baseline among the couples who eventually achieved a pregnancy. For couples that did not achieve pregnancy, acceptability declined over time and relationships became more strained.

The researchers concluded that their findings suggest fertility monitoring does not have a negative influence and may even have a positive influence on the couples' relationship, in particular in enhancing communication. Although gaining knowledge of fertility initially helped to keep stress and anxiety at a minimum, for couples that did not achieve a pregnancy, stress and anxiety reentered into the relationship after unsuccessful attempts to achieve a pregnancy.

Unlike the NICE guidelines that indicate fertility focused intercourse is stressful and not

recommended, the authors felt that using the electronic fertility device was better than using nothing for two reasons, 1) it provided clear knowledge of the optimum time to have intercourse, and 2) the high tech monitor could bolster their confidence that conception will happen.

Comments

In the first article, the rationale of the author, H.K.A. Snick, is not clear. Snick criticizes fertility focused intercourse as causing too much stress in a couple who wishes to achieve pregnancy. NFP users know that the fertile phase of the menstrual cycle is the most advantageous for trying to achieve pregnancy. Research shows that the two optimal days to achieve a pregnancy are the two days before ovulation, therefore, targeting these days (for infertile couples) makes sense and increases the probability of achieving pregnancy.[6]

It is interesting that the NICE evidenced based guidelines for recommending intercourse for couples' attempting to achieve pregnancy, is based on one study, that of Wilcox, et al. 1995 *(New England Journal of Medicine)*, in which 221 women had intercourse once in the menstrual cycle and achieved pregnancy. That study defined the 6 day fertile window. However, the study did not measure whether having fertility focused intercourse was stressful. Furthermore, the study was not a randomized control trial of couples having random intercourse with couples having fertility focused intercourse. The only recommendation that Wilcox gave was that frequent intercourse did not seem to decrease time to pregnancy (i.e., addressing the concern that frequent intercourse will diminish sperm count).[7]

Snick mentioned from his retrospective time to pregnancy study, that 96% of his couples achieved a pregnancy within 12 months. Those cumulative pregnancy rates are not what will be found in the general public which is around 84-85% over one year with unprotected intercourse. Therefore, if the cumulative pregnancy rate can be increased to 95-96% by having fertility focused intercourse, then maybe that practice is warranted. The NICE guidelines are impressive in that they are evidenced based, however, the evidence for their timing of intercourse is thin, and the evidence that fertility focused intercourse is stressful is nonexistent and might be false. As pointed out in the study assessing the electronic fertility monitor, knowing the fertile time and having intercourse during the optimal fertile days might increase confidence and lower anxiety and stress. I agree that NFP promoters and scientists need better evidence for their claims of effectiveness and pregnancy rate and in particular the need for evidence based on randomized control trials. (RJF)

1. Snick, H.K.A. **Should spontaneous or timed intercourse guide couples trying to conceive?** *Human Reproduction,* 2005;10:2976-77.
2. Hilgers, T.W., Daly, K.D., Prebil, A.M., & Hilgers, S.K. **Cumulative pregnancy rates in patients with apparently normal fertility and fertility-focused intercourse.** *Journal of Reproductive Medicine,* 1992;37:864-866.
3. Gnoth, C., Godehardt, D., Godehardt, E., Frank-Hermann, P., & Freundl, G. **Time to pregnancy: results of the German prospective study and impact on the management of infertility.** *Human Reproduction,* 2003;18:1959-1966.
4. NICE Guideline (2004) Clinical Guidelines 11. **Fertility: assessment and treatment for people with fertility problems.** February 2004. (http://www.nice.org.uk/pdf/CG011niceguideline.pdf)
5. Severy, L.J., Robison, J., Findley-Klein, C., & McNulty, J. **Acceptability of a home monitor used to aid in conception: psychological factors and couple dynamics.** *Contraception*, 2006;73:65-71.
6. Dunson, D.B., Baird, D.D., Wilcox, A.J., & Weinberg, C.R. **Day-specific probabilities of clinical pregnancy based on two studies with imperfect measures of ovulation.** *Human Reproduction,* 1999;14:1835-1839.
7. Wilcox, A.J., Weinberg, C.R., & Baird, D.D. **Timing of sexual intercourse in relation to ovulation: effects on the probability of conception, survival of the pregnancy, and sex of the baby.** *The New England Journal of Medicine,* 1995;333:1517-1521.

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BREASTFEEDING/MENSTRUAL CYCLE

Determining Fertility While Breastfeeding and not Ovulating

For women and couples who use NFP to avoid pregnancy, determining fertility while breastfeeding is often difficult. Anticipating the first true "fertile window" and the first ovulation can be frustrating and the transition from not ovulating to being in normal cycles is a time when couples become pregnant not intending to. Although the traditional use of monitoring changes in cervical mucus (and the eventual basal body temperature shift if temperature is used) has been useful and successful for many women, cervical mucus monitoring can be confusing at times and its use often over estimates the actual fertile time by a considerable amount of days.

Researchers from Marquette and Saint Louis University recently conducted a small pilot study with 10 breastfeeding women who were not ovulating to test a protocol using an electronic hormonal fertility monitor.[1] The protocol involved creating artificial 20 day cycles and using the monitor to test for threshold levels of E3G and an eventual LH surge in the urine. The 10 participants observed their cervical mucus on a daily basis and the "low," "high" and "peak" readings provided by the hand held fertility monitor through their first complete menstrual cycle. The electronic monitor provided a "high" reading when a threshold level of E3G was reached and "peak" reading when a threshold level of urinary LH was reached. The monitor was designed to read antibody impregnated test-strips that were held under the urine stream for 3 seconds. The researchers compared the amount of days of fertility as indicated by cervical mucus as compared to the high and peak readings on the monitor through the first complete menstrual cycle.

The mean number of days from the first day of charting through the first complete menstrual cycle was 147 days (SD=62.8), the mean number of fertile days as indicated by cervical mucus ratings was 73.5 days (SD = 38.8) or 49.7% of the total days monitored. The mean number of high and peak reading on the electronic monitor was 25.7 days (SD=17.6) or 17.4% of the total. There was a significant difference between the mean number of fertile mucus days as compared to the fertile monitor days ($t = 3.65$; $p<0.01$). The authors concluded that although the protocol needs further testing, the fertility monitor protocol does provide women with a simple and objective method of determining fertility while breastfeeding.

Comments

A disadvantage of the electronic fertility monitor is that it costs approximately $200 and the test strips about $50 for a package of 30. However, the average cost of using the monitor, once the woman is ovulating on a regular basis, is about $18 per cycle. A criticism of the protocol and research is that to be a fair comparison, determination of the basic infertile pattern (BIP) of continuous mucus needs to be figured into the calculations. The women in this small study graded the mucus from 1 to 8, with a 1 = to a dry sensation and no mucus present to 7-8 = to clear, stretchy, slippery mucus. For the study, a 4 or greater reading was considered to be a fertile day. This level of mucus is often an indication of a transition into a fertile phase. (RJF)

1. Fehring, R.J., Barron, M.L., & Schneider, M. **Protocol for determining fertility while breastfeeding and not in cycles.** *Fertility and Sterility*, 2005;84:805-807.

Menstrual Cycle Lengths between 30-31 days Associated with Highest Fecundity

Epidemiologists from Emory University (Atlanta) prospectively followed 470 women who kept menstrual cycle diaries and recorded the length of their menstrual cycles and menstrual bleeds.[1] These women participants also provided two urine samples per cycle. The urine samples were tested by the researchers for human chorionic gonadotropin to confirm pregnancy. The participants were followed for one year or until the end of a clinical pregnancy. The purpose of this research was to determine whether menstrual cycle characteristics are associated with fertility and pregnancy outcomes.

The researchers found that menstrual cycle lengths between 30-31 days preceded cycles with the highest fecundity. Shorter cycles (i.e., less than 30 days) were less likely to be followed by conception. They also found menstrual cycles with menstrual bleeds of 5 days had the highest fecundity and menstrual cycles with menstrual bleeds 4 days or less had lower fecundity. Furthermore, menstrual cycles which were shorter than 30 days or longer than 31 were more likely to be followed by conception cycles that ended with spontaneous abortions. The researchers concluded menstrual cycle characteristics are associated with fecundity and spontaneous abortion.

Comments

The obvious implication for NFP use is that women who generally have 30-31 day cycle lengths and 5 days of menses can be comfortable they most likely have hormonally normal cycles. Another earlier study that investigated menstrual cycle characteristics among 309 working women between the ages of 20-44 and who produced 1,139 menstrual cycles of information (including daily urine samples assayed for estrogen and progesterone levels) found that mean cycle length and phase lengths were significantly associated with length of the prior luteal phase.[2] This result could help confirm the NFP rule used for STM methods that state if a woman experiences a clear BBT shift followed by a normal luteal phase, then the first 5 days of the next menstrual cycle can be considered infertile. (RJF)

1. Chanley, S.M., Manatunga, A.K., Klein, M., Feigelson, H.S., Dominquez, C.E., McChesney, R., & Marcus, M. **Menstrual cycle characteristics: associations with fertility and spontaneous abortion.** *Epidemiology*, 2006;17:52-60.
2. Liu, Y., Gold, E.B., Lasley, B.L., & Jonson, W.O. **Factors affecting menstrual cycle characteristics.** *American Journal of Epidemiology*, 2004;160:131-140.

Lunch Time determined to be Best Time for Urine LH Surge Determination

Researchers from the United Kingdom conducted a study to determine the most likely time to detect the onset of the LH surge by use of over the counter urinary LH assay dipsticks. Another purpose was to determine the optimal time for intrauterine insemination from the onset of the LH surge. They conducted a prospective study in which they generated 1540 inseminations with 362 women between 23-45 years of age from one IVF clinic. The women participants were asked to collect 4 daily urine samples i.e., early morning (04:00-10:00), lunch-time (11:00-15:00), tea-time (16:00-20:00) and bed time (21:00-00:00). In addition, they were instructed to test only the lunch-time urine sample (after not urinating for 4 hours). If the lunch time urine was positive for LH, other samples were tested retrospective by the researchers. Of the 1540 cycles of insemination, 951 resulted in an LH surge followed by a negative result.

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The researchers found that the first positive LH test occurred in the morning sample 27% (N=257) of the time, 44.5% (N=423) of the time with the lunch-time samples, the tea-time samples only produced 15.7% (N=149), and the night-time sample produced the least with 12.8% (N=122) of the samples. It was clear by percentage and by use of chi square analysis that the largest number of positive LH tests were obtained during lunch-time. They also found the best time for IUI was 24-42 hours after the first detection of LH.

Although the researchers were concerned about the best time for initiating artificial inseminations to produce a live birth, the purpose of including this article was for the information about urinary LH testing (for determining or estimating the day of ovulation). The researchers concluded from this study that lunch-time is the optimal time to check for the LH surge with urine dip sticks.

Comments

It is interesting that the researchers wanted to determine the best time of the day to use urine LH dipstick test kits (Clearblue, Unipath) to determine the onset of the LH surge. Although, lunch-time was determined to be the best time, the women had to make sure that they avoided urinating at least 4 hours before taking a test. This might not be convenient for the woman user of these test kits. Furthermore, the researchers did indicate that with early morning testing, even if the lunch-time was when the LH surge began, the surge will be detected the next day in the early morning urine. This study does not show that a greater percentage of LH surges will be detected from lunch-time testing versus early morning testing. (RJF)

1. Khattab, A., Mustafa, F., & Taylor, P. **The use of urine LH detection kits to time intrauterine insemination with donor sperm.** *Human Reproduction*, 2005; 20:2542-2545

Weight Loss Best Predictor of Menstrual Cycle Regularity among Obese PCOS Patients

Researchers from the United Kingdom (Department of Reproductive Medicine - The General Infirmary, Leeds, UK) recently conducted a placebo-controlled, double blind multi-center study to investigate the effects of Metformin on menstrual cycle regularity, weight loss (i.e., arthropometric measurements) and endocrine parameters (i.e., lipid sensitivity and lipid profiles) with obese patients diagnosed with polycystic ovary syndrome (PCOS).[1] The researchers randomly assigned 143 obese PCOS patients (between 18 and 39 years) with a basal body mass (BMI) of >30 kg / m2 from 8 centers over a 4 year period (1999-2003) to either a metformin (MET) or placebo control group. The MET group participants (N=69) were instructed to take one tablet of metformin (850 mg) every 12 hours for 6 months, the control group received an identical placebo pill and were given the same instructions. All participants were assessed by a dietitian and provided individual diet plans high in carbohydrates (50%) and low in fats (10%). In addition, they were encouraged to increase their exercise patterns (i.e., walking, using stairs) by 15 minutes each day.

Although participants in both groups showed significant improvements in menstrual cycle regularity and weight loss and no significant improvements in insulin sensitivity or lipid profiles, there were no significant differences between the 2 groups on all outcome measures. The researchers also correlated menstrual cycle regularity with metformin use, percentage of weight loss, initial BMI, and age, and found only the percentage of weight loss to correlate with menstrual cycle regularity. The researchers concluded that use of metformin among obese PCOS patients does not improve menstrual frequency or weight loss. How-

ever, life style changes that include weight loss and moderate exercise does improve menstrual cycle regularity.

Comments

The measure of menstrual cycle improvement was rather imprecise, since it was measured by frequency of menses over a 6 month time period. I would be more comfortable with this outcome if the women participants were charting other parameters of the menstrual cycle, such as cervical mucus changes, basal body temperature shift, and or urinary LH surge. However, the results of this study support another recent randomized control trial of life style modification and use of metformin.[2] The researchers in this study (involving 38 obese women with PCOS as participants) found the greatest improvement in ovulation rate was with those women who lost weight. In this study ovulation was determined by urine assays of pregnanedial glucuronide.

The relevance of these studies for NFP are if women have long cycles (especially long anovulatory cycles) due to PCOS and are obese, and wish to use NFP methods, then helping them loose weight might be the first step towards menstrual cycle regularity. If weight loss normalizes cycle length then NFP methods will be easier to use. I would want to find out if weight loss not only normalizes cycle length but also biological markers of fertility like cervical mucus and basal body temperature. I would imagine there would be less false positive LH surges with normalized cycle lengths. (RJF)

1. Tang, T., Glanville, J., Hayden, C.J., White, D., Barth, J.H., & Balan, A.H. **Combined lifestyle modification and metformin in obese patients with polycystics ovary syndrome. A randomized, placebo-controlled, double-blind multicentre study.** *Human Reproduction*, 2006;21:80-89.
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OF INTEREST

Oral Contraceptive Use Associated with Decreased Levels of Sex Hormone-binding Globulin and Androgen Levels

This study was carried out by researchers from the Department of Endocrinology and Urology at Boston University Medical Center.[1] The purpose of the study was to determine sex hormone-binding globulin (SHBG) levels before and after the discontinuation of oral contraceptives (OCs) and in comparison with women who never were on OCs. Previous studies have shown that SHBG levels are increased with OC users and that androgen levels are decreased. SHBG is a protein that binds with testosterone and thus makes it biologically unavailable. Adequate testosterone levels are necessary for healthy sexual functioning. Low levels of testosterone could lead to a low or diminished sexual drive. Decreased androgen levels and increased SHBG are associated with sexual dysfunction.

The participants were 124 pre-menopausal women with sexual health complaints for greater than 6 months. The researchers defined 3 groups of women, group one (N=62; mean age 32) were women who were on OCs for at least 6 months and continued to take them, group two (N=39; mean age 33) were women who were on OCs but had discontinued them

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for at least 6 months, and group three (N=23; mean age 36) included women who never had taken OCs. The main outcome measure was SHGB levels.

The researchers found that SHGB levels were 4 times higher in the continued OC users compared to the discontinued users of OCs. Furthermore, the discontinued users (even after 6 months post discontinuing OCs) had significantly higher SHBG levels compared to the never users. The researchers concluded that sexual, metabolic, and mental health problems could result from long term elevations of SHBG due to OCs.

Comments

This is not a randomized control trial, therefore results need to be discussed with caution. An obvious benefit for NFP users is that women who use natural methods will not have to worry about elevations of SHBG and potential sexual health problems due to decreased androgen levels. It is also interesting that in a web site report from Medical News Today (1/9/2006) - the lead author Dr. Claudia Panzer stated, "it is important for physicians prescribing oral contraceptives to point out to their patients potential sexual side effects, such as decreased desire, arousal, decreased lubrication and increased sexual pain. Also if women present with these complaints, it is crucial to recognize the link between sexual dysfunction and the oral contraceptive and not to attribute these complaints solely to psychological causes." Women on OCs might become more interested in natural methods if they are experiencing sexual dysfunction and a low sexual drive. (RJF)

1. Panzer, C., Wise, S., Fantini, G., Kang, D., Munarriz, R., Guay, A., & Goldstein, I. **Impact of oral contraceptives on sex hormone-binding globulin and androgen levels: a retrospective study in women with sexual dysfunction.** *Journal of Sexual Medicine,* 2006;3:104.

Decrease in Marriage, Delay in Planning First Child, and No Desire for Children Contribute to Low European Fertility Rates: Children & Family are Low Priority

The double impact of an aging population and low fertility rates are a concern in European countries. The fertility rates in the European Union are well below the replacement level of 2.1 (See Table 3). The lowest fertility rates are those in the Southern countries (e.g., Italy and Spain) with a slightly higher rate among Northern countries. Demographers from the University of Rome recently analyzed socio-demographic factors that have contributed to these low fertility rates. They determined postponement of marriage and delay in having children once married are the two most significant contributing factors.[1] In addition, low fertility rates are modified somewhat in countries (e.g., Sweden) where institutions support women's careers and have family friendly support systems (e.g., generous maternity leave). The authors also list non-traditional family systems (e.g., cohabitation) as contributing factors to the declining fertility rates.

In Germany, researchers from the University of Leipzig referenced the problem of low fertility rates and conducted a study to determine reasons for a desire to have or not have children among the German people.[2] They surveyed a representative sample of 785 women and 795 men with a mean age of 34.8 years (range of 14 to 50 years) and found 82% of their total sample either had no or little wish for a child. Furthermore, 77% of the childless participants had little or no desire for children as well. Among childless participants, men had significantly less desire for a child, and women between the ages of 21 and 30 years of

age the greatest desire to have children. Fifty-three percent of the participants identified "two" as the ideal number of children. Eighty percent wanted to have 2 or less. Desire for "emotional stabilization" was listed as the strongest motivation to have a child and "economic reasons" were given as the biggest barrier. When asked to prioritize life values with family life and having children, the respondents listed having a child as number six behind health, income and financial stability, work, partnership and sexuality, and living conditions (in that order).

The authors speculated that increased individualism and alternative life paths (especially career) are increasingly more important than children and family life. They also cited economic concerns, i.e., when the cost of living increases, it becomes too expensive, especially in terms of educational costs, to have more. In addition, as women become more educated they experience less desire to have children. Based on their findings, the authors identified the need for more governmental support (i.e., social services) to increase the desire to have more children. They also indicated that educating couples about fertility being a positive resource should be promoted. Finally they stated because living standards and per capital income is increasing in Europe, but the birth rate is declining, there is no expectation for population growth in the next few years.

Comments

The researchers reported that 8% of the German population and about 8% of their respondents wished to have a large family (i.e., 4 or more children). They also stated this rate has remained constant over the last decade. I found it interesting they did not look at other factors that might contribute to a desire to have children, such as religiosity (i.e., the practice of religion), marriage, divorce, and cohabitation. (RJF)

Table 3:

Fertility rates (number of children per woman) in the United States and Select Countries in Europe (Stöbel-Richter, 2005)

Country	Fertility Rate
Spain	1.25
Italy	1.26
Germany	1.40
Great Britain	1.64
Sweden	1.65
France	1.88
Ireland	1.97
USA	2.06

1. Pinnelli, A. & Di Cesare, M.. **Human fertility: socio-demographic aspects.** *Contraception,* 2005;72:303-307.
2. Stöbel-Richter, Y., Beutel, M.F., Finck, C., & Brahler, E. **The wish to have a child, childlessness, and infertility in Germany.** *Human Reproduction,* 2005;20:2850-57.

UNDER THE MICROSCOPE

Recent Studies Explore Problems (Physical and Ethical) with IVF Procedures and Oocyte Donation

Small but significant increase in major birth defects found after in-vitro fertilization

One of the largest studies to determine risk of birth defects after use of in-vitro fertilization (IVF) techniques as compared to natural reproduction was recently conducted at the University of Iowa.[1] The researchers compared a cohort of children conceived by IVF (i.e.,

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conceived either by intracytoplasmic sperm injection or by culturing the oocytes and spermatozoa together) with a cohort of children conceived by intrauterine insemination (IUI), and with a cohort of naturally conceived children. The cohort of 864 IVF children and the 270 IUI were conceived at the University of Iowa Hospital from 1989 through 2002. These children were matched (by maternal age, plurality, year of birth, and race) with 6,374 naturally conceived children selected from a 65 county birth registry in Iowa. By state law all births involving a birth defect must be reported in the Iowa Birth Defects Registry. The researchers used this registry to ascertain if birth defects existed in the study cohorts.

The University of Iowa researchers found a significant increase in major birth defects among children conceived by IVF techniques compared with children naturally conceived. There were no differences in birth defects between children conceived by IUI and natural controls. These findings existed whether the children were singletons or not. A greater proportion of major cardiovascular, musculoskeletal, and syndrome type defects were found in the IVF cohort compared with controls, whether the children were conceived as singletons or not. In addition, male children were at a higher risk for major birth defects after IVF than female children.

According to the researchers, although there was a significant increase in major birth defects with IVF, this increase is small, i.e., not enough to dissuade couples from seeking this type of infertility treatment. Speculation as to the cause of the increase cited the use of intra cytoplasmic sperm injection (i.e., the selection of defective sperm not weeded out through the natural process), the effects of cryopreservation of embryos, the effects of the culture media used in IVF, and genetic defects inherited from the parents. With the increasing numbers of couples using IVF for conception (currently 1% of all children in the US are conceived by IVF) the authors concluded there is a need for a systematic evaluation of birth outcomes for children conceived by IVF along with long term follow-up.

A study conducted by researchers in Australia found an increased rate of parenting difficulties (including psychological adjustment and self-reported mood disturbances) among women who underwent assisted reproductive techniques compared to the general population.[2] Although some of the increase could be due to an increased age among couples seeking IVF treatments and a higher rate of multiple births, the Australian researchers recommended that health professionals be aware of the risk of mood disturbances and early parenting difficulties among ART mothers, especially among older women and those with multiple birthing outcomes.

A recent study by researchers in Finland was conducted to determine the frequency of health complications among 9,175 Finish women who underwent IVF, and among10,254 who received ovulation induction (OI) treatments from 1996-1998 and were reported in the Finland National registry through the year 2000.[3] The Finnish researchers found serious cases of ovarian hyperstimulation syndrome (OHSS) in 14 women per 1000 IVF treatment cycles, for the first cycle of treatment, but a rate of 23 per 1000 for the entire study. The rate of OHSS for OI was low (0.3 per 1000). The rate of ectopic pregnancy per 1000 women was 9 for the IVF-treated women and 8 for the OI-treated women, and the rate of miscarriages was 42 per 1000 for both IVF and OI treated women. Finally, they found 15% of the IVF and 8% of the OI women experienced hospital stays due to complications of their reproductive procedure. The Finish researchers concluded that although the risk of complications from a first cycle of IVF treatment is low, repeated attempts will result in many women experiencing serious health complications.

High rates of embryo wastage in the United States

Besides an increase in major birth defects, parental difficulties, and complications as the result of IVF treatments, other major problems with IVF in the United States are the high rates of embryo wastage and the number of "excess" embryos in frozen storage. Although there has been a decrease in embryo wastage in the past ten years, a recent study showed that in 2001, 84.9% of embryos transferred did not result in a live birth (indicating approximately 169,000 embryos wasted in one year alone).[4] From 1995 (when the wastage was 90.8%) through 2001, over 1,000,000 embryos have been wasted through IVF. Although the rate has gone down since 1995 (due to better live birth outcomes and a decrease in the number of embryos transferred), the actual number of embryos wasted has increased due to the increase in IVF attempts (See Figure 2).

Furthermore, there are estimates of approximately 400,000 embryos currently in frozen storage that have accumulated from IVF procedures since 1985.[5] This problem has been exacerbated by recent efforts and promotions to have excess embryos donated to infertile couples or for research purposes. The American Society for Reproductive Medicine has published ethical guidelines for use of embryos for research and in 2002, the U.S. Department of Health and Human Services spent $900,000 to promote embryo donation.[6] The guardians and counselors of embryo donation for infertile couples, however, are the staff of the infertility clinics and/or the embryonic stem cell researchers.

A recent study by University of Wisconsin-Madison researchers illustrates some of the problems with IVF programs and full disclosure of oocyte donation and embryo management.[7] The UW researchers conducted interviews with 122 potential egg donors for their IVF program. Potential donors were informed of numerous ways to determine the fate of their donated oocytes and future embryo management. The 16 possible scenarios presented to the potential donors included donating oocytes: to lesbian and homosexual couples; for posthumous reproduction; to recipients who are HIV positive; to recipients who are on psychotropic drugs; and recipients wishing to use donated sperm from a family member (father/brother). Of these 122 potential donors, 29% (N=35) did not have any concerns regarding the hypothetical scenarios. Sixty-five percent (N=79) stated they would still donate their eggs

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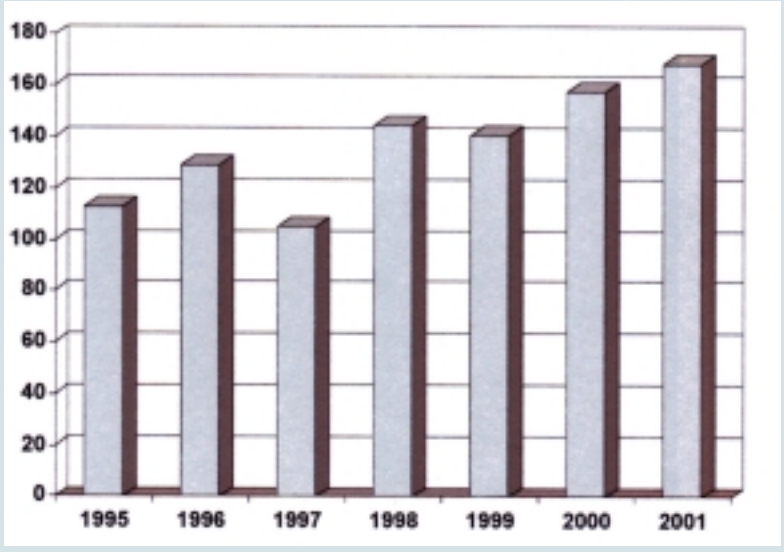
Figure 2:

Number of Embryos Wasted per Year by IVF Procedures in the United States



Current Medical Research, a supplement of ***NFP Forum (Diocesan Activity Report)***, is published biannually. Richard Fehring, DNSc, RN is the editor. Theresa Notare, MA, is the managing editor. The purpose of the supplement is to serve the Roman Catholic diocesan NFP programs of the United States through providing them with up-to-date information on research within the field of fertility, family planning, and related issues. The diocesan NFP teacher should be equipped to understand the various methods of contraception and be able to explain their incompatibility with the practice of the natural methods of family planning.

and trusted the program's judgment, but would prefer their eggs not be given in some of the suggested scenarios (however, the only scenario with lower than 50% approval was donating oocytes to HIV positive recipients). Only 6% (N=8) of the respondents stated they would not donate if their oocytes would be used for certain of the scenarios (but again, only 4 scenarios had less than 50% approval).

Comments

IVF clinics are "big business" in the United States. Some think the potential profits from stem cell research and resultant products are enormous.[7] In addition, money provided by various state governments, private foundations, and countries like South Korea (researchers here were found to have falsified their reports and claims)for stem cell research is substantial. In the United States women are routinely paid from $4,000 to $5,000 for egg donations.[7] In 2002, 13,183 donated eggs were used in IVF procedures, representing 11.4% of a total of 115,392 cycles.

One does not need a very active imagination to see the potential for major ethical problems among the IVF clinics and embryonic stem cell research centers in the United States. The recent scandal in South Korea which involved fraud as well as pressure for egg donation among female research assistants, is certainly not the only known case of pressure for egg donation. Although guidelines have been developed by the ethics committee of the American Society for Reproductive Medicine on recruitment of human egg donors and for donation of "spare" embryos for stem-cell research, I wonder what these guidelines are based upon when they declare that it is ethically permissible to use cells from human embryos and they ensure no oversight to determine whether the guidelines are followed or not.[8,9]

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