ORIGINAL ARTICLE: ENVIRONMENT AND EPIDEMIOLOGY

Peri-implantation intercourse lowers fecundability

Anne Z. Steiner, M.D., M.P.H.,[a] David A. Pritchard, M.S.,[b] Steven L. Young, M.D., Ph.D.,[a] and Amy H. Herring, Sc.D.[b,c]

[a] Department of Obstetrics and Gynecology, [b] Department of Biostatistics, and [c] Carolina Population Center, University of North Carolina, Chapel Hill, North Carolina

Objective: To determine the impact of sexual intercourse around the time of implantation on the probability of achieving a pregnancy.
Design: Time-to-pregnancy cohort using day-specific probability of pregnancy modeling to account for intercourse during the fertile window.
Setting: Community cohort.
Patient(s): Women trying to conceive naturally, ages 30–44, without known infertility.
Intervention(s): None.
Main Outcome Measure(s): Positive pregnancy test.
Result(s): A total of 564 women provided 1,332 complete cycles for analysis. Intercourse frequency during the fertile window and during the peri-implantation window were significantly correlated. Cycles in which couples had 2 or more days with intercourse during the implantation window were significantly less likely to result in a positive pregnancy test compared with cycles in which couples did not have intercourse in this window, after adjusting for age, race, history of regular menstrual cycles, previous pregnancy, and body mass index (fecundability ratio, 0.62; 95% confidence interval, 0.42–0.91).
Conclusion(s): Intercourse during the peri-implantation window may be detrimental to natural fertility. Methods that allow couples to time intercourse to the fertile window may decrease time to pregnancy by not only increasing the probability of fertilization but also decreasing the probability of failed implantation. (Fertil Steril® 2014;■:■–■. ©2014 by American Society for Reproductive Medicine.)
Key Words: Intercourse, fecundability, implantation, time-to-pregnancy

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/steinera-peri-implantation-intercourse-fecundability/

Use your smartphone to scan this QR code and connect to the discussion forum for this article now.*

* Download a free QR code scanner by searching for "QR scanner" in your smartphone's app store or app marketplace.

Previously, Wilcox et al. showed that the fertile window includes the 6 days before and including the day of ovulation (1). For natural conception to occur, procreative intercourse must occur during this window. Theoretically, couples, who are having intercourse at least twice a week should succeed in having intercourse during this interval. However, previous studies have shown that methods that allow a couple to time intercourse to the fertile window lead to higher pregnancy rates (2, 3). One possible explanation for this finding is that intercourse during both the fertile and nonfertile window affects pregnancy rates.

Hypothetically, intercourse around the time of implantation could result in uterine contractions, disrupting the implantation process, displacing the implanted embryo, or expelling the embryo from the uterus. Previous studies have shown increased myometrial activity during intercourse; myometrial activity increases with female orgasm (4). Uterine contractions around the time of ET during assisted reproductive technology lowers pregnancy rates (5, 6). Medications used to inhibit myometrial contractions around the time of ET have been shown to improve implantation rates (7). Based on these theories, some clinicians recommend that couples abstain from intercourse after ET during assisted reproductive technology cycles.

Seminal fluid also contains many potent factors that modify and directly elicit a complex maternal immune response (8). Seminal factors include IL8, CXCL12, CCL2, soluble HLA-G, TGF-beta, and PGE series prostaglandins, as well as specific antigens presented on the sperm cells (8). The introduction of semen rapidly induces a strong inflammatory response by the female reproductive tract, as shown in multiple species, whose superficial

Received December 19, 2013; revised February 26, 2014; accepted March 11, 2014.
A.Z.S. reports consulting fees from Roche Diagnostics. D.A.P. has nothing to disclose. S.L.Y. has nothing to disclose. A.H.H. has nothing to disclose.
This study was supported by the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health, grant nos. R21 HD060229 and R01 HD067683, and by the National Institute of Environmental Health Sciences, grant no. T32ES007018.
Reprint requests: Anne Z. Steiner, M.D., M.P.H., Associate Professor, Department of Obstetrics and Gynecology, UNC School of Medicine, CB #7570, Old Clinic Building, Chapel Hill, North Carolina 27599 (E-mail: asteiner@med.unc.edu).

Fertility and Sterility® Vol. ■, No. ■, ■ 2014 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2014.03.017

cervical and endometrial tissues undergo large changes in leukocyte population that last about 2 days (9–11). Although human data are limited, they support actions of seminal fluid very similar to those seen in animal models (12). After the initial inflammatory response to semen, a secondary tolerogenic response occurs that is likely protective for pregnancy (8). Thus, sexual intercourse at the time of embryo implantation could theoretically induce an unwanted proinflammatory response that could interfere with normal embryo implantation.

We sought to determine whether intercourse around the time of implantation affected fecundability, the probability of achieving a positive pregnancy test in a given cycle. We hypothesized that intercourse during the peri-implantation window, including implantation and the first couple of days after implantation, would lower the probability of conceiving in a given cycle.

MATERIALS AND METHODS

This study was a secondary analysis of data obtained from Time to Conceive (TTC), a prospective time-to-pregnancy study designed to determine the ability of biomarkers of ovarian aging to predict reproductive potential (13, 14). Institutional Review Board approval was obtained for this research. Women were recruited to TTC from the community using flyers; mass e-mail; informational letters; Internet, radio, and television advertising; print ads; and community blogs. All advertising materials directed interested women to an informational website or study telephone number. Women were screened for eligibility using a telephone interview. Women who were eligible for TTC were between the ages of 30 and 44, had been attempting to conceive naturally for 3 or fewer months, and did not have risk factors for infertility (e.g., history of polycystic ovarian syndrome, endometriosis, or pelvic inflammatory disease). After consent was obtained, participants completed a self-reported, online baseline survey of demographics, height, weight, and medical history—for both themselves and their male partners—as well as behaviors including tobacco, alcohol, and caffeine use. While attempting to conceive, women completed an online daily diary for up to 4 months or up to the time of pregnancy detection, in which they recorded vaginal bleeding, intercourse, results of ovulation prediction testing (ovulation predictor kit or cervical mucus monitoring), and results of pregnancy tests. Women were not required to monitor for ovulation but were asked to record the results if they did check their cervical mucus and/or use an ovulation predictor kit. Participants were provided free home pregnancy tests (sensitivity = 20 mIU hCG/mL) and standardized pregnancy test instructions. Initially women were instructed to test with missed menses. Later the protocol was modified to instruct women to test on cycle days 28, 31, 34, and so on until a positive test was noted or menses began.

Data from the baseline survey and daily diary were used to construct menstrual cycles. The start of a menstrual cycle was defined by [1] at least 2 consecutive days of bleeding (not spotting), [2] 3 or more days of bleeding and spotting occurring at least 15 days from the start of the last cycle, or [3] participant-reported last menstrual period (if entire cycle not observed). For each menstrual cycle, day of ovulation was estimated using the calendar method (15). Ovulation was assumed to have occurred 14 days before the first day of menses or first positive home pregnancy test, with the fertile window designated as extending from 5 days before to 3 days after the estimated day of ovulation, as defined above (2, 16). The peri-implantation window was defined as extending from 5 days after ovulation to 9 days after ovulation. Using the calendar method this corresponds to the 3–9 days before the end of the menstrual cycle (whether ending in menses or a positive pregnancy test). For this analysis, cycles were not included in the analysis if the entire fertile window and peri-implantation window were not observed.

The number of days with intercourse during the peri-implantation window was determined for each cycle by responses in the daily diary. For analyses, number of days with intercourse during the peri-implantation window was categorized as none, one, or two or more. Pregnancy, the outcome for this study, was defined by the first report of a positive home pregnancy test.

Pearson correlations, Kruskal-Wallis tests, and χ^2-tests were used to compare demographics and potential covariates (subject age, race, education level, previous pregnancy, body mass index [BMI], ovulation predictor kit use, smoking, hormonal contraception in the preceding year, partner age, partner race, and partner education) between categories of peri-implantation intercourse. For the models, we included those covariates that were strongly associated with fecundability in our study or that had been identified in multiple prior studies as related to fecundability, even if these variables were not statistically significant in our study. Potential covariates that were highly correlated with other predictors thought to have a greater relevance (i.e., partner age is highly correlated with subject age) were also excluded from the primary analysis.

The day-specific probabilities model by Scarpa and Dunson (17) (which was also used in prior analyses) (13, 14) was used. Intercourse patterns are accommodated through inclusion of indicators of intercourse on each day of the fertile window that restrict the probability of conception on a nonintercourse day to be 0. This model provides Bayesian estimates of the fecundability ratio (FR) and an accompanying 95% confidence interval (CI). In this model an FR <1.0 suggests reduced fecundability. The day-specific probabilities model allows one to determine the effect of peri-implantation intercourse on achieving a pregnancy independent of intercourse during the fertile window via inclusion of indicator variables for number of peri-implantation intercourse days as a covariate. Other covariates used in the model include maternal age (collapsed into three categories for modeling: 30–34, 35–37, and 38–44), race (non-Hispanic white or non–white), history of previous pregnancy (dichotomized as any/none), maternal BMI, and self-reported history of regular menstrual cycles (yes/no). To address the need for left truncation, attempt cycle at enrollment was added to the model as a covariate; however, addition of the covariate