Effect of ejaculatory abstinence period on the pregnancy rate after intrauterine insemination

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Objective: To determine the optimal interval of ejaculatory abstinence for couples undergoing IUI.
Design: Retrospective analysis.
Setting: Reproductive endocrinology and infertility center.
Patient(s): Infertile couples undergoing ovulation induction and IUI with partner's semen.
Intervention(s): Ovulation induction with clomiphene citrate and a single IUI procedure per cycle.
Main Outcome Measures(s): Clinical pregnancy rates as a function of abstinence intervals.
Result(s): Four hundred seventeen women underwent 929 cycles from June 1999 to October 2002 for a median of 4 IUI attempts per couple. The median ejaculatory abstinence interval was 4 days (range 0–30) with an overall pregnancy rate of 12% per cycle. Abstinence correlated positively with inseminate sperm count but negatively with motility. Variations in inseminate parameters did not correlate with pregnancy rates. However, abstinence intervals significantly affected pregnancy rates. The highest pregnancy rate was observed with an abstinence interval of 3 days or less (14%) and the lowest pregnancy rate seen with an abstinence interval of 10 days or more (3%).
Conclusion(s): An abstinence interval of 3 days or less was associated with higher pregnancy rates following IUI. Prolonged abstinence decreases pregnancy rates, independent of other sperm parameters, perhaps as a result of sperm senescence and functional damage not readily identified by standard semen analysis. Abstinence intervals should be controlled for in studies examining pregnancy outcome in assisted reproduction. (Fertil Steril® 2005; 84:678–81. ©2005 by American Society for Reproductive Medicine.)

Key Words: Infertility, ovulation induction, intrauterine insemination, ejaculatory abstinence, semen analysis, sperm parameters, sperm senescence, sperm DNA damage

There is no consensus in the literature as to the optimal period of ejaculatory abstinence for achieving maximum semen quality. In 1952, McLeod and Gold (1) surveyed fertile couples and reported that their average coital frequency was two to three times per week. Less frequent ejaculation intervals may result in delayed fecundity by missing the ovulatory window and/or by affecting sperm characteristics. Several studies have shown that increasing ejaculatory abstinence generally increases sperm concentration (2–6) but decreases motility (5, 7). Sperm morphology seems to be less dependent on abstinence intervals (5, 7). However, the direct influence of abstinence intervals on pregnancy rate has not been evaluated.

Many investigators have described how standard semen parameters impact on pregnancy rates in couples undergoing intrauterine insemination (IUI). Arny and Quagliarello (8) concluded that sperm motility is the parameter most predictive of conception in IUI cycles. Horvarth et al. (9), described that at least a total motile sperm (TMS) count >1 million was necessary for pregnancy to occur and agreed with Miller et al. (10) and Van Voorhis et al. (11) that an inseminate TMS of 10 million was the statistical threshold for discriminating between pregnant and nonpregnant cycles. However, none of these parameters have proven to be reliable predictors of pregnancy (12). Interestingly, the ejaculatory abstinence interval was not strictly controlled for in these studies, and in fact there are no studies looking at the direct effect of abstinence duration on pregnancy rates.

Because of the known and unknown effects of abstinence on semen parameters, and subsequently pregnancy rates, controlling for the influence of this variable may yield valuable information for counseling couples and infertile patients undergoing fertility treatment. The goal of this study is to investigate the influence of ejaculatory abstinence intervals on the pregnancy rates of infertile couples undergoing treatment with ovulation induction and intrauterine insemination.

MATERIALS AND METHODS

This retrospective analysis was approved by the Johns Hopkins University Institutional Review Board. We reviewed 929 IUI attempts involving 417 women from June 1999

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through October 2002. In this study, couples diagnosed with unexplained infertility or oligomenorrhea (with a normal comprehensive semen analysis and at least one patent fallopian tube in an otherwise normal hysterosalpingogram) underwent ovulation induction and IUI. Patients received clomiphene citrate (50 mg/d for 5 days) beginning on the 3rd or the 5th day of the menstrual cycle. Ovulation was monitored with ultrasound beginning on the 10th or 12th day of the cycle in addition to serum E_2 and LH. A single IUI per cycle was performed with the partner's semen using an Inseminator-Cath catheter (Cook Ob/Gyn, Spencer, IA) either 36 hours after (hCG) administration (10,000 IU IM when the leading follicle measured at least 17 mm in diameter) or 24 hours after a spontaneous LH surge (serum LH >25 mIU/mL). The data included only couples for whom an ejaculatory abstinence period was documented by the andrology laboratory staff on the day of semen collection for IUI. Pregnancy was defined as the presence of an intrauterine gestational sac seen on transvaginal ultrasound (clinical pregnancy).

Whole semen samples (ejaculates) obtained on the day of insemination were processed using density gradient separation technique. Briefly, a maximum of 2 cc of ejaculate was gently overlaid on a column consisting of 1 cc of 50% and 1 cc 90% density gradient Isolate (Irvine Scientific, Santa Ana, CA) in a 15 cc conical tube. If the ejaculate volume was greater than 2 cc, a separate column was used. After centrifugation at 300 *g* for 15 minutes at room temperature, the pellet was suspended and combined in 5 cc of sperm washing medium containing modified human tubal fluid medium (mHTF; Irvine Scientific) and 10% synthetic serum substitute (SSS; Irvine Scientific). Following centrifugation at 300 *g* for 8 minutes, the pellet was resuspended in 0.5 cc of wash medium. The sample was then assessed using a Makler chamber (Sefi-Medical instruments, Haifa, Israel) under a phase contrast microscope for concentration, motility, forward progression (0 = nonmotile to 4 = rapid) and TMS.

We evaluated the correlation between ejaculatory abstinence intervals and semen parameters (concentration, motility, forward progression, and TMS) in both ejaculate and inseminate, semen parameters (ejaculate and inseminate) and pregnancy rates, and abstinence intervals and pregnancy rates by Spearman's correlation analysis. Logistic regression including each of the semen parameters (ejaculate and inseminate) and abstinence intervals was performed to assess the influence of each of these variables on pregnancy rate. Mann-Whitney and Kruskal-Wallis tests were used to compare means. Unless otherwise specified, values are reported as mean ± SD or median (range). All statistical calculations were performed using the SPSS 12.0 software (SPSS, Chicago, IL).

RESULTS

The median number of IUI cycles per patient was 4 (1–13). The mean male and female partner ages were 37.1 ± 13.3 and 35.2 ± 4.5 years, respectively. The median interval of ejaculatory abstinence was 4 days (0–30) resulting in an overall pregnancy rate per IUI cycle of 12% (113/929). The range in semen parameters for the study group is shown in Table 1.

Ejaculatory abstinence had a significant impact on semen parameters. Correlation analysis revealed that as the abstinence interval increased, sperm concentration and TMS significantly increased but motility decreased ($P<.05$). Forward progression was not affected by abstinence intervals. Ejaculatory abstinence correlated negatively with pregnancy rates ($P<.05$). There were no significant correlations between sperm concentration, motility, forward progression, or TMS and pregnancy rates. These relationships were constant for both ejaculate and inseminate specimens.

Combining all variables (ejaculate parameters, inseminate parameters and abstinence intervals) in a logistic regression model with pregnancy as the outcome, only abstinence interval had a significant impact on pregnancy rates ($P<.05$). Table 2 shows the trend in declining pregnancy rates with increasing abstinence intervals. The sharpest drop in pregnancy rates was seen after 10 days of abstinence. No pregnancies were observed with an abstinence interval greater

TABLE 1

Parameters for the prestudy comprehensive semen analysis, whole semen specimen prior to processing (ejaculate), and processed semen for insemination (inseminate). Values are median (range).

	Comprehensive semen analysis	Ejaculate	Inseminate
Concentration (million/mL)	69 (19–238)	59 (12–174)	67 (2–457)
Motility (%)	64 (34–90)	59 (13–90)	85 (10–99)
Forward progression	4 (1–4)	3 (1–4)	4 (2–4)
Total motile sperm	129 (8–665)	85 (10–399)	25 (2–105)
Morphology (% normal, strict Krueger's)	6 (2–21)	N/A	N/A

Jurema. Abstinence and pregnancy after IUI. Fertil Steril 2005.