ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Does duration of abstinence affect the live-birth rate after assisted reproductive technology? A retrospective analysis of 1,030 cycles

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Objective: To study influence of abstinence period on the live-birth rate after assisted reproductive technology (ART).
Design: Retrospective cohort study.
Setting: Reproductive medicine unit, university-level hospital.
Patient(s): A total 1,030 ART cycles evaluated from 2011 to 2015.
Intervention(s): Group I, abstinence period 2–7 days, and group II, abstinence period >7 days, were compared. Two subgroups Ia (2–4 days) and Ib (5–7 days) were also compared with group II.
Main Outcome Measure(s): Primary outcome was live birth per ET. Secondary outcomes included implantation, clinical pregnancy, and miscarriage rates.
Result(s): The live-birth rate (34.1 % vs. 24.1%; odds ratio [OR], 1.6; 95% confidence interval [CI], 1.1–2.4), clinical pregnancy rate (44.4 % vs. 32.7%; OR, 1.6; 95% CI, 1.1–2.3), and implantation rate (26.4% vs. 18.2%) were significantly higher in group I compared with group II. Other secondary outcomes of fertilization rate and miscarriage rate did not differ between groups I and II. The adjusted odds ratio (aOR) for live birth (aOR, 1.6; 95% CI, 1.1–2.5) and clinical pregnancy rates (aOR, 1.7; 95% CI, 1.2–2.5) were significantly higher for group I compared with group II. The live-birth rate was significantly higher in group Ia (36.1% vs. 24.1%) compared with group II.
Conclusion(s): An abstinence period of more than 7 days may impact ART outcomes adversely when compared with an abstinence period of 2–7 days. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: Abstinence, IVF, ICSI, live birth

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Semen analysis is an important investigation in the evaluation of the subfertile couple. The abstinence period before semen collection can influence the seminal parameters, with short or long abstinence being linked to abnormal results (1). For standardization, the World Health Organization guidelines recommend a 2–7 days abstinence period before semen analysis during routine infertility workup (2). The European Society of Human Reproduction and Embryology advises 3–4 days of abstinence before semen analysis (3).

The role of abstinence period and its impact on sperm DNA fragmentation has been studied, and conflicting reports have emerged. While one study reported an increase in immature sperm chromatin after 1 day of abstinence, another found reduced sperm DNA fragmentation after a similar duration of abstinence (4, 5). While the effect of abstinence period on seminal parameters and sperm quality has been extensively reported in the literature, its overall impact on clinical outcomes of therapeutic interventions such as in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) is not clear (6). One study found higher pregnancy rates in the shorter abstinence group after ICSI and reduction in pregnancy rates after abstinence of ≥5 days (7).

Received May 16, 2017; revised July 30, 2017; accepted August 25, 2017.
A.J.P. has nothing to disclose. G.M. has nothing to disclose. M.K. has nothing to disclose. A.M.M. has nothing to disclose. A.T.K. has nothing to disclose. M.S.K. has nothing to disclose.
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Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2017.08.034

In clinical practice, advice regarding period of abstinence during assisted reproductive technology (ART) has largely been extrapolated from existing recommendations for diagnostic semen analysis. There is a felt need for greater clarity on the issue of abstinence for couples undergoing ART. The literature investigating the effect of abstinence period on clinical outcomes after ART is sparse. We decided to evaluate the influence of abstinence period on clinical pregnancy and live-birth rates after ART.

MATERIALS AND METHODS

A retrospective study was conducted in the Reproductive Medicine Unit of a university-level teaching hospital. Data from all the ART cycles performed during January 2011 to December 2015 were analyzed. Ethics approval was given by the Institutional Review Board.

We included all ART cycles that resulted in a fresh ET irrespective of indication. Type of ART treatment included ICSI or a combination of IVF and ICSI. We excluded the following: [1] women $\geq$40 years, [2] cycles where surgically retrieved sperms or cryopreserved samples were used for ICSI, [3] IVF only cycles, [4] poor responders ($\leq$3 oocytes retrieved), and [5] cycles where all the embryos were cryopreserved.

The included cycles were divided into two main groups: group I, abstinence between 2 and 7 days (standard abstinence period), and group II, abstinence period of >7 days (long abstinence period). We further divided group I into two subgroups: group Ia, abstinence period of 2–4 days, and group Ib, abstinence period of 5–7 days.

We used standard long GnRH agonist, ultralong, or GnRH antagonist protocols. For controlled ovarian hyperstimulation, 100–300 IU of recombinant FSH (Recagon, Organon) was used, and follicular monitoring was done using serial ultrasounds. When at least three follicles >17 mm developed, 5,000 IU of injected hCG (Pregnyl, Organon) was administered. Oocyte retrieval was planned after 35 hours, after hCG trigger. Between one and three embryos were transferred either at cleavage (day 2 or 3) or blastocyst stage (day 5). For luteal support, micronized P, 400 mg twice a day intravaginally (Naturogest, German Remedies), along with IM P, 100 mg (Gestone, Ferring) twice weekly was given. The serum beta hCG level was checked on day 18 after oocyte retrieval.

Data regarding abstinence detail were collected from questionnaires filled out by the male partner on the day of sample collection during the treatment cycle. These questionnaires were safely kept along with embryological details in the ART laboratory records section. Information regarding other clinical and ART variables such as age, indication, oocyte numbers, embryo quality, and numbers transferred was obtained from the unit ART database. The pregnancy outcomes were collected from the women through e-mails and telephone contacts. Collected data were entered in SPSS, and data were analyzed using STATA, version 13.1 (Statacorp).

Outcomes Measured

The primary outcome was live-birth rate per ET. Live birth is defined as delivery of a live baby after 24 weeks of gestation. Secondary outcomes included fertilization rates after IVF and ICSI, development of top-quality embryos, and implantation, clinical pregnancy, and miscarriage rates.

The fertilization rate is defined as the number of fertilized oocytes by the total number of inseminated oocytes (IVF) or injected oocytes (ICSI). A top-quality cleavage-stage embryo is defined as the total number of grade I embryos on day 2/3 of insemination or injection. Clinical pregnancy is defined as evidence of a gestational sac on ultrasound. Implantation rate is defined as the number of sacs seen on ultrasound divided by the number of embryos transferred. The miscarriage rate is absence of cardiac activity or loss of embryo or fetus before 24 completed weeks of gestation divided by the number of clinical pregnancies.

Statistical Methods

Data were summarized using mean (SD) for continuous variables and frequency (percentage) for categorical variables. Analysis of variance (followed by post hoc test) and χ^2 test were used to check the relation between the duration of abstinence and the outcome variables. A logistic regression was performed for the dichotomous outcomes (live birth, miscarriage, and clinical pregnancy), mutually adjusting the potential confounders such as severe oligozoospermia (<5 million/mL) and asthenozoospermia (progressive motility <1%) and male age. The effect is given as odds ratio (OR) with 95% confidence interval (CI). A multiple linear regression was used to assess the influence of predictors over the continuous outcome, mutually adjusting the confounders and expressed as β (95% CI).

RESULTS

A total of 1,345 ART cycles were performed during the study period. After screening, 315 cycles were excluded for reasons such as [1] female confounders (n = 269), [2] frozen semen sample used (n = 16), [3] IVF only (n = 5), and [4] data unavailable (n = 25). In the final analysis, 1,030 cycles were included, among which group I had 868 and group II had 162 cycles.

There were no significant differences in baseline clinical characteristics between group I and group II (Table 1). Mean duration of abstinence in group I was 4.33 $\pm$ 1.31 days and in group II, 18.4 $\pm$ 29.69 days.

Among ART variables, the dose of gonadotropins, the duration of stimulation, the number of oocytes retrieved, and the mean number of embryos transferred were not significantly different in main group comparisons (group I vs. II). The method of fertilization (ICSI or IVF+ICSI) was significantly different between the two main groups (P=.001). Mean progressive motility was significantly higher in group I (36.71 $\pm$ 20.2 vs. 30.6 $\pm$ 19.1; P<.001) compared with group II (Table 2).

The live-birth rate per ET (34.1 % vs. 24.1%; OR 1.6; 95% CI, 1.1–2.5; P=.01) and clinical pregnancy rate per ET (44.4 % vs. 32.7%; OR, 1.6; 95% CI, 1.1–2.3; P=.008) were significantly higher in group I compared with group II (Tables 3 and 4). The implantation rate (26.4% vs. 18.2%; P<.001) was also significantly higher in group I versus group II. Other secondary outcomes of fertilization rate, development