Predictive factors for pregnancy after intrauterine insemination (IUI): An analysis of 1038 cycles and a review of the literature

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Objective: To determine the predictive factors for pregnancy after IUI.
Design: Retrospective study.
Setting: A single university medical center.
Patient(s): One thousand thirty-eight IUI cycles in 353 couples were studied between 2002 and 2005.
Intervention(s): Ovarian stimulation via SC injection of FSH or hMG was performed daily; IUI was then performed 36 hours after triggering ovulation if at least one follicle measuring >16 mm and an endometrial thickness of >7 mm (with triple-line development) were obtained.
Main Outcome Measure(s): Clinical pregnancy rates were analyzed according to the woman's age, the type of infertility, the spermogram characteristics, the total motile spermatozoa (TMS) count, the E_2 level before hCG injection, and the number of mature follicles.
Result(s): The couple with the best chance of pregnancy can be described as follows: an under 30 woman with cervical or anovulatory infertility and a man with a TMS ≥5 million spermatozoa. The "ideal" stimulation cycle enables the recruitment of two follicles measuring >16 mm with an E_2 concentration >500 pg/mL on the day of hCG administration. The best results are obtained when IUI is performed using a soft catheter.
Conclusion(s): This study enabled the characterization of many prognostic factors for pregnancy and particularly those for women at risk of multiple pregnancies after IUI. (Fertil Steril® 2010;93:79–88. ©2010 by American Society for Reproductive Medicine.)

Key Words: Intrauterine insemination, ovarian stimulation, spermogram, clinical pregnancy rate, twin pregnancy

At present, 16% of prospective parents seek medical advice for infertility. Some of these couples will need to undergo IUI using the prospective father's fresh sperm. This method of assisted reproductive technology is indicated in cases of cervical infertility, relative male factor infertility, anovulation, endometriosis with a healthy fallopian tube, and, lastly, unexplained infertility.

In the literature, many factors have been reported as influencing pregnancy rates after IUI: the woman's age, the length of infertility, indications (type of infertility), the sperm count in the initial analysis or in the catheter, the number of mature follicles, the E_2 concentration on the day of hCG administration, and the type of catheter used. However, the various investigators have not agreed on the nature and ranking of these criteria.

In France, the clinical pregnancy rate per IUI cycle is only 11.8%, and the rate of childbirth per cycle is below 9% (1).

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The aim of this retrospective study was to report on 4 years of IUI practice (1038 cycles) at Amiens University Medical Center and determine the predictive factors for successful pregnancy and birth.

MATERIALS AND METHODS

Before each course of treatment, the following tests were performed: hysterosalpingography, serum hormone assays on the third day of the menstrual cycle (estradiol-17β, FSH, LH, and PRL), semen analysis (notably the total motile spermatozoa [TMS] count), and a postcoital test (Hühner's test).

After centrifugation of a semen sample in a discontinuous density gradient column (Puresperm, Nidacon, Mölndal, Sweden), the TMS count was obtained by multiplying the total sperm count by the prewash percentage of mobility. Sperm morphology was rated according to the World Health Organization (WHO) criteria (2). IUIs with donor sperm were excluded from the present study.

The postcoital test was positive when more than 10 motile spermatozoa were observed in the endocervical sample with an Insler score >10. If the postcoital test remained negative despite the administration of additional vaginal estrogens or ovarian stimulation (i.e., cervical infertility), then IUI was considered to be appropriate.

Anovulatory infertility corresponded to polycystic ovary syndrome (diagnosed according to the Rotterdam criteria), and ovarian insufficiency was defined as a serum FSH level >9.5 IU/L at the beginning of the menstrual cycle.

A laparoscopy with tubal permeability evaluation was performed when the salpingography suggested fallopian tube infertility or when a combination of dysmenorrhea and dyspareunia suggested endometriosis as a cause of infertility. Only American Fertility Society (AFS) stage I or II pelvic endometriosis was considered to be an indication for IUI.

After this assessment, IUI was effectively indicated if all the following conditions were met: at least one permeable fallopian tube, an FSH level below 12 IU/L, and more than 500,000 motile, normal spermatozoa.

Ovarian Stimulation

All the IUI cycles were combined with gonadotropic ovarian stimulation. The treatment was initiated on the second day of the cycle and was continued until ovulation or observation of an LH initiating rise. We used urinary FSH (Fostimon; Genevrier, Sophia-Antipolis, France), recombinant FSH (Gonal-F; Ares-Serono, Geneva, Switzerland; or Puregon, Organon International Inc, Roseland, NJ), or hMG (Menopur, Ferring SAS, St. Prex, Switzerland). The administration of GnRH agonist or antagonist was not required. The initial dose of gonadotropin prescribed (37.5–100 IU/day) depended on the woman's hormonal profile and age and the duration of infertility. The initial dose was maintained until the first sixth day of stimulation and thereafter adapted as a function of the ovarian response.

The evaluation combined serum hormone assays (estradiol-17β and LH) and a vaginal ultrasound examination evaluating follicle number and size and endometrial maturation. E_2 and LH were measured using time-resolved immunochemoluminescence assays with an ACS:180 Plus analyser and E2-6II and LH2 kits (Bayer Corporation, Tarrytown, NY). The detection limits of the E_2 and LH assays were 10 pg/mL and 0.07 IU/L, respectively. This evaluation was begun on the seventh day of treatment and repeated after 2 or 3 days, depending on the follicular growth. Ovulation triggering was achieved by SC injection of 250 μg of recombinant hCG (Ovitrelle, Ares-Serono). Insemination was performed 2 days later (i.e., 36 hours after the hCG injection). The criteria used for triggering ovulation were as follows: at least one follicle measuring >16 mm and triple-line preovulatory, endometrial maturation, with a thickness over 7 mm. If an LH initiating rise was observed (i.e., serum LH elevated by around 180% compared with the previous level), the insemination was delayed until the following day.

IUI and Luteal Support

Two hours before the insemination and after 48–72 hours of abstinence, semen was collected at the laboratory. After a motility determination, the spermatozoa were washed free from seminal liquid and prepared for insemination (postwash TMS = number of spermatozoa inseminated). Abnormal spermatozoa were rated according to the WHO criteria. Teratospermia was defined as an abnormal sperm rate of over 70%.

A soft catheter (the Frydman series from CCD, Paris, France) was used for the insemination process. The end of the catheter was placed in the center of the uterine cavity, and the sperm preparation (0.2–0.4 mL) was injected slowly (over 15 seconds). If the soft catheter was unable to pass the cervix, a hard catheter was used (the TDT series from CCD). A 2-week course of daily treatment with 400 mg of micronized P (Utrogestan, Cassenne-Aventis, Paris, France) was prescribed. After this time, the woman was allowed to perform a pregnancy test (a serum β-hCG assay). If the test was positive, it was repeated 7 days later to check the β-hCG time course (micronized P was withdrawn at the same time). Clinical pregnancies were defined as those with a fetal heart beat on ultrasound. The pregnancy was qualified as ongoing when it reached 12 weeks of amenorrhea.

Statistical Methods

Results were expressed as means $\pm$ SD. Categorical variables were compared using a χ^2-test, and continuous variables were analyzed using Student's t-test. $P<.05$ was considered statistically significant. Multivariate logistic regression analysis was used to test for correlations between clinical/biological variables and the occurrence of pregnancy. To determine informative covariates, we performed backward variable selection by evaluation of the multivariate normality of estimates. The variables were normally distributed, and some were collinear, such as [1] the woman's age and cycle number and [2] spermatozoa mobility and the number of inseminated spermatozoa. Odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated separately for each factor. CIs exclusive of unity were considered to be statistically significant. The study protocol was approved by the local independent ethics committee.

RESULTS

We studied a total of 1038 IUI cycles in 353 couples between 2002 and 2005. On average, each couple underwent 2.6 $\pm$ 1.6 IUI cycles (range, 1–9). The infertility had a female cause in 24.3% of cases, a male cause in 32.6% of cases, and combined male and female causes in 32.6% of cases. In 10.5% of cases, no cause could be found (i.e., unexplained infertility). The female causes could be broken down as follows, in order of prevalence: cervical infertility (31.5%), anovulation (22.2%), ovarian insufficiency (15.1%), AFS stage I and II pelvic endometriosis (8.1%), and fallopian tube anomalies (2.3%). Two causes were present in 20.9% of cases.

At the time of the first IUI cycle, the woman's mean age was 31.5 $\pm$ 4.4 years, and the mean body mass index (BMI) was 23.6 $\pm$ 14.4 kg/m^2. More than a third of the women (33.9%) had achieved a prior, spontaneous pregnancy (and with their current partner in two-thirds of these cases). The precycle hormonal evaluation gave the following mean