Prognosis factors of pregnancy after intrauterine insemination with the husband's sperm: conclusions of an analysis of 2,019 cycles

Laka Dinelli, M.D.,[a] Blandine Courbière, M.D., Ph.D.,[a,b] Vincent Achard, M.D., Ph.D.,[a,c] Elisabeth Jouve, M.Sc.,[d] Carole Deveze, M.D.,[a] Audrey Gnisci, M.D.,[a] Jean-Marie Grillo, M.D., Ph.D.,[a,c] and Odile Paulmyer-Lacroix, M.D., Ph.D.[a,c]

[a] Department of Gynecology-Obstetric and Reproduction, Gynepôle, AP-HM La Conception, Marseille; [b] IMBE, Biogénotoxicologie, Santé Humaine & Environnement UMR 6116, Aix-Marseille Université, Marseille FR CNRS 3098, ECCOREV, Aix-en-Provence; [c] Department of Histology-Embryology, Faculty of Medicine, Aix-Marseille University, Marseille; and [d] CIC-CPCET, Data Management and Biostatistics, AP-HM, Marseille, France

Objective: To identify the prognostic factors for pregnancy after intrauterine insemination with the husband's sperm (IUI-H).
Design: Retrospective study.
Setting: A single university medical center.
Patient(s): 851 couples, for 2,019 IUI-H cycles.
Intervention(s): After controlled ovarian stimulation, IUI-H performed 36 hours after ovulation triggering or 24 hours after a spontaneous luteinizing hormone (LH) surge.
Main Outcome Measure(s): Clinical pregnancy rate per cycle (PR) and delivery rate per cycle (DR).
Result(s): The overall PR was 14.8% and DR 10.8%. Higher PR and DR were observed for patients presenting with ovulation disorders (particularly polycystic ovary syndrome) or with male infertility. Secondary infertility in the woman appeared to be a positive prognostic factor as did a basal follicle-stimulating hormone (FSH) level $\leq$7 IU/L and ovulation triggering over spontaneous LH rise. The other parameters influencing the results were the women's age, the number of mature follicles obtained ($\geq$2), the endometrial thickness (10–11 mm), and the number of progressive motile spermatozoa inseminated (>1 million).
Conclusion(s): In women aged $\leq$38 years, IUI-H should be considered as an option, particularly in cases of female infertility from ovulation disorders, in cases of a normal ovarian reserve, in cases of secondary infertility, or when $\geq$1 million progressive sperm are inseminated. Bifollicular stimulation is required. In other cases, in vitro fertilization should be discussed as the first-line treatment. (Fertil Steril® 2014;101:994–1000. ©2014 by American Society for Reproductive Medicine.)
Key Words: Delivery rate, husband's sperm, intrauterine insemination, pregnancy rate, prognosis factor

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/dinellil-prognosis-factor-pregnancy-intrauterine-insemination-sperm/

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.

Intrauterine insemination with husband's sperm (IUI-H), the oldest first-line approach for treatment of infertile couples when at least one healthy fallopian tube is diagnosed, is widely used around the world. In the United States, the National Survey Family Growth (NSFG) (1) study showed that treatments other than assisted reproductive technology (ART), such as IUI-H, are the most commonly used. In Europe, the European Society of Human Reproduction and Embryology (ESHRE) data report that 162,843 IUI-H cycles were performed in 2009 compared with 135,621 cycles of classic in vitro fertilization (IVF) during the same period (2). Treatment with IUI-H is shorter, less invasive, and less expensive (3), with a lower multiple delivery rate (10.4%

Received September 9, 2013; revised and accepted January 6, 2014; published online February 15, 2014.
L.D. has nothing to disclose. B.C. has nothing to disclose. V.A. has nothing to disclose. E.J. has nothing to disclose. C.D. has nothing to disclose. A.G. has nothing to disclose. J-M.G. has nothing to disclose. O.P.-L. has nothing to disclose.
Reprint requests: Odile Paulmyer-Lacroix, M.D., Ph.D., Department of Gynecology-Obstetric and Reproduction, AP-HM, La Conception, 147 Bd Baille, 13005 Marseille, France (E-mail: odile.lacroix-paulmyer@ap-hm.fr).

Fertility and Sterility® Vol. 101, No. 4, April 2014 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2014.01.009

vs. 20.2%) and lower morbidity than IVF (2). The pregnancy rate per cycle (PR) with IUI-H is otherwise comparable to that observed after IVF with mild ovarian stimulation (4).

However, despite technical improvements in sperm preparation (5, 6) and controlled ovarian stimulation, the success rates with IUI-H have been limited: ESHRE data show a PR per cycle of 12.4% after IUI-H compared with 28.9% after IVF (7), and this PR has been relatively stable from year to year (2). Several factors such as women's age and indication, the number of mature follicles obtained, and the sperm quality (8, 9) have been reported to influence the PR after IUI-H, and no consensus has established IUI-H over IVF as a first line of treatment. Our study analyzed IUI-H cycles to determine which prognostic factors contribute to positive pregnancy outcomes.

MATERIALS AND METHODS

Patients

We retrospectively analyzed the IUI-H cycles performed in the reproductive department of a university medical center in France from January 2005 to December 2011. The data were collected from the medical records of couples. The study protocol was approved by the local ethics committee.

Before treatment, the couples underwent an infertility assessment, including at least two semen analyses, serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) assays on the second or third day of the menstrual cycle, a hysterosalpingography, and safety tests.

We then proposed IUI-H to couples for the following indications: [1] female infertility: cervical pathology, unilateral tubal obstruction, endometriosis with healthy fallopian tubes, ovulation disorders including central anovulation, idiopathic ovulation disorder, polycystic ovary syndrome (PCOS), or diminished ovarian reserve (DOR); [2] moderate male infertility, according to World Health Organization (WHO) criteria (10, 11) using a modified (12) David classification (13), with at least 1 million motile spermatozoa recovered after sperm preparation; [3] use of cryopreserved sperm (performed before a potentially sterilizing treatment or in cases of ejaculatory disorders) when the postthaw test of one straw showed at least 1 million motile spermatozoa; [4] mixed infertility; or [5] unexplained infertility. Furthermore, some couples benefited from IVF conversion to IUI in cases of hyporesponse to controlled ovarian stimulation (COS) with less than four mature follicles and normal semen analysis. When IUI-H was proposed to women $\leq$40 years old, it was limited to four attempts, except in cases of ovulation disorder (central anovulation, idiopathic, or PCOS), in which case up to six attempts were permitted if needed (8).

The recorded parameters were related to couple factors (duration of infertility, indications, number of attempts), female characteristics (age, parity, serum hormone levels), male characteristics (age, semen parameters), technical aspects of IUI (COS protocol, estradiol and LH levels, endometrial thickness, number of mature follicles assessed on the day of ovulation triggering, sperm quality before and after treatment, number of motile sperm inseminated, and insemination time interval). The IUI outcome and pregnancy outcome were also noted.

Controlled Ovarian Stimulation

We started COS on the second day of the cycle and continued until ovulation triggering or detection of a spontaneous LH rise, defined as serum levels $\geq$20 IU/L. The COS cycle was stimulated by antiestrogens (clomiphene citrate, Clomid; Sanofi-Aventis) or by gonadotropins (Menopur, Ferring SAS; Fostimon, Genevrier; Gonal F, Merck-Serono; or Puregon, Schering-Plough). The initial dose was 50 mg/day for clomiphene citrate (CC) (days 3–8) or of 50 IU/day for gonadotropins, and the dosage was modulated by the woman's age, indication, rank of the attempt, and previous responses to stimulation. The initial dose of gonadotropins was maintained for the first 6 days of stimulation, after which it was adapted according to the ovarian response.

Ovulation monitoring was performed by vaginal ultrasound to evaluate the growth, number, and size of ovarian follicles and the endometrial thickness; and by serum hormone assays for measuring estradiol and LH (VIDASPC Analyser; bioMERIEUX). The first test was conducted after 8 days of stimulation, then repeated every 2 or 3 days depending on the ovarian response. When at least one mature follicle was assessed to range in size between 16–18 mm with gonadotropins, or 20–22 mm with CC, and the serum estradiol levels had reached 100 to 300 pg/mL per mature follicle, we performed ovulation triggering via intramuscular injection of urinary human chorionic gonadotropin (5,000 IU of hCG; Schering-Plough) or by subcutaneous injection of recombinant hCG (250 μg of Ovitrelle; Merck-Serono). We cancelled the IUI cycle when no mature follicles were obtained or when more than three mature follicles were observed. Insemination was performed 36 to 40 hours after hCG injection or 24 hours after a spontaneous LH rise.

Semen Collection and Sperm Preparation

After 2 to 5 days of abstinence and 2 hours before insemination, semen was collected at the laboratory. After 30 minutes of liquefaction at 37°C, semen analysis was performed, and 1 to 2 mL of ejaculate were prepared for insemination by centrifugation on a density gradient (PureSperm; Nicadon International), diluted in Ferticult IVF medium (FertiPro NV). After 20 minutes of centrifugation at 1,300 rpm, the most concentrated phase, containing the most mobile spermatozoa, was collected and resuspended in Ferticult and centrifuged for 10 minutes at 1,500 rpm. The resulting pellet was dried and resuspended in 0.15 mL of Ferticult. After a number and motility evaluation, all recovered spermatozoa were inseminated. In cases of self-cryopreservation, frozen semen was processed in the same conditions as for fresh semen.

Intrauterine Insemination and Luteal Phase Support

Insemination was performed by one of the ART center's gynecologists in a room adjacent to the laboratory. The end of the soft catheter (Frydman type; CCD) or hard catheter if the soft catheter could not pass (TDT; CCD) was inserted into the center of the uterine cavity, and the sperm preparation (0.15 mL) was injected slowly.