

Influence of follicle rupture and uterine contractions on intrauterine insemination outcome: a new predictive model

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Objective: To correlate the detection of follicle rupture and the number of uterine contractions per minute with the outcome of IUI and to build a predictive model for the outcome of IUI including these parameters.

Design: Retrospective cohort study.

Setting: Fertility clinic.

Patient(s): We analyzed data from 610 women who underwent homologous or donor double IUI from 2005 to 2010 and whose data of uterine contractions or follicle rupture were recorded.

Intervention(s): None.

Main Outcome Measure(s): Live-birth rate.

Result(s): Nine hundred seventy-nine IUI cycles were included. The detection of follicle rupture (odds ratio [OR], 1.98; 95% confidence interval [CI], 1.30–3.01) and the number of uterine contractions per minute (OR, 1.67; 95% CI, 1.02–2.74) assessed after the second insemination procedure of a double IUI were positively correlated with the live-birth rate. A multiple logistic regression model showed that sperm origin, maternal age, follicle count at hCG administration day, follicle rupture, and the number of uterine contractions observed after the second insemination procedure were significantly associated with the live-birth rate.

Conclusion(s): Follicle rupture and uterine contractions are associated with the success of an IUI cycle. This may open new possibilities to improve the methodology of IUI. (*Fertil Steril*® 2014;102:1034–40. ©2014 by American Society for Reproductive Medicine.)

Key Words: Intrauterine insemination, follicle rupture, uterine contraction, predictive model, clinical pregnancy rate, live-birth rate

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IUI is the artificial introduction of sperm cells into the uterus using a catheter. The sperm cells are purified from seminal plasma performing sperm washing methods like swim-up or density gradients (1, 2). This is a simple and cost-effective technique to treat infertile couples with cervical factor, mild male factor, anovulatory

infertility, or unexplained infertility (3–6). IUI is commonly used in combination with controlled ovarian hyperstimulation, based on the administration of clomiphene citrate with/or gonadotropins (2).

The efficacy of IUI in terms of pregnancy rate is around 10%–20% per patient (1, 7). Many studies have reported

factors that affect the outcome of this technique: maternal age, motile sperm count, length and type of infertility, number of previous insemination treatments, ovarian stimulation regimen, type of catheter used, and, on the day in which hCG is administered, the number of preovulatory follicles and blood E₂ level (8–17). Regarding the sperm origin, insemination results are generally better using donor sperm than using the sperm of the partner (2).

However, the relationship of some relevant factors with the outcome of IUI still needs an in-depth analysis. One of these factors is uterine contractility, which has been proposed to

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facilitate the transport of sperm cells towards the fallopian tubes (18–21). In assisted reproductive techniques, uterine contractions during ET in IVF cycles have a negative effect on pregnancy rates (22–24), whereas their impact on IUI is unknown. Another poorly analyzed prognosis factor is the occurrence of follicle rupture the day the artificial insemination is performed. A recent study found a positive correlation between pregnancy rate and the detection of follicle rupture (a sign of ovulation) just after the IUI procedure (25).

Our aim in this retrospective study was to analyze the value of two parameters to predict cycle outcome: follicle rupture and the number of uterine contractions per minute measured after each of the insemination procedures performed in a double IUI protocol.

MATERIALS AND METHODS

Patients

We selected from our database 610 patients with data on uterine contractions and follicle rupture recorded during their IUI cycles, which were performed between February 2005 and December 2010 at the clinic IVI Sevilla. A total of 979 cycles were included in this retrospective cohort study. Of the 610 patients, 420 were inseminated with sperm from the couple (668 cycles), and 190 patients were inseminated with donor sperm (311 cycles). All patients met the clinic criteria to undergo IUI: attempting pregnancy for at least 1 year, at least one permeable fallopian tube, and a total motile sperm count of more than 3 million sperm cells after sperm preparation. This study was approved by the local ethics committee.

Controlled Ovarian Hyperstimulation

The stimulation treatment began the second or third day of the menstrual cycle. An initial dose of 50 IU of recombinant FSH (rFSH; Puregon, MSD) or 75 IU of hMG (hMG-Lepori, Angelini Farmacéutica S.A.) was administered every day to the patients. An ultrasound scan was performed the fourth day of stimulation to monitor the follicular growth. Subsequent controls were performed every 24–72 hours (ultrasound machine Voluson 730 Pro, GE Healthcare). The daily dose of rFSH or hMG was adjusted according to the observed growth rate of the ovarian follicles. Once the dominant follicle reached a diameter of 17 mm, the ovulation was induced that night or the next one by administering 250 μ g of Ovitrelle (Merck). To avoid multiple pregnancies, the stimulation was cancelled if we observed more than three follicles with an average diameter of 16 mm or larger in any of the controls.

Sperm Preparation and IUI

Patients underwent two consecutive IUIs, performed 12 and 36 hours (\pm 1 hour) after hCG administration. In homologous IUI (H-IUI), the partner produced the sperm sample by masturbation 60 minutes before the scheduled insemination. In IUI with donor sperm (D-IUI), the assigned donor samples were thawed 90 minutes before the appointment. No frozen samples were used for H-IUI. Once collected or thawed, the samples were prepared using a three-layer density gradient

(SpermGrad, Vitrolife). The total motile sperm count was measured using a Makler Chamber (Sefi-Medical Instruments). A final volume of 0.3–0.5 mL of culture media (HTF, Irvine Scientific) containing the prepared sperm cells was introduced into the uterus through a soft flexible catheter (Emtrac Delphin, Gynetics).

Uterine Contractions and Follicle Rupture Assessment

From 2005 onward, the clinic staff was trained to assess uterine contractions and follicle rupture after an IUI procedure to record data for further studies. After each insemination of the cycle, a transvaginal ultrasound scan was performed to measure uterine contractions. The ultrasound probe was not covered in gel, and it was introduced carefully into the vagina, immediately after the catheter's removal. Uterine contractions were counted for 1 minute by a nurse using a timer. Each contraction event was defined as a rhythmic movement of the uterus similar to a wave, which could not be confused with an image skip caused by the movement of the probe or the patient. We created three categories to record this data: (A) no contractions, (B) one to three contractions, and (C) four or more contractions per minute.

Follicle rupture was also assessed by ultrasound after the second insemination of the cycle, and it was confirmed when free fluid was present and there was no sign of the dominant follicle. This was interpreted as a sign of ovulation. Once these assessments were finished, the patient rested for 15 minutes in the supine position.

Luteal Support

After the insemination procedure, the luteal phase was supported by vaginal administration of 100 mg of P (Progeffik, Effik; or Utrogestan, SEID S.A.) every 12 hours. This treatment began the night after the second insemination and continued until the beta-hCG pregnancy test. In case of a positive result, luteal support was kept until the 10th week of pregnancy.

Predictor and Outcome Variables

The predictor variables were the presence of follicle rupture after the second IUI procedure and the number of uterine contractions per minute assessed after each IUI procedure. The second predictor variable was divided into three ascending categories: no contractions per minute, one to three contractions per minute, and four or more contractions per minute.

The main outcome variable of this study was live-birth rate. Other outcome variables were clinical pregnancy, multiple pregnancy, and miscarriage rate. Clinical pregnancy was confirmed when a gestational sac with heartbeat was observed in the uterus by ultrasound examination, performed 2–3 weeks after the positive result of the beta-hCG pregnancy test.

Statistical Analysis

We used SPSS versions 19 software for data analysis. Probability values under 5% were considered statistically significant. Patient characteristics are expressed as the mean and

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