Success of Intrauterine Insemination Using Cryopreserved Donor Sperm Is Related to the Age of the Woman and the Number of Preovulatory Follicles

RUDIGER U, PITTOF,1,2 ADEL SHAKER,3 NICOLA DEAN,1 JINAN S. BEKIR,1 STUART CAMPBELL,1,2 and SEANG-LIN TAN1,3

Submitted: June 16, 1995
Accepted: August 29, 1995

Objective: Our objective was to assess parameters associated with a successful outcome of intrauterine insemination (IUI) using cryopreserved donor sperm.

Design: We analyzed 750 consecutive donor IUI cycles undertaken by 363 women in an assisted conception clinic. The main outcome measure was clinical pregnancy.

Results: IUI was performed in 94.7% of the 750 IUI treatment cycles commenced and 180 clinical pregnancies occurred. The clinical pregnancy rate per cycle was 26.4%. The rate was significantly related to the patient’s age (30.5% for age <35 years and 18.1% for age >35 years; P < 0.05) and whether there was one or more than one preovulatory follicles (20.9, 34.4, and 31.5% for one, two, and three or four follicles with a mean diameter of 14 or more mm at the time of human chorionic gonadotropin (hCG) administration; P = 0.006). Two to four preovulatory follicles were present in 12.6% of the natural cycles, 43.6% of clomiphene citrate or tamoxifen, and 59.9% of gonadotropin stimulated cycles. The difference in the number of preovulatory follicles between stimulated and unstimulated cycles was highly significant (P < 0.0001). Pregnancy rates were 29.9% in gonadotropin-stimulated cycles, 23.6% in clomiphene citrate- or tamoxifen-stimulated cycles, and 20.1% in unstimulated cycles. The difference in pregnancy rates between gonadotropin-stimulated and natural cycles was significant (P = 0.038). Cycle fecundity rates were not significantly affected by the number of previous treatment cycles, duration of infertility, gravidity and parity of the patient, presence of a spontaneous luteinizing hormone (LH) surge before the administration of hCG, or number of motile sperm in the insemination specimen.

Conclusions: Success of IUI using cryopreserved donor sperm is related to the age of the women and whether there is one or more than one preovulatory follicles.

KEY WORDS: donor intrauterine insemination; ovarian stimulation.

INTRODUCTION

Therapeutic insemination with donor sperm is a common treatment for couples with severe male-factor infertility. Because of the potential risk of transmitting infectious disease, only cryopreserved semen, quarantined for a minimum of 6 months, is permitted for clinical use (1). Unfortunately cryopreservation reduces the percentage of motile sperm following the thawing process and higher pregnancy rates are achieved if fresh rather than cryopreserved donor sperm is used (2).

Chaffkin and colleagues (3) showed that ovarian stimulation increased cycle fecundity rates in ovulatory women undergoing intrauterine insemination (IUI) treatment. In their study, fresh sperm from the partners of the patients were used and the conclusions might not necessarily apply to patients undergo-
ing IUI using cryopreserved donor sperm. As there are relatively few data on the usefulness of ovarian stimulation for IUI in the context of cryopreserved donor sperm, we related the outcome of IUI to ovarian stimulation in a group of women undergoing insemination with cryopreserved donor sperm.

MATERIALS AND METHODS

Couples who underwent IUI using cryopreserved donor sperm at The London Women's Clinic between January 1, 1992, and July 15, 1994, were studied. The primary indications for treatment were azoospermia or severe oligospermia.

Pretreatment screening tests for all patients included cervical cytology, cervical swab for chlamydia, and high vaginal swab for microbiological culture. A midluteal serum progesterone concentration was measured to confirm spontaneous ovulation, and serum follicle stimulating hormone (FSH) levels were measured on day 2 of the menstrual cycle in women over 40 years of age. Patency of at least one fallopian tube was confirmed in all patients by a pretreatment hysterosalpingogram of laparoscopy and chromohydrotubation.

IUI was performed either in unstimulated cycles or with ovarian stimulation. In stimulated cycles patients received clomiphene citrate (50 or 100 mg) (Merrel Dow, Uxbridge, England) or tamoxifen citrate (20–40 mg) (Kabi Pharmacia, Milton Keynes, England) orally, from day 2 to day 6 of the menstrual cycle in women over 40 years of age. Patency of at least one fallopian tube was confirmed in all patients by a pretreatment hysterosalpingogram of laparoscopy and chromohydrotubation.

IUI was performed either in unstimulated cycles or with ovarian stimulation. In stimulated cycles patients received clomiphene citrate (50 or 100 mg) (Merrel Dow, Uxbridge, England) or tamoxifen citrate (20–40 mg) (Kabi Pharmacia, Milton Keynes, England) orally, from day 2 to day 6 of the menstrual cycle, or gonadotropins (Humegon, Organon, Cambridge, UK, or Metrodin, Serono, Welwyn Garden City, England), usually 150 to 300 IU on alternate days starting on day 3 of the menstrual cycle.

All patients underwent serial transvaginal ultrasound monitoring of follicular growth using an Acuson XP128/10 with a 5-MHz endovaginal probe. A baseline scan was performed on the second day of the menstrual cycle, and a second scan on day 9 of the cycle. Subsequent scans were performed at 1- to 2-day intervals until the mean diameter of the dominant follicle reached 18 mm. An intramuscular injection of 10,000 IU human chorionic gonadotropin (hCG; Pregnyl, Organon, Cambridge, England) was given to induce ovulation. IUI was generally performed 40 hr after the administration of hCG. Patients, in whom a spontaneous onset of an endogenous luteinizing hormone (LH) surge was suspected underwent a qualitative LH urine test (Conceive, Quidel, San Diego, CA). If a spontaneous LH surge was confirmed, 10,000 IU hCG was administered immediately and the IUI performed 18 to 24 hr later.

On the day that the mean diameter of the largest follicle reached or exceeded 18 mm, the sizes of the other follicles were also determined. Patients underwent IUI only if there was a maximum of three preovulatory follicles (mean follicular diameter, ≥14 mm) or if the serum estradiol concentration was below 3500 pM in patients with four preovulatory follicles. If ovarian response exceeded these criteria, the cycle was either abandoned or, following the administration of hCG, converted to in vitro fertilization (IVF) or peritoneal oocyte and sperm transfer (POST) (4).

All semen donors had been screened according to guidelines issued by the British Andrological Society. One (0.5-ml) or two (0.25-ml) straws containing frozen sperm were thawed and the specimen was prepared for IUI using a mini-Percoll gradient by a technique modified slightly from Ord and colleagues (5).

A vaginal speculum was used to expose the cervix. The ectocervix and the upper vagina were cleansed with sterile water and wiped with a cotton swab to remove cervical mucus. IUI was performed using a Frydman catheter. Sperm (0.5 ml) was injected high into the uterine cavity. The patient was allowed to rest for several minutes at her request.

Patients who were administered gonadotropins received luteal support either in the form of progesterone pessaries (Cyclogest, Hoechst, Hounslow, England), 400 mg twice daily for 16 days starting on the day of the IUI, or hCG, 1500 IU intramuscularly on the third and sixth day after the IUI, depending on their choice.

All pregnancies were diagnosed using a sensitive urine assay for β-hCG 16 days after the insemination. Clinical pregnancy was confirmed by ultrasound examination 2 weeks later.

Statistical Analysis

Differences in results in the different groups were compared using the Student t test or chi-square test. A value of P < 0.05 was considered significant. Logistic regression was used to examine the effect of covariants such as age, duration of infertility, and parity.

RESULTS

Three hundred sixty-three patients underwent a total of 750 treatment cycles. There was no significant