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Pregnancy outcomes using donor sperm insemination after failed in vitro fertilization with intracytoplasmic sperm injection cycles in couples with complex infertility disorders

Marsha J. Gorrill, M.D., Kenneth A. Burry, M.D., and Phillip E. Patton, M.D.

Oregon Health and Science University, Portland, Oregon

Objective: To evaluate alternatives for couples with severe male factor infertility who fail to conceive with IVF-intracytoplasmic sperm injection (ICSI).

Design: Outcomes of couples using artificial insemination with donor sperm (AID) after failed IVF-ICSI, assessing multiple risk factors affecting prognosis.

Setting: University infertility service.

Patient(s): Nineteen patients with complex infertility disorders who failed IVF-ICSI and subsequently used AID (1 to 7 cycles).

Intervention(s): Artificial insemination with donor sperm was performed 36 hours after detection of an LH surge or hCG injection.

Main Outcome Measure(s): Pregnancy outcomes were determined.

Result(s): Seventeen pregnancies occurred in 16 women associated with AID for a pregnancy rate per cycle of 27.9% within a mean of 3.2 ± 18 cycles. Live birth rate per cycle was 24.6%.

Conclusion(s): A high pregnancy rate was achieved with AID in women who failed IVF-ICSI. Given the low cost and effectiveness of AID in this series, consideration of AID is a reasonable and effective option even in couples with poor prognosis who fail to conceive with IVF-ICSI. (Fertil Steril® 2003;80:936–8. ©2003 by American Society for Reproductive Medicine.)

Key Words: Failed IVF-ICSI, AID, donor sperm

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Address correspondence to: Marsha J. Gorrill, M.D., University Fertility Consultants, 1750 S.W. Harbor Way, Suite 100, Portland, Oregon 97201-5133 (FAX: 503-418-3708; E-mail: gorrillm@ohsu.edu).

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Intracytoplasmic sperm injection (ICSI) is a procedure that represents a major advance in the treatment of severe male factor infertility. The decision to use IVF-ICSI is generally based on the desire for each partner to have an equal genetic contribution to future offspring. However, couples may consider alternative reproductive options after an unsuccessful IVF-ICSI cycle, such as artificial insemination with donor sperm (AID), egg donation, or adoption.

The growing experience with IVF and ICSI indicates that success rates are dependent on both oocyte-related and sperm-related factors. When couples have mixed or complex infertility disorders, the probability of a successful cycle of IVF-ICSI is reduced, and repeated cycles may be necessary but unacceptable, secondary to economic costs and other considerations. When multiple infertility factors coexist, the comparison and selection of the other treatment options can be difficult. This report reviews pregnancy outcomes after AID in an unselected population of couples who failed to conceive after IVF-ICSI. Our results indicate that AID represents a viable reproductive choice for couples with multiple and complex infertility disorders.

MATERIALS AND METHODS

From 1994 through 2001, a total of 561 IVF-ICSI cycles was completed at the Oregon Health Sciences University infertility program. The methods of ovarian hyperstimulation, oocyte and sperm preparation, and embryo cul-

ture for IVF and ICSI have been described elsewhere (1). During this interval we identified a total of 19 couples who failed to achieve pregnancy in a total of 32 ICSI cycles and elected to use donor sperm for artificial insemination. Records from their IVF-ICSI cycles were reviewed for the following risk factors associated with a reduced pregnancy potential: evidence of a poor ovarian response (<4 mature follicles or peak E_2 concentration of <100 pg/mL) and/or evidence of poor embryo quality (<4 blastomeres in embryos transferred on day 3, ≤2 expanded blastocysts transferred by day 6 of extended culture, or a cancelled ET secondary to embryonic arrest).

For therapeutic donor insemination, the methods of patient screening, sperm processing, and insemination have been described elsewhere (2). Briefly, each woman received a single IUI that was performed 24 to 36 hours after detection of the LH surge using conventional urine kits (OvuQuick or OvuKit; Quidel Corporation, San Diego, CA) or after administration of exogenous hCG. After insertion of the insemination catheter (Shepard catheter; Cook Ob/Gyn, Bloomington, IN; or a 17-g intracath; Intracath-Deseret, Sandy, UT) through the cervical os into the upper fundal area of the uterine cavity, the suspension of processed sperm was injected during a period of 10 to 20 seconds.

Ovulation parameters were evaluated retrospectively after each insemination with the use of basal body temperature records, midcycle urine LH detection kits, and midluteal P assay results, as indicated. Abnormalities in ovulatory function were treated with either clomiphene citrate (50 mg to 150 mg, 8 women) or injectable gonadotropins (2 women).

All pregnancies were confirmed using standard serum assays for hCG. Clinical pregnancies were defined by ultrasound evidence of an intrauterine gestational sac. The pregnancy rate per cycle and live birth rate per cycle were determined.

RESULTS

After the introduction of ICSI, we observed an overall clinical pregnancy rate of 40% per ET with IVF-ICSI (201 pregnancies in 500 transfers; 61 cycles did not have an ET). Of the 19 women reported in this study, a total of 32 IVF-ICSI cycles were initiated. Eight cycles were canceled in eight women secondary to a poor ovarian response (25%) before oocyte retrieval (2 women had low E_2 levels and 6 women developed ≤4 follicles). In an additional 12 cycles (38%), arrested embryonic development or poor embryo quality was noted. Taken together, poor embryo quality or cycle cancellation occurred in 63% of IVF-ICSI cycles (Table 1).

A total of 61 AID cycles was completed during the period of observation. The mean age of the population was 33.7 ± 4.9 years, with 52.6% of the women aged ≥35 years. Sixteen couples conceived (84.2%) within seven cycles of donor insemination, resulting in 17 pregnancies with 15 live births and 2 spontaneous abortions (Table 2). The mean (SEM) number of donor insemination cycles performed to achieve pregnancy was 3.2 (± 1.8), and the fecundity rate was 27.9%. Three women did not conceive (ages 37 years, 39 years, and 40 years) after one to seven cycles of donor insemination.

TABLE 1

Poor prognostic factors and outcome of AID.

Patient no.	IVF-ICSI cycle cancellation	Poor embryo quality/ embryonic arrest	Multiple IVF-ICSI cycles (n)	AID pregnancy
1	No	No	Yes (2)	Yes
2	Yes	Yes	Yes (2)	Yes
3	Yes	No	Yes (4)	Yes
4	No	Yes	No (1)	Yes
5	Yes	Yes	Yes (2)	Yes
6	Yes	Yes	Yes (2)	Yes
7	No	Yes	No (1)	Yes
8	No	No	No (1)	Yes
9	Yes	No	No (1)	No
10	No	Yes	No (1)	No
11	No	Yes	No (1)	No
12	No	Yes	Yes (2)	Yes
13	Yes	No	Yes (3)	Yes
14	No	Yes	No (1)	Yes
15	Yes	No	No (1)	Yes
16	No	No	Yes (3)	Yes
17	Yes	No	No (1)	Yes
18	No	Yes	Yes (2)	Yes
19	No	Yes	No (1)	Yes

Note: AID = artificial insemination with donor sperm; ICSI = intracytoplasmic sperm injection.

Gorrill. Donor sperm after failed IVF-ICSI. Fertil Steril 2003.

TABLE 2

Outcomes of AID cycles in women who failed IVF-ICSI.

Variable	Outcome
Pregnancy rate per patient, n (%)	16/19 (84.2)
Pregnancy rate per cycle (%)	27.9
Live birth rate per cycle (%)	24.6
No. of AID cycles	
Range	1–7
Mean (SEM)	3.2 (±1.8)
Conception cycles with ovarian stimulation (n)	
Gonadotropins	2
Clomiphene citrate	8
None	7

Note: AID = artificial insemination with donor sperm; ICSI = intracytoplasmic sperm injection.

Gorrill. Donor sperm after failed IVF-ICSI. Fertil Steril 2003.

DISCUSSION

Before the introduction of assisted reproductive technology (ART), AID was routinely recommended when infertility secondary to a severe male factor was diagnosed. The use of third-party donor sperm was inexpensive and successful but was not satisfactory to couples that desired a child with a genetic link to both parents. For these couples, IVF or IVF-ICSI provided a new alternative and rapidly became a highly used treatment for male-factor infertility, representing nearly half of all ART procedures performed.

Nevertheless, a pregnancy will not occur in many IVF-ICSI cycles. Although many pregnancy failures are secondary to sperm-related disorders, it is now well recognized that both sperm-related and egg-related factors contribute to the overall success rates for IVF-ICSI. Advanced maternal age, diminished ovarian reserve, suboptimal response to gonadotropins, inadequate endometrial development, and poor embryo quality are among identified maternal factors that can impair pregnancy outcome. In this report, we evaluated reproductive outcome in couples who had multiple infertility factors and who failed IVF-ICSI and subsequently used AID.

In our series, AID was highly successful in couples with a high degree of both sperm-related and oocyte-related problems. Of the 19 couples that failed an IVF-ICSI procedure, we observed an overall clinical pregnancy rate of 84% and a live birth rate of 88%. The monthly fecundity rate for AID in this series was 27.9%. In our clinic's AID program, monthly fecundity rates for all women undergoing donor insemination between 1994 and 2001 ranged from 8.4% to 19.4%. In this series, the majority of inseminations occurred between 2000 and 2001, and the overall AID program monthly fecundity rates were 19.4% and 18.1%, respectively. Acceptable pregnancy rates were achieved despite the observation of a high cycle cancellation rate, poor ovarian response to ovarian hyperstimulation, and suboptimal embryo development in many of the antecedent IVF-ICSI cycles. Although it is unlikely that the high pregnancy and fecundity rates observed in this report will persist with more extended clinical experience, the data are supportive of the consideration of AID for couples who fail to conceive after IVF-ICSI, even when multiple and complex infertility factors are present.

Our results suggest that repeated cycles of AID may overcome some of the potential obstacles of coexistent maternal and paternal factors when compared with the case of a single cycle or a limited number of cycles of IVF-ICSI. This concept may be particularly relevant in women of advanced maternal age. In previous studies in women of advanced maternal age, Trimbos-Kemper (3) reported a 48% intrauterine pregnancy rate in women >40 years of age after tubal reanastomosis. Other sources have confirmed these clinical findings with reported pregnancy rates ranging from 43% to 71% in women aged >40 years after a tubal reanastomosis (4, 5). Recently, Fuchs and Burt (6) reported pregnancy outcomes after vasectomy reversal in men who were thought previously to have a poor prognosis. Overall, the investigators reported a 29% live birth rate in women 36 to 40 years of age after surgery in their male partners, who had a vasectomy reversal ≥15 years after vasectomy. In women aged >40 years, the overall pregnancy rate was 28%, with a live birth rate of 19%.

Although the size of our series and the selective nature of this report limit any definitive conclusions, we believe that our results are clinically relevant to clinicians offering general infertility care as well as to ART specialists. In 1998, the Society for Assisted Reproductive Technology Registry reported a 32% live birth rate in couples undergoing ICSI for male factor infertility (7). Although repeated cycles of IVF-ICSI may result in pregnancy, the economic costs associated with ART procedures may prohibit multiple attempts. When both oocyte-related and sperm-related problems are identified during an infertility investigation, the use of donor oocytes with ICSI is a highly successful alternative. However, donor oocyte procedures are limited by the supply of adequately screened donors and the high costs associated with the procedure. Therefore, an awareness of alternative reproductive options and clinical outcomes in this clinical setting is relevant to clinicians who provide infertility services.

The use of AID in couples with coexisting infertility disorders is a tenable option that has received little emphasis. This report demonstrates an acceptable pregnancy rate with donor insemination in women who have a poor prognosis for pregnancy and who have failed at multiple attempts of ART. Although our results are encouraging, a much larger experience will be necessary to accurately evaluate pregnancy potential in these couples. On the basis of our results, a 6-month trial of donor insemination is a reasonable, cost-effective reproductive option in couples who fail to conceive with IVF-ICSI procedures.

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