

In Vitro Fertilization—Embryo Transfer in Three Women with Ovarian Failure

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Attempts at in vitro fertilization—embryo transfer (IVF-ET) for women with hypergonadotropic hypogonadism and bilateral tubal disease demonstrated a very low fertilization rate and no clinical pregnancies.

KEY WORDS: in vitro fertilization—embryo transfer (IVF-ET); ovarian failure; poor fertilization.

INTRODUCTION

Ovulation induction in women with ovarian failure has been described employing human menopausal gonadotropins (hMG) following suppression of the endogenous elevated gonadotropins with either estrogen or leuprolide acetate (1,2). Although pregnancies have been achieved using these techniques, the pregnancy rate in comparison to the number of ovulations has been quite low.

Three 44-year-old women with bilateral tubal occlusion and hypergonadotropic amenorrhea provided a unique opportunity to evaluate the incidence and quality of fertilization in these patients.

MATERIALS AND METHODS

Three patients were chosen who had previously demonstrated the ability to ovulate in response to the gonadotropin suppression/hMG stimulation

technique. All three women were treated daily with leuprolide acetate (LA), 1 mg subcutaneously and exclusively for a minimum of 10 days until the gonadotropins were within a normal range. The LA was then continued with the initiation of hMG, 150 IU twice daily, for 4 days. At this time serum estradiol (E₂) levels were measured by radioimmunoassay (RIA) method and size and number of follicles were determined by transvaginal sonography. A serum E₂ level of 100 pg/ml or greater indicated a reduction to 150 IU hMG per day; a level of 50–100 pg/ml required the continuance of 300 IU hMG per day and less than 50 pg/ml, an increase to 450 IU hMG per day.

Since a large number of follicles was not expected, the hMG was to be discontinued and human chorionic gonadotropins (hCG) was given (10,000 U intramuscularly) if at least one mature follicle was seen on ultrasound and the serum E₂ level measured ≥ 200 pg/ml.

The ova were retrieved 30 to 32 hr following the administration of hCG with transvaginal ultrasound guidance. All three patients had uneventful retrievals followed by a quick recovery period and were discharged accordingly.

RESULTS

Patient 1 had five ovulation induction cycles, with 14 oocytes recovered in four of the five cycles. All four cycles produced multiple ova, with fertilization occurring in 5 of the 14 oocytes (35.7%); 3 demonstrated polyspermy (60%) and 2 were normal (40%). One transfer was performed with one normally cleaved two-cell embryo (20%) and one prezygote. No pregnancy resulted. "Empty fol-

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lices" were encountered in 15 of 29 follicles aspirated (52%). The highest serum E_2 achieved in any cycle was 1691 pg/ml.

Patient 2 had seven ovulation induction cycles, with four oocytes recovered in four of the seven cycles. No more than one ovum per cycle was ever retrieved. The spouse demonstrated oligospermia with decreased motility and progression. Fertilization occurred in two of the four oocytes recovered (50%). One oocyte inseminated with the husband's sperm resulted in polyspermy (25%), while one oocyte inseminated by donor sperm 24 hr after failure with husband's sperm resulted in a normally fertilized and cleaved embryo. The three-cell embryo was frozen for future transfer. "Empty follicles" were seen in 8 of the 12 follicles aspirated. The highest serum E_2 achieved was 386 pg/ml and the maximum number of follicles was nine.

Patient 3 had only one ovulation induction cycle, in which one follicle was aspirated; it was an "empty follicle." A large cumulus was collected in the fourth flush, with no oocyte evident.

Thus overall there were 13 IVF cycles in these three patients, 42 follicles aspirated, and 18 oocytes recovered, 7 of which fertilized but only 3 of which fertilized normally. No pregnancies resulted.

DISCUSSION

These three cases demonstrate that the "empty follicle" syndrome was common in these ovarian failure patients following ovulation induction (3,4). There were only 18 eggs recovered of 42 follicles (43%), whereas normally we recover 63% of oocytes from follicles. Although the fertilization rate was low, at 16%, compared to our normal rate of 52.3% (reported to S.A.R.T., 1988), nevertheless, normal fertilization and cleavage did occur.

Until recently, whenever one follicle was attained and the serum E_2 measured at least 200 pg/ml, hCG

would have been used. More recently, because of the improved pregnancy success when transferring multiple embryos during IVF-ET, higher amounts of hMG were used in these cases, hopefully to induce more follicles. Patient 1 demonstrated that although large amounts of hMG may be needed, induction of multiple follicles is possible. A total of 7050 IU of hMG with as much as 750 IU per day was used in patient 1 to achieve multiple folliculogenesis, but only five fertilized eggs and two normal fertilized eggs resulted. Thus, high doses of hMG did not improve the number of eggs retrieved.

The data are so poor that women with hypergonadotropic amenorrhea should not be encouraged to try IVF-ET with the technique described herein. Probably they should be steered in the direction of donor egg IVF-ET.

CONCLUSIONS

In vitro fertilization-embryo transfer (IVF-ET) was attempted in three patients, age 44, with ovarian failure. Although successful fertilization and cleavage did occur rarely, the reduced rate of embryogenesis per mature follicle which was seen was probably related to poor egg quality and increased incidence of empty follicles.

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