

6 HOURS MORE EXPOSURE OF -HCG MAY SALVAGE MORE THAN 70% OF ART EMPTY FOLLICLE SYNDROME (EFS) CYCLES. H. Sahebkhaf, Z. Alamoti, K. Soudmand, M. Kamgar, M. Sahand, S. Sahebkhaf. Reproductive Endocrinology and Infertility, Navid's Institute of Infertility, Tehran, Islamic Republic of Iran.

OBJECTIVE: The term of empty follicle syndrome (EFS) was first described by Coulam et al. for in-vitro fertilization (IVF) cycles during which no oocytes could be retrieved. Although there are cases in which the etiology of EFS remains unknown, it is clear that decreased HCG availability, whatever its origin, seems to be a fundamental cause in many of the published cases of EFS. We presented the preliminary results in the 2004 ASRM meeting. We undertook this study to evaluate the effect of longer duration of exposure to HCG on salvage of empty follicle syndrome cycles in a larger scale of patients.

DESIGN: Prospective evaluation of empty follicle syndrome (EFS) patients.

MATERIALS AND METHODS: 12,656 cycles of Rapid ICSI-ZIFT, in-vitro fertilization (IVF) and ICSI were performed between March 21st, 1998, and March 21st, 2007 at Navid's Institute of Infertility using long protocol Buserelin Acetate (Superfact, UK) and Human Menopausal Gonadotropin (HMG) or Gonal-F (rFSH). Buserelin Acetate and Gonadotropin were stopped and 10,000 IU of HCG (Profasi, Serono or Pregnyl, Organon) were administered I.M. when it was estimated that patients would have two or more follicles >17 mm diameter. Transvaginal ultrasound directed follicle aspiration was performed 36 h after HCG injection. All oocyte collections in the unit were performed by experienced operators. There were 119 cases in 108 patients in which no oocyte was recovered despite performing multiple flushes of present follicles. In all these cases, inquiries informed that the HCG used had not expired, was properly stored, and was administered at the right time and blood serum HCG was positive. Follicle aspiration was abandoned when no egg was retrieved halfway into the procedure and after waiting 6 hours more follicle puncture was programmed.

RESULTS: Twenty seven patients (25%) were 35 years of age or older at the time of their EFS cycle. Of the total 12,656 ART cycles, 119 EFS cycle were noted as no oocytes were obtained from any of 108 patients when performing oocyte retrieval under standard conditions (36 h after the indicated 10,000 IU HCG injection). In these cases, after waiting 6 hours more and re-programming of follicle puncture, oocytes were recovered from 85 patients with a mean of 8 ± 4.3 mature oocytes per woman EFS. Other patients' demographics were similar when compared, including age, type of infertility and stimulation protocols.

CONCLUSIONS: In most women with empty follicle syndrome, reprogramming of aspiration 6 hours later, may salvage the ART cycle.

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P-529

DIRECT OVARIAN STIMULATION BY OVARIAN INJECTION OF rFSH AND SOMATROPIN FOR THE POOR RESPONDERS IN IVF-ET PROGRAM. J. Jung, H. C. Kwon, J. W. Kim, B. H. Kim, S. E. Lee, S. J. Lee. Department of Ob/Gyn, Mirae and Heemang Ob/Gyn Clinic, Seoul, Korea; Laboratory of Infertility, Mirae and Heemang Ob/Gyn Clinic, Seoul, Korea.

OBJECTIVE: To assess the effect of direct ovarian stimulation by ovarian injection of rFSH and somatropin (DOS) on oocyte recovery, embryo development and cycle outcome in the poor responders undergoing IVF-ET program.

DESIGN: The design of this study was prospective.

MATERIALS AND METHODS: One hundred forty-nine patients participated in this study. The patients were divided into 3 groups based on their prior response and application of DOS to the COH: Group 1 (control, mean age: 34.2 ± 5.6): 98 patients with prior normal response, Group 2 (Non-DOS, mean age: 39.9 ± 4.2): 23 patients with a prior poor response, to whom DOS did not be applied, and Group 3 (DOS, mean age: 40.7 ± 3.4): 26 patients with a prior poor response, to whom DOS was applied. Patients with endometriosis, uterine pathology and PCOS were excluded. Ovarian stimulation for all patients was initiated with 150~225 IU of rFSH and 75IU of hMG with the standard GnRH-a long-protocol. For

DOS, 0.4 cc of culture media (Quin's Advanced Fertilization media, SAGE, USA) containing 30 IU of rFSH (Gonal-F^a, Merk Serono S.A., USA) and 0.2 IU of Somatropin (Decalge inj^a, LG Life Science, Korea) was injected on each ovarian stroma with 19 gauge needle (Chiba needle^a, Angiomed, Germany) on the cycle day 2 and additional injection on the cycle day 4 was decided after due consideration of an ovarian responsiveness.

RESULTS: The summarized results were in the following Table 1 and 2.

TABLE 1. Number and quality of retrieved oocytes and their development of embryo in each group (^{1,2,3}; $P < 0.05$, in ANOVA test)

Variables (n)	Control (98)	Non-DOS (23)	DOS (26)
No. of Oocytes	$12.4 \pm 8.2^{1,2}$	$1.57 \pm 0.9^{2,3}$	$6.3 \pm 4.8^{1,3}$
Good Oocytes (Mature, inter-1, 2)	$7.7 \pm 5.4^{1,2}$	$1.1 \pm 0.5^{2,3}$	$4.3 \pm 3.8^{1,3}$
Good Embryos (Grad 1, 1-1, 2)	4.7 ± 2.7^1	$0.42 \pm 0.1^{1,2}$	3.2 ± 2.1^2
Cumulative Embryo Score	131.2 ± 74.9^1	42.8 ± 32.6^1	93.6 ± 70.1

TABLE 2. Pregnant Outcome ($P = ns$ in CROSSTAB)

Variables (n)	Control (98)	Non-DOS (23)	DOS (26)
None Pregnancy	59	20	19
Chemical Abortion	4 (4.1%)	2 (8.7%)	0 (0%)
Clinical Abortion	5 (5.1%)	1 (4.3%)	3 (11.5%)
Ongoing Pregnancy (≥ 12 wks)	30 (30.6%)	0 (0%)	4 (15.4%)

CONCLUSIONS: An alternative approach of DOS in addition to the standard GnRH-a long-protocol for the patients with prior poor response enhances the ovarian response, thereby improves the quality of transferred embryos and the clinical outcome. This may be due to increase the concentration of FSH and somatropin in early follicular phase with concomitant augmentation of angiogenesis by estrogen in the treated ovaries.

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P-530

GnRH ANTAGONIST USE IS ASSOCIATED WITH INCREASED PREGNANCY RATES IN OVULATION INDUCTION/INTRAUTERINE INSEMINATION (OI/UI) TO IVF CONVERSIONS, INDEPENDENT OF AGE AND ESTRADIOL LEVEL AT RETRIEVAL. A. M. Quaas, S. A. Missmer, E. S. Ginsburg. Center for Reproductive Medicine, Department of Ob/Gyn, Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To determine if the use of gonadotropin releasing hormone (GnRH) antagonist in cycles converted from OI/UI to in-vitro fertilization (IVF) affects cycle outcome and pregnancy rates.

DESIGN: Case-control study of 182 consecutive OI/UI to IVF conversions undergoing oocyte retrieval conducted at a university-based infertility clinic from 2004 to 2006.

MATERIALS AND METHODS: All OI/UI to IVF conversions 2004-2006 were identified. Data were collected on female age, GnRH antagonist use, cycle characteristics and pregnancy outcome. The primary outcome was fetal cardiac activity on early ultrasound. We used multivariable logistic regression to estimate odds ratios (OR) and 95% confidence intervals (CI) to evaluate the relation between observation of fetal heartbeat and GnRH antagonist exposure. Linear regression was used to estimate the difference in intermediate cycle outcomes by antagonist exposure.

RESULTS: For patients treated with a GnRH antagonist, the OR for achieving pregnancy was 2.13 (95% CI = 1.03-4.39, $P = 0.04$) compared to untreated patients, independent of age and E2 levels on day of HCG. Patients treated with antagonist had 1.6 more follicles ($P = 0.07$), 2.1 more oocytes retrieved ($P = 0.06$), 1.9 more mature oocytes ($P = 0.04$), 2.3 more fertilized oocytes ($P = 0.007$), and the fertilization rate was 9.7% higher ($P = 0.01$).