



Polycystic ovary syndrome in IVF

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Abstract

Objective: To compare the pregnancy outcome of women with polycystic ovary syndrome (PCOS) and other cause of infertility.

Design and methods: Retrospective, clinical study in Academic tertiary center. We retrospectively examined the cycles of 2,491 women undergoing IVF therapy at Taipei Medical University from August 1995 to March 2009. Main Outcome Measures using pregnancy rates, fertilization rates, implantation rates, number of good embryos.

Results: Women with PCOS had very good pregnancy outcome in this study. As compared to the other causes of infertility, the women with PCOS had significantly higher peak E2 levels (2213 ± 216.6 vs. 1312 ± 21.7 , $p < 0.001$), more retrieved oocytes (15.0 ± 1.1 vs. 8.3 ± 0.1 , $p < 0.001$), more good embryos (2.8 ± 0.3 vs. 2.2 ± 0.1 , $p < 0.001$), more frozen embryos (4.4 ± 0.7 vs. 0.9 ± 0.1 , $p < 0.001$), higher implantation rates (21.5 ± 3.3 vs. 11.6 ± 0.1 , $p < 0.001$), and higher pregnancy rates (50.8 ± 6.3 vs. 29.9 ± 0.9 , $p = 0.003$). However, the women with PCOS had a higher percentage of severe ovarian hyperstimulation syndrome (4.8% (3/63) vs. 0.8% (20/2428), $p = 0.001$).

Conclusions: Women with PCOS had excellent pregnancy outcome in IVF procedure. There were more retrieved oocytes, more fertilized embryos, and more available frozen embryos. However, the quality of oocytes/embryos of women with PCOS was not impaired.

Introduction

Polycystic ovarian syndrome (PCOS) occurs in 6-8% of all women of reproductive age and about 20% of women presenting with sub-fertility. Because of the problem of chronic anovulation, a significant proportion of these women will ultimately need assisted reproductive techniques (ART). The typical outcome of ART in women with PCOS were more retrieval oocyte than women with other indication, however, the number of retrieved oocytes and pregnancy outcome have been published with controversial results (1-6). We then conduct this study to compare the oocyte quality and pregnancy outcome of women with PCOS and other indication.

Materials and methods

This study was approved by the Institutional Review Board of Taipei Medical University Hospital, Taipei, Taiwan.

We performed a retrospective analysis of IVF-ET cycles at Taipei Medical University from August 1995 to March 2009. All women were chosen by computer to meet the following criteria: (1) women were between 20 and 42 years old; (2) their IVF cycles had undergone down-regulation with leuprolide acetate, followed by ovarian stimulation with exogenous gonadotropins; (3) their IVF cycles had at least one embryo transfer; (4) there had been no donation of oocytes or reception of embryos; (5) only the data from first cycles were used; and, (6) their IVF cycles used fresh nondonor eggs and embryos.

A total of 2,491 women were classified according to the indication of infertility as PCOS and Non-PCOS. Embryos were evaluated by their morphological appearance just before transfer (about 66–72 hours after insemination). Embryo quality was judged by the implantation rate. In this study, we defined the implantation rate as the number of gestational sacs seen with ultrasound at 6 to 7 weeks of pregnancy, divided by the number of embryos replaced per transfer (7, 8).

IVF protocol

The cycles for all of the women were suppressed with the gonadotropin-releasing hormone (GnRH) agonist. Ovarian stimulation was performed using the gonadotropins available at the time of treatment. The stimulation protocol and starting dose were chosen according to the woman's age and an assessment of her ovarian function. Each woman's cycle was monitored by vaginal ultrasound from cycle day 6 of ovarian stimulation. The dosage of FSH was adjusted individually (usually in a step-down manner) after cycle day 7 for all the women. HCG (Profasi, Serono Laboratories, Randolph, MA) 10,000 IU i.m. was administered when three or more follicles were >16 mm at their largest diameters. Transvaginal follicular aspiration was performed 35–36 hours later. Progesterone supplementation (50 mg/day i.m.) and/or Utrogestone (micronised progesterone), (Laboratoire Pilette International S. A., Beinhem, France) (100 mg) was begun on the day of transfer and was continued until a pregnancy test was performed. If the test was positive, progesterone supplementation was given until week 10 of the pregnancy. A clinical pregnancy was defined as the presence of a gestational sac by ultrasound at 6 to 7 weeks. All oocytes were assessed at aspiration for corona/oocyte morphology (corona density, ooplasm color, oocyte shape, and nuclear morphology) and fertilization outcome.

Transfer of the embryos into the uterus was performed approximately 70–72 hours post-sperm injection or insemination (day 3 transfers). Embryos were transferred in a transfer medium consisting of HTF Medium (Irvine Scientific, Santa Ana, California), supplemented with 10% Plasmanate (Talecris Biotherapeutics, Inc., Research Triangle Park, NC), and loaded into a TDT SET (Laboratoire CCD, Paris, France). The number of embryos to be transferred was determined immediately before the transfer based upon the quality of embryo and women's age. The excess embryos were cryopreserved (cleaving stage). Only the results of "fresh" transfers were considered in this study.

Embryo quality grading

The morphological condition (grading) of cleaving embryos was assessed immediately before transfer following the criteria outlined by Veeck (9). The grading system is as follows, with Grade 1 representing the best morphological condition: Grade 1: Preembryo with blastomeres of equal size, no cytoplasmic fragments; Grade 2: Preembryo with blastomeres of equal size, minor cytoplasmic fragments or blebs; Grade 3: Preembryo with blastomeres of distinctly unequal size, few or no cytoplasmic fragments; Grade 4: Preembryo with blastomeres of equal or unequal size, significant cytoplasmic fragmentation; and, Grade 5: Preembryo with few blastomeres of any size, and severe or complete fragmentation. Good embryos are defined as grade 1 or 2 embryos (8).

Statistical analysis

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL). Data are presented as mean $\pm$ standard deviation. More than two groups' means were compared using one-way ANOVA post hoc range (Dunnett's) tests, with equal variances not assumed. Correlations were performed using Pearson's correlation coefficient. Data are presented as mean $\pm$ standard error. P levels <0.05 were considered significant.

Results

The cycles of 2,491 women (average age 34.4 ± 4.2 , range 20–40 years old) resulting in pregnancy rates with 30.4% were analysed. Results showed the causes of infertility and their pregnancy outcome among the 2,491 women. Causes of infertility included: endometriosis (34.6%, 863/2491); male infertility (23.23%, 579/2491); tubal factor infertility (19.4%, 483/2491); polycystic ovary syndrome (PCOS) (2.5%, 63/2491); combined multiple infertility causes (11.9%, 296/2491); and, others (8.3%, 207/2491). The pregnancy rates of various indication of infertility as following: Endometriosis (32.7 ± 1.6), Male factor infertility (25.9 ± 1.8), Tubal factor infertility (29.6 ± 2.1), PCOS (50.8 ± 6.3), Combined factors (35.8 ± 2.8), Others (21.7 ± 2.9). Women with PCOS had the best pregnancy outcome in this study. As compared to the other causes of infertility, the women with PCOS had significantly higher peak E2 levels (Mean $\pm$ Standard Error; 2213 ± 217 vs. 1312 ± 22 , $p < 0.001$), more retrieved oocytes (15.0 ± 1.1 vs. 8.3 ± 0.1 , $p < 0.001$), more good embryos (2.8 ± 0.3 vs. 2.2 ± 0.4 , $p = 0.003$), more frozen embryos (4.4 ± 0.7 vs. 0.9 ± 0.1 , $p < 0.001$), higher implantation rates (21.5 ± 0.7 vs. 11.6 ± 0.1 , $p < 0.001$), and higher pregnancy rates (50.8 ± 6.3 vs. 29.9 ± 0.9 , $p = 0.001$). However, the women with PCOS had a significantly higher percentage of severe ovarian hyperstimulation syndrome (4.8% (3/63) vs. 0.8% (20/2428), $p = 0.001$).

Discussion

To compare with other indication of infertility in the treatment of IVF, women with PCOS had excellent pregnancy outcome in IVF procedure. There were more retrieved oocytes, more fertilized embryos, and more available frozen embryos. However, the better implantation rates of embryo from women with PCOS implied that the quality of oocytes/embryos of women with PCOS was not impaired.

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Table-1: Pregnancy outcome in PCOS & non-PCOS responders

	Total	PCOS	Non-PCOS	p-value
Cases	2491	63	2428	NS
Age	34.4±0.1	34.4±0.5	34.4±0.1	
Range of oocyte number	2-40	3-38	2-40	
Duration of infertility	3.8±0.1	3.3±0.3	3.8±0.1	NS
Oocytes Number	8.5±0.1	15.0±1.1	8.3±0.1	<0.001
peak Estradiol	1334.2±22.0	2212.5±216.6	1311.9±21.7	<0.001
Fertilization Rates %	66.6±0.4	64.7±0.2	66.7±0.1	NS
Implantation Rates %	11.9±0.4	21.5±3.3	11.6±0.1	<0.001
Pregnancy Rates %	30.4±0.1	50.8±6.3	29.9±0.9	0.001
Abortion Rates %	23.0±1.5	18.8±7.0	23.1±1.6	NS
Live birth Rates %	23.4±8.5	41.3±7.3	23.0±0.1	0.001
Number of Embryo transfer	3.2±0.1	3.5±0.1	3.2±0.1	0.014
Number of Fertilized egg	5.4±0.1	9.5±0.8	5.3±0.1	<0.001
Number of Good embryo	2.2±0.1	2.8±0.3	2.2±0.1	0.003
Number of Frozen embryo	1.0±0.1	4.4±0.7	0.9±0.1	<0.001
Ovarian Hyperstimulation Case and %	23 (0.01%)	3 (0.5%)	20 (0.01%)	0.001

Data presentation with Mean $\pm$ Standard Error