Taiwanese Journal of Obstetrics & Gynecology 55 (2016) 821–825

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Impact of the number of retrieved oocytes on pregnancy outcome in *in vitro* fertilization

Ming-I Hsu [a, b], Chia-Woei Wang [a], Chi-Huang Chen [a], Chii-Ruey Tzeng [a, *]

[a] Department of Obstetrics and Gynecology, Taipei Medical University Hospital, Taipei Medical University, Taipei, Taiwan
[b] Department of Obstetrics and Gynaecology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

ARTICLE INFO

Article history:
Accepted 20 May 2015

Keywords:
IVF
number of retrieved oocytes
ovarian response
pregnancy outcome

ABSTRACT

Objective: To evaluate the impact of the number of retrieved oocytes on pregnancy outcome.
Materials and Methods: We retrospectively examined the cycles of 2491 women undergoing *in vitro* fertilization therapy at Taipei Medical University (Taipei, Taiwan) from August 1995 to March 2009. We divided them into three groups based on their response rate (where H = high, M = middle, and L = low). We conducted this study to evaluate and compare pregnancy outcome in these three groups.
Results: The total number of retrieved oocytes had a significantly positive correlation with peak E2 levels, and the number of fertilized oocytes, good quality embryos, and available frozen embryos. The number of retrieved oocytes had a positive correlation with pregnancy rates and a negative correlation with fertilization rates. The implantation and abortion rates among the three groups were essentially the same. Compared to the middle and higher responders, the pregnancy rates for lower responders were significantly lower. The pregnancy rates for middle responders and higher responders were not significantly different.
Conclusion: The benefits of more retrieved oocytes between the lower and the middle responders were obvious. However, the benefits and risks for retrieving more oocytes for the middle and the higher responders remained controversial.

Introduction

Ovarian response during controlled ovarian hyperstimulation (COH) is the most important factor for evaluating the pregnancy outcome in assisted reproductive technique. Age and ovarian reserve are both major predictive factors for *in vitro* fertilization (IVF) outcome [1]. The higher responders produced more oocytes with a smaller dose of exogenous gonadotropins. The lower responders required a higher dose of gonadotropins to produce a smaller number of oocytes [2–4]. Furthermore, the higher and lower responders usually registered higher and lower serum E2 levels, respectively [2,4]. The oocytes obtained from various responders should be under different endocrine milieu [5]. We question whether there are any differences between the quality and developmental potential of oocytes obtained from the various responders.

Numerous studies about the number of retrieved oocytes and pregnancy outcome have been published with controversial results [5–10]. While remaining within the margins of safety required to prevent ovarian hyperstimulation syndrome, some authors suggested that the more oocytes obtained, the higher the chance of conception [6,7]. Others proposed that mild ovarian stimulation with a modest number of retrieved oocytes would optimize implantation rates [9].

Understanding the relationship between the number of retrieved oocytes and the quality of oocytes/embryos is critically important when the ovarian stimulation protocol is determined. We conducted this study to determine the number of retrieved oocytes during COH and to evaluate their impact on oocyte/embryo development potential and pregnancy outcome.

* Corresponding author. Department of Obstetrics and Gynecology, Taipei Medical University Hospital, 252 Wu Hsing Street, Taipei 110, Taiwan.
E-mail address: tzengcr@tmu.edu.tw (C.-R. Tzeng).

http://dx.doi.org/10.1016/j.tjog.2015.05.009

Materials and methods

This study was approved by the Institutional Review Board of Taipei Medical University Hospital, Taipei, Taiwan (101IVF-TMU 01).

We performed a retrospective analysis of IVF-embryo transfer cycles at Taipei Medical University from August 1995 to March 2009. All women were chosen by computer to meet the following criteria: (1) women who were between 20 years old and 42 years old; (2) their IVF cycles had undergone downregulation with leuprolide acetate, followed by ovarian stimulation with exogenous gonadotropins; (3) their IVF cycles had at least one embryo transfer; (4) only the data from first cycles were used; (5) their IVF cycles used fresh nondonor eggs and embryos.

To rank ovarian response, the cycles of a total of 2491 women were arbitrarily classified according to the number of oocytes harvested as middle (M), higher (H), and lower (L) responders. Group M consisted of the middle responders (retrieved oocytes: 5–11, $n = 1298$); group H comprised the higher responders (retrieved oocytes: >11, $n = 579$); and group L consisted of the lower responders (retrieved oocytes: <5, $n = 614$). Oocytes were evaluated by their fertilization rates. Embryos were evaluated by their morphological appearance just prior to the transfer (about 66–72 hours after insemination). Oocyte 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 6–7 weeks of pregnancy, divided by the number of embryos replaced per transfer [11,12].

IVF protocol

The cycles for all of the women were suppressed with the gonadotropin-releasing hormone 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 6 days after ovarian stimulation. The dosage of follicle-stimulating hormone was adjusted individually (usually in a step-down manner) 7 days after ovarian stimulation for all women. HCG (Profasi; Serono Laboratories, Randolph, MA, USA) 10,000 IU [intramuscularly (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/d, i.m.) and/or utrogesterone (micronized progesterone; 100 mg) (Laboratoire Piette International S.A., Beinheim, France) 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 6–7 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 postsperm injection or insemination (Day 3 transfers). Embryos were transferred in a transfer medium consisting of HTF Medium (Irvine Scientific, Santa Ana, CA, USA), supplemented with 10% Plasmanate (Talecris Biotherapeutics, Inc., Research Triangle Park, NC, USA), and loaded into a TDT SET (Laboratoire CCD, Paris, France). The number of embryos to be transferred was determined immediately prior to the transfer based on the quality of the 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 prior to the transfer following the criteria outlined by Veeck [13]. 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; Grade 5—preembryo with few blastomeres of any size, and severe or complete fragmentation. Good embryos are defined as Grade 1 or Grade 2 embryos [12].

Statistical analysis

Statistical analysis was performed using SPSS 13.0 for Windows (SPSS, Inc., Chicago, IL, USA). Data are presented as mean ± standard error. More than two groups' means were compared using one-way analysis of variance *post hoc* range (Dunnett's) tests, with equal variances not assumed (Table 1; Figures 1 and 2). Correlations were performed using Pearson's correlation coefficient. Data are presented as mean ± standard error. A p level < 0.05 was considered statistically significant.

Results

The cycles of 2491 women (average age, 34.4 ± 4.2 years; range, 20–40 years) resulting in pregnancy rates with 30.4% were analyzed. Table 1 shows the causes of infertility and their pregnancy outcome among the 2491 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). Women with PCOS had the best pregnancy outcome in this study. Compared to the other causes of infertility, the women with PCOS had significantly higher peak E2 levels (2213 ± 1663 vs. 1311 ± 1049, $p < 0.001$), more retrieved oocytes (15.0 ± 8.5 vs. 8.3 ± 5.1, $p < 0.001$), more good embryos (2.8 ± 2.0 vs. 2.2 ± 1.7, $p < 0.001$), more frozen embryos (4.4 ± 5.5 vs. 0.9 ± 2.4, $p < 0.001$), higher implantation rates (21.5 ± 26.4 vs. 11.6 ± 20.3, $p < 0.001$), and higher pregnancy rates (50.8 ± 50.4 vs. 29.9 ± 45.8, $p = 0.003$). However, the women with PCOS had a significantly lower percentage of good embryos in fertilized eggs (35.6 ± 24.1 vs. 47.2 ± 33.1, $p = 0.006$), and a higher percentage of severe ovarian hyperstimulation syndrome [4.8% (3/63) vs. 0.8% (20/2428), $p = 0.001$].

In the analysis of correlations for all 2491 cycles, the total number of retrieved oocytes had a significantly positive correlation with the peak estradiol level ($\gamma = 0.559$, $p < 0.001$), as well as the number of fertilized oocytes ($\gamma = 0.834$, $p < 0.001$), good embryos ($\gamma = 0.329$, $p < 0.001$), and available frozen embryos ($\gamma = 0.617$, $p < 0.001$). The number of retrieved oocytes had a positive correlation with pregnancy rates ($\gamma = 0.120$, $p < 0.001$), and a significantly negative correlation with fertilization rates ($\gamma = -0.236$, $p < 0.001$). The number of retrieved oocytes also had a positive correlation with implantation ($\gamma = 0.076$, $p < 0.001$), and a significantly negative correlation with the percentage of good embryos ($\gamma = -0.269$, $p < 0.001$).

Table 2 shows the ovulation and pregnancy outcome according to the ovarian responses of the women. There was no significant difference in average age among the higher (H), middle (M), and lower (L) responders. The parameters for comparison of the groups