Reproductive BioMedicine Online (2013) 27, 147–153

www.sciencedirect.com
www.rbmonline.com

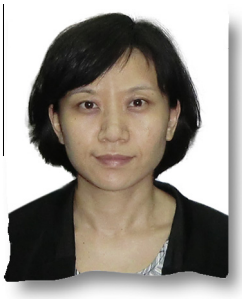
ARTICLE

Prediction of IVF/ICSI outcome based on the follicular output rate

Ning Zhang [a,b], Cui-Fang Hao [b], Li-Li Zhuang [a,b], Xiao-Yan Liu [b], Harvest F Gu [c], Shan Liu [a,d,e,f], Zi-Jiang Chen [a,d,e,f,*]

[a] *Center for Reproductive Medicine, Provincial Hospital Affiliated to Shandong University, 250021 Jinan, China;* [b] *Center for Reproductive Medicine, Yantai Yuhuangding Hospital, 264000 Yantai, China;* [c] *Rolf Luft Center for Diabetes Research, Department of Molecular Medicine and Surgery, Karolinska Hospital, Karolinska Institutet, 17176 Stockholm, Sweden;* [d] *National Research Center for Assisted Reproductive Technology and Reproductive Genetics, 250021 Jinan, China;* [e] *The Key Laboratory for Reproductive Endocrinology of Ministry of Education, 250021 Jinan, China;* [f] *Shandong Provincial Key Laboratory of Reproductive Medicine, Jinan, China*

[*] Corresponding author. *E-mail addresses:* chenzijiang@hotmail.com, yyyzhangning@126.com (Z.-J. Chen).



Dr Ning Zhang is an associate professor of Yantai Yuhuangding Hospital, Yantai, China. She received her MD degree from Shandong University, Shandong, China, in 2007. Since 2009, she has been pursuing her PhD degree at the Center for Reproductive Medicine of Shandong University, which is one of the largest IVF centres in China and a pioneer in reproductive endocrinology, genetic diseases and oocyte cryopreservation. Dr Ning Zhang has engaged in reproductive endocrinology and assisted reproductive technology for 13 years. She is especially interested in the study of polycystic ovary syndrome.

Abstract This study assessed the true accuracy of follicular output rate (FORT) as a prognostic indicator of response to FSH and reproductive competence after IVF/intracytoplasmic sperm injection. A total of 1643 cycles, including 140 polycystic ovary syndrome (PCOS) patients who underwent ovarian stimulation, were studied. FORT was calculated as the ratio of preovulatory follicle count on the day of stimulation × 100/small antral follicle count (3–10 mm in diameter) at baseline. Low, medium and high FORT groups were defined according to tertile values. Among 1503 non-PCOS cycles, numbers of retrieved oocytes and of all embryos that could be transferred, as well as rates of good-quality embryos, embryo implantations and clinical pregnancies, progressively increased with FORT. In PCOS patients, FORT were significantly lower in patients who achieved clinical pregnancy compared with those who did not (0.56 ± 0.21 versus 0.66 ± 0.29, $P = 0.031$). Fertilization and good-quality embryo rates were significantly higher with medium FORT than low and high FORT ($P = 0.001$ and $P = 0.047$, respectively). Medium FORT in PCOS patients and high FORT in non-PCOS patients may predict better outcomes for IVF/ICSI.

KEYWORDS: embryo transfer, follicular output rate, IVF, ICSI, ovarian stimulation, polycystic ovary syndrome

1472-6483/$ - see front matter
http://dx.doi.org/10.1016/j.rbmo.2013.04.012

Introduction

Ovarian stimulation is a key procedure in assisted reproduction technology. This stimulation is achieved by the administration of exogenous gonadotrophin to increase follicular recruitment and oocyte yields. Although the regulatory mechanisms determining the extent of the sensitivity of individual antral follicles to FSH remains to be elucidated, the appropriate response of antral follicles to FSH and a high quality of oocytes may result in a good outcome after IVF/intracytoplasmic sperm injection (ICSI).

There is no marker that can predict both ovarian response and oocyte competence. The antral follicular count (AFC) comprises the number of follicles of 3—10 mm diameter measured in ovaries at the start of the menstrual cycle (Chang et al., 1998; de Carvalho et al., 2008). The AFC may reflect the size of the remaining primordial pool in women with proven natural fertility (Kline et al., 2005; Scheffer et al., 1999) and is highly correlated to the number of oocytes retrieved (Bancsi et al., 2002; Broer et al., 2009). Otherwise, AFC can be used in the prediction of ovarian response but not of oocyte/embryo quality or IVF outcome (Melo et al., 2009). The number of preovulatory follicles obtained at the end of ovarian stimulation is not a reliable reflection of antral follicle sensitivity to FSH, as it is greatly influenced by the number of small antral follicles available before treatment. To evaluate follicular responsiveness to exogenous FSH, the use of the follicular output rate (FORT) as an innovative measure has been suggested (Genro et al., 2011). FORT is assessed by the ratio of the preovulatory follicle count (PFC; 16—22 mm) obtained in response to FSH administration on the day of human chorionic gonadotrophin (HCG) to the small antral follicle count (3—10 mm) observed after the complete suppression of endogenous gonadotrophins by gonadotrophin-releasing hormone agonist (GnRHa) (FORT = PFC × 100/AFC) (Gallot et al., 2012; Genro et al., 2011, 2012). Gallot et al. (2012) found that FORT may be a qualitative reflector of ovarian follicular competence only in patients with regular menstrual cycles. The values of FORT as a predictor of IVF/ICSI outcome in polycystic ovary syndrome (PCOS) and non-PCOS patients were unknown. The aim of the present investigation was to assess the true accuracy of FORT as a prognostic indicator of the response to FSH and the reproductive competence reflected by the outcomes of oocytes and embryos after IVF/ICSI treatment.

Materials and methods

Subjects

In total, 1643 cycles of IVF/ICSI treatment from January 2010 to December 2011 were included in the present study. Women from 23 to 44 years of age were included if they fulfilled the following criteria: (i) both ovaries present; (ii) FSH <12 IU/l, oestradiol <80 pg/ml and prolactin in the normal range before ovarian stimulation; (iii) presence of a normal uterine cavity; (iv) normal thyroid-stimulating hormone concentration or euthyroid as determined by the investigator; and (v) no current or past diseases affecting the administration of gonadotrophin. Indications for IVF/ICSI were: (i) female factors, 1063 cycles (64.7%), such as tubal factor, endometriosis or ovulation dysfunction; (ii) male factors, 176 cycles (10.7%); and (iii) both factors, 404 cycles (24.6%).

Among all patients, 1503 cases were non-PCOS and 140 cases were diagnosed as PCOS based on the presence of two out of three criteria of The Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group (2004), including oligo- and/or anovulation, clinical and/or biochemical signs of hyperandrogenism and polycystic ovaries. Other aetiologies (congenital adrenal hyperplasias, androgen-secreting tumours and Cushing's syndrome) were excluded. The median age was 32 in both the PCOS and non-PCOS groups. Among the patients with PCOS, there were 79 cases (56.43%) with oligo- and/or anovulation + hyperandrogenism + polycystic ovaries, 46 cases (32.86%) with oligo- and/or anovulation + polycystic ovaries, 11 cases (7.86%) with oligo- and/or anovulation + hyperandrogenism and four cases (2.86%) with hyperandrogenism + polycystic ovaries.

Treatment protocol

All patients underwent standard pituitary down-regulation protocol with GnRHa (triptorelin, Diphereline; Ipsen Pharma Biotech, France) 0.05 mg between day 5—7 after ovulation or on day 21 of the oral contraceptive cycles. Fourteen days later, complete pituitary desensitization was confirmed by the detection of serum oestradiol concentrations <50 pg/ml, LH <3 IU/l, no follicles >10 mm in diameter and endometrial thickness <7 mm by ultrasound examination. Gonadotrophin was administered with recombinant FSH (Gonal F; Merck Serono, Switzerland) 150—300 IU/day until the day of HCG administration (250 μg, Ovidrel; Merck Serono, Switzerland).

On the day of recombinant FSH and HCG administration, ovarian ultrasound scans were performed using a transvaginal probe (Aloka Medical, Japan). FORT was calculated as PFC on the day of HCG × 100/AFC at baseline (the first day of FSH).

Transvaginal oocyte retrieval was performed 34—36 h after the administration of HCG. Oocytes were fertilized either via conventional insemination or ICSI based on the couple's history. Fertilization was assessed 16—18 h after IVF or ICSI. Embryo transfers were performed 3 days after oocyte retrieval. No more than three embryos per patient were transferred; surplus embryos were cryopreserved. Progesterone vaginal tablets (Besins, Iscovesco, France) were administered 600 mg/day as luteal support from the day of the oocyte retrieval. Clinical pregnancy was defined as the presence of a gestational sac confirmed 5 weeks after embryo transfer by ultrasonography.

Informed consent was received from all subjects. The study were approved by the local ethics committee of Yantai Yuhuangding Hospital (YYH 2011-12-19, granted 19 December 2011).

Statistical analysis

Data were statistically described in terms of means ± SD. The data were analysed using a two-tailed Student's t-test, ANOVA and Turkey's post-hoc test for independent data. For comparing categorical data, the Pearson chi-squared test