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ARTICLE

Assisted reproductive outcomes in women with different polycystic ovary syndrome phenotypes: the predictive value of anti-Müllerian hormone

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Abstract This cross-sectional study aimed to evaluate IVF/intracytoplasmic sperm injection (ICSI) outcomes in different polycystic ovary syndrome (PCOS) phenotypes (A, B, C and D) compared with a control group and the predictive values of serum anti-Müllerian hormone (AMH) in PCOS phenotypes for main outcomes. This study evaluated 386 PCOS women and 350 patients with male factor infertility. Women with phenotypes A and C had significantly higher concentrations of AMH than those with phenotype B ($P < 0.001$). Clinical pregnancy rate (CPR) in the phenotype D group (53.3%) was higher than other groups (32.5%, 26.4% and 36.8%, respectively, in phenotypes A, B and C), but not to a significant level. Multivariable regression analysis, after adjusting for women's age and body mass index, revealed that PCOS phenotypes A and B were associated with a decreased CPR compared with the control group (odds ratio [OR]: 0.46, confidence interval [CI]: 0.26–0.8, $P = 0.007$ and OR: 0.34, CI: 0.18–0.62, $P = 0.001$, respectively). It seems a combination of hyperandrogenism and chronic anovulation is associated with a negative impact on the CPR in these patients. These results demonstrated that AMH concentration is related to PCO morphology but not predictive for CPR and live birth rate.

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Introduction

Polycystic ovary syndrome (PCOS) is a common cause of female infertility and affects 15–25% of women, based on the Rotterdam criteria (Livadas and Diamanti-Kandarakis, 2013). PCOS constitutes a continuous spectrum of symptoms starting from the early prepubertal years and continuing after menopause. Phenotypes are the clinical features resulting from the interaction between heredity and environment in a disease or syndrome (Moran et al., 2012). The phenotypic expression of PCOS varies through time and depends on several internal (e.g. genetic influence (Cui et al., 2015), ovarian/adrenal steroidogenesis and insulin resistance) and external (e.g. quality and quantity of diet, exercise and lifestyle) factors (Livadas and Diamanti-Kandarakis, 2013). Moreover, the emergence of new definitions with the use of ovarian morphology as well as chronic anovulation and hyperandrogenism, as diagnostic criteria, has developed the phenotypic variety of PCOS (Livadas and Diamanti-Kandarakis, 2013). To our knowledge, very few studies have evaluated the outcomes of assisted reproductive technology (ART) in the different phenotypes of PCOS women (Palomba et al., 2010).

Recently, anti-Müllerian hormone (AMH) has been considered a diagnostic or even prognostic marker of PCOS (Karkanaki et al., 2011). Tal et al. (2014) in a recent study stated that the concentration of serum AMH might be related to the severity of PCOS and correlate with its clinical diagnostic hallmarks (i.e. hyperandrogenism, oligo/anovulation and polycystic ovary morphology [PCOM]). Pregnancy rates are likely to decrease with the exacerbation of PCOS (Sahmay et al., 2013). Although some studies have suggested a reverse relationship between the AMH concentration and pregnancy rates (Xi et al., 2012), some others have found a positive relationship between the AMH concentration, embryo quality and clinical pregnancy rates (Tal et al., 2014).

On the other hand, an elevated concentration of basal LH due to enhanced pulsatile gonadotrophin-releasing hormone (GnRH) release is one of the hallmark endocrinological disturbances in PCOS women. Increased LH concentrations are observed in about 70% of PCOS patients with elevated LH pulse amplitude and an increased LH pulse frequency, which causes a two- to threefold elevation in serum LH concentrations versus FSH concentrations (Piouka et al., 2009). The potential impact of a high concentration of LH, and specifically a high LH/FSH ratio on human reproduction, is still under debate. Some studies reported negative impacts of high LH or LH/FSH ratio on the number of follicles as well as the number and maturity of oocytes (Tarlatzis et al., 1995), embryo quality and clinical pregnancy rates (CPR) (Wiser et al., 2013); however, other studies could not find any adverse effects (Geng et al., 2013; Mendoza et al., 2002). Elsewhere, Brodin et al. (2009) concluded that a low FSH concentration combined with high LH probably shows a well-preserved ovarian reserve and is associated with high pregnancy rates in IVF/ICSI cycles.

PCOS has its unique properties such as increased antral follicle count, serum AMH and LH/FSH ratio. Therefore, the prediction of clinical pregnancy in women with PCOS is more challenging than non-PCOS women (Sahmay et al., 2013). The present study was designed to evaluate: (i) ART outcomes in different PCOS phenotypes compared with the control group; and (ii) the predictive values of serum AMH and LH/FSH ratio in PCOS phenotypes for ART outcomes.

Materials and methods

Patients

This cross-sectional study was performed in the Royan Institute from June 2012 to January 2014. The Institutional Review Board and Ethics Committee of Royan Institute approved the study protocol on 15 June 2015 (reference number EC90/1010). The study was performed in accordance with the Helsinki Declaration and adhered to the guidelines of the Committee of Publication Ethics. All the participants signed the informed consent. All infertile women diagnosed with PCOS who underwent the first IVF/ICSI cycle were enrolled during the study period. Other causes of infertility including severe endometriosis, hydrosalpinx, uterine factor, severe male factor (oligo-tetrato-asthenozoospermia), and age factor (≥40) or diminished ovarian reserve (AMH < 1 ng/ml, FSH > 12 IU/l) were excluded. Only patients with mild/moderate male factor and/or tubal factor infertility were included. Meanwhile smokers and diabetic patients were excluded from the study.

PCOS cases were diagnosed based on the Rotterdam criteria (2004), and the presence of at least two of the following criteria: menstrual irregularity (cycle length <26 days or >35 days or variation between consecutive cycles of >10 days); clinical (presence of hirsutism evaluated by a Ferriman-Gallwey score >8, severe acne and alopecia) or biochemical (total testosterone concentration >0.5 ng/ml and/or free testosterone >3.5 pg/ml) hyperandrogenism; or ultrasound evidence of polycystic ovaries. Hirsutism was assessed according to the Ferriman-Gallwey-score and examination of nine body areas for coarse terminal hair, including upper lip, chin and chest, upper and lower areas of the abdomen, thighs and upper arms. In each part, the severity of hirsutism was graded from 1 to 4 and the participants with the total score of 8 and above considered as having hirsutism. PCOM was defined as the presence of 12 or more ovarian cysts with 2–10 mm diameter per ovary and/or ovarian volume ≥10 cm^3. Vaginal ultrasound was performed by an ultrasound specialist and radiologist using an Aloka α-10 with a transvaginal 6–7.5 MHz probe (Japan). Patients with other differential diagnoses, including hyperprolactinaemia, thyroid dysfunction, hypothalamic amenorrhoea, Cushing's syndrome and ovarian failure, were detected via hormonal tests and excluded from the study. PCOS patients were categorized to four phenotype groups according to the Rotterdam criteria: (i) phenotype A: the coexistence of hyperandrogenism, chronic anovulation and polycystic ovaries (HA+AO+PCO); (ii) phenotype B: chronic anovulation and hyperandrogenism without the polycystic ovaries

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