Progesterone levels on the hCG day and outcomes in vitro fertilization in women with polycystic ovary syndrome

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Abstract

Background The purpose of this study was to determine the incidence of premature luteinization in patients with polycystic ovary syndrome and compared the main determinants of success in in-vitro fertilization in PCOS patients with and without premature luteinization.

Methods Retrospective analysis of 180 PCOS women of Chinese Han origin with infertility who underwent controlled ovarian hyperstimulation (COH) with an exogenous gonadotropin/GnRH antagonist protocol. Hormone levels on the hCG day and IVF outcomes were assessed.

Results The incidence of premature luteinization was 23.3 %. Compared with PCOS patients without premature luteinization, PCOS patients with premature luteinization (PL) had a higher number of oocytes retrieved (18.20 ± 6.6 vs 15.08 ± 7.3 , $p=0.037$) and a higher fertilization rate (72.9 ± 1.9 vs 63.1 ± 2.3 , $p=0.033$), but clinical pregnancy rates were no statistical significance (53.3 vs 56.0 , $p=0.836$). Though the implantation rate was higher in no premature luteinization

patients, but the difference was not statistically significant (37.7 vs 30.3 , $p=0.115$).

Conclusion The PCOS patients with premature luteinization had a higher fertilization rate and high number of oocytes retrieved, and the similar implantation rate and clinical PRs as PCOS patients without premature luteinization.

Keywords Controlled ovarian hyperstimulation · In vitro fertilization · Premature luteinization · Progesterone · Polycystic ovary syndrome

Background

Polycystic ovary syndrome (PCOS, OMIM 184700) is an endocrine disorder that affects reproductive aged women and is characterized by clinical and/or biochemical hyperandrogenism, oligomenorrhea/amenorrhea and polycystic ovaries on ultrasonography [1]. PCOS patients who fail to conceive can be treated with clomiphene citrate followed by gonadotropins. In vitro fertilization (IVF) and embryo transfer provide an additional line of treatment for PCOS patients with recombinant human FSH (rFSH) alone or in combination with gonadotrophin-releasing hormone agonist (GnRHa).

GnRH antagonists were introduced into clinical practice to prevent premature luteinization in controlled ovarian hyperstimulation (COH) protocols [2–4]. Despite pituitary down-regulation, premature luteinization is a frequent event in COH cycles [5]. The possible effect of increased progesterone (P) levels secondary to GnRH antagonism on IVF outcomes is controversial in general people for several years. One study indicated that premature luteinization did not appear to have a negative impact on ongoing pregnancy rate (PR) in an oocyte donation program [6]. However, a lower implantation rate and PR were observed in patients with high P levels, with a 38.3 % incidence of premature

Capsule Progesterone levels on the hCG day was not an obstacle to successful IVF outcomes in women with polycystic ovary syndrome patients undergoing COH.

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luteinization when P levels were 1.2 ng/ml in patients (excluding PCOS patients) [3]. Additional studies have reported similar results [7], whereas others have reported increased PR associated with premature luteinization and elevated serum P concentration in an oocyte donation program [8]. A number of similar studies have produced either negative or controversial results regarding the role of P and premature luteinization on IVF outcomes.

But, the incidence of premature luteinization has been rarely evaluated in PCOS patients. Previous studies have not adequately characterized the IVF outcomes of PCOS patients undergoing COH with and without premature luteinization.

Furthermore, most previous reports did not discriminate between short and long COH protocols, which is important, as the short regimen more frequently leads to premature luteinization [9]. The majority of data on premature luteinization and IVF outcomes have been collected from groups of patients that may or may not have excluded PCOS patients and therefore cannot be extrapolated to patients with PCOS undergoing COH.

In the present study, we performed a retrospective analysis of a large number of PCOS patients who underwent a GnRHa long COH protocol for IVF. We determined the incidence of premature luteinization and compared clinical outcomes with and without premature luteinization.

Methods and materials

Patients

A total of 180 patients with PCOS participating in an IVF program from June 2008 until February 2010 at the Reproductive & Genetic Hospital of CITIC-XIANGYA were included in this retrospective study. PCOS patients were referred to our department for IVF because of menstrual disturbance or biochemical signs of hyperandrogenism, and all PCOS patients had polycystic ovaries upon ultrasound scan. All subjects enrolled in this study were from unrelated families. Some patients had been investigated by hysterosalpingography and laparoscopy. All patients could enter the study only once. The fecundities of all male partners were normal according to World Health Organization criteria [10].

The diagnosis of PCOS was based on the 2003 American Society for Reproductive Medicine/European Society for Human Reproduction and Embryology (ASRM/ESHRE) joint consensus criteria, which state that PCOS is diagnosed on the basis of having two out of three criteria: oligo- or anovulation, signs of clinical and/or biochemical hyperandrogenism and polycystic ovaries on ultrasonography after exclusion of specific identifiable disorders (congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome, thyroid dysfunction, hyperprolactinemia) [11]. Body

mass index (BMI) was calculated as body weight (kg) divided by height squared (m^2).

Controlled ovarian hyperstimulation

In PCOS patients, GnRHa was administered 3 weeks after a progestin-induced withdrawal bleed or spontaneous menstruation. On the 21st day of the cycle, patients received Decapeptyl® (0.5 mg/day; Ferring, Kiel, Germany), the initial dose was 0.5 mg/day. COH began on cycle day 4 with rFSH (Gonal-f®; Serono, Geneva, Switzerland), and dose adjustments were based on the individual dose response. When at least two follicles were ≥ 18 mm in diameter, 10,000 IU of hCG was administered. Treatment was monitored with serial blood samples to assess serum estradiol (E2), luteinizing hormone (LH) and P levels. Follicle development was evaluated by ultrasound. Oocyte retrieval was scheduled 34–36 h after hCG administration by vaginal ultrasound. On the third day after insemination, the morphology of each embryo was measured for number of cells, extent of fragmentation and blastomere symmetry. Good-quality embryos were defined as containing ≥ 6 equal-sized blastomeres with < 20 % fragmentation. According to our routine procedure, two or three embryos were transferred on day 3 after oocyte retrieval. In the luteal phase, all patients received muscular administration of 60 mg natural P supplementation, starting from the day of oocyte retrieval until pregnancy testing 11 days after embryo transfer. Clinical pregnancy was defined as the presence of gestational sacs detectable by ultrasound.

Blood samples and hormone measurements

Hormonal assessment of each patient during COH monitoring was performed on day 4 of stimulation and on the day of hCG administration (hCG day). Blood samples were obtained from each patient. Serum E2, LH and P concentrations were measured with the Abbott Ax System (Abbott Diagnostics, Abbott Park, IL). Baseline levels of FSH, LH, total T and E2 were measured with the Abbott Ax System (Abbott Diagnostics) in blood samples obtained from PCOS patients during a period of amenorrhea and from ovulatory women between cycle days 2–4 of the menstrual cycle preceding IVF. Premature luteinization has been defined as the presence of elevated serum P concentrations on the day of hCG administration, but the definition varies across studies. In the present study, a P level of 1.2 ng/mL was used as the discriminatory value for premature luteinization by the reference [3].

Statistical analysis

The patients data were reported as means $\pm$ SD. The serum hormone levels and fertilization rates were analyzed using

Student's *t* test, and the χ^2 test was used for comparisons of the clinical pregnancy rates and implantation rates. In all tests, $p < 0.05$ was considered statistically significant by two-tailed analysis. Statistical analysis was done with the Statistical Package for Social Sciences for Windows, version 11.0 (SPSS, Chicago, IL).

Results

According to the reference [3], PCOS patients were divided into two patient groups with or without premature luteinization according to P concentration on the day of hCG administration: $P < 1.2$ ng/mL (without premature luteinization) and $P \geq 1.2$ ng/mL (with premature luteinization; Table 1). Of the 180 PCOS patients who underwent COH only once each, 42 patients developed premature luteinization based on hCG day P levels ≥ 1.2 ng/mL and the incidence of premature luteinization was 23.3 %.

A retrospective analysis of 180 PCOS patients undergoing COH for IVF suggested that there were no significant differences in age, BMI, length of infertility (years) and induced length (days) between the two patient groups ($p = 0.410$, $p = 0.856$, $p = 0.767$, $p = 0.797$, respectively) (Table 1). No statistically significant difference was also observed in rFSH administered between the two patient groups ($p = 0.573$). Baseline FSH, LH, E2 and T were also not different in the PCOS patients without premature luteinization compared with in the patients with premature luteinization (Table 1). The peak LH level was similar in both patients groups on hCG day. Whereas, the peak E2 levels of patients without premature luteinization was lower compared with that of patients with premature luteinization (2316.3 ± 821.5 vs. 2618.8 ± 892.6) ($p = 0.026$) and the peak P level was also significantly lower (0.74 ± 0.2 vs. 1.42 ± 0.3) ($p < 0.001$) on hCG day (Table 1).

Statistically significant differences were observed in PCOS patients with or without premature luteinization with regard to the number of retrieved oocytes and fertilization rates (Table 2). More oocytes (18.20 ± 6.6) were retrieved from PCOS patients with premature luteinization, who also had higher E2 and P levels on hCG day, compared with PCOS patients without premature luteinization (15.08 ± 7.3 , $p = 0.037$). A higher fertilization rate (72.9 ± 1.9 %) of retrieved oocytes was observed in PCOS patients with premature luteinization compared with those without premature luteinization (63.1 ± 2.3 %) ($p = 0.033$). However, the number of good-quality embryos on day 3 after egg retrieval and good-quality embryo rate were similar between the two groups (Table 2). The patients without premature luteinization had a higher implantation rate and clinical PR compared with the patient with premature luteinization, but the difference was not statistically significant. In the patients with premature luteinization, mean number of embryos transferred was subtle difference compared with in the patients without premature luteinization, but no statistical significance was observed ($p = 0.836$ and $p = 0.643$, respectively; Table 2).

Discussion

Polycystic ovary syndrome (PCOS) is a common clinical disorder affecting 5 %–10 % of young women [12]. The disorder is associated with hirsutism, obesity and multiple cysts in the ovaries [13]. In a significant proportion of PCOS patients, insulin resistance (IR) is a common phenotype predisposing patients to type 2 diabetes and atherosclerosis [1, 14–19]. The etiology of PCOS remains poorly understood, however, progesterone is believed to play some role in the responsiveness of these patients to COH.

Despite the role of down-regulation of the pituitary-gonadal axis in IVF protocols, several researchers have

Table 1 Demographic data and clinical characteristics of PCOS patients with and without premature

Value	$P < 1.2$ ng/mL ($n = 138$)	$P \geq 1.2$ ng/mL ($n = 42$)	p Value
Age (years)	29.9 ± 3.5	30.3 ± 3.7	0.410
BMI (kg/m^2)	24.6 ± 3.2	25.8 ± 2.5	0.856
Length of infertility (years)	5.4 ± 2.3	5.6 ± 2.9	0.767
Induction length (days)	10.5 ± 1.8	10.6 ± 1.3	0.797
rFSH administration	2689.2 ± 548.0	2388.3 ± 907.4	0.573
Baseline FSH (mIU/L)	6.7 ± 1.5	6.5 ± 1.7	0.486
Baseline LH (mIU/L)	7.2 ± 4.6	6.8 ± 1.9	0.746
Baseline E ₂ (pg/mL)	44.1 ± 16.9	43.8 ± 21.2	0.423
Baseline T (ng/mL)	0.56 ± 0.4	0.54 ± 0.2	0.810
hCG day E ₂ (pg/mL)	2316.3 ± 821.5	2618.8 ± 892.6	0.026
hCG day P (ng/mL)	0.74 ± 0.2	1.42 ± 0.3	<0.001
hCG day LH (mIU/L)	2.7 ± 2.4	2.3 ± 0.9	0.370

Values are reported as mean $\pm$ SD and were analyzed by Student's *t* test, with $p < 0.05$ considered statistically significant. BMI body mass index, FSH follicle-stimulating hormone, LH luteinizing hormone, E₂ estrogen, T testosterone, P progesterone, rFSH recombinant FSH, IVF in vitro fertilization, COH controlled ovarian hyperstimulation

Table 2 Outcomes in PCOS patients with and without premature luteinization undergoing COH for IVF

Value	$P < 1.2$ ng/mL ($n = 138$)	$P \geq 1.2$ ng/mL ($n = 42$)	p Value
No. of oocytes retrieved ^a	15.08±7.3	18.20±6.6	0.037
No. of day 3 good-quality embryos ^a	6.6±3.7	7.2±4.7	0.475
Good-quality embryo rate (%) ^a	67.0±2.3	70.9±2.8	0.440
No. of embryos transferred ^a	2.0±0.8	2.0±0.4	0.643
Implantation rate (%) ^b	37.7	30.3	0.115
Fertilization rate (%) ^a	63.1±2.3	72.9±1.9	0.033
Clinical PR (%) ^b	56.0	53.3	0.836

^a Values are reported as mean±SD and were analyzed by Student's t test

^b Values were analyzed by χ^2 test

$p < 0.05$ was considered statistically significant

IVF in vitro fertilization, COH controlled ovarian hyperstimulation

described a phenomenon of premature luteinization in COH cycles [20]. There may have been a number of problems in interpreting the results of previous studies due to varying diagnostic criteria for premature luteinization, use of different ovarian stimulation methods [21] and differences in initial rFSH dose during ovarian stimulation [22]. High P levels have been shown to adversely affect embryo quality and pregnancy rates in IVF and oocyte donation programs [23]. In one study, premature luteinization during COH had no adverse effect on oocyte and embryo quality [24], while others have reported that premature luteinization during GnRH antagonist IVF-embryo transfer cycles was frequently observed and associated with lower pregnancy and implantation rates [3]. In the present study, in the only PCOS patients with excluding no PCOS patients, a serum P level of ≥ 1.2 ng/mL on the day of hCG was defined as the break point for premature luteinization. Patients underwent a GnRHa down-regulation long COH protocol for IVF. Adjustments of the dose of rFSH were based on the individual dose response, which excluded a number of problems in interpreting our results in favour of our study.

Previous studies were based on the general groups who were not strictly distinguishing patients with and without PCOS. Therefore, premature luteinization in PCOS patients and the impact on IVF outcomes has rarely been studied. In this study, we measured the incidence of premature luteinization and its possible effect on IVF outcomes in a large population of PCOS patients. The incidence of premature luteinization ranges from 2 % to 40 % in IVF general patients [4, 25–27]. Bosch et al. reported frequent premature luteinization and diminished PR with the introduction of a GnRH antagonist to their COH protocol for IVF in patients [3]. The incidence of premature luteinization was 38.3 % in

patients and premature luteinization was associated with lower pregnancy and implantation rates [3]. Bosch's study excluded PCOS patients. The incidence of premature luteinization was 23.3 % in PCOS patients in our report, which was similar to that of general patients. Although patients with premature luteinization ($P \geq 1.2$ ng/mL on the day of hCG administration) had statistically significantly higher E2 and P levels on the hCG day and statistically significantly higher numbers of oocytes retrieved, they had a similar number of day 3 good-quality embryos and good-quality embryo rates as patients without premature luteinization when using the GnRH antagonist long COH protocol. Moreover, we found that despite an increased number of oocytes retrieved from PCOS patients with premature luteinization compared with PCOS patients without premature luteinization, the differences in PR, implantation rates and number of embryos transferred were not statistically significant. However, a significantly higher fertilization rate was observed in PCOS patients with premature luteinization. These results suggested that premature luteinization in PCOS patients does not have a statistically significant adverse effect on implantation rate and PR, but premature luteinizing may be beneficial increase in the number of oocytes. In fact, the heterogeneous nature of PCOS patients was very important to evaluate the premature luteinization level and IVF outcome. PCOS consists of a heterogeneous set of signs and symptoms with a spectrum of mild to severe disturbances in reproductive endocrine and metabolic functions in women. The abnormalities include hyperandrogenism, insulin resistance, abnormal LH-to-FSH ratios, and an abnormal follicular hormone environment and obesity. So, a larger prospective study is needed to confirm these results by the heterogeneous nature of PCOS patients.

In conclusion, our study showed that the premature luteinization incidence was 23.3 % in PCOS patients, which was similar to that of general patients. Furthermore, the study suggests that premature luteinization PCOS patients undergoing IVF may not reflect the discriminatory value compared with nonpremature luteinization PCOS patient. But, the differences in our findings compared with previous reports may be due to variations in patient group, induction protocol, individual genetic background, lifestyle and other factors. Despite the differences, our results suggest that premature luteinization—defined by P concentration ≥ 1.2 ng/mL on the day of hCG administration—was not an obstacle to successful IVF outcomes in PCOS patients undergoing COH.

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Conflicts of Interest The authors declare that they have no conflicts of interest.

Authors' Contributions All authors were responsible for data collection, analysis, and interpretation presented in the manuscript. All authors read and approved the final manuscript.

References

1. Broekmans FJ, Knauff EA, Valkenburg O, Laven JS, Eijkemans MJ, Fauser BC. PCOS according to the Rotterdam consensus criteria. Change in prevalence among WHO-II anovulation and association with metabolic factors. *BJOG-INT J Obstet Gy.* 2006;113:1210–7.
2. Papanikolaou EG, Kolibianakis EM, Pozzobon C, Tank P, Tourayne H, Bourgain C, Steirteghem A, Devroey P. Progesterone rise on the day of human chorionic gonadotropin administration impairs pregnancy outcome in day 3 single-embryo transfer, while has no effect on day 5 single blastocyst transfer. *Fertil Steril.* 2009;91:949–52.
3. Bosch E, Valencia I, Escudero E, Crespo J, Simon C, Remohi J, Pellicer A. Premature luteinization during gonadotropin-releasing hormone antagonist cycles and its relationship with in vitro fertilization outcome. *Fertil Steril.* 2003;80:1444–9.
4. Edelstein MC, Seltman HJ, Cox BJ, Robinson SM, Shaw RA, Muasher SJ. Progesterone levels on the day of human chorionic gonadotropin administration in cycles with gonadotropin-releasing hormone agonist suppression are not predictive of pregnancy outcome. *Fertil Steril.* 1990;54:853–7.
5. Martinez F, Coroleu B, Clua E, Tur R, Buxaderas R, Parera N, Barri PN, Balasch J. Serum progesterone concentrations on the day of HCG administration cannot predict pregnancy in assisted reproduction cycles. *Reprod Biomed Online.* 2004;8:183–90.
6. Melo MA, Meseguer M, Garrido N, Bosch E, Pellicer A, Remohi J. The significance of premature luteinization in an oocyte-donation programme. *Hum Reprod.* 2006;21:1503–7.
7. Fanchin R, de Ziegler D, Taieb J, Hazout A, Frydman R. Premature elevation of plasma progesterone alters pregnancy rates of in vitro fertilization and embryo transfer. *Fertil Steril.* 1993;59:1090–4.
8. Legro RS, Ary BA, Paulson RJ, Stanczyk FZ, Sauer MV. Premature luteinization as detected by elevated serum progesterone is associated with a higher pregnancy rate in donor oocyte in-vitro fertilization. *Hum Reprod.* 1993;8:1506–11.
9. Filicori M, Cognigni GE, Arnone R, Carbone F, Falbo A, Tabarelli C, Ciampaglia W, Casadio P, Spettoli D, Pecorari R. Role of different GnRH agonist regimens in pituitary suppression and the outcome of controlled ovarian hyperstimulation. *Hum Reprod.* 1996;11(Suppl3):123–32.
10. World Health Organization. WHO laboratory manual for the examination of human semen and sperm–cervical mucus interaction. 4th ed. Cambridge: Cambridge University Press; 1999.
11. The Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group, Fauser BCJM. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Hum Reprod.* 2004;19:41–7.
12. Ehrmann DA, Barnes RB, Rosenfield RL, Cavaghan MK, Imperial J. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care.* 1999;22:141–6.
13. Knochenhauer ES, Key TJ, Kahsar-Miller M, Waggoner W, Boots LR, Azziz R. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States. A prospective study. *J Clin Endocrinol Metab.* 1998;83:3078–82.
14. Christian RC, Dumesic DA, Behrenbeck T, Oberg AL, Sheedy 2nd PF, Fitzpatrick LA. Prevalence and predictors of coronary artery calcification in women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2003;88:2562–8.
15. Glueck CJ, Morrison JA, Wang P. Insulin resistance, obesity, hypofibrinolysis, hyperandrogenism, and coronary heart disease risk factors in 25 pre-perimenarchal girls age <14 or =14 years, 13 with precocious puberty, 23 with a first-degree relative with polycystic ovary syndrome. *J Pediatr Endocrinol Metab.* 2008;21:973–84.
16. Legro RS. Polycystic ovary syndrome and cardiovascular disease: a premature association? *Endocr Rev.* 2003;24:302–12.
17. Legro RS, Kunselman AR, Dodson WC, Dunaif A. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome. a prospective, controlled study in 254 affected women. *J Clin Endocrinol Metab.* 1999;84:165–9.
18. Ovalle F, Azziz R. Insulin resistance, polycystic ovary syndrome, and type 2 diabetes mellitus. *Fertil Steril.* 2002;77:1095–105.
19. Mehrabian F, Khani B, Kelishadi R, Ghanbari E. The prevalence of polycystic ovary syndrome in Iranian women based on different diagnostic criteria. *Endokrynologia Polska/Polish Journal of Endocrinology.* 2011;62:238–42.
20. Elnashar AM. Progesterone rise on the day of HCG administration (premature luteinization) in IVF. An overdue update. *J Assist Reprod Genet.* 2010;27:149–55.
21. Bukulmez O, Rehman KS, Langley M, Carr BR, Nackley AC, Doody KM. Precycle administration of GnRH antagonist and microdose HCG decreases clinical pregnancy rates without affecting embryo quality and blastulation. *Reprod Biomed Online.* 2006;13:465–75.
22. Li R, Qiao J, Wang L, Zhen X, Lu Y. Serum progesterone concentration on day of HCG administration and IVF outcome. *Reprod Biomed Online.* 2008;16:627–31.
23. Yovel I, Yaron Y, Amit A, Peyser MR, David MP, Kogosowski A, Lessing JB. High progesterone levels adversely affect embryo quality and pregnancy rates in in vitro fertilization and oocyte donation programs. *Fertil Steril.* 1995;64:128–31.
24. Hofmann GE, Bentzien F, Bergh PA, Garrisi GJ, Williams MC, Guzman I, Navot D. Premature luteinization in controlled ovarian hyperstimulation has no adverse effect on oocyte and embryo quality. *Fertil Steril.* 1993;60:675–9.
25. Givens CR, Schriock ED, Dandekar PV, Martin MC. Elevated serum progesterone levels on the day of human chorionic gonadotropin administration do not predict outcome in assisted reproduction cycles. *Fertil Steril.* 1994;62:1011–7.
26. Schoolcraft W, Sinton E, Schlenker T, Huynh D, Hamilton F, Meldrum DR. Lower pregnancy rate with premature luteinization during pituitary suppression with leuprolide acetate. *Fertil Steril.* 1991;55:563–6.
27. Ubaldi F, Smitz J, Wisanto A, Joris H, Schiettecatte J, Derde MP, Borkham E, Steirteghem AV, Devroey P. Oocyte and embryo quality as well as pregnancy rate in intracytoplasmic sperm injection are not affected by high follicular phase serum progesterone. *Hum Reprod.* 1995;10:3091–6.