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Serum anti-mullerian hormone levels in the main phenotypes of polycystic ovary syndrome

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ABSTRACT

Objective: To characterize the difference in circulating anti-Müllerian hormone (AMH) levels between the main polycystic ovary syndrome (PCOS) phenotypic groups and evaluate the role of AMH in predicting the severity of PCOS.

Study design: Cross-sectional, retrospective study. A total of 251 women were divided into four groups based on the main features of PCOS, as follows: Group 1 (polycystic ovarian morphology [PCOM]+/oligo-anovulation [OA]+/hyperandrogenism [HA]+), Group 2 (PCOM+/OA+/HA−), Group 3 (PCOM+/OA−/HA+), and Group 4 (PCOM−/OA+/HA+). AMH and other hormone levels were measured in serum. The main outcome was serum AMH concentrations in the main phenotypes of PCOS.

Result(s): The mean serum AMH levels were 9.50 ± 6.1 ng/mL in Group 1; 8.02 ± 6.2 ng/mL in Group 2; 6.12 ± 3.6 ng/mL in Group 3; and 3.06 ± 2.4 ng/mL in Group 4. Circulating AMH levels in Group 1 (PCOM+/OA+/HA+) were three times higher than those in Group 4 (PCOM−/OA+/HA+).

Conclusions: The highest AMH levels were found in cases where all three main diagnostic criteria existed. AMH levels correlate best with PCOM. In addition, oligo-anovulation contributes to increased AMH levels. Hyperandrogenism criteria were found to have less influence on AMH levels. AMH levels seem to have a diagnostic role in determining the severity of PCOS.

1. Introduction

Anti-Müllerian hormone (AMH), also referred to as Müllerian-inhibiting substance, is a member of the transforming growth factor (TGF)-beta superfamily [1]. In females, it is produced by the granulosa cells of pre-antral and small antral follicles. It was recently demonstrated that oocytes from early pre-antral, late pre-antral, and pre-ovulatory follicles upregulate AMH mRNA levels in granulosa cells, and that this increase is dependent upon the developmental stage of the oocyte. These findings suggest that oocyte-mediated regulation of AMH expression may play a role in intra- and inter-follicular coordination of follicle development [2].

AMH serum levels are age-dependent. Production starts in females in the 36th week of intrauterine life and peaks in puberty [3]. AMH levels plateau until the age of 25 years, and from the age of 25 years onward, serum AMH levels correlate inversely with age [4].

In addition to being a reliable marker of ovarian reserve, AMH is also gynecologically useful in predicting poor responders to assisted reproduction [5] and patients with ovarian hyperstimulation syndrome [6]. Although it has been thought that AMH levels were not beneficial in predicting pregnancy, recent studies show that AMH levels may predict pregnancy potential in high responders [7]. AMH levels also increase during pregnancy [8].

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, with an estimated prevalence between 5 and 10% [9,10]. The three main diagnostic criteria of PCOS are polycystic ovarian morphology (PCOM), oligo-anovulation (OA), and hyperandrogenism (HA) [11]. Diagnosis is typically subjective, especially for girls in adolescence, which can sometimes lead to a diagnostic dilemma. The heterogeneity of clinical presentations and wide spectrum of phenotypes in PCOS may lead clinicians to create new subphenotypes.

Many studies have investigated the relationship of PCOS with serum AMH levels. Patients with PCOS have significantly higher serum AMH levels as compared with control subjects [12,13]. This is due to the increase in the number of follicles in PCOS patients, as well as the increase in AMH production per follicle. Thus, in the diagnosis of PCOS, AMH levels are gaining importance as a diagnostic criterion.

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The wide differences in AMH levels among patients with PCOS may be linked to the severity of the syndrome. Studies in this area support this idea.

Serum androgen concentrations are tightly correlated with the excessive number of 2- to 9-mm antral follicles seen on ultrasonography [14,15]. One pathophysiological hypothesis states that intraovarian androgens play a major role in the disturbed folliculogenesis of PCOS [16]. Contrary to this hypothesis, Diamanti-Kandarakis et al. [17] showed that serum concentrations of AMH correlated with the severity of symptoms; the ovulatory group had lower concentrations of AMH compared to those who were equally hyperandrogenic, but anovulatory.

AMH levels reflect the severity of PCOS, which is traditionally defined by its two cardinal elements: anovulation and HA [18]. La Marca et al. [19] reported that AMH was higher in amenorrheic women as compared with oligomenorrheic women with PCOS. Fleming et al. [20] observed that AMH levels were higher in insulin-resistant PCOS women than in patients with normal insulin sensitivity. The demonstration by La Marca et al. [21] that AMH was higher in amenorrheic women than in oligomenorrheic women with PCOS could indicate a role for AMH in the pathogenesis of PCOS-related anovulation.

In our study, we examined the relationship between three cardinal features of PCOS (PCOM, OA, and HA) and AMH concentration with respect to PCOS severity. To gain further insights into the relationship of AMH with these three main features of PCOS and evaluate the role of AMH in predicting the severity of the syndrome, we compared serum AMH levels among four different phenotypes.

2. Materials and methods

Between January 2008 and November 2011, samples were analyzed from each of 251 consecutive patients who were admitted to our reproductive endocrinology and infertility clinic with a diagnosis of PCOS according to the Rotterdam consensus [11]. Patients with PCOM had at least 12 follicles of 2- to 9-mm diameter per ovary and/or oligo-amenorrhea and/or showed clinical and/or biochemical signs of HA.

In this cross-sectional, restrospective study, subjects were divided into four different phenotypic groups based on PCOM, OA, and HA criteria as follows: Group 1, PCOM+/OA+/HA+; Group 2, PCOM+/OA+/HA−; Group 3, PCOM+/OA−/HA+; and Group 4, PCOM−/OA+/HA+.

Informed consent was obtained from all women, and approval from the Human Ethics Committee of Istanbul University was obtained. On days 3–5 of the women's normal cycle, we performed a routine gynecological examination, a basic vaginal ultrasound, a basal hormone profile evaluation (follicle-stimulating hormone [FSH], luteinizing hormone [LH], total testosterone [total T], free testosterone [free T], dehydroepiandrosterone-sulfate [DHEA-S], and 17-OH-progesterone), and measurement of AMH. Age and body mass index (BMI) were recorded in a standardized manner.

The inclusion criteria were as follows: <40 years of age, no previous history of ovarian surgery, no thyroid or prolactin hormone level abnormalities, no non-classic.

21-hydroxylase deficiency [basal 17-hydroxyprogesterone (17-OHP) <5 nml/l and no hormonal therapy in the 6 months before entering the study.

All blood samples for AMH measurement were collected in a lithium-heparin tube. AMH concentrations were measured with an enzymatically amplified two-sided immunoassay (DSL-10-14400 Active Müllerian Inhibiting Substance/AMH enzyme-linked immunosorbent assay [ELISA] kit, Diagnostic Systems Laboratories [DSL], Webster, TX). The theoretical sensitivity of the method was 0.006 ng/mL, the intra-assay coefficient of variation for high values was 3.3%, and the inter-assay coefficient of variation for high values was 6.7%. Serum levels of estradiol, testosterone, FSH, and LH were measured using an Immulite 2000 (Diagnostic Products Corp., Los Angeles, CA).

For sonographic imaging, we used a 6.5-MHz vaginal transducer (model EUB-415; Hitachi Medical Corp., Tokyo, Japan). PCOM was defined as the presence of 12 or more 2- to 9-mm diameter follicles in each ovary or an increased ovarian volume of >10 mL. The ovaries were localized and scanned. OA was defined as the presence of oligomenorrhea (menstrual cycle of >35 days) or amenorrhea (i.e., no menstrual bleeding during the last 3 months). HA was clinically defined as the presence of clinical signs of hirsutism (modified Ferriman & Gallwey score of >6), acne, seborrhea or hair loss, and/or high biochemical levels of androgen (free testosterone of >3 nmol/L).

Statistical analysis was performed using SPSS 17.0 for Windows. Group means were compared using one-way analysis of variance (ANOVA) for age. All other data were evaluated by one-way Kruskal–Wallis variance analysis with post hoc least-squares means pair-wise comparisons (after log transformation of the values) with Bonferroni's corrected Mann–Whitney *U* test. All data are presented as the mean ± standard deviation (SD). Receiver operating characteristic (ROC) curves of AMH levels were constructed to examine the diagnostic test performance for the four groups of PCOS-related phenotypes. We evaluated the correlation between AMH levels and PCOS-related phenotype groups by determining the two-tailed Pearson correlation coefficient. Differences among groups were considered to be significant if the *P* value was <0.05.

3. Results

Of the 251 subjects who participated in this study, 119 (47.4%) had PCOM+/OA+/HA+ (Group 1), 61 (24.3%) had PCOM+/OA+/HA− (Group 2), 45 (17.9%) had PCOM+/OA−/HA+ (Group 3), and 26 (10.3%) had PCOM−/OA+/HA+ (Group 4). Data obtained from the four groups are shown in Table 1. No statistically significant differences were found among the four groups in terms of age and BMI. No significant relationships were found between circulating AMH levels in the four groups and the BMI and age of the patients.

The mean serum AMH levels were 9.50 ± 6.1 ng/mL in Group 1, 8.02 ± 6.2 ng/mL in Group 2, 6.12 ± 3.6 ng/mL in Group 3, and 3.06 ± 2.4 ng/mL in Group 4. The highest AMH levels were found in Group 1. The circulating AMH levels in Group 1 were three times higher than those in Group 4 (Groups 1–4, $P < 0.001$). Table 1 presents the *P* values of the differences among groups in AMH and other hormone levels.

Fig. 1 presents the mean serum AMH levels of the four groups based on PCOS-related phenotypes. Women with PCOM+/OA+/HA− (Group 2) had higher serum AMH levels than those with PCOM+/OA−/HA+ (Group 3), but this difference was not statistically significant ($P > 0.05$). There were no statistically significant differences among the four groups in terms of total T and DHEA-S levels. FSH levels differed among Groups 1, 2 and 3 ($P = 0.01$). LH as a variable differed among Groups 1 through 4 ($P = 0.002$) and Groups 2 through 4 ($P = 0.004$). E2 as a variable differed among Groups 1 through 4 ($P = 0.009$).

Serum AMH levels were also evaluated as quartiles, and a Pearson's correlation analysis showed statistically significant correlations between AMH and the four groups of PCOS-related phenotypes ($r = -0.408$, $P < 0.01$) (Table 2). As the levels increased, the prevalence of the PCOM+/OA+/HA+ group increased from 11.6% in the <25th quartile-AMH group to 37.9% in the >75th quartile-AMH group.

The ROC curves of the serum AMH concentrations in discriminating Group 1 from Group 4 and Group 1 from Group 3 are depicted in Fig. 2. The areas under the curves (AUC) were

Table 1
Biochemical and demographic data of subjects.

	PCOM+/OA+/HA+	PCOM+/OA+/HA−	PCOM+/OA−/HA+	PCOM−/OA+/HA+
Patient number (%)	119 (47.4%)	61 (24.3%)	45 (17.9%)	26 (10.3%)
Age (years)	24.73 ± 4.8	24.77 ± 5.5	24.73 ± 4.4	23.12 ± 5.9
BMI (kg/m^2) min–max	26.16 (19–35)	25.02 (19–35)	25.25 (19–35)	27.57 (19–35)
AMH (ng/ml)	9.50 ± 6.1[a,b,c]	8.02 ± 6.2[c]	6.12 ± 3.6[c]	3.06 ± 2.4
FSH (mIU/ml)	4.50 ± 1.35[b]	4.77 ± 1.48	5.62 ± 3.27	4.46 ± 1.85
LH (mIU/ml)	5.86 ± 4.65[c]	5.65 ± 3.21[c]	4.86 ± 3.92	3.72 ± 3.19
E2 (pg/ml)	41.23 ± 19.2[c]	35.18 ± 15.4	37.39 ± 15.2[c]	29.60 ± 13.5
DHEA-S (nmol/l)	358.9 ± 143.2	348.4 ± 151.4	358.3 ± 164.7	350.1 ± 171.8
17-OHP (nml/l)	1.60 ± 1.09[a]	1.14 ± 0.65	1.60 ± 1.22	1.68 ± 1.37
Total T (nmol/l)	110.4 ± 50.6	108.3 ± 44.1	113.3 ± 34.7	102.1 ± 52.2
Free T (nmol/l)	2.23 ± 2.16	1.71 ± 1.13	2.08 ± 1.73	2.24 ± 1.64

PCOM, polycystic ovary morphology; OA, oligoanovulation; HA, hyperandrogenism; BMI, body mass index; AMH, antimullerian hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; Total T, total testosterone; Free T, free testesterone; DHEA-S, dehydroepiandrosterone-sulfate; 17-OHP, 17-OH-progesterone.
Values are means ± SD. Significant difference: $P < 0.05$ compared with PCOS groups [a]2, [b]3 and [c]4.

Table 2
Groups according to AMH quartiles.

Quartil %	AMH[a] (ng/ml)	Group-1 (%)	Group-2 (%)	Group-3 (%)	Group-4 (%)
<25	<4.00	11.6	17.6	33.3	42.9
25–50	4.01–6.00	26.3	33.3	23.1	28.8
50–75	6.01–10.20	24.2	25.5	33.3	14.3
>75	>10.21	37.9	23.5	10.3	14.3

[a]Pearson correlation test: $r = -0.408$, $P < 0.01$.

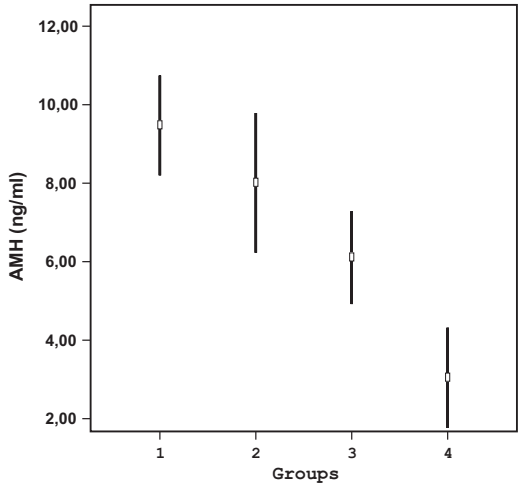

Fig. 1. The mean serum AMH levels (ng/ml) of all groups.

0.889 (95% confidence interval [CI], 0.806–0.972) and 0.677 (95% CI, 0.581–0.772), respectively. Significance in discrimination of AMH levels between Groups 2 and 4 and between Groups 3 and 4 was also found (AUC, 0.855 and 95% CI, 0.742–0.968 versus AUC, 0.791 and 95% CI, 0.657–0.925, respectively).

4. Comments

In this study, AMH levels were compared among four main PCOS phenotypes using the three main generally accepted criteria (PCOM, OA, and HA) for investigating the factors affecting the severity of this syndrome.

Studies have shown that serum AMH levels are increased in women with PCOS as compared with normo-ovulatory women, a finding that corresponds to the follicle excess seen on ultrasonographic examination [22]. Some authors, however, have argued that the increased serum AMH is due to increased production per granulosa cell, suggesting intrinsic granulosa cell dysregulation in PCOS. Assays of follicular fluid from small follicles [23] and in cell-conditioned media from cultured granulosa cells in vitro [24] support this hypothesis.

Our study showed a three-fold increase in circulating AMH levels in Group 1 as compared with Group 4, where PCOM was the only distinctive symptom between two groups. These results indicate that PCOM is the most effective factor influencing AMH levels. In addition, statistically significant relationships were found among Groups 2 through 4 and between Groups 3 and 4.

Lin et al. divided all patients into three groups: high AMH (>11 ng/mL), moderate AMH (4–11 ng/mL), and low AMH (<4 ng/mL). As the AMH level increased, the prevalence of PCOS increased significantly from 21% in the low-AMH group to 37% in the moderate-AMH group and 80% in the high-AMH group [25]. These results support our findings. Histological examination has shown that PCOS exhibits the same number of primordial follicles, whereas the number of developing and subsequent atretic follicles is doubled as compared with normo-ovulatory controls [26]. Smaller follicles that are not readily detected on ultrasound may contribute to serum AMH levels.

Our findings suggest that the other factor affecting AMH levels in patients with PCOS is OA. The present study showed that a statistically significant difference in AMH values was found between Groups 1 and 3, where OA was the only distinctive symptom between two groups (Groups 1–3, $P = 0.002$). AMH serum levels correlated well with parameters indicative of the extent of ovarian dysfunction, such as oligo/anovulatory periods.

As shown in Table 1, there was only a slight difference in AMH levels between groups 1 (PCOM+/OA+/HA+) and 2 (PCOM+/OA+HA−). According to the Androgen Excess Society, however, HA is considered to be a main indicator in the diagnosis of PCOS. There was no statistically significant difference among the four groups in terms of total T and DHEA-S levels.

Hyperandrogenic (Group 1) PCOS patients have AMH concentrations statistically different to those of non-hyperandrogenic (Group 2) PCOS patients; but this difference had the least impact when we evaluated the four groups. Parallel with our results, Rosenfield et al. found similar AMH levels between

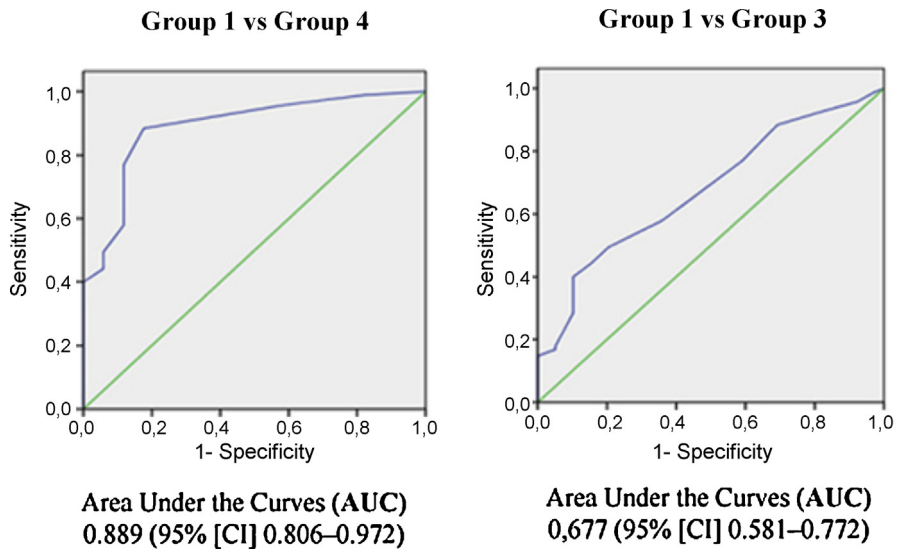

Fig. 2. Receiver operating characteristic (ROC) curves of serum AMH in discrimination of group 1 vs group 4 and group 1 vs group 3.

hyperandrogenic and non-hyperandrogenic PCOS patients. The AMH value for discrimination between the two groups had a very low sensitivity [27]. In contrast to our results, Guastella et al. found higher DHEA-S levels in hyperandrogenic PCOS patients than normoandrogenic PCOS patients [28]. There are several hypotheses stating that androgens may play a role in increased AMH secretion by potentiating the growth-promoting effects of oocytes in a mechanism that involves the androgen receptor [29]. According to those hypotheses, in PCOS, ovulation as well as a reduction in androgen levels may be required to decrease the numbers of pre-antral and small antral follicles, thus lowering AMH levels.

Piouka et al. reported that AMH levels were higher in anovulatory and hyperandrogenic women with NIH-defined "classical" PCOS without PCOM as compared with both ovulatory women with PCOM and HA and anovulatory women with PCOM but normal androgen levels. In contrast to their results, we showed that serum AMH concentrations were positively influenced by PCO morphology. Similarly, they found the highest serum AMH levels in the PCOM+/OA+/HA+ group [18].

Our results show that HA is the least effective factor influencing serum AMH levels. Also OA is the more reliable criterion than HA for increased AMH levels. The most important criterion affecting serum AMH levels is PCOM, followed by OA.

The highest AMH level was associated with the three main diagnostic criteria. If we divide our results into percentiles according to AMH levels (Table 2), the AMH value increases in proportion to the increase in the severity of PCOS. The highest AMH levels were found in Group 1, and the prevalence increased from 11% in the <25th quartile to 37% in the >75th quartile. On the other hand, the lowest level of AMH was found in Group 4 (PCOM−/OA+/HA+), and the prevalence of PCOM was lower with low AMH levels. The ROC curves of the serum AMH concentration in discriminating Group 1 from Group 4 and Group 1 from Group 3 are depicted in Fig. 2. Evaluation of the above findings demonstrates that AMH levels reflect the severity of PCOS.

In conclusion, our study showed that the highest AMH level was associated with the presence of the three main diagnostic criteria. AMH levels correlate best with PCOM. In addition, OA contributes to increased AMH levels. HA criteria were found to have less influence on AMH levels. We assume that AMH levels are highly correlated with follicle number. AMH levels seem to have a diagnostic role in determining the severity of PCOS.

Conflict of interest

All authors have nothing to disclose.

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References

[1] Cate RL, Mattaliano RJ, Hession C, et al. Isolation of the bovine and human genes for Müllerian inhibiting substance and expression of the human gene in animal cells. Cell 1986;45:685–98.
[2] Salmon NA, Handyside AH, Joyce IM. Oocyte regulation of anti-Müllerian hormone expression in granulosa cells during ovarian follicle development in mice. Dev Biol 2004;266:201–8.
[3] de Vet A, Laven JS, de Jong FH, et al. Anti-Müllerian hormone serum levels: a putative marker for ovarian aging. Fertil Steril 2002;77:357–62.
[4] Lie Fong S, Visser JA, Welt CK, et al. Serum anti-Mullerian hormone levels in healthy females: a nomogram ranging from infancy to adulthood. J Clin Endocrinol Metab 2012;97:4650–5.
[5] Sahmay S, Cetin M, Ocal P, et al. Serum anti-Müllerian hormone level as a predictor of poor ovarian response in in vitro fertilization patients. Reprod Med Biol 2011;10:9–14.
[6] Ocal P, Sahmay S, Cetin M, et al. Serum anti-Müllerian hormone and antral follicle count as predictive markers of OHSS in ART cycles. J Assist Reprod Genet 2011;28:1197–203.
[7] Weghofer A, Kim A, Barad DH, et al. Follicle stimulating hormone and anti-Müllerian hormone per oocyte in predicting in vitro fertilization pregnancy in high responders: a cohort study. PLoS One 2012;7:e34290.
[8] Sahmay S, Demirayak G, Guralp O, et al. Serum anti-Müllerian hormone, follicle stimulating hormone and antral follicle count measurement cannot predict pregnancy rates in IVF/ICSI cycles. J Assist Reprod Genet 2012;11.
[9] Franks S. Polycystic ovary syndrome. N Engl J Med 1995;333:853–61.
[10] Knochenhauer ES, Key TJ, Kahsar-Miller M, et al. 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.
[11] Rotterdam ESHRE/ASRM-sponsored PCOS Consensus Workshop Group Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod 2004; 19:41–47.
[12] Siow Y, Kives S, Hertweck P, et al. Serum Müllerian-inhibiting substance levels in adolescent girls with normal menstrual cycles or with polycystic ovary syndrome. Fertil Steril 2005;84:938–44.
[13] Hart R, Doherty DA, Norman RJ, et al. Serum anti-Müllerian hormone (AMH) levels are elevated in adolescent girls with polycystic ovaries and the polycystic ovarian syndrome (PCOS). Fertil Steril 2010;94:1118–21.
[14] Jonard S, Robert Y, Cortet-Rudelli C, et al. Ultrasound examination of polycystic ovaries: is it worth counting the follicles? Hum Reprod 2003;18:598–603.

[15] Chen MJ, Yang WS, Chen CL, et al. The relationship between anti-Müllerian hormone, androgen and insulin resistance on the number of antral follicles in women with polycystic ovary syndrome. Hum Reprod 2008;23:952–7.
[16] Jonard S, Dewailly D. The follicular excess in polycystic ovaries, due to intra-ovarian hyperandrogenism, may be the main culprit for the follicular arrest. Hum Reprod Update 2004;10:107–17.
[17] Diamanti-Kandarakis E, Piouka A, Livadas S, et al. Anti-Müllerian hormone is associated with advanced glycosylated end products in lean women with polycystic ovary syndrome. Eur J Endocrinol 2009;160:847–53.
[18] Piouka A, Farmakiotis D, Katsikis I, et al. Anti-Müllerian hormone levels reflect severity of PCOS but are negatively influenced by obesity: relationship with increased luteinizing hormone levels. Am J Physiol Endocrinol Metab 2009;296:E238–43.
[19] La Marca A, Malmusi S, Giulini S, et al. Anti-Müllerian hormone plasma levels in spontaneous menstrual cycle and during treatment with FSH to induce ovulation. Hum Reprod 2004;19:2738–41.
[20] Fleming R, Deshpande N, Traynor I, et al. Dynamics of FSH-induced follicular growth in subfertile women: relationship with age, insulin resistance, oocyte yield and anti-Müllerian hormone. Hum Reprod 2006;21:1436–41.
[21] La Marca A, Broekmans FJ, Volpe A, et al. ESHRE Special Interest Group for Reproductive Endocrinology-AMH Round Table. Anti-Müllerian hormone (AMH): what do we still need to know? Hum Reprod 2009;24:2264–75.
[22] Laven JS, Mulders AG, Visser JA, et al. Anti-Müllerian hormone serum concentrations in normoovulatory and anovulatory women of reproductive age. J Clin Endocrinol Metab 2004;89:318–23.
[23] Das M, Gillott DJ, Saridogan E, et al. Anti-Müllerian hormone is increased in follicular fluid from unstimulated ovaries in women with polycystic ovary syndrome. Hum Reprod 2008;23:2122–6.
[24] Pellatt L, Hanna L, Brincat M, et al. Granulosa cell production of anti-Müllerian hormone is increased in polycystic ovaries. J Clin Endocrinol Metab 2007;92:240–5.
[25] Lin YH, Chiu WC, Wu CH, et al. Anti-Müllerian hormone and polycystic ovary syndrome. Fertil Streil 2011;96:230–5.
[26] Hughesdon PE. Morphology and morphogenesis of the Stein-Leventhal ovary and of so-called hyperthecosis. Obstet Gynecol Surv 1982;37:59–77.
[27] Rosenfield RL, Wroblewski K, Padmanabhan V, et al. Anti-Müllerian hormone levels are independently related to ovarian hyperandrogenism and polycystic ovaries. Fertil Steril 2012;98:242–9.
[28] Guastella E, Longo RA, Carmina E. Clinical and endocrine characteristics of the main polycystic ovary syndrome phenotypes. Fertil Steril 2010;94:2197–201.
[29] Hickey TE, Marrocco DL, Amato F, et al. Androgens augment the mitogenic effects of oocyte-secreted factors and growth differentiation factor 9 on porcine granulosa cells. Biol Reprod 2005;73:825–32.