Anti-Müllerian hormone concentrations in androgen-suppressed women with polycystic ovary syndrome

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BACKGROUND: Current data suggest that excessive androgen exposure can lead to the development of polycystic ovaries and polycystic ovary syndrome (PCOS). Anti-Müllerian hormone (AMH) levels reflect the number of small antral follicles in the ovaries and are elevated in PCOS. We hypothesized that protracted reduction of circulating androgens and/or insulin resistance would reduce circulating AMH concentrations in women with PCOS.

METHODS: A prospective, randomized, double-blind 26 week long study was undertaken in 50 women with PCOS. They all received diet and lifestyle counselling, and metformin 850 mg three times daily. Concomitantly, they were randomized to either dexamethasone 0.25 mg daily (n = 25) or placebo (n = 25). Thirty-eight women completed the study. AMH (primary outcome) and other hormone levels were measured at inclusion and after 8 and 26 weeks of treatment.

RESULTS: At baseline in univariate regression analyses, AMH levels associated positively with testosterone levels (P = 0.041) and ovarian volume (P = 0.002). In multivariate regression analyses, AMH associated positively with testosterone (P = 0.004), and negatively with dehydroepiandrosterone sulphate (DHEAS) (P = 0.001) and C-peptide levels (P = 0.020). Circulating AMH concentrations were unaffected by 6 months of lifestyle counselling with metformin and placebo treatment. AMH levels were also unaffected by 6 months of androgen suppression with dexamethasone in addition.

CONCLUSIONS: AMH levels in untreated PCOS women associated positively with testosterone, and negatively with DHEAS and C-peptide levels. Six months of androgen suppression by either metformin or low-dose dexamethasone treatment failed to influence circulating AMH levels.

Key words: androgens / dexamethasone / anti-Müllerian hormone / polycystic ovary syndrome

Introduction

PCOS is probably multifactorial in origin, and intrauterine androgen exposure, post-natal insulin resistance and hyperinsulinemia are all important pathogenic factors (Norman et al., 2007). Insulin stimulates androgen synthesis directly in both the adrenals and the ovaries (Nestler, 1997; Franks et al., 1999; la Marca et al., 1999). Insulin may also be involved in the development of PCO (Norman et al., 2007). However, androgens may also induce PCOS and the changes seen in PCO (Jonard and Dewailly, 2004). This is supported both by direct animal studies (Abbott et al., 2002) and by the high prevalence of PCO seen in women with congenital adrenal hyperplasia as recently reviewed by Xita and Tsatsoulis (2006).
Circulating levels of anti-Müllerian hormone (AMH), secreted by the granulosa cells of early developing pre-antral and small antral follicles, are seen as a marker of ovarian follicular reserve in normal women (Visser et al., 2006) and in PCOS (Pigny et al., 2006; Chen et al., 2008). However, in animal models, AMH acts as an inhibitor of primary follicle recruitment and decreases the sensitivity of follicles for the FSH selection for dominance (Visser et al., 2006). Women with PCOS show increased development of antral follicles compared with normal women (Pigny et al., 2006). Accordingly, their circulating levels of AMH levels are two to three times increased (Pigny et al., 2006; Somunkiran et al., 2007). There is now a consensus that both in normally menstruating women and in PCOS women, circulating AMH represents the number of antral follicles as evaluated by transvaginal ultrasound estimation (Laven et al., 2004; Eldar-Geva et al., 2005; Fleming et al., 2005, 2006; Pigny et al., 2006; Chen et al., 2008). The granulosa cells from small antral follicles of women with PCOS appear to secrete AMH in greater quantities than in normal women, so the total amount of AMH in the circulation may derive from a combination of increased follicle counts and increased specific secretion (Rice et al., 2007).

It is established that metformin treatment of women with PCOS usually results in reduction of circulating androgens and a modest improvement of ovulation frequency (Costello et al., 2007). Short-term (1 week) treatment with metformin in women with PCOS does not change AMH while the number of antral follicles may be reduced (Bayrak et al., 2007). There are two reports that suggest that after protracted (several months) metformin treatment AMH is reduced (Fleming et al., 2005; Piltonen et al., 2005), while ovarian volume is unchanged or reduced (Fleming et al., 2005).

The present study was performed to explore the possible roles of altered circulating androgens and insulin on the development of small antral follicles in PCOS women. In this prospective, randomized, placebo controlled study, we primarily explored the roles of suppression of androgens. Further, in the placebo-treated control group, the effect of reduction of insulin resistance by metformin was examined. This was performed in PCOS women treated with a single session program of diet and lifestyle recommendations. At the same time, they were started on metformin, and randomized to placebo or dexamethasone in a double-blind design over 26 weeks. The effects on circulating androgens were measured directly, and the effects on small antral follicle changes were evaluated indirectly, by way of circulating levels of AMH.

Materials and Methods

Fifty women with PCOS were recruited from either our University Hospital (Trondheim), gynecological outpatient clinic or by advertisement in the local newspaper, and results from the primary study have been published previously (Vanky et al., 2004). Inclusion criteria were age between 18 and 40 years and PCO (≥ 9 sub-capsular follicles visualized in one plane with a diameter of 3–8 mm), verified by transvaginal ultrasonography. Ultrasonographic examinations were performed at inclusion, and week 26. Patients were examined in the supine position with a 6 MHz probe. All recordings were performed using a MultiSync MS500 Synergy, Diasonic Ultrasound instrument (Israel). Patients with serum progesterone levels >4.0 nmol/l, indicating the luteal phase, were reexamined 2 weeks later. Both ovaries were measured in three dimensions (i.e. length, depth and height) three times. A mean value was calculated for each of the three dimensions. The ovarian volume was calculated using the following equation: length × depth × height × 0.5.

In addition, at least one of the following criteria had to be fulfilled: testosterone >2.5 nmol/l, sex hormone-binding globulin (SHBG) <30 nmol/l, fasting C-peptide >1.0 nmol/l, oligo-amenorrhea (length of menstrual cycle >35 days or <10 periods per year) or hirsutism, judged clinically as male pattern growth of body hair. In retrospect, evaluating ovarian volume (right and/or left) >10 ml, free testosterone index (total testosterone × 10/SHBG) >0.6 and menstrual pattern, we could conclude that all the participants also fulfilled the ‘Rotterdam 2003’ criteria for PCOS (The Rotterdam European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine -sponsored PCOS consensus workshop group, 2004).

Exclusion criteria included pregnancy, breastfeeding, known liver disease or alanine aminotransferase >60 IU/l, creatinine >130 μmol/l, known alcohol abuse, diabetes mellitus and treatment with oral glucocorticoids or hormonal contraceptives. Patients could be included if hormonal contraception had been discontinued at least 1 month previously. Only 4 of the 38 participants who completed the study used hormonal contraceptives and had a 1 month of wash out before inclusion. Congenital adrenal hyperplasia was excluded by 17-hydroxprogesterone measurements and all participants had normal prolactin levels (<784 mIU/l).

Of the original 50 patients, 4 patients became pregnant, despite being instructed to use non-hormonal contraception during the study period (three in the dexamethasone group and one in the placebo group). Three patients withdrew due to gastrointestinal side effects of metformin (nausea or frequent diarrhoea lasting more than 3 weeks). Two patients withdrew due to motivation failure, two withdrew without giving any reason and in one woman early ovarian failure had been overlooked. Accordingly, 38 women completed the whole study, 18 in the dexamethasone group and 20 in the placebo group.

Venous blood samples were drawn from an antecubital vein, between 8:00 and 10:00 a.m. after an overnight fast at randomization and at the end of the study (26 weeks after inclusion). Blood samples were centrifuged at room temperature within 30 min and stored at -80°C until analysis (1–9 months for androgens and C-peptide, 3–4 years for AMH) as described below.

Study protocol

All participants received individual, written and verbal diet and lifestyle counselling at inclusion (Week 0). Thereafter no such advice was given. Concomitant with diet and lifestyle counselling, all the participants were started on metformin 850 mg (metformin hydrochloride, Metformin®, Weifa A/S, Oslo, Norway). All the patients used metformin once daily during the first week, twice daily during the second week and thereafter three times daily for the rest of the study period. At inclusion (Week 0), the participants were also randomized to additional treatment with either dexamethasone 0.25 mg (dexamethasone natriumphosphate, Decadron®, MSD, Drammen, Norway) or identical placebo, daily at bedtime. Accordingly, our study has two arms; one with women treated with diet and lifestyle advice, metformin and placebo, and the other with women treated with diet and lifestyle advice, metformin and dexamethasone. Both groups were treated for 26 weeks. Dexamethasone and identical placebo capsules were produced and packed by our local hospital pharmacy.

The primary outcome measure was circulating AMH levels, while testosterone, androstenedione, dehydroepiandrosterone sulphate (DHEAS), C-peptide and ovarian volume (mean of right + left ovary, or only the contralateral ovary if a follicle >10 mm was seen) were secondary outcome measures for correlation analyses.
The Committee for Medical Research Ethics of Health Region IV, Norway, and The Norwegian Medicines Agency approved the study. A written informed consent was obtained from each patient before inclusion, and the declaration of Helsinki was followed throughout the study.

**Assays**

AMH was estimated by single measurements by an enzyme-linked immunoassay provided by Diagnostic Systems Laboratories (Webster, TX, USA) using the reagents and calibrators supplied by the manufacturer. Values are presented as nanograms per millilitre (conversion factor to pmol/l = ng/ml \times 7.1). AMH estimation was done in one single run with one kit. Reference values for the normal population were not available from the manufacturer as the kit was for research purposes only.

Testosterone and androstenedione were measured by a double-antibody technique on an Elecsys 2010 analyser (Roche Diagnostics GmbH, Mannheim, Germany) using reagents and calibrators supplied by the manufacturer. DHEAS concentrations were measured using a competitive immunoassay on an Immulite 2000 analyser using the reagents and calibrators supplied by the manufacturer (Diagnostic Products Corporation, Los Angeles, CA, USA). C-peptide was analysed on an Immulite 2000 analyser using reagents, methods and calibrator obtained from the instrument supplier (Diagnostic Products Corporation). For AMH the intra-assay coefficient of variation was 8.9%, for testosterone 5.5%, for androstenedione 8.4%, for DHEAS 4.4% and for C-peptide 4.5%.

**Statistical analysis**

All statistical procedures were performed using the Statistical Package for the Social Sciences (SPSS) version 15.0i for Windows SPSS Inc. (Chicago, IL, USA). Sample size calculations were performed for the original study. We achieved 23–23 patients in each group at 90% of power to detect 1.0 nmol/l change in testosterone between groups. SDs were estimated to 0.6 nmol/l. We anticipated a 5–10% possible ‘drop out’ and included 25 patients in each group.

Mann–Whitney test for independent samples and Wilcoxon signed ranks test for paired samples were used for comparisons as appropriate. Treatment effects were investigated with analysis of covariance adjusted for patient age. Values are reported as means and SD. Uni- and multivariate linear regression analyses were used for correlation analyses. In regression analyses, values are reported as mean and 95% confidence intervals (CI). P-values < 0.05 were considered significant. No adjustments for multiple comparisons were performed.

**Results**

**The study population**

The mean age of the participants who completed the study was 30.6 ± 5.9 and 26.4 ± 3.8 years in the placebo and dexamethasone groups, accordingly (P = 0.019) (Table I). BMI, age at menarche and bleedings per year were equal between groups. All biochemical variables, except DHEAS, were equal between study groups at inclusion (Table II). The apparent difference in DHEAS levels disappeared after adjustment for age.

At inclusion the patients who withdrew from the study were equal to those who completed the study with respect to age, body weight, BMI, DHEAS, androstenedione, testosterone, C-peptide, age at menarche and bleeding per year (data not shown). However, AMH was lower in those who withdrew (7.55 ± 3.28 versus 14.01 ± 9.95 ng/ml; P = 0.043).

**Changes in androgens during the study**

Table II shows that treatment with metformin and lifestyle advice (placebo group) resulted in increases in DHEAS and decreases in androstenedione, testosterone and C-peptide. In the dexamethasone group, DHEAS, androstenedione and testosterone decreased during the study period. Comparisons at Week 26 showed that testosterone was significantly lower in the dexamethasone group than placebo (P = 0.033), while DHEAS tended to be lower (P = 0.082).

**Metformin and dexamethasone effects on AMH concentrations and ovarian volume**

Table III shows that baseline AMH levels in the patients who completed the study were in the upper normal range, and that there were no differences between the treatment groups. Our normal data are derived from women aged 30 to 37 years undergoing IVF, and whose egg yields were the average ± SD. The range so calculated is 3.8 to 18 pmol/L. After 26 weeks of treatment, AMH concentrations showed no indications of change in either treatment group. Baseline and 26 weeks AMH levels were equal both in the dexamethasone (P = 0.98) and in the placebo (P = 0.60) groups. Ovarian volumes were also unchanged over the 26 week study period.

Separate uni- and multivariate analyses in the dexamethasone and placebo groups revealed no significant association between individual changes in AMH levels from inclusion to study Week 26 and changes in DHEAS, androstenedione, testosterone, C-peptide or ovarian volume (data not shown).

**AMH and relationship with other factors prior to and during the study period**

At baseline, univariate regression analyses in untreated PCOS women (at inclusion, before diet and lifestyle advice and any medication), AMH associated positively with circulating testosterone (P = 0.041) and ovarian volume (P = 0.002) (Table IV). However, in multivariate regression analyses, AMH associated negatively with DHEAS (P = 0.001) and C-peptide (P = 0.020) and positively with testosterone (P = 0.004).

In univariate regression analyses in the placebo group after 26 weeks of treatment AMH levels associated positively with androstenedione (P = 0.013) and ovarian volume (P = 0.001). In multivariate regression analyses, AMH levels associated positively with

**Table I Baseline characteristics of the study participants with PCOS who completed the study**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 20)</th>
<th>Dexamethasone (n = 18)</th>
<th>P-value *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.6 ± 5.9</td>
<td>26.4 ± 3.8</td>
<td>0.019</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.4 ± 7.5</td>
<td>32.8 ± 6.7</td>
<td>0.81</td>
</tr>
<tr>
<td>Age at menarche (years)</td>
<td>12.9 ± 1.4</td>
<td>12.5 ± 1.6</td>
<td>0.22</td>
</tr>
<tr>
<td>Bleedings per year (no.)</td>
<td>4.4 ± 3.9</td>
<td>4.9 ± 3.2</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*The study groups were compared with Mann–Whitney test for independent samples.
A reduction of androgens over a protracted period, sufficient to explore effects from the earliest stages of follicle development, also failed to modify AMH levels and ovarian volume according to study groups through treatment with either metformin or a combination of metformin and dexamethasone. Dexamethasone administration in women with PCOS also failed to modify circulating AMH concentrations (Table II). Furthermore, protracted treatment with either metformin or a combination of metformin and dexamethasone did not influence ovarian volumes.

Our findings are perhaps surprising given both direct and circumstantial evidence supporting a role for androgens in follicular development and survival although other mechanisms have also been proposed (Visser et al., 2006). Androgens play a role in stimulating early (FSH independent) stages of follicular growth (Vendola et al., 1998; Weil et al., 1999), and occupation of the androgen receptor appears to be a critical step in growth factor mechanisms (Hickey et al., 2005). In female-to-male transsexuals, testosterone administration results in PCOS-like changes (Futterweit and Deligdisch, 1986; Spinder et al., 1989; Pache et al., 1991). During this high-dose androgen treatment in women, gonadotrophins become suppressed, and ovaries enlarged with morphological changes meeting the criteria of PCO. Under these circumstances, androgens appear to induce PCO-like ovarian changes in humans, independent of the effect of gonadotrophins. These studies suggest that testosterone (androgens) contributes directly to the pathogenesis of PCO and PCOS, and the accompanying elevation of AMH concentrations, not only by intrauterine androgen exposure as recently reviewed (Xita and Tsatsoulis, 2006), but also in adult women when exposed to hyperandrogenism.

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**Discussion**

These results demonstrate that, contrary to our hypothesis, reducing biosynthesis and circulating concentrations of androgens using dexamethasone in women with PCOS failed to modify circulating AMH concentrations. Furthermore, protracted treatment with either metformin or a combination of metformin and dexamethasone did not influence ovarian volumes.

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circulating androgen levels and also reductions in AMH levels (Fleming et al., 2005; Pitkonen et al., 2005). The present study, with its 6 month treatment period, does not confirm these observations, as AMH levels remained unchanged in the control group despite reduced insulin levels as evaluated by reduced C-peptide levels. This might indicate that the effect of metformin on AMH emerges only after 6 months treatment. However, it may also indicate that the modest changes seen in those two reports are related to normal time-dependent evolution of AMH rather than an effect of treatment per se (Visser et al., 2006). However, it should be noted that the age of the participants in the two previous studies is comparable to the age of the participants in the present study.

The baseline associations between AMH and other factors in untreated women with PCOS, support data reported previously. Univariate analyses revealed that AMH associated positively with testosterone and ovarian volume. In multivariate analyses, both C-peptide and DHEAS became negatively associated with AMH while the positive association with testosterone was strengthened. The association between AMH and ovarian volume, testosterone and insulin has been reported previously (Fleming et al., 2005; Chen et al., 2008). However, the possible association with the adrenal androgen precursor DHEAS has not been described before.

In the control group, i.e. PCOS women treated with diet and lifestyle advice, and metformin, the associations between AMH and other factors both in univariate and multivariate analyses were essentially unchanged during the study. However, in the dexamethasone group (metformin + dexamethasone-treated women), all associations were abolished by treatment. This effect applied to ovarian volume and DHEAS as well as the circulating androgens, which may be

### Table IV Linear regression analyses of AMH (ng/ml) in women with PCOS

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th></th>
<th></th>
<th></th>
<th>Multivariate</th>
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<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>B</td>
<td>95% CI</td>
<td>P-value</td>
<td>B</td>
<td>95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>At baseline (de novo PCOS women; n = 38)</td>
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<td></td>
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<tr>
<td>DHEAS (µmol/l)</td>
<td></td>
<td>-0.61</td>
<td>-1.60 to 0.39</td>
<td>0.23</td>
<td>-2.07</td>
<td>-3.21 to 0.93</td>
<td>0.001</td>
</tr>
<tr>
<td>Androstenedione (nmol/l)</td>
<td></td>
<td>0.43</td>
<td>-0.05 to 0.91</td>
<td>0.079</td>
<td>0.24</td>
<td>-0.32 to 0.81</td>
<td>0.39</td>
</tr>
<tr>
<td>Testosterone (nmol/l)</td>
<td></td>
<td>2.11</td>
<td>0.10 to 4.13</td>
<td>0.041</td>
<td>4.47</td>
<td>1.52 to 7.43</td>
<td>0.004</td>
</tr>
<tr>
<td>C-peptide (nmol/l)</td>
<td></td>
<td>-1.67</td>
<td>-5.95 to 2.61</td>
<td>0.43</td>
<td>-4.84</td>
<td>-8.86 to 0.82</td>
<td>0.020</td>
</tr>
<tr>
<td>Ovarian volume (cm³)</td>
<td></td>
<td>0.88</td>
<td>0.35 to 1.40</td>
<td>0.002</td>
<td>0.33</td>
<td>-0.18 to 0.84</td>
<td>0.20</td>
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<tr>
<td>After 26 weeks of treatment (placebo group; n = 20)</td>
<td></td>
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<tr>
<td>DHEAS (µmol/l)</td>
<td></td>
<td>-0.87</td>
<td>-2.67 to 0.93</td>
<td>0.32</td>
<td>-3.42</td>
<td>-5.97 to 0.87</td>
<td>0.013</td>
</tr>
<tr>
<td>Androstenedione (nmol/l)</td>
<td></td>
<td>1.05</td>
<td>0.25 to 1.43</td>
<td>0.013</td>
<td>0.06</td>
<td>-0.99 to 1.12</td>
<td>0.90</td>
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<tr>
<td>Testosterone (nmol/l)</td>
<td></td>
<td>4.47</td>
<td>-0.14 to 9.07</td>
<td>0.056</td>
<td>11.0</td>
<td>2.00 to 20.1</td>
<td>0.020</td>
</tr>
<tr>
<td>C-peptide (nmol/l)</td>
<td></td>
<td>3.08</td>
<td>-9.35 to 15.52</td>
<td>0.61</td>
<td>-11.9</td>
<td>-22.5 to 0.13</td>
<td>0.031</td>
</tr>
<tr>
<td>Ovarian volume (cm³)</td>
<td></td>
<td>1.19</td>
<td>0.54 to 1.84</td>
<td>0.001</td>
<td>0.20</td>
<td>-0.59 to 0.99</td>
<td>0.60</td>
</tr>
<tr>
<td>After 26 weeks of treatment (dexamethasone group; n = 18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHEAS (µmol/l)</td>
<td></td>
<td>0.53</td>
<td>-1.91 to 2.96</td>
<td>0.65</td>
<td>-0.13</td>
<td>-4.43 to 4.18</td>
<td>0.95</td>
</tr>
<tr>
<td>Androstenedione (nmol/l)</td>
<td></td>
<td>-0.31</td>
<td>-2.04 to 1.43</td>
<td>0.71</td>
<td>-1.50</td>
<td>-5.12 to 2.13</td>
<td>0.37</td>
</tr>
<tr>
<td>Testosterone (nmol/l)</td>
<td></td>
<td>1.70</td>
<td>-5.86 to 9.27</td>
<td>0.64</td>
<td>0.74</td>
<td>-16.38 to 17.86</td>
<td>0.92</td>
</tr>
<tr>
<td>C-peptide (nmol/l)</td>
<td></td>
<td>-4.52</td>
<td>-13.45 to 4.42</td>
<td>0.30</td>
<td>0.55</td>
<td>-16.69 to 17.80</td>
<td>0.94</td>
</tr>
<tr>
<td>Ovarian volume (cm³)</td>
<td></td>
<td>1.45</td>
<td>-0.26 to 3.18</td>
<td>0.089</td>
<td>1.98</td>
<td>-0.58 to 4.53</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Our observations add support to the concept that circulating AMH does not hold a simple linear relationship with follicle number, as previously suggested by the observation that AMH is more elevated in hyperandrogenic compared with normoandrogenic women with PCO despite comparable numbers of small follicles (Eldar-Geva et al., 2005). The markedly decreased AMH levels seen in PCOS women with diabetes type I compared with non-diabetic PCOS women, despite comparable androgen levels, is also compatible with this view (Codner et al., 2007).

It is also possible that the partial suppression of androgens seen in the present study is insufficient to reduce the biological effect on ovarian androgen receptors. Thus, the underlying pathology may relate to androgen receptor sensitivity as much as circulating androgen concentrations (Shah et al., 2008). Blocking the androgen receptor, as in treatment with the anti-androgen flutamide, induces a much larger reduction in the biological androgen effect at the cellular level, and further exploration of effects upon follicular dynamics represented by AMH output is awaited. Accordingly, our study indicates that suppression of adrenal androgens, either with or without modification of insulin sensitivity using metformin, is not a clinically valid approach to normalization of ovarian morphology or follicular dynamics in women with PCOS.

Two previous reports of protracted treatment with the insulin sensitizer metformin resulted in improved insulin sensitivity, reduced follicular development, does not result in ovarian changes as represented by AMH output, suggesting that numerous mechanisms are responsible for the induction and maintenance of the morphological changes observed in the ovaries of women with PCOS. It also indicates that androgen-mediated support for follicular growth, development and survival is not a simple direct cause and effect relationship.

Between AMH and ovarian volume, testosterone and insulin has a negative association. The association between AMH and other factors in untreated women with PCOS, support data reported previously. Univariate analyses showed that AMH associated positively with testosterone and ovarian volume. In multivariate analyses, both C-peptide and DHEAS became negatively associated with AMH while the positive association with testosterone was strengthened. The association between AMH and ovarian volume, testosterone and insulin has been reported previously (Fleming et al., 2005; Chen et al., 2008). However, the possible association with the adrenal androgen precursor DHEAS has not been described before.
confused by assay sensitivity limitations. An obvious explanation would be that the modification of adrenal androgens by dexamethasone actively disrupts the usual mechanisms regulating the latter stages of follicular growth and development in PCOS. This, in turn, suggests possible effective inter-organ relationships. However, why or how adrenal androgen suppression should disrupt relationships while maintaining follicular profiles is difficult to explain. It is interesting to note that in PCOS women treated with GnRH-agonists for down-regulation during IVF treatment, levels of DHEAS and DHEA decrease, further supporting an ovarian—adrenal interplay (Kjøtrød et al., 2008). In this context, further exploration of the mineralocorticoid receptor activity in normal and PCOS ovaries may prove rewarding.

In conclusion, 6 months of androgen suppression by low-dose dexamethasone failed to modify follicular dynamics as represented by the changes in circulating AMH levels in women with PCOS treated with diet, lifestyle advice and metformin.

Author’s role
S.M.C. had the original idea, performed the statistical analyses and was responsible for preparing the manuscript. E.V. performed the initial statistical analyses and preparation of the manuscript. R.F. took part in developing the hypothesis, interpretation of results and preparation of the manuscript.

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