Variation of luteinizing hormone and androgens in oligomenorrhoea and its implications for the study of polycystic ovary syndrome

M.H.A. van Hooff\textsuperscript{1}, M. van der Meer, C.B. Lambalk and J. Schoemaker

Research Institute for Endocrinology, Reproduction and Metabolism, Department of Obstetrics and Gynaecology, Division of Reproductive Endocrinology and Fertility, Medical Centre Free University, PO Box 7057, 1007 MB Amsterdam, The Netherlands

\textsuperscript{1}To whom correspondence should be addressed

We measured luteinizing hormone (LH) and androgen concentrations in patients at different phases of the oligomenorrhoeic cycle and compared the results with those of patients with normogonadotrophic amenorrhoea. Several blood samples separated by \( \geq 7 \) days were obtained from each of 72 patients with oligomenorrhoea and 18 with normogonadotrophic amenorrhoea. The oligomenorrhoeic cycle was divided into five phases: the postmenstrual phase week 1 (day 1–7) and week 2 (day 8–14), the specific oligomenorrhoeic phase (SOP, day 15 after a menstruation) and the premenstrual phase (days 10–1 before menstruation). The SOP, when the endocrinology is comparable with that of normogonadotrophic amenorrhoea. Several studies showed temporary normalization of high LH concentrations or abnormal LH pulse patterns after either an ovulation or progesterone administration (Minakami et al., 1988; Homburg et al., 1988; Prelevic et al., 1990; Anttila et al., 1992; Taylor et al., 1997). Furthermore, androgen concentrations decrease after ovulation (Taylor et al., 1997) or progesterone administration (Anttila et al., 1992). These studies suggest that ovulation not only influences hormone concentrations in the luteal phase but also during the first 14 days of the next menstrual cycle. This implies the importance of timing of blood sampling in the endocrine evaluation of oligomenorrhoea. We describe for the first time the influence of blood sample timing on the intra-individual variation in LH concentrations and on the prevalence of elevated LH concentrations in oligomenorrhoeic women with and without polycystic ovaries detected using ultrasound. Furthermore, we compared gonadotrophin, androgen and oestradiol concentrations in blood samples taken at different phases of the oligomenorrhoeic cycle and from women with normogonadotrophic secondary amenorrhoea.

Materials and methods

Population

Several repeated blood samples were obtained from all new patients with chronic anovulation or oligo-ovulation who attended our fertility clinic during 1993. These patients presented with the clinical symptom of secondary amenorrhoea (no menstruation during the previous 6 months) or oligomenorrhoea (mean length of the menstrual cycle \( > 41 \) days). Table I shows the characteristics of the study population. One hundred and six patients, mean age 28.7 years, range 19–37, entered the study. Subsequently, patients with the following conditions were excluded: hypergonadotrophic hypoestrogenaemic amenorrhoea (FSH \( > 20 \) IU/l and oestradiol \( < 90 \) pmol/l), hypogonadotrophic hypoestrogenaemic amenorrhoea (FSH \( < 1 \) IU/l and oestradiol \( < 90 \) pmol/l) (World Health Organization, 1993; ESHRE Capri Workshop, 1995; British Fertility Society 1995), hyperprolactinaemia (prolactin \( > 0.75 \) IU/l) and a macroadenoma on magnetic resonance imaging, Ashermann’s syndrome, regular ovulatory cycles during the study. Those who visited our outpatient clinic only once were also excluded. Sixty-two patients with oligomenorrhoea and 28 patients with normogonadotrophic secondary amenorrhoea and normal FSH concentrations (FSH 1–10 IU/l and oestradiol \( > 90 \) pmol/l) were included. Ten patients who presented with normogonadotrophic secondary amenorrhoea had a menstruation during the study period and were defined as having oligomenorrhoea and analysed as such. Thus, for the purposes of analysis, there were 72 oligomenorrhoeic and 18 normogonadotrophic patients.

The study was approved by the Committee on Ethics of Research involving Human Subjects of the Free University Hospital.

Introduction

Oligomenorrhoea is a key feature of the polycystic ovary syndrome. Elevated luteinizing hormone (LH) concentrations are common in all reported studies of women with this condition (Franks, 1995) and have an adverse effect on fertility and outcome of pregnancy (Shoham et al., 1993; Balen et al., 1995).

In oligomenorrhoeic women, ovulatory cycles may alternate with anovulatory cycles (Franks, 1995). Several studies showed temporary normalization of high LH concentrations or abnormal LH pulse patterns after either an ovulation or progesterone administration (Minakami et al., 1988; Homburg et al., 1988; Prelevic et al., 1990; Anttila et al., 1992; Taylor et al., 1997). Furthermore, androgen concentrations decrease after ovulation (Taylor et al., 1997) or progesterone administration (Anttila et al., 1992). These studies suggest that ovulation not only influences hormone concentrations in the luteal phase but also during the first 14 days of the next menstrual cycle. This implies the importance of timing of blood sampling in the endocrine evaluation of oligomenorrhoea. We describe for the first time the influence of blood sample timing on the intra-individual variation in LH concentrations and on the prevalence of elevated LH concentrations in oligomenorrhoeic women with and without polycystic ovaries detected using ultrasound. Furthermore, we compared gonadotrophin, androgen and oestradiol concentrations in blood samples taken at different phases of the oligomenorrhoeic cycle and from women with normogonadotrophic secondary amenorrhoea.

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Key words: androgens/LH/oligomenorrhoea/PCOS/specific oligomenorrhoeic phase
Variation of hormones in oligomenorrhoea in Amsterdam. Informed consent was obtained from all participating women.

**Phases of the oligomenorrhoeic cycle**

The oligomenorrhoeic cycle was divided into five phases (Figure 1): the premenstrual phase (10–1 days before a menstruation), the postmenstrual phase week 1 (days 1–7 after a menstruation), the postmenstrual phase week 2 (days 8–14 after a menstruation), the specific oligomenorrhoeic phase (day 15 after a menstruation to day 21 before a subsequent menstruation), and the possibly peri-ovulatory phase (days 21–11 before a menstruation). The terms postmenstrual, possibly peri-ovulatory and premenstrual phase were used instead of follicular, peri-ovulatory and luteal because ovulation was not necessarily documented. Menstruation was defined as vaginal bleeding for several days recognized by the patient as a period.

**Definition of the specific oligomenorrhoeic phase**

A new concept, the specific oligomenorrhoeic phase (SOP), is introduced. This phase is defined as the period from 15 days after the first day of a menstruation until 21 days before the next. The duration of the SOP varies with the duration of the menstrual cycle, e.g. 1 week in a 6 week cycle and 7 weeks in a 12 week cycle.

The definition of the beginning of the SOP is based on a study (Minakami et al., 1988) which showed that elevated LH concentrations in women with oligomenorrhoea gradually declined after an ovulation (suggested by an increase in the basal body temperature) to the normal or near normal range by the end of the luteal phase and during the early follicular phase of the next cycle. The lower LH concentrations gradually increased again from the beginning of menstruation and were always above the normal range after day 14 of the next cycle. Subsequently, LH concentrations varied around their plateau.

The definition of the ending of the SOP is based on the notion that peri-ovulatory hormonal changes may start a few days before ovulation. This, when added to the normal length of the luteal phase, defines a time span of up to 21 days before the next menses in which hormone values may be altered due to growth of a dominant follicle, or to ovulation or luteinization. To separate possibly peri-ovulatory values from premenstrual values, the latter phase was defined as the 10 days before the next menses (minimum length of the luteal phase; Lenton et al., 1984). The possibly peri-ovulatory phase (21–11 days before a menstruation) were given arbitrarily wide limits to exclude the possibility that hormone values in other phases would be confounded by peri-ovulatory values.

**Timing of blood sampling**

In both oligomenorrhoeic and amenorrhoeic patients, the first blood sample was obtained on the day that the patient visited our clinic for the first time. Three to five blood samples were taken subsequently, with at least 7 days between consecutive samples.

The methodology of the study implied that not all oligomenorrhoeic patients would provide blood samples in all defined phases of the oligomenorrhoeic cycle. Of the 72 patients analysed as oligomenorrhoeic (including 10 amenorrheic patients who had a menstruation during the study and were therefore transferred to the oligomenorrhoeic group), 70 had a sample taken in the oligomenorrhoeic phase, 18 had a sample taken in the postmenstrual phase week 1, 26 had a sample taken in the postmenstrual phase week 2, 35 a sample taken in the premenstrual phase and 40 a sample taken during the possibly peri-ovulatory phase. Of the latter, 20 (50%) showed LH values compatible with a midcycle LH surge.

Excluding all 40 samples taken during the possibly peri-ovulatory phase, 38 patients provided samples in the SOP and in at least one other phase (Table Ic), of whom 26 provided samples in the SOP and in at least two other phases.

Of the 38 patients with a sample taken in the SOP and at least one sample taken in another phase, 16 patients had samples taken both

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**Table I. Characteristics of the study population**

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Unselected population</td>
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</tr>
<tr>
<td>Oligomenorrhoea</td>
<td>74</td>
</tr>
<tr>
<td>Secondary amenorrhoea</td>
<td>42</td>
</tr>
<tr>
<td>Total</td>
<td>116</td>
</tr>
<tr>
<td>b. Patients excluded</td>
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</tr>
<tr>
<td>Hypergonadotrophic hypoestrogenic amenorrhoea</td>
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<tr>
<td>Hypogonadotrophic hypoestrogenic amenorrhoea</td>
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</tr>
<tr>
<td>Hyperprolactinaemia</td>
<td>2</td>
</tr>
<tr>
<td>Ashermann’s syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Regular ovulatory cycles</td>
<td>6</td>
</tr>
<tr>
<td>No blood samples obtained after first visit</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
</tr>
<tr>
<td>c. Patients included</td>
<td></td>
</tr>
<tr>
<td>Oligomenorrhoea:</td>
<td></td>
</tr>
<tr>
<td>one sample in the SOP and one in at least one other phase</td>
<td>38</td>
</tr>
<tr>
<td>all samples in the SOP</td>
<td>22</td>
</tr>
<tr>
<td>no samples in the SOP</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>62</td>
</tr>
<tr>
<td>Normogonadotropic secondary amenorrhoea:</td>
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</tr>
<tr>
<td>amenorrhoea during the study</td>
<td>18</td>
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<tr>
<td>menstruation during the study and included as oligomenorrhoea with</td>
<td>10</td>
</tr>
<tr>
<td>one sample in the SOP and one in at least one other phase</td>
<td>total</td>
</tr>
</tbody>
</table>

*SOP = specific oligomenorrhoeic phase (see text).

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Figure 1. Phases of the oligomenorrhoeic cycle.
in the postmenstrual phase week 1 and the SOP. 24 patients had samples taken both in the postmenstrual phase week 2 and the SOP and 35 patients had samples taken both in the premenstrual phase and the SOP. Nine patients had samples taken in both the postmenstrual phase week 1 and the postmenstrual phase week 2.

Of the 26 patients with a sample taken in the SOP and a sample taken in at least two other phases, nine patients had samples taken in the postmenstrual phase week 1, the postmenstrual phase week 2 and the SOP, 10 patients had samples taken in the premenstrual phase, postmenstrual phase week 2 and the SOP and seven patients had samples taken in the premenstrual phase, postmenstrual phase week 1 and the SOP.

Only three patients had samples taken in all four phases, i.e. the SOP, the premenstrual phase, the postmenstrual phase week 1 and the postmenstrual phase week 2.

As the study was initially focused on the variation in LH concentrations, this was determined in all samples. FSH, testosterone, androstenedione and oestradiol were determined only in the first two samples. For the oligomenorrhoic patients, these hormones were determined in 46 samples taken in the SOP, 22 taken in the premenstrual phase, 14 taken in the postmenstrual phase week 1 and 14 taken in the postmenstrual phase week 2. Furthermore, these hormones were determined in samples from all 18 patients with normogonadotrophic secondary amenorrhoea.

Hormone assays and reference values

Plasma LH, FSH and oestradiol concentrations were determined by using immunofluorometric assays (Amerlite, Amersham, UK). For the LH assay the lower limit of detection was 0.3 IU/l. The intra-assay coefficient of variation (CV) was 5% at a concentration of 10 IU/l, 3% at concentrations of 20 IU/l and 40 IU/l. The inter-assay CV was 10% at a concentration of 2 IU/l and 6% at a concentration of 40 IU/l. For the FSH assay the lower limit of detection was 0.5 IU/l. The intra-assay CV was 6% at a concentration of 5 IU/l and 5% at concentrations of 15 IU/l and 40 IU/l. The inter-assay CV was 9% at a concentration of 3 IU/l and 5% at a concentration of 35 IU/l. The detection limit for the oestradiol assay was 90 pmol/l. The intra-assay CV was 13% at a concentration of 350 pmol/l and 9% at a concentration of 1100 pmol/l. The inter-assay CV was 11% at a concentration of 160 pmol/l. Serum androstenedione and testosterone were determined by using a radioimmunoassay (Coat a Count®; DPC, Los Angeles, CA, USA). For the testosterone assay the lower limit of detection was 1.0 nmol/l. The intra-assay CV was 6% at a concentration of 4 nmol/l. The inter-assay CV was 12% at a concentration of 2.5 nmol/l. For the androstenedione assay the lower limit of detection was 0.4 nmol/l. The intra-assay CV was 5% at a concentration of 1 nmol/l and 8% at a concentration of 3 nmol/l. The inter-assay CV was 11% at a concentration of 3 nmol/l and 8% at a concentration of 11 nmol/l.

In our clinic, LH concentrations >6.5 U/l are considered to be elevated, excluding peri-ovulatory and postmenopausal values. For the purpose of this study reference values of LH were re-examined. The 95th centile for the LH concentration of 125 tubal factor IVF patients with regular menstrual cycles was 6.6 IU/l in blood samples taken between cycle days 2 and 5. In this study a LH concentration >6.5 IU/l was defined as elevated.

Ultrasound of the ovaries

Vaginal ultrasound was performed using an Ultramark-4 ultrasound equipment (ATL, Bothell, WA, USA) with a 5 MHz vaginal probe. The ultrasounds were recorded on video-tape. patients' names were coded to numbers and the ultrasound appearance of the ovaries was judged by two of the authors (MvdM and MvH) without knowledge of the endocrine or clinical data. Ovaries were defined as polycystic according to well known criteria (Adams et al., 1986). The ultrasound appearance of the normal ovary changes during the menstrual cycle and is not well defined in the literature. Therefore, ovaries not meeting the criteria for polycystic were classified as normal.

Multifollicular ovaries were only seen in hypogonadotrophic patients.

Statistics

If more than one sample was available in a particular phase only the result of the first sample was used in the analysis. This method avoids bias from the selection of samples with the highest values.

To compare the intra-individual variance in LH between the SOP and one other phase, paired t-tests were employed. Analysis of variance for repeated measurements was used for patients with blood samples in the SOP and in two other phases. McNemar's χ² test for paired data was used to compare the within patient variation in elevated LH concentrations in the different menstrual phases. Results are expressed as mean ± SD.

Analysis of variance with subsequent non-paired t-tests was used to compare hormone concentrations in normogonadotrophic amenorrhoic women with those found during the different phases of the cycle in oligomenorrhoic women.

P values < 0.05 in two-sided tests were considered significant.

Results

In three patients with oligomenorrhea, no ultrasound of the ovaries was performed and in two patients an unequivocal interpretation of the ultrasound was not possible. These five patients were not diagnosed on ultrasound. Thus, 39 patients with oligomenorrhea and polycystic ovaries at ultrasound and 28 with normal ovaries at ultrasound were included. These groups did not differ in age (29.1 versus 28.6 years), body mass index (27.9 ± 6.2 versus 25.6 ± 5.0 kg/m²), average number of menstrual cycles in the past year (4.1 ± 2.1 versus 4.8 ± 1.7 menstruations) and prevalence of hirsutism (39 versus 29%).

Figure 2 shows the intra-individual variation of LH in the different phases of the oligomenorrhoeic cycle. LH concentrations during the specific oligomenorrhoeic phase were significantly higher than those in all other phase of the oligomenorrhoeic cycle, excluding those values around a possible ovulation. LH concentrations in samples taken in the postmenstrual phase week 2 were significantly higher than those taken in postmenstrual phase week 1. Analysis of variance with repeated measurements with data from 26 patients who had blood sampled in three different phases showed a significant increase in LH concentrations (P = 0.002) in nine of these patients whose blood samples were obtained in the postmenstrual phase week 1, the postmenstrual phase week 2 and the SOP. In another 10 of these patients whose blood samples were obtained in the premenstrual phase, postmenstrual phase week 2 and the SOP a significant increase in LH was also documented (P = 0.005). In the other seven of these patients whose blood samples were obtained in the premenstrual phase, postmenstrual phase week 1 and the SOP, LH concentrations declined from the premenstrual to the postmenstrual phase week 1 and subsequently increased to the highest concentrations in the SOP (P = 0.04). Only
Variation of hormones in oligomenorrhea

Figure 2. Intra-individual variation in LH concentrations in different phases of the oligomenorrheic cycle. Pre = premenstrual phase, Post-1 = postmenstrual phase week 1, post-2 = postmenstrual phase week 2, SOP = specific oligomenorrheic phase. Individual values and * mean ± SD are presented. Paired t-test P < 0.05 for all comparisons.

Table II. Comparison of elevated LH concentrations (>6.5 IU/l) within patients in the different phases of the oligomenorrheic cycle

<table>
<thead>
<tr>
<th>Paired samples</th>
<th>n</th>
<th>Both elevated</th>
<th>Both normal</th>
<th>A Elevated</th>
<th>A Normal</th>
<th>McNemar’s X^2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postmenstrual phase week 1 (A) and week 2 (B)</td>
<td>9</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>5</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Postmenstrual phase week 1 (A) and SOP (B)</td>
<td>16</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>9</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Postmenstrual phase week 2 (A) and SOP (B)</td>
<td>24</td>
<td>14</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>Premenstrual phase (A) and SOP (B)</td>
<td>35</td>
<td>11</td>
<td>12</td>
<td>1</td>
<td>11</td>
<td></td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

three patients provided blood samples in all four phases. This subgroup was too small for statistical analysis.

Table II shows the results of a paired analysis confirming the effect of timing of blood sampling on the prevalence of elevated LH concentrations within individuals. Considering the top two rows in Table II, in 14 out of 16 (88%) patients with elevated LH concentrations, LH concentrations were normal in the postmenstrual phase week 1 while they were elevated in the specific oligomenorrheic phase or postmenstrual phase week 2. Of the premenstrual samples (row four of Table II), 11 out of a total of 23 (48%) samples showed normal values although they had shown elevated values in the specific oligomenorrheic phase.

Figure 3 shows a comparison between gonadotrophin, androgen and oestradiol concentrations in the different phases of the oligomenorrheic cycle and in normogonadotrophic secondary amenorrhea. Although there were a variety of significant differences in endocrine concentration between secondary amenorrhea and the postmenstrual phase week 1, postmenstrual phase week 2 or the premenstrual phase, no significant differences were found in gonadotrophin, androgen or oestradiol concentrations between a specific oligomenorrheic phase and normogonadotrophic amenorrhea.

In oligomenorrheic cycles LH, androstenedione and testosterone concentrations increased in the order postmenstrual phase week 1, postmenstrual phase week 2 and SOP. LH and androstenedione concentrations during the postmenstrual phase week 2 were also significantly lower than during the SOP. LH concentrations during the postmenstrual phase week 2 were also significantly lower than during the SOP. The variation in testosterone concentrations was less and was not significant. FSH concentrations were lower and oestradiol concentrations were higher during the premenstrual phase compared to the SOP.

LH and oestradiol concentrations did not differ between women with normal or polycystic ovaries in any phase of the oligomenorrheic cycle or secondary amenorrhea. FSH concentrations were significantly lower in women with PCO compared to those with normal ovaries during the postmenstrual phase week 2 (4.4 ± 1.2 versus 5.9 ± 1.6; P = 0.02), the SOP (4.8 ± 1.3 versus 5.8 ± 2.1; P = 0.02) and secondary amenorrhea (5.2 ± 1.3 versus 7.1 ± 1.9; P = 0.03). The LH/FSH ratio was significantly higher in women with PCO during the SOP (2.0 ± 0.9 versus 1.5 ± 0.8; P = 0.02). Androstenedione concentrations were higher in women with PCO than in those with normal ovaries in the postmenstrual phase week 1 (9.0 ± 1.9 versus 4.7 ± 0.8; P = 0.01), the postmenstrual phase week 2 (10.0 ± 3.1 versus 7.0 ± 2.0; P = 0.03) and the SOP (11.3 ± 4.0 versus 7.5 ± 2.8; P < 0.001). Testosterone concentrations were significantly higher in women with PCO in the SOP (2.2 ± 0.8 versus 1.7 ± 0.6; P = 0.03). For women with PCO and women with normal ovaries LH, androstenedione and testosterone concentrations increased in the order: postmenstrual phase week 1, postmenstrual phase week 2 and SOP. The increase was significant for LH in women with PCO (ANOVA, P =
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Figure 3. Comparison of gonadotrophins, androgens and oestradiol concentrations in various phases of the oligomenorrhoeic cycle and normogonadotrophic amenorrhoea. A = premenstrual phase (n = 22–35, i.e. lowest and highest number of determinations dependent on hormone studied), B = postmenstrual phase week 1 (n = 14–19); C = postmenstrual phase week 2 (n = 14–26), D = specific oligomenorrhoeic phase (n = 46–70), SA = normogonadotrophic amenorrhoea (n = 18). *Student’s t-test P < 0.05 compared to normogonadotrophic amenorrhoea; §Student’s t-test P < 0.05 compared to the specific oligomenorrhoeic phase. Results are expressed as mean ± SD.

Discussion

We defined a phase in the cycle of oligomenorrhoeic patients in which hormone concentrations are minimally influenced by events such as ovulation and progesterone production. By definition this phase only exists in menstrual cycles longer than 5 weeks, as seen in oligomenorrhoea, and we introduced the name specific oligomenorrhoeic phase (SOP). We have shown that in a non-selected population of oligomenorrhoeic patients, hormone values from blood sampled during this phase are fully comparable with those found in patients with amenorrhoea who also lack the influences of major ovarian changes. From a practical point of view, blood samples can easily be obtained in the SOP. A blood sample can be obtained at the first visit if the start of the last menses was more than 14 days previously. It should be verified whether the sample was obtained 3 weeks before the start of the next menses. In our clinic this is done by a telephone appointment. If at the time of the first visit the start of the last menses was less than 14 days earlier, or if a menstruation occurred within 3 weeks after the first sample, then the sampling should be planned for 2 weeks after the beginning of the menses. Again the start of the next menstruation after the sampling should be verified. Additional measurement of progesterone in a sample only allows identification of premenstrual samples.

Another new aspect of our study is the finding of a clear intra-individual variation in LH values, not only in oligomenorrhoeic patients with polycystic ovaries but also in those whose ovaries appear normal at ultrasound. A similar intra-individual variation for oligomenorrhoeic women with polycystic and those with normal ovaries was shown previously following progesterone administration (Anttila et al., 1992). Other studies have clearly indicated the relationship of LH concentrations to prior progesterone administration and ovulation in patients with oligomenorrhoea, but there have been no longitudinal studies and the ovarian ultrasound appearance was not described (Goldenberg et al., 1973; Molloy et al., 1984; Petsos et al., 1986; Blankstein et al., 1987; Buckler et al., 1988; Homburg et al., 1988; Minakami et al., 1988; Prelevic et al., 1990). The important influence of timing of blood sampling on the prevalence of elevated LH concentrations within individuals (Table II) has not been described before.

Our study focused on the evaluation of longitudinal changes in LH. Other hormones such as androstenedione and testosterone were measured only in the first two samples, which unfortunately allowed cross-sectional analysis only. Nevertheless, we were able to confirm earlier observations that androgen concentrations also depend on timing of prior progesterone administration (Anttila et al., 1992) or ovulation (Taylor et al., 1997).

In our study LH, androstenedione and testosterone concentrations in the specific oligomenorrhoeic phase were not different
from the concentrations found in patients with normogonadotrophic secondary amenorrhoea. This is in line with the concept that normogonadotrophic secondary amenorrhoea represents a very long specific oligomenorrhoeic phase. Timing of sampling in the specific oligomenorrhoeic phase will provide more homogeneous endocrine values in oligomenorrhoeic and normogonadotrophic amenorrhoeic women, and supports our rationale for obtaining blood samples.

Although elevated LH concentrations are associated with adverse effects on fertility and outcome of pregnancy (Shoham et al., 1993; Balen et al., 1995), the value of elevated LH concentrations in the diagnosis of the polycystic ovary syndrome remains controversial. However, many studies have obtained samples from the first week after a menstruation or did not take into account the timing of blood during sampling obtained samples from the first week after menstruation or syndrome remains controversial. However, many studies have obtained samples from the first week after a menstruation or did not take into account the timing of blood during sampling obtained samples from the first week after a menstruation or


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References


