Prolactin secretion in polycystic ovary syndrome (PCO): correlation with the steroid pattern

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Abstract. To evaluate the prevalence of hyperprolactinaemia in PCO patients and its possible correlation with a steroid pattern, we studied prolactin secretion (basal and after TRH stimulation) in 40 women affected by typical PCO. LH, FSH, testosterone, oestradiol, oestrone, DHEA-s and 17-OHP serum levels were also evaluated. Twenty-one patients had prolactin (Prl) values in the normal range both in baseline conditions and after TRH stimulation; 10 patients had normal basal values of Prl but an exaggerated response to TRH stimulation; 9 patients had high Prl basal values and an exaggerated response to TRH. The presence of hyperprolactinaemia was associated with increased serum levels of oestrone (P < 0.01), DHEA-s (P < 0.01) and 17-OHP (P < 0.05). In conclusion, hyperprolactinaemia is a relatively frequent condition which affects almost half the patients suffering from PCO and is probably related to an increase of serum oestrogens, mostly oestrone. Moreover, in patients with PCO and hyperprolactinaemia, the production of some other steroids is also affected.

During recent years prolactin hypersecretion has been reported in the polycystic ovary syndrome (PCO). After some isolated observations (Thorner et al. 1974; Seppälä & Hirvonen 1975), Jaffe et al. (1978) reported that in a study of 12 women affected by PCO, 5 patients had hyperprolactinaemia. Similar data have been reported by other investigators (Wortsman & Hirschowitz 1980; Falaschi et al. 1980; Carmina et al. 1981) although Yen et al. (1976) observed normal prolactin secretion in patients affected by typical PCO.

On the other hand, those authors who reported the presence of hyperprolactinaemia in cases of PCO did not demonstrate its dependence on a particular steroid pattern (Jaffe et al. 1978; Falaschi et al. 1980). It is not yet clear therefore whether hyperprolactinaemia is a rare phenomenon in PCO or whether it represents an important endocrine aspect of this disease. Furthermore, it has not yet been possible to ascertain whether hyperprolactinaemia is simply the consequence of a particular steroid pattern, or whether it is the expression of a diencephalic alteration which occurs in some cases of PCO (Goldzieher 1981).

We report our findings on the Prl secretion in 40 women affected by PCO. The steroid pattern was also evaluated in order to establish any correlation with hyperprolactinaemia. Since it is possible that many of the disagreements in previous reports may have been due to the heterogeneous nature of the cases studied, only patients with typical PCO were included in our study. These all had an increase in ovarian size and hirsutism.

Materials and Methods

Forty women (aged 15–38 years) with typical PCO were studied. Diagnosis of PCO was based on the following criteria: hirsutism, chronic anovulation, menstrual disorders (hypo-oligomenorrhea or amenorrhoea), celioscopic and/or echographic evidence of bilaterally enlarged polycystic ovaries. Ovarian scannings were made with a full bladder using the Picker model 80L echotomograph and an Aloka model 250 with 3.5 MHz probe. Criteria for echographic diagnosis of PCO have been al-
ready presented (Comparetto et al. 1982). Only patients with a maximum longitudinal diameter of the ovary greater than 35 mm were selected for this study.

None of the subjects had ever been pregnant and all had been free from medication and hormonal treatment for at least 3 months before this investigation.

In the morning after overnight fasting and bed rest, the following tests were performed:

- determination of basal serum levels of LH, FSH and Prl (at least 4 blood samples taken at 30 min intervals)
- determination of serum Prl response to TRH stimulation (200 µg iv and samples drawn every 30 min for 120 min)
- determination of serum levels of oestradiol-17β (E2), oestrone (E1), testosterone (T), 17-hydroxyprogesterone (17-OHP), dehydroepiandrosterone sulphate (DHEA-s) (at least 2 blood samples on 2 different days).

In menstruating patients the study was performed during the follicular phase of the cycle (days 5–8). Twenty-three normally cycling women served as controls. LH, FSH, Prl, oestrone and DHEA-s were determined by RIA using commercial kits purchased from Biodata (Milano). Oestradiol, testosterone and 17-OHP were assayed by RIA using commercial kits provided by Sorin (Saluggia). The statistical analysis was performed by Student's t-test.

Results

The results of the hormone assays in PCO patients and normal controls are summarized in Table 1. Normal ranges were determined as mean ± SD.

a Prolactin

In PCO patients, the mean serum level of Prl (mean of the medium baseline levels) was significantly higher (P < 0.01) than in normal women. After TRH stimulation, the mean Prl peak was 79.54 ± 49.06 ng/ml, significantly higher (P < 0.01) than in normal women. Twenty-one patients with PCO had Prl values in the normal range both in baseline conditions (mean ± SD 11.94 ± 4.91 ng/ml) and after TRH stimulation (mean peak ± SD 41.60 ± 14.37 ng/ml). Ten PCO patients showed normal basal values of Prl (mean ± SD 14.97 ± 4.37 ng/ml) but an exaggerated response to TRH stimulation (mean peak ± SD 101.97 ± 48.53 ng/ml). Finally, 9 patients had Prl basal values above the normal range (mean ± SD 30.75 ± 8.98 ng/ml, range 24–50 ng/ml) and an exaggerated response to TRH stimulation (mean peak ± SD 123.88 ± 42.51 ng/ml). To sum up, 52.5% of the patients proved to be normoprolactinaemic, while 22.5% had hyperprolactinaemia in basal conditions and 25% showed an exaggerated reserve of Prl in the pituitary gland.

b Gonadotrophins

In PCO patients, the serum levels of LH were significantly (P < 0.01) higher than in normal controls. The mean serum levels of FSH were similar to those of the control group. No differences were observed in the serum levels of LH and FSH in normoprolactinaemic and hyperprolactinaemic PCO patients.

Table 1.

| Hormone levels (mean ± SD) in serum of 23 normal women (days 5–8) and of 40 PCO patients. |
|-----------------------------------------------|-------------------|-------------------|
| LH mUI/ml                                      | 9.40 ± 2.74       | 25.89 ± 9.66*     |
| FSH mUI/ml                                     | 8.96 ± 2.51       | 8.46 ± 2.69       |
| Prl ng/ml                                      |                   |                   |
| basal                                          | 11.21 ± 5.40      | 17.05 ± 9.64*     |
| peak after TRH 200                             | 40.64 ± 11.32     | 79.54 ± 49.06*    |
| Testosterone ng/100 ml                         | 29.81 ± 10.23     | 86.76 ± 21.80*    |
| Oestradiol pg/ml                               | 56.10 ± 18.16     | 54.91 ± 35.56     |
| Oestrone pg/ml                                 | 61.43 ± 18.75     | 119.05 ± 42.88*   |
| DHEA-s µg/ml                                   | 2.21 ± 0.69       | 4.65 ± 1.84*      |
| 17-OHP ng/ml                                   | 0.56 ± 0.18       | 1.32 ± 0.42*      |

* Indicates statistical differences significant at P < 0.01.
Serum levels of oestradiol (□) and oestrone (■) in 40 women with typical PCO divided on the basis of Prl behaviour. Group a = normoprolactinaemic patients. Group b = patients with normal basal levels of Prl but exaggerated response to TRH. Group c = hyperprolactinaemic patients.

c Testosterone
The mean serum levels of testosterone were significantly higher ($P < 0.01$) than those of the control group. No differences in the serum levels of testosterone were observed between normoprolactinaemic and hyperprolactinaemic patients.

d Oestrogens
The serum levels of oestradiol were similar to those observed in the controls. Instead, the mean serum levels of oestrone were significantly higher ($P < 0.01$) in PCO patients than in the control women. The patients with PCO therefore, presented a modified oestrone/oestradiol ratio in favour of oestrone (2.16:1). As indicated in Fig. 1, a progressive increase was observed in the levels of oestrone and oestradiol ranging from the normoprolactinaemic patients to those with increased reserve of Prl and from the latter to those with high Prl basal values.

Table 2.
Serum levels (mean ± sd) of some steroids in 40 PCO patients. Group a = 21 normoprolactinaemic patients; group b = 10 patients with exaggerated Prl response to TRH; group c = 9 patients with high basal levels of Prl.

<table>
<thead>
<tr>
<th></th>
<th>Group a</th>
<th>Group b</th>
<th>Group c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Testosterone ng/100 ml</td>
<td>86.40 ± 25.41</td>
<td>82.33 ± 16.90</td>
<td>92.11 ± 18.03</td>
</tr>
<tr>
<td>Oestradiol-17β pg/ml</td>
<td>48.52 ± 25.10</td>
<td>55.40 ± 36.83</td>
<td>74.11 ± 44.83</td>
</tr>
<tr>
<td>Oestrone pg/ml</td>
<td>86.66 ± 45.75</td>
<td>125.02 ± 20.17**</td>
<td>142.57 ± 38.55**</td>
</tr>
<tr>
<td>17-OH-P ng/ml</td>
<td>1.20 ± 0.34</td>
<td>1.21 ± 0.31</td>
<td>1.70 ± 0.51*</td>
</tr>
<tr>
<td>DHEA-s µg/ml</td>
<td>3.69 ± 1.43</td>
<td>4.44 ± 1.71</td>
<td>5.72 ± 0.19**</td>
</tr>
</tbody>
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The differences from group a are significant at $P < 0.05*$ and $P < 0.01**$. 

![Fig. 1.](image-url)
17-OHP and DHEA-s levels in 40 women with typical PCO divided on the basis of Prl behaviour. Group a = normoprolactinaemic patients. Group b = patients with normal basal levels of prolactin but exaggerated response to TRH. Group c = hyperprolactinaemic patients.

Discussion

The present study demonstrates that hyperprolactinaemia is a relatively frequent condition which affects almost half the patients suffering from PCO, in the form of an increase of basal Prl levels or of an increased reserve of Prl in the pituitary gland. It is surprising that evidence of such a frequent phenomenon was discovered only a few years ago (Jaffe et al. 1978; Wortsman & Hirschowitz 1980; Falaschi et al. 1980). It is interesting to observe that the heterogeneity of Prl secretion behaviour noted in PCO patients is not a phenomenon limited to this hormone, but, on the contrary, seems to be a characteristic of the syndrome. In fact, an analogous heterogeneity may be found in most of the other hormonal parameters including those that more classically define the endocrine features of the syndrome such as, for example, the hypersecretion of LH and oestrone (De Vane et al. 1975; Givens et al. 1976). It is common knowledge, in fact, that it is relatively frequent for patients affected by PCO to have normal levels of LH
and/or oestrone. It is possible that such heterogeneity of the endocrine parameters of PCO reflects heterogeneity in the aetiopathogenetic mechanisms, which determine the development of the disease.

Moreover, our data suggest that hyperprolactinaemia in PCO patients merely reflects the existence of hyperoestrogenism since we demonstrated a progressive increase in the levels of circulating oestrogens, ranging from the normoprolactaemic patients to those with an exaggerated response to TRH and from the latter to those with basal hyperprolactinaemia. Basically, this phenomenon concerns the increase in oestrone alone, given that it was not possible to show statistically valid variations for oestradiol. Bearing in mind that oestrogens stimulate the secretion of prolactin (Yen et al. 1974), it may be presumed that hyperprolactinaemia is present in those patients in whom there is a greater secretion of oestrogens, and in particular, oestrone. On the other hand, our data do not permit us to identify the genesis of the hyperoestrogenism in such patients since oestrone is to a great extent a product of the peripheral conversion of androstenedione, which may be secreted both by the ovaries and by the adrenal glands (Hatch et al. 1981).

Some other abnormalities of steroid secretion proved to be in statistical correlation with hyperprolactinaemia, and we observed that in patients with PCO and hyperprolactinaemia there was an increase in serum levels of DHEA-s and 17-OHP.

The increase of DHEA-s was to some extent predictable, as it has been reported many times in recent years that hyperprolactinaemia determines a hypersecretion of DHEA-s (Bassi et al. 1977; Lobo et al. 1980; Glickman et al. 1982). However, we were unable to find reports of the presence of high levels of DHEA-s in patients with hyperprolactinaemia associated with PCO.

In contrast, the increase of serum levels of 17-OHP that we observed in hyperprolactinaemic PCO patients is a relatively surprising result, since in patients with hyperprolactenaemia from other causes serum levels of 17-OHP are generally reported to be normal. However, it has recently been reported that 17-OHP shows an exaggerated increase when stimulated with ACTH in patients with pituitary prolactinomas (Glickman et al. 1982). Our data on DHEA-s and 17-OHP serum levels seem to indicate that in patients with PCO, hyperprolactinaemia produces an alteration in steroid production which may contribute to the development of a particular clinical and endocrine pattern of the syndrome.

In conclusion, we have shown that in PCO hyperprolactinaemia is a frequent condition related to multiple steroid abnormalities.

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References


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