Leptin concentrations in hirsute women with polycystic ovary syndrome or idiopathic hirsutism: influence on LH and relationship with hormonal, metabolic, and anthropometric measurements*

P.M.Spritzer1,2,4, M.Poy1, D.Wiltgen1,2, L.S.Mylius1 and E.Capp2,3

1Gynecological Endocrinology Unit, Division of Endocrinology, Hospital de Clínicas de Porto Alegre, 2Department of Physiology and 3Department of Obstetrics and Gynecology, Universidade Federal do Rio Grande do Sul, 90.050-170, Porto Alegre, RS, Brazil
4To whom correspondence should be addressed at: Departamento de Fisiologia, Instituto de Ciências Básicas da Saúde, Universidade Federal do Rio Grande do Sul, Rua Sarmento Leite 500, 90 170 050 Porto Alegre, RS, Brazil. E-mail: spritzer@vortex.ufrrgs.br

BACKGROUND: The known association between leptin, obesity and insulin action suggests that leptin may have a role in polycystic ovarian syndrome (PCOS) but this has only been addressed peripherally. METHODS: We assessed the influence of leptin on LH and investigated the relationship between leptin and body mass index (BMI), waist:hip ratio (WHR), androgen concentrations, fasting insulin and insulin:glucose ratio (IGR) in 27 women with PCOS and in 20 age- and weight-matched women with regular, ovulatory menstrual cycles and idiopathic hirsutism (IH). RESULTS: Leptin concentrations were significantly higher in obese PCOS women than in normal weight women with either PCOS or IH (P = 0.0028), but did not differ between obese women with PCOS and IH. WHR, insulin concentrations and IGR were significantly higher in obese PCOS patients in comparison with the three other groups. In IH patients, the association between leptin concentrations and WHR was lost after adjustment for BMI. In PCOS patients, a significant correlation was observed between leptin and fasting insulin concentrations, IGR, WHR and LH. After adjustment for BMI, only the correlation with LH remained significant. A stepwise regression model was set up with LH as the dependent variable to test the hypothesis that the concentrations of leptin might be modulating the concentrations of LH in PCOS patients. The relationship of LH concentrations with IGR was found to be BMI dependent. In contrast, leptin concentrations contributed negatively and significantly to LH concentrations, independently of either BMI or IGR. CONCLUSIONS: We speculate that the known attenuation in basal or stimulated response of LH in obese PCOS patients might be related to leptin resistance, which could influence LH hypersecretion. In IH ovulatory patients, normal LH concentrations suggest the presence of preserved regulatory mechanisms of GnRH pulsatility. Further studies are needed to specifically investigate the proposed correlation between leptin and GnRH modulation in PCOS.

Key words: idiopathic hirsutism/insulin resistance/leptin/LH/polycystic ovary syndrome

Introduction

Leptin, a protein containing 167 amino acids, transcribed from the obesity (ob) gene, is associated with the regulation of body fat stores. In rodents, leptin contributes to the regulation of energy balance (Halaas et al., 1995) and reduces the percentage of body fat. In humans, however, leptin resistance is involved in the development of obesity, and is closely related to the metabolism of insulin and glucose (Auwerx and Staels, 1998).

In vitro, leptin seems to attenuate the phosphorylation of insulin receptor-1 (IRS-1), while increasing the association of IRS-1 with phosphatidylinositol 3-kinase. Therefore, leptin may antagonize some actions of insulin, and thus may have a role in obesity-induced insulin-resistance (Cohen et al., 1996). Moreover, leptin receptors have been reported in the pancreas, suggesting that leptin may also regulate insulin release as part of an adipo-insulin feedback (Wang et al., 1998). Polycystic ovarian syndrome (PCOS) is a heterogeneous clinical condition, characterized by hirsutism, irregular menstrual cycles, infertility, and endocrine abnormalities such as hyperandrogenism and inappropriate LH secretion. Moreover, a considerable percentage of PCOS women present insulin resistance and compensatory hyperinsulinemia (Dunaif et al., 1989; Holte et al., 1994a; Ehrmann et al., 1995). These metabolic defects are more prevalent in PCOS women than in
normal women within similar age groups. Also, insulin resistance seems to be more frequent and/or to cause a higher metabolic impact on obese PCOS women than in non-obese PCOS women. At least 20% of the obese PCOS patients present glucose intolerance or diabetes, versus ~5% of the healthy age- and weight-matched population (Dunaif et al., 1987; Spritzer et al., 1998; Ehrmann et al., 1999).

Taking into consideration the known association between leptin, obesity and insulin action, it is possible to assume that leptin might have a role in PCOS. However, so far this point has been addressed only peripherally, and with contradictory results: some investigators report a significant increase in leptin concentrations in PCOS (Brzechffa et al., 1996), while others report that the significance of the increase is lost when leptin concentrations are adjusted for BMI (Chapman et al., 1997; Laughlin et al., 1997; Mantzoros et al., 1997; Rouru et al., 1997; Carmina et al., 1999; Mantzoros et al., 2000).

There is some evidence that, at the level of the central nervous system, leptin may stimulate gonadotrophin-releasing hormone (GnRH) release from the hypothalamus, and LH and FSH release from the pituitary. This is probably accomplished by the action of leptin on its own receptor and by the promotion of nitric oxide release (Yu et al., 1997). A synchronicity between LH and leptin pulses in the mid–late (Licinio et al., 1998) and early follicular (Sir-Petermann et al., 1999) phase of the menstrual cycle has been recently reported in healthy women, suggesting that leptin may regulate the minute-to-minute oscillations in LH plasma concentrations. Elevated concentrations of LH, or an elevated LH:FSH ratio, both basal and in response to GnRH or GnRH agonist administration, are known to be associated with PCOS. This abnormality has been thought to result from inappropriate hypothalamic GnRH secretion (Yen et al., 1970; Rebar et al., 1976; Burger et al., 1985). Nevertheless, whereas hypersecretion of LH and heightened LH responses to GnRH are evident in non-obese PCOS patients, the presence of obesity in PCOS women attenuates these neuroendocrine abnormalities (Dale et al., 1992; Grulet et al., 1993; Holte et al., 1994b; Morales et al., 1996; Arroyo et al., 1997; Taylor et al., 1997). It is possible that in these women, hyperprolactinaemia could interfere with the mechanism of LH hypersecretion.

Therefore, the objective of the present study was to assess the influence of leptin on LH, and to investigate the potential association of leptin with body mass index (BMI), waist:hip ratio (WHR), androgen concentrations, fasting insulin and insulin:glucose ratio in women with PCOS and in age- and weight-matched women with regular, ovulatory menstrual cycles and idiopathic hirsutism (IH).

Material and methods

Patients

The study population included women treated for hirsutism, seen consecutively during a 2 year period at the Gynecological Endocrinology Unit at Hospital de Clínicas de Porto Alegre, Brazil. Late-onset (non-classic) congenital adrenal hyperplasia patients were excluded on the basis of a high plasma concentration of 17-hydroxyprogesterone (>15.1 nmol/l) and/or its marked increase after adenocorticotrophic hormone stimulation (>30 nmol/l) (Spritzer et al., 1990; Aziz et al., 1994). Patients with hyperprolactinaemia (serum prolactin concentrations >20 µg/l on two different occasions) were also excluded.

Forty-seven patients, aged 13–39 years, were selected for the study. None had received any drugs known to interfere with hormonal concentrations for at least 3 months before the study. The mean score for hirsutism, assigned by the original published method (Ferriman and Gallwey, 1961), was 19 ± 6. Twenty-seven patients were diagnosed as having PCOS and 20 as having idiopathic hirsutism (IH). Twenty-six were overweight or obese, with a BMI >25 kg/m² (18 in the PCOS group and eight in the IH group).

The diagnosis of PCOS was based on the physical features of hyperandrogenism, disturbed menstrual cycles, elevated serum LH concentrations or LH:FSH ratio, increased concentrations of serum testosterone and/or androstenedione, ultrasound evidence of bilateral enlarged polycystic ovaries (Adams et al., 1986; Herter et al., 1996) and absence of ovarian or adrenal neoplasm or Cushing’s syndrome.

Idiopathic hirsutism was diagnosed, as previously described (Spritzer et al., 2000), in hirsute patients with regular, ovulatory cycles (luteal phase progesterone concentrations >3.8 ng/ml), normal androgen concentrations, and without any known underlying disease. Since IH women presented the same age, BMI, and degree of hirsutism as PCOS women, but without the chronic anovulation, menstrual disturbances, and hormonal alterations that characterize PCOS, in the present study these hirsute ovulatory women were considered as a control group. For the assessment of leptin concentrations and metabolic variables, the population was stratified into four groups, according to diagnosis and BMI: normal weight PCOS patients; normal weight IH patients; overweight (BMI >25 kg/m²) PCOS patients; and overweight IH patients.

Table I shows the baseline clinical features and hormone profiles of the patients with PCOS and IH, and a comparison with reference features and hormone concentrations in a group of 13 normal women. The study protocol was approved by the local Ethics Committee, and written informed consent was obtained from all subjects.

Study protocol

Anthropometric measurements included body weight, height, waist: hip ratio (WHR) (waist circumference was recorded at the narrowest point or at the umbilicus, and hip circumference at the level of the greater trochanter), and BMI (current measured weight in kg divided by height in m²).

All studies were performed after a 3 day 300 g carbohydrate diet. The hormonal and metabolic assessment was made between days 2 and 10 of the menstrual cycle or on any day when the patients were amenorrhoeic. After an overnight fast, blood samples were drawn from an antecubital vein for determination of plasma glucose and insulin. Blood samples were also drawn for leptin, LH, FSH, sex hormone binding globulin (SHBG), total testosterone and androstenedione determinations. All samples were obtained between 08:00 and 10:00.

The free testosterone index was estimated as testosterone (nmol/l)/SHBG (nmol/l)×100. Fasting insulin:glucose ratio (IGR, µIU/mg) was calculated by dividing fasting serum insulin by fasting serum glucose, as previously reported (Spritzer et al., 1998). The threshold hold value to define hyperinsulinaemia was arbitrarily established at 23 µIU/ml, taking into consideration the upper normal limit for insulin (25 µIU/ml) and for glucose (110...
mg/dl), and confirmed by receiver operating characteristic (ROC) curve analysis.

**Assays**
Glucose was measured by the glucose oxidase technique using Mega Merck Kits (Darmstadt, Germany). Serum LH and FSH were measured by specific immunofluorimetric assay (Wallac, Turku, Finland) with intra- and inter-assay coefficients of variation (CV) of 6.7 and 11% respectively for LH, and 6.6 and 10.2% for FSH. The sensitivity of the assays was 0.12 IU/l for LH and 0.05 IU/l for FSH. Serum androstenedione (A) concentrations were measured using the radioimmunoassay method (Diagnostic Products Corp., Los Angeles, CA, USA) with an assay sensitivity of 0.06 ng/ml, and intra- and inter-assay CV of 4.2 and 7.8% respectively. Total serum testosterone concentrations were measured with the radioimmunoassay method (Diagnostic Products Corp.) with an assay sensitivity of 0.04 ng/ml, and intra- and inter-assay CV of 8.5 and 10.3% respectively. SHBG was measured by chemiluminescent enzyme immunoassay (DPC, Los Angeles, CA, USA) with an assay sensitivity of 0.2 nmol/l, and intra- and inter-assay CV of 6.1 and 8.0% respectively. A double antibody radioimmunoassay (CIS Bio International, Bedford, MA, USA), measured serum insulin concentrations with an assay sensitivity of 2.0 μIU/ml, and intra- and inter-assay CV of 7.5 and 9%, respectively. Serum leptin concentration was measured with specific leptin immunoradiometric assay kit (Diagnosis Systems Laboratories, Inc., Webster, TX, USA) with an assay sensitivity of 0.10 ng/ml, and intra- and inter-assay CV of 5.7 and 6.3%, respectively.

**Statistical analysis**
Results are presented as means ± SD, unless otherwise noted. Comparisons between group means were analysed by two-way analysis of variance (ANOVA) followed by the Student-Newman-Keuls test; comparisons between median values were analysed using the Kruskal-Wallis and Dunn tests. Spearman’s rank correlation coefficients were calculated between variables using a two-tailed test for significance. Partial correlations of fasting insulin concentrations and IGR, LH and androgen concentrations with leptin were calculated (adjusted for BMI). A forward stepwise multiple regression model was also calculated for patients with PCOS in order to explore the relationship between LH concentration as a dependent variable and leptin, IGR and BMI as independent variables. Log_{10} transformation was used to normalize the distribution of non-Gaussian variables and mean values were back-transformed for presentation.

All analyses were performed using the Statistical Packages for the Social Sciences (SPSS, Chicago, IL, USA). Data were considered to be significant at P < 0.05.

**Results**
Table II shows leptin measurements and anthropometric and metabolic data for patients with PCOS and IH. For this analysis, patients were stratified into four groups according to BMI: normal weight PCOS patients; normal weight IH; overweight (BMI > 25 kg/m²) PCOS patients; and overweight IH patients. Leptin concentrations were significantly higher in obese PCOS women than in normal-weight women with either PCOS or IH (P = 0.0028), but did not differ between obese women with PCOS and IH. Waist:hip ratios, insulin concentrations and IGR were significantly higher in obese PCOS patients in comparison with all the other groups. As shown in Figure 1, there was a strong correlation between serum leptin concentrations and BMI and WHR in both PCOS and IH women.

Table III shows the correlation between leptin and fasting insulin concentrations, fasting IGR, LH and androgen concentrations in PCOS and IH patients. In IH patients, leptin concentrations were correlated only to WHR. However, the significance was lost after adjustment for BMI. In PCOS patients, a significant correlation was observed between leptin and fasting insulin concentrations, IGR, WHR and LH. After adjustment for BMI, only the correlation between leptin and LH remained significant.

Taking into consideration the results of the BMI-adjusted analysis, in which a negative correlation between leptin and LH was observed only in PCOS patients, independently of BMI, a stepwise regression model was set up with LH as the dependent variable to test the hypothesis that the concentrations of leptin might be influencing the concentrations of LH (Table I). This analysis also aimed at eliminating the influence of hyperinsulinaemia as a possible confounding factor in PCOS patients, and therefore BMI, IGR and leptin concentrations

<table>
<thead>
<tr>
<th>Table I. Clinical and hormonal data for hirsute patients with polycystic ovary syndrome (PCOS) and idiopathic hirsutism (IH) and for normal women</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS (n = 27)</td>
</tr>
<tr>
<td>Age (years)b</td>
</tr>
<tr>
<td>Clinical score for hirsutismb</td>
</tr>
<tr>
<td>Body mass index (kg/m²)b</td>
</tr>
<tr>
<td>Testosterone (ng/ml)b</td>
</tr>
<tr>
<td>Androstenedione (ng/ml)b</td>
</tr>
<tr>
<td>LH (IU/l)c,d</td>
</tr>
<tr>
<td>LH:FSH ratioc,d</td>
</tr>
</tbody>
</table>

aReference values refer to women with regular menstrual and ovulatory cycles and without hirsutism, from the same geographical region and with socio-economic characteristics similar to the study group.
bValues are expressed as mean ± SD.
cValues are expressed as median and 95% confidence interval.
dP < 0.05 versus IH and/or normal women by analysis of variance and Newman-Keuls test (Kruskal-Wallis test followed by Dunn’s test).
Leptin concentrations in PCOS and idiopathic hirsutism

Table II. Leptin concentrations, anthropometric and metabolic data for hirsute patients with polycystic ovary syndrome (PCOS) and idiopathic hirsutism (IH) stratified according to BMI

<table>
<thead>
<tr>
<th></th>
<th>IH (n = 20)</th>
<th></th>
<th>PCOS (n = 27)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMI ≤25</td>
<td>BMI &gt;25</td>
<td>BMI ≤25</td>
<td>BMI &gt;25</td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(n = 8)</td>
<td></td>
<td>(n = 9)</td>
<td>(n = 18)</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.73 ± 0.06</td>
<td>0.81 ± 0.04*</td>
<td>0.73 ± 0.02</td>
<td>0.90 ± 0.07†</td>
</tr>
<tr>
<td>Fasting insulin (µIU/ml)b</td>
<td>16.04 ± 4.66</td>
<td>21.48 ± 11.50</td>
<td>17.5 ± 8.27</td>
<td>34.12 ± 15.29†</td>
</tr>
<tr>
<td>Insulin:glucose ratio (µIU/mg)b</td>
<td>18 ± 5</td>
<td>23 ± 11</td>
<td>20 ± 9</td>
<td>37 ± 16†</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>9.52 ± 1.90</td>
<td>17.04 ± 2.20</td>
<td>11.21 ± 2.10</td>
<td>21.74 ± 2.50‡</td>
</tr>
</tbody>
</table>

*aValues are expressed as kg/m², means ± SD (analysis of variance + Newman-Keuls test).

*P < 0.05 versus IH BMI ≤25; †P < 0.05 versus other three groups; ‡P < 0.05 versus PCOS or IH BMI ≤25.

*bHyperinsulinaemia: insulin >25 µIU/ml and/or insulin:glucose ratio >23 µIU/mg.

Figure 1. (A and C) Correlation between serum leptin concentrations and body mass index (BMI) for polycystic ovarian syndrome (PCOS) and idiopathic hirsutism (IH) patients respectively. (B and D) Correlation between serum leptin concentrations and waist:hip ratio (WHR) for PCOS and IH patients respectively (Spearman’s rank correlation coefficients).

were included as independent variables. These variables were significantly correlated with LH (data not shown).

As shown in Table IV, the relationship of LH concentrations with IGR in PCOS patients was found to be BMI dependent. In contrast, leptin concentrations contributed negatively and significantly to LH concentrations, independently of either BMI or IGR.

Discussion

Women with PCOS are characterized by hyperandrogenaemia, increased LH concentrations, and high incidence of hyperinsulinaemia/insulin resistance and obesity. Thus, PCOS patients may serve as a reliable model to assess the relationship of hyperinsulinaemia and androgen excess with leptin concentrations beyond the association of leptin with obesity per se.
et al. these three parameters with BMI, as previously reported modulated by internal or external factors; such an explanation such a correlation was accounted for by the association of be viewed as a consequence of the activity of an oscillator.

In general, the pattern of pituitary hormone secretion may

Table III. Correlation between fasting insulin concentrations, fasting insulin:glucose ratio, LH and androgen concentrations with leptin concentrations (Spearman’s rank correlation coefficients)

<table>
<thead>
<tr>
<th>Leptin versus:</th>
<th>IH</th>
<th>Adjusted for BMI</th>
<th>PCOS</th>
<th>Adjusted for BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>P</td>
<td>r</td>
<td>P</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.5714</td>
<td>0.021</td>
<td>0.2447</td>
<td>0.379</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.1218</td>
<td>0.630</td>
<td>0.1176</td>
<td>0.664</td>
</tr>
<tr>
<td>Insulin:glucose ratio</td>
<td>0.1623</td>
<td>0.520</td>
<td>0.6022</td>
<td>0.014</td>
</tr>
<tr>
<td>Total testosterone</td>
<td>−0.662</td>
<td>0.801</td>
<td>0.0162</td>
<td>0.952</td>
</tr>
<tr>
<td>Androstenedione</td>
<td>0.2996</td>
<td>0.243</td>
<td>0.1618</td>
<td>0.549</td>
</tr>
<tr>
<td>Free testosterone index</td>
<td>−0.2986</td>
<td>0.229</td>
<td>−0.5460</td>
<td>0.029</td>
</tr>
</tbody>
</table>

IH = idiopathic hirsutism; PCOS = polycystic ovarian syndrome; R = correlation coefficient; r = partial correlation coefficient.

Table IV. Model-fitting results for stepwise regression of LH concentrations versus body mass index (BMI), insulin:glucose ratio (IGR) and leptin concentrations with significantly correlated variables for polycystic ovary syndrome.

<table>
<thead>
<tr>
<th>LH concentrations versus independent variables</th>
<th>Coefficient ± SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>1.950 ± 0.803</td>
<td>0.032</td>
</tr>
<tr>
<td>Leptin</td>
<td>−0.880 ± 0.349</td>
<td>0.027</td>
</tr>
<tr>
<td>IGR</td>
<td>−0.506 ± 0.323</td>
<td>0.143</td>
</tr>
</tbody>
</table>

*Values for leptin, BMI, IGR and LH are log_{10}-transformed. Model regression (analysis of variance) three predictors: constant, BMI, IGR, leptin.

In the present study, PCOS women were assessed and compared with a group of IH women. We believe that these ovulatory IH women are an especially apt control group, since their age, BMI and degree of hirsutism are similar to those of PCOS women; however, they do not present the clinical and hormonal alterations that are typical of PCOS.

Recent studies have shed some light on the possible effects of insulin and/or insulin resistance on leptin, and insulin has been shown to modulate leptin gene expression (Saladin et al., 1995; Friedman and Halaas, 1998). In addition, a number of studies have examined the relationship between leptin and insulin resistance or insulin concentration independently of obesity, although with contradictory results.

In this study, both insulin and IGR were used as markers of insulin sensitivity. Previous reports have shown that in non-diabetic subjects, fasting insulin is closely correlated with more direct measures of insulin resistance (Laakso, 1993). Moreover, insulin:glucose ratio or glucose:insulin ratio have also been shown to be useful measures of insulin resistance in women with PCOS (Parra et al., 1994; Legro et al., 1998; Spritzer et al., 1998).

We observed a correlation between serum leptin concentrations and fasting serum insulin and IGR in PCOS. However, such a correlation was accounted for by the association of these three parameters with BMI, as previously reported (Chapman et al., 1997; Laughlin et al., 1997; Mantzoros et al., 1997; Rouru et al., 1997). Regarding the association of leptin with PCOS, as serum leptin concentrations were similar in PCOS patients and in BMI-matched IH women, the idea (Brzechffa et al., 1996) that circulating leptin concentrations would be elevated in insulin resistant states, such as PCOS, independently of obesity, is not supported by our data, in agreement with other studies (Laughlin et al., 1997). In addition, the correlation between BMI and WHR with serum leptin concentrations, observed in both PCOS and IH patients, and previously reported (Considine et al., 1996; Chapman et al., 1997; Gennarelli et al., 1998), is consistent with the presence of leptin in the circulation in amounts strongly linked to the quantity of adipose tissue and to the high correlation between body fat stores and BMI. Together, these findings provide evidence that circulating leptin in PCOS is related to the overall and central adiposity that is frequently associated with this syndrome, and not directly related to PCOS itself.

Despite the increasing knowledge regarding leptin physiology (Ahima et al., 1996), the relationship between the LH axis and leptin has only recently become the focus of attention. Laughlin et al. observed a BMI-dependent inverse correlation between 24 h mean LH concentrations and 24 h mean LH pulse amplitude and leptin concentrations in PCOS patients, but not in normal cycling women (Laughlin et al., 1997). Moreover, another study (Sir-Petermann et al., 1999) demonstrated a weaker synchronicity, as well as a phase shift between LH and leptin pulses in PCOS patients in comparison with normal cycling women.

In the present paper, we observed a negative correlation between leptin and LH concentrations in PCOS patients, but not in ovulatory women with IH. This correlation remained significant even after adjustment for BMI. Furthermore, a stepwise regression model showed that the negative correlation between leptin and LH concentrations is independent of either BMI or IGR. The independent negative association of leptin and LH concentrations reported here was only evident for patients with PCOS.

In general, the pattern of pituitary hormone secretion may be viewed as a consequence of the activity of an oscillator modulated by internal or external factors; such an explanation could account for the modulatory effect of leptin on GnRH-
LH secretion (Yu et al., 1997; Sir-Petermann et al., 1999). In PCOS, there is a basal pathological condition of increased GnRH pulsatility and hypersecretion of LH. This is characteristically expressed by high LH concentrations under basal conditions or in response to GnRH administration, except in a considerable number of obese patients (Givens et al., 1976; Laatikainen et al., 1983; Dale et al., 1992; Gruet et al., 1993; Oppermann et al., 1993; Holte et al., 1994b; Morales et al., 1996; Taylor et al., 1997). Thus, we speculate that the attenuation in basal or stimulated response of LH in obese PCOS patients might be related to a weaker modulation of the GnRH oscillator by a leptin-resistant state. In IH ovulatory Gennarelli, G., Holte, J., Wide, L. et al. PCOS patients might be related to a weaker modulation of the weight in mammals. Diabetes Care, 22, 141–146.


Leptin concentrations in PCOS and idiopathic hirsutism


References


Received on October 17, 2000; accepted on March 14, 2001