Clomiphene Citrate and LH Pulsatility in PCO Syndrome

Teresa Sir, F. Alba, L. Devoto and W. Rossmanith
University of Chile, Santiago, Chile and Universitäts-Frauenklinik, Universität Ulm, Ulm, Germany

Introduction

Although administration of Clomiphene citrate (CC) is effective in inducing ovulation in patients with polycystic ovary syndrome (PCO), 15 to 20% of PCO patients do not ovulate in response to CC treatment (*Garcia, Jones* and *Wentz* 1977). The purpose of this study was to compare the endocrine dynamics (LH pulsatile patterns, FSH and steroid hormone secretion) of PCO patients who ovulated and those who failed to ovulate in response to CC therapy.

Methodology

The study was conducted in patients with endocrinologically and morphologically confirmed PCO disease. 12 PCO women were subjected to CC administration (up to 100 mg CC/day from cycle day 5 to 9) for three consecutive cycles. 6 women showed an increase in progesterone (P) concentrations of more than 6 ng/ml 11–18 days after initiation of CC treatments and were thus considered to have ovulated (PCOS). 6 other women did not respond to this CC regimen with increased P levels (PCOR). At the beginning of the study, a single blood sample for the determination of basal hormone levels (LH, FSH, prolactin (PRL), testosterone (T), dehydroandrosterone-sulfate (DHAS), 17-OH-progesterone (17-OHP), estrone (E1) and sex hormone binding globulin (SHBG)) was obtained from all women. In the first cycle (control), blood was collected at 15 min intervals for 4 hrs on day 9 in all women, and this regimen was repeated on day 9 of the subsequent cycle (treatment: CC 100 mg/day from day 5 to 9). LH was then determined in all samples and FSH and estradiol (E2) every 60 min by RIA (*Devoto, Soto, Magofke* and *Sierralta* 1980). In addition, follicular maturation was assessed by transabdominal ultrasounds in both cycles. Ovulatory cycles were established by observation of increased body temperatures and serum P levels (exceeding 6 ng/ml) at the latest on day 10 after discontinuation of CC therapy. LH pulsatile activity was assessed by a pulse algorithm (*Veldhuis, Rogol* and *Johnson* 1985).

Results

No significant differences were observed in the clinical parameters (age, body mass index, degree of hirsutism, ovarian volumes) and endocrinological characteristics (LH, FSH, E1, E2, PRL, T, DHAS, 17-OHP, SHBG) between PCOS and PCOR women. During the control cycle, the LH pulse amplitudes and transverse mean LH levels were higher ($P < 0.05$) in PCOR than in PCOS patients. The LH pulse frequency, however, was similar in both groups. In response to CC, the LH amplitudes and transverse mean LH levels of PCOR patients did not change, while they increased ($P < 0.05$) in PCOS women. FSH and E2 concentrations were comparable in both groups in the control cycle. During CC administrations, FSH and E2 concentrations remained unchanged in PCOR; by contrast, they increased ($P < 0.05$ or less) in PCOS.

Discussion

Although it is known that the LH pulsatility is abnormal in PCO patients in terms of exaggerated LH pulse amplitudes and transverse mean levels (*Yen* 1980), this abnormal LH secretory pattern is not corrected during CC administration in both PCOS and PCOR women. On the contrary, the exaggerated LH pulsatile activity is even further increased during CC treatments in PCOS women. Therefore, it is suggested that other factors than modulations of LH pulsatility may account for the differences in ovarian responses in PCOR and PCOS patients during CC therapies. Since we found significant increases in FSH concentrations during CC administrations exclusively in PCOS patients, we propose that an increase of FSH secretion during CC treatments may be critical and thus may determine the ovulatory responsiveness of PCO patients.

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Requests for reprints should be addressed to:

Dr. W. Rossmanith
Universitäts-Frauenklinik
Universität Ulm
Prittwitzstr. 43
D-7900 Ulm/Donau (Germany)

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