Gonadotropin dysfunction in women with polycystic ovary syndrome

Ann E. Taylor, M.D.

Pfizer Global Research and Development, Groton, Connecticut

Abnormal gonadotropin secretion, especially increased mean LH levels, is one of the most common findings in women with polycystic ovary syndrome (PCOS). Increased LH pulse frequency and amplitude is detected if blood is sampled frequently and long enough (at least every 10 min) (1). Follicle-stimulating hormone may be normal or low, leading to an elevated LH/FSH ratio compared with normally cycling early follicular phase young control women.

Recent studies have demonstrated, somewhat surprisingly, that LH tends to be more normal, rather than worse, in obese women with PCOS. Lean women with PCOS have the highest LH pulse amplitude compared with very overweight women with PCOS who can have relatively normal LH pulse amplitudes (2). A similar inverse correlation is observed with serum insulin levels. In a pilot study, women with PCOS who lost weight over 3 to 6 months of a diet program tended to have an increase in serum LH, suggesting that something associated with weight was the driver for the modification of LH secretion. This finding may suggest that some metabolic factor may modulate gonadotropin secretion in women with PCOS. Pulse frequency does not associate with body mass index (BMI), suggesting that the metabolic factor could impact pulse amplitude at either the pituitary or the hypothalamus.

Another strong factor influencing LH secretion is recent ovulation. When the assessment of pulsatile LH secretion is normalized for time from last spontaneous menses, women who have recently ovulated (in the luteal phase or early follicular phase [before day 7] after a spontaneous ovulation) have relatively normal LH levels. We hypothesize that the negative feedback from normal progesterone secretion from the corpus luteum is adequate to provide normal negative feedback to the hypothalamus and pituitary in PCOS women. This observation is consistent with recent reports from others suggesting that women with PCOS may be less sensitive to low levels of progesterone but respond normally to high levels (3, 4).

These findings, that both recent ovulation and body size independently influence LH secretion in women with PCOS, likely explain many of the differences in the PCOS literature regarding the prevalence of LH defects. In our studies, when recent ovulation is excluded and LH is normalized for BMI, up to 90% of women meeting clinical National Institutes of Health criteria for PCOS have abnormal gonadotropin secretion. We expect that lower rates of LH defects will be detected when last menstrual period is not recorded, when subjects are studied after a progesterone induced withdrawal bleed, or when the studied population is mostly overweight.

To investigate whether exaggerated LH secretion is related to polycystic ovarian (PCO) morphology by ultrasound, we studied women with regular ovulatory menstrual cycles, 21 with PCO morphology and 24 with normal ovarian morphology (4). The LH levels were identical in daily samples and in frequent sampling sessions between the two groups of women, although androgen levels were higher in women with the PCO morphology. This finding suggests that elevated LH levels are not required for increased ovarian androgen secretion, and it is consistent with in vitro studies of human ovarian samples indicating that the PCOS ovary hypersecretes androgens independent of circulating stimuli.

REFERENCES