Preovulatory Serum Gonadotropin Levels in hMG Stimulated Menstrual Cycles in Pregnant and Nonpregnant Patients

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Summary. In a group of patients undergoing in vitro fertilization, 10 pregnant and 10 nonpregnant, cycles were analysed in retrospect in relation to gonadotropin and steroid hormones. All patients were similar in terms of age, body surface area and initial stimulation protocol. The increase in follicles stimulating hormone (FSH) was significantly higher in the pregnant group through cycle day 8 as compared with cycle day 3 before stimulation. A significant increase in the nonpregnant group was never detectable; the mean FSH levels rather decreased to the baseline value during stimulation after a slight nonsignificant increase. The levels of luteinizing hormone (LH) decreased significantly in pregnant and nonpregnant patients during stimulation. No significant difference in the FSH/LH ratio between the pregnant and nonpregnant group was encountered. Although the mean serum estrogen in the follicular phase and the serum estrogen and progesteron values in the luteal phase were higher in the pregnant patients, no statistically significant difference between groups could be demonstrated, until luteal day 11. It is believed from this study, that a 15–20% increase in serum FSH levels over baseline during the early and mid follicular phase is required for adequate follicular development and steroidogenesis. The determination of serum gonadotropins in the follicular phase in patients who failed to conceive, might reveal differences, which can account for failures in hMG induced cycles.

Key words: IVF – Gonadotropins – Ovulation induction

Introduction

Inappropriate levels of gonadotropins may be the cause of inadequate preovulatory follicular development and subsequent luteal phase dysfunction. Specifi-
cally, adequate serum FSH levels seem to be mandatory throughout the follicular phase for normal folliculogenesis and steroidogenic function of the preovulatory follicle and subsequent corpus luteum [20].

The program of in vitro fertilization at Norfolk has recently reported the analysis of steroid hormones in pregnant and nonpregnant patients with irreparable tubal disease, stimulated by human menopausal gonadotropins (hMG)/human chorionic gonadotropin (hCG) for the purpose of in vitro fertilization. Pregnancy rates seem to be related to the peripheral estradiol (E2) responses and progesterone (P) levels in the luteal phase of the cycle [12, 16].

Since ovarian steroid production is a result, among other factors, of normal gonadotropin secretion observed during the menstrual cycle, an attempt was made in this study to correlate peripheral gonadotropin levels in induced menstrual cycles with steroid hormones levels, specifically E2 and P, in patients who did and did not achieve pregnancy. Furthermore, as a FSH-dose related response in follicular recruitment and steroidogenesis has been described [1, 10], it seemed appropriate to analyze the hormonal patterns only in patients with a similar stimulation protocol, age and body surface area.

Patients and Methods

Between April 1982 and December 1983 (Norfolk Series 4–12) 263 cycles in 216 patients were stimulated with 2 ampules hMG$^1$ (150 IU of FSH/150 IU of LH) per day, starting on cycle day 3. Fifty-four pregnancies resulted. Twenty cycles from twenty patients, 10 pregnant and 10 nonpregnant, were selected from these series in regard of similar body mass and composition, age and initial stimulation protocol, for the purpose of this study. All patients were cycling normally and had no endocrine dysfunction at the time of the stimulation. All these patients had irreparable tubal disease. The mean age at the time of treatment showed no difference in the pregnant and nonpregnant patients: 32.12 ± 0.95 years (mean ± SEM) and 33.66 ± 1.24 years respectively. The body surface area [4], calculated by weight and height was similar for both groups (1.59 ± 0.03 m² and 1.70 ± 0.04 m² respectively). All pregnant patients carried their pregnancy to term except for one patient who had a premature delivery at 27 weeks due to a true knot in the umbilical cord.

Blood was drawn at approximately 8.00 am daily for E2 determinations during the follicular phase and, for E2 and P evaluation every other day during the luteral phase; luteral day 1 being the day of laparoscopy.

Serum values for E2 and P were measured by direct and indirect radioimmunoassay respectively [9] (Pantex Corp., Santa Barbara, California). The minimum concentration of E2 and P detectable was 10 pg/ml and 0.5 ng/ml respectively. The interassay and intraassay coefficients of variation were 10% and 8.3% for E2 and 11.2% and 9.4% for P. Serum FSH and LH were measured in a single assay to avoid interassay variation, utilizing a modified radioimmunoassay kit for LH [9, 18] (Diagnostic Products, Los Angeles, California). The minimum concentration of gonadotropin detectable was 1 mIU/ml for FSH and 1.5 mIU for LH. The intraassay coefficient of variation was 5.7% for LH and 6.9% for FSH.

Beginning on day 3 of the menstrual cycle, all patients were stimulated with hMG administered intramuscularly at 4.00 pm daily. Determinations of the karyopyknotic index in the vaginal smear, cervical mucus examinations and ultrasound measurements of the follicle size were made daily after day 6 of the cycle according to a protocol published previously [5, 11]. The stimulation schedule for cycle days 3, 4, 5, 6 and 7 was in all patients 2 ampules of hMG per day and not statistically significant different during the entire treatment. HMG was discontinued when the serum E2

$^1$ Pergonal (Serono, Randolph, MA) was administered in the clinic and the FSH/LH ratio was always close to 75 IU FSH/75 IU LH