

Estradiol production during controlled ovarian hyperstimulation correlates with treatment outcome in women undergoing in vitro fertilization–embryo transfer

Mohamed F. M. Mitwally, M.D.,^{a,c} Helmata S. Bhakoo, Ph.D.,^{a,b} Kent Crickard, M.D.,^{a,d}
Michael W. Sullivan, M.D.,^{a,d} Ronald E. Batt, M.D.,^a and John Yeh, M.D.^a

^aDepartment of Gynecology-Obstetrics, School of Medicine and Biomedical Sciences, and ^bBiotechnical and Clinical Laboratory Sciences, State University of New York, Buffalo, New York; ^cDivision of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Wayne State University, Bloomfield Hills, Michigan; and ^dInfertility and IVF Associates, Snyder, New York

Objective: To study the value of E₂ production during controlled ovarian hyperstimulation (COH) in predicting IVF-ET outcome.

Design: Historical cohort.

Setting: Academic infertility center.

Patient(s): A cohort of 270 patients who completed 324 consecutive IVF-ET treatment cycles.

Intervention(s): None.

Main Outcome Measure(s): Area under the curve for E₂ levels (AUC-E₂) from the first day of COH until the day of hCG administration was calculated and cycles grouped into low, average, and high AUC-E₂ groups. Clinical pregnancy rates per cycle were compared among the three groups, and correlations with AUC-E₂ values were calculated for all patients and after sub-grouping according to age, COH protocol and infertility diagnosis.

Result(s): Cycles with low and high AUC-E₂ values had significantly lower pregnancy rates particularly in patients 35 years or older. There was a positive correlation between AUC-E₂ and pregnancy rates up to a certain AUC-E₂ level above which a negative correlation was found. The turning point between positive and negative correlations occurred at a significantly lower AUC-E₂ level in patients 35 years or older.

Conclusions: Estradiol production during COH correlates with IVF-ET outcome. Women >35 years of age seem more vulnerable to high E₂ levels. (Fertil Steril® 2006;86:588–96. ©2006 by American Society for Reproductive Medicine.)

Key Words: Area under the curve, controlled ovarian hyperstimulation, estradiol, IVF-ET

Since the birth of Louise Brown in 1978, IVF-ET has become the therapeutic mainstay for female infertility, with rapid expansion of IVF clinics worldwide resulting in >1% of children being conceived by some form of assisted reproduction (1). In most IVF-ET cycles, gonadotropins are used alone or in combination to stimulate the growth and maturation of multiple oocytes, a process called controlled ovarian hyperstimulation (COH). This is essential because of the need to recruit a greater number of follicles, which allows retrieval of several oocytes. This would improve the chance of fertilization and allow an increased number of embryos for transfer to give acceptable success rates. It is clear that supraphysiologic levels of E₂ are inevitably attained during COH owing to the development of multiple ovarian follicles, each contributing significantly to E₂ production which can

reach levels up to 10 times or more those found during spontaneous cycles (2, 3).

The effect of such supraphysiologic E₂ levels on the outcome of IVF-ET has been the subject of intense debate with conflicting evidence (4, 5). Some investigators have shown that supraphysiologic levels of E₂ have a detrimental influence on endometrial receptivity and IVF outcome (6–16). However, others did not find high E₂ levels to be detrimental to IVF outcome (17–25).

Most of the studies observed E₂ concentrations attained on the day of hCG administration rather than considering E₂ levels along the whole period of ovarian stimulation. Calculating the area under the curve for E₂ levels (AUC-E₂) along the several days of COH is expected to reflect more accurately the amount of E₂ produced, because it takes into consideration both the duration of ovarian stimulation and several E₂ levels rather than a single level on the day of hCG administration. Recently, we reported that although the overall AUC-E₂ correlated with E₂ concentrations attained on the day of hCG administration, there was no uniform correlation between successive individual patients, and that different

Received July 12, 2005; revised and accepted February 2, 2006.
Presented in part at the 59th Annual Meeting of the American Society for Reproductive Medicine, October 11–15, 2003, San Antonio, Texas.
Reprint requests: John Yeh, M.D., Department of Gynecology and Obstetrics, State University of New York, 239 Bryant Street, Buffalo, New York 14222 (FAX: 716-888-3833; E-mail: jyeh@buffalo.edu).

conclusions can be obtained when studying E₂ levels attained during COH by looking at E₂ levels on the day of hCG administration rather than AUC-E₂ (26). The present study looks at the correlation between E₂ levels attained during COH calculated as AUC-E₂ and the outcome of IVF-ET treatment as achievement of clinical pregnancy.

METHODS

After obtaining approval from the State University of New York at Buffalo's Institutional Review Board, we retrospectively analyzed data from charts of patients who underwent completed IVF-ET cycles and had a fresh ET.

The study was conducted in conjunction with the Infertility and In Vitro Fertilization Associates of Western New York, an academic tertiary referral IVF-ET center affiliated with the Department of Gynecology-Obstetrics, State University of New York, Buffalo.

Data were obtained from charts of the patients who underwent IVF-ET treatment during the period from January 2001 to July 2002. The study included patients who received COH and had E₂ levels checked at least every other day from the first day of COH until the day of hCG administration. We included patients who had their E₂ levels assayed at the same laboratory, applying immunoassay methods that had similar intraassay and interassay coefficient factors.

We found 270 patients, who completed 324 IVF-ET cycles, who met the admission criteria. Stimulation was performed with a starting dose of 150–225 IU recombinant FSH or a combination with highly purified FSH. The starting dose was decided based on the patient's clinical profile, including age, body mass index, and response in a prior gonadotropin stimulation cycle. The dose was adjusted to reach an optimum number of three follicles of ≥18 mm present on ultrasound; at that time, final oocyte maturation was achieved by administration of 10,000 IU hCG. Pituitary down-regulation was done as previously described according to the long GnRH agonist (27) or microdose (28) protocols. Owing to the retrospective nature of this study, we could not obtain embryo quality data that was valuable enough for comparison between the different groups. This was mainly due to the use of different embryo scoring systems.

Analysis of Data

Area under the curve for E₂ levels was calculated for each IVF-ET treatment cycle. The AUC-E₂ was calculated from the available E₂ concentrations along the follicular phase starting on the first day of COH until the day of hCG administration. The AUC was calculated as previously described (48).

Treatment cycles were grouped into cycles with low, medium, and high AUC-E₂. The low AUC-E₂ group included cycles in which AUC-E₂ was less than the mean minus 1 SD, the high AUC-E₂ group included cycles in

which AUC-E₂ was more than the mean plus 1 SD, and the medium AUC-E₂ group included cycles in which AUC-E₂ was between that of the other two groups (mean ± 1 SD). Clinical pregnancy (defined as confirmation of fetal cardiac activity with transvaginal ultrasound approximately 4–6 weeks after embryo transfer) rates per cycle were compared among the three study groups in all cycles and after subgrouping according to age (<35 and ≥35 years), protocol applied for COH (long GnRH agonist and microdose), and infertility diagnosis (tubal, male, anovulatory, unexplained, and combined [more than one factor]).

To look at the correlation between AUC-E₂ and clinical pregnancy rate per cycle, treatment cycles were grouped according to AUC-E₂ values (increments of 3,000 pg/mL per day). Correlation between AUC-E₂ and clinical pregnancy rate per cycle was calculated for all cycles and for subgroups of cycles according to age, COH protocol, and infertility diagnosis.

RESULTS

Table 1 shows the patients' characteristics, including age, duration of infertility, number of prior IVF-ET cycles, and gravidity. These characteristics were compared among the study groups (low, medium, and high AUC-E₂) for all cycles. It is interesting that there were no statistically significant differences in any of those characteristics (data not presented).

Table 2 shows the mean value of AUC-E₂ (pg/mL per day) for the three study groups (low, medium, and high AUC-E₂) for all cycles and after subgrouping according to age and stimulation protocol. Although the mean of AUC-E₂ tended to be higher in cycles for patients <35 years old and in long GnRH agonist stimulation protocol cycles, the difference was not statistically significant. The closeness of the value of the median for AUC-E₂ to the value of the mean in all subgroups indicates a normal distribution of the AUC-E₂ values around the median. Such normal distribution is seen in Figure 1, showing the percentage distribution of AUC-E₂ values among cycles for patients <35 and ≥35 years old (Fig. 1A) and long GnRH agonist and microdose stimulation protocols (Fig. 1B). As the figures show, the low and high

TABLE 1

Patient characteristics.

Characteristic	Mean	Median	SD	Range
Age (y)	35.1	34	3.9	20–44
Duration of infertility (mo)	35.8	36	25	6–184
Number of prior IVF cycles	0.86	1	0.61	0–4
Gravidity	0.85	1	1.1	0–6

Mitwally. E₂ production and IVF outcome. Fertil Steril 2006.

Download English Version:

<https://daneshyari.com/en/article/3940982>

Download Persian Version:

<https://daneshyari.com/article/3940982>

[Daneshyari.com](https://daneshyari.com)