
REPRODUCTIVE SCIENCE

The Significance of Basal Follicular Stimulating Hormone and Luteinizing Hormone of Previous Cycle in Prediction of the Outcome of In Vitro Fertilization

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ABSTRACT

Objective To determine the effect of basal follicular stimulating hormone level on day 3 of previous cycle on the ovarian response and clinical pregnancy rate in the treatment of infertility by IVF-ET.

Design A prospective descriptive study.

Setting A tertiary infertility service in an academic university hospital.

Subjects Thirty-eight infertile patients without male factor treated with IVF-ET under long protocol using GnRH agonist. Blood samples were taken on day 3 of previous cycle prior to ovarian stimulation.

Main outcome measures Numbers of ampoule of FSH and hMG, peak serum E₂, numbers of oocytes collected, and clinical pregnancy rate.

Results Numbers of ampoule of FSH and hMG used were significantly lower in high FSH group (> 8 IU/L). Clinical pregnancy rate in the low, medium, and high FSH group were 20%, 11.8%, and 0% respectively.

Conclusion The results suggested that a high basal serum FSH level is associated with a higher cancellation rate, a lower peak serum E₂ level, lower number of oocytes retrieved and a lower clinical pregnancy rate.

Key words : In Vitro Fertilization, FSH, LH, outcome prediction

Multiple variables affect the likelihood of conception from assisted reproduction. Several investigators have demonstrated the role of

hormonal regulation during ovulation, fertilization, and implantation period.⁽¹⁾ Since the advent of in vitro fertilization (IVF), improved pregnancy rates

per embryo transfer have remained a constant but elusive goal. Despite the rapid development in assisted reproduction, the pregnancy rate has remained at about 15-20% per treatment cycle.⁽²⁾ Much research has been done recently to look for prognostic indicators in vitro fertilization. Various authors have shown that a high serum follicular stimulating hormone (FSH) level after clomiphene citrate correlated to cancellation of the cycle⁽³⁾ due to a poor ovarian response^(4,5) and is predictive of pregnancy outcome.⁽⁶⁾ We used gonadotropin stimulation protocol which consisted of both FSH and LH for ovarian stimulation. Toner et al⁽⁷⁾ and Khalifa et al⁽⁸⁾ also reported on the predictive value of basal FSH levels but patients with different stimulation protocols were included. Hughes et al⁽⁹⁾ have shown that for those patients with a poor response to stimulation with clomiphene citrate and gonadotropins, they appeared to benefit from the use of gonadotropin releasing hormone agonist (GnRH-a) treatment. Hence, whether basal serum gonadotropin level is predictive of IVF outcome with this regimen of ovarian stimulation needs to be clarified. The purpose of this report is to assess

whether basal FSH and luteinizing hormone (LH) are predictive of the ovarian response and outcome during treatment with IVF when GnRH-a are also used in the stimulation protocols.

Materials and Methods

From October 1994 to April 1995, infertile patients without male factor treated with IVF at the Department of Obstetrics and Gynaecology, Chulalongkorn University Hospital, were recruited for the study. Blood was taken for serum FSH, LH, and estradiol (E₂) on day 3 of the previous cycle prior to ovarian stimulation. Treatment was started in the next cycle when there was no abnormality detected by ultrasound and the baseline E₂ level was below 50 pg/ml. Intranasal Buserelin (Suprefact; Hoechst AG, Germany), 600 mg daily, was started on day 21. On day 2 of the next cycle, 150 IU of FSH (Metrodin ; Sereno, England) and 150 IU of human menopausal gonadotrophin (hMG; Humegon, Organon, The Netherlands) were given for three days, followed by 150 IU of hMG daily. (Fig.1)

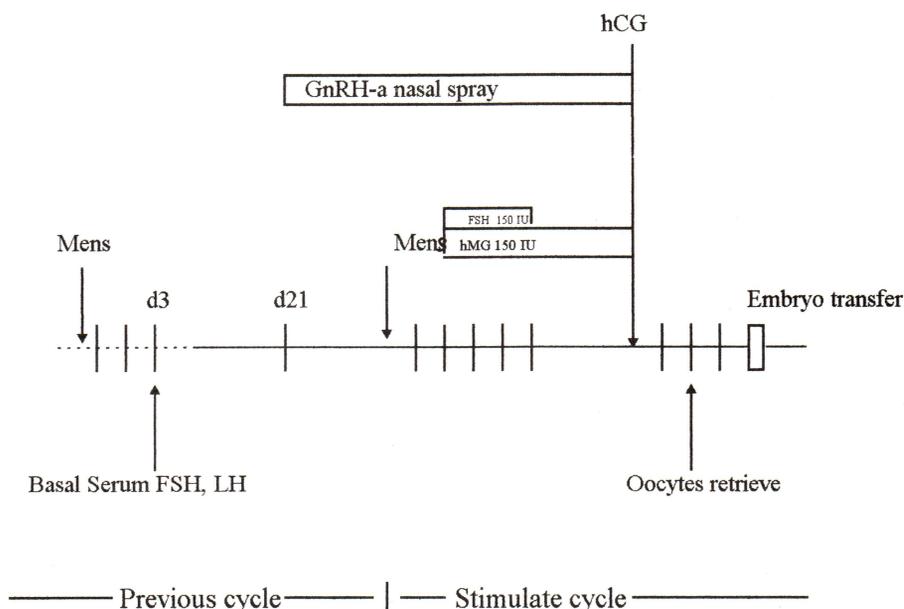


Fig. 1. Diagram of ovarian stimulation protocol.

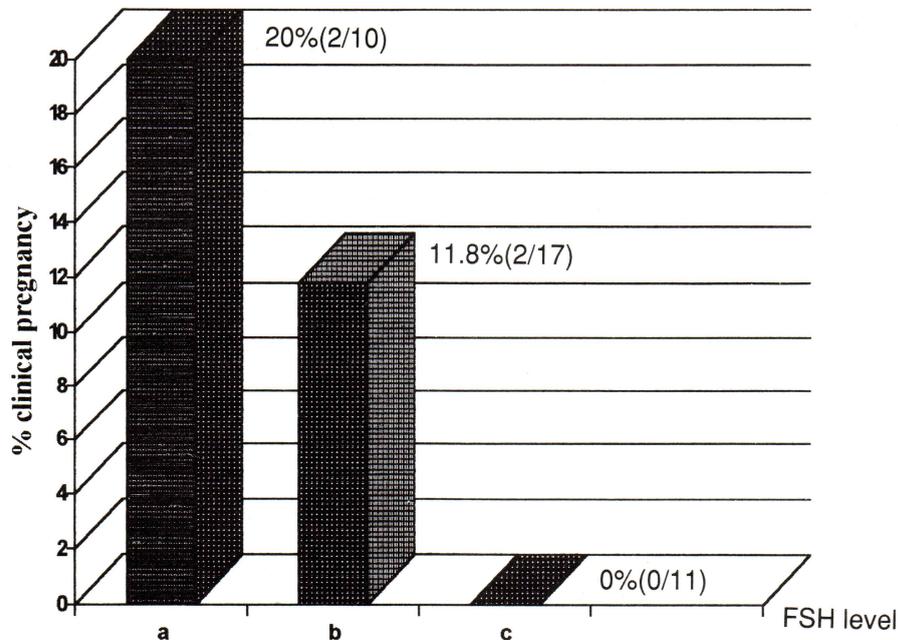


Fig. 2. Clinical pregnancy in patients of each group, (a) Low FSH (< 4 IU/L), (b) Medium FSH (4-8 IU/L), (c) High FSH (> 8 IU/L).

Table 1. The comparison of age and the parameters of ovarian response in patients with different day 3 serum FSH levels

	Basal day 3 serum FSH		
	Low (< 4 U/L)	Medium (4-8 IU/L)	High (> 8 IU/L)
Age (year)	33.2 ± 4.8	35.3 ± 5.4	36.2 ± 5.1
No. of ampoule FSH, hMG	19.1 ± 4.3	22.6 ± 9.4	28.6 ± 10.2*
Peak serum E ₂ (pg/ml)	3,104 ± 1,012	2,480 ± 1,403	1,981 ± 1,214*
No. of oocytes retrieved	16.2 ± 5.4	12.8 ± 6.2	8.4 ± 4.2*
% of fertilization	61.4 ± 30.8	61.2 ± 34.6	62.1 ± 31.4
Cancel cycle	0	0	1
	N = 10	N = 17	N = 11

*Statistically significant, P < 0.05

The ovarian response was monitored with daily serum E₂ level and ultrasonogram starting on day 4. After day 8, serum LH, and E₂ were measured daily and pelvic ultrasonogram was also performed. Human chorionic gonadotrophin (hCG ;

Pregnyl, Organon, The Netherlands) 10,000 IU, was given intramuscularly in the evening when (a) the leading follicle was > 18 mm in diameter, (b) the serum E₂ was > 600 pg/ml, and (c) there were at least three follicles.

Transvaginal ultrasound - guided oocyte retrieval was performed 34-36 hr after hCG injection. The oocytes were incubated for a period of 4 to 6 hr before insemination. Up to four cleaving embryos were transferred about 48 hr after insemination.

Serum FSH, LH and E₂ levels were measured by fluorescent immunoassay.

Analysis of data and statistics were performed using SPSS/PC plus software. The results were expressed as mean ± standard deviation. The differences in the means between the different groups were compared by Student t-test.

Results

Thirty-eight cycles of IVF in patients excluding male factor were evaluated.

All of our patients' serum FSH levels were below menopausal range. The patients were subdivided into three groups based on the day 3 serum FSH levels (a) low, < 4 IU/L (b) medium, 4-8 IU/L (c) high, > 8 IU/L and their ovarian response and outcome are shown in Table I. There was statistically significant differences in the amount of FSH/ hMG required, peak serum E₂ level, number of follicles aspirated, number of oocytes obtained, number of embryos replaced, percentage of cycles canceled, and number of clinical pregnancies per cycle initiated between the low and high - basal serum FSH groups

However, when based on cycle day 3 serum LH levels, the patients were again divided into three groups, the same as FSH. There was no statistically significant difference in the number of ampoules of FSH/hMG used, the peak serum E₂ level, the number of oocytes obtained, or clinical pregnancies among the three groups.

Discussion

The results in this study showed that in

patients stimulated with a combination of GnRH agonists and FSH and hMG in an IVF programme, a high basal serum FSH level is associated with a higher cancellation rate, a lower peak serum E₂ level, lower number of oocytes retrieved and embryos replaced, and a lower clinical pregnancy rate. These results agreed with those previously reported in patients on various types of treatment regimens for ovarian stimulation.^(5,6) Unlike the results of Hughes et al,⁽⁹⁾ our results showed that the addition of GnRH - a to the stimulation regimen could not correct the poor ovarian response. All these results point to the fact that the level of day 3 serum FSH is an indicator of the functional potential of the ovary. The basic control of LH and FSH is by a negative feedback system involving the hypothalamus, anterior pituitary, and ovary. Each component can adjust its activity in proportion to the output of the other components in a dose - related manner. Though none of the patients studied here had FSH level in the menopausal range, a relatively higher level might indicate a lower ovarian functional reserve. This may explain the observation of a poorer ovarian response, which would definitely affect the peak serum E₂ levels, number of oocytes retrieved, and number of embryos replaced. Gindoff and Jewelewicz⁽¹⁰⁾ stated that serum FSH is the most sensitive marker to delineate perimenopausal state and thus it would not be surprising that basal FSH levels could also predict the pregnancy rate.

There was no significant relationship between the ovarian response and the day 3 serum LH. It was shown previously, in patients undergoing IVF treatment given clomiphene citrate and hMG for ovarian stimulation, that the fertilization rate and implantation rate were significantly reduced in those with high basal serum LH.⁽¹¹⁾ Urinary LH cycles was higher than those in conception cycles.⁽¹²⁾ These observations are all

consistent with our findings. However, the predictive value of day 3 serum FSH was better than that of serum LH.

In conclusion, the day 3 serum FSH level is one prognostic indicator in IVF treatment and is especially useful in predicting the ovarian response. It may help the clinician to adjust the ovarian stimulation regimen on an individual basis and also provide further information for counselling of couples who wish to be enrolled in the IVF programme. Although a high day 3 serum LH may be associated with a poor outcome, it is not useful in predicting ovarian response and pregnancy.

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