Which is the Best Predictive Factor of Ovarian Response; Age, Basal FSH or Basal Estradiol

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OBJECTIVE: We have investigated the association between basal estradiol, FSH, age and ovarian response in the present study.

STUDY DESIGN: Three- hundred twenty- nine cycles from 285 patients who admitted to Cukurova University IVF Unit were evaluated. Hormone analysis was done at one day between 3rd-5th day of the menstruel cycle. A long stimulation protocol was used with GnRHa / HMG or recFSH / HCG. 34-35h after HCG injection, an ultrasound guided transvaginal ovum pick up was performed under general anesthesia.

RESULTS: The mean age of the patients was 32.49 ± 0.29 range (19-45). The mean basal FSH levels were 7.40±0.24 mIU/ml (11.38-39.69), mean LH levels were 5.9<±0.19 mIU/ml (1.26-24.68) and mean basal E2 levels were 59.40±1.20 pg/ml (17.102). The mean number of follicles which were ≥18mm and aspirated was 7.04±0.29 with a maximum of 22 follicles. The mean of oocytes picked up was 6.14±0.27 with a maximum of 21. Cycle cancellation rate after IVF was found lower in patients younger than 40, have FSH level < 12 mIU/ml. and estradiol level < 80 pg/ml.

CONCLUSIONS: We found that basal FSH was more useful in evaluation of ovarian response when compared with basal estradiol and age. Combination of basal FSH and E2 is safer to use together for the evaluation of ovarian response.

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Key Words: Ovarian response, Age, FSH, Estradiol

Introduction

Cycle cancellation has negative effect on cost and it is a psychological problem for patients. As well as it costs time. For these reasons it is very important to find out the patients with low ovarian response.[1-3] Advanced maternal age and diminished ovarian reserve may be associated with poor ovarian response.[4] Several hypotheses have been suggested for poor ovarian response such as poor follicular blood flow[5], dysfunctions of cytokines and the growth factor network[6,7], and the presence of ovarian autoantibody.[8]

Reproductive ageing is related to both a quantitative and a qualitative reduction of the primordial follicle pool.[9] There is still no concensus on the topic of predicting the ovarian response. Evaluation of ovarian response gives us an estimation of the result and also important for patient the give and selection. Different clinics use various parameters for this reason.[10-12] Basal FSH[13], basal inhibin B[14], ultrasonographic count of the antral follicles[15] and anti-Müllerian hormone[16] have all been performed in order to assess response to gonadotrophins. The aim of this study is to evaluate which of the factor (s) of age, basal FSH, basal estradiol levels in the ovarian response.

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Material and Methods

In this retrospective study the basal FSH, basal estradiol and chronological age were evaluated in 329 cycles of 285 patients who admitted to IVF Unit of Çukurova University Faculty of Medicine. Radioimmunoassay was used for FSH and estradiol measurements. Minimum detectable value was 0.54 mIU/ml for FSH and 10 pg/ml for estradiol. Hormone analysis was done at one day between 3rd-5th day of the menstruel cycle. A long stimulation protocol was used with GnRHa/HMG or recFSH/HCG. 34-35h after HCG injection, an ultrasound guided transvaginal ovum pick up was performed under general anesthesia. Oocytes were checked 16-20 hour after insemination. Statistical analysis were performed by SPSS 8.0 statistical software, using the oneway ANOVA and Kruskal-Wallis tests.

Results

The mean age of the patients was 32.49±0.29 range (19-45). The mean basal FSH levels were 7.40±0.24 mIU/ml (11.38-39.69), mean LH levels were 5.9<±0.19 mIU/ml (1.26-24.68) and mean basal E2 levels were 59.40±1.20 pg/ml (17.102). The mean number of follicles which were ≥18mm and aspirated was 7.04±0.29 with a maximum of 22 follicles. The mean of oocytes picked up was 6.14±0.27 with a maximum of 21.

The distribution of patients according to the age groups, and the number of cycles,number of oocytes and the cycle cancellation rate was shown in Table 1. The distribution of patients according to the basal FSH levels, and the number of cycles,number of oocytes and the cycle cancellation rate was shown in Table 2. The distribution of patients according to the basal estradiol levels, and the number of cycles,number of oocytes and the cycle cancellation rate was shown in Table 3.

Table 1: Number of cycle,oocytes and percentage of cycle cancellation according to chronological age

Age	<30	30-34	35-39	>40	P value
Cycle	85	100	94	15	
Nr.oocytes	8.0	6.3	4.8	2.8	<0.001
Cycle cancellation (%)	10.6	12.0	17.0	40.0	>0.05

Table 2: Number of cycle,oocytes and percentage of cycle cancellation according to basal FSH levels

Basal FSH mIU/ml	<10	10-11.9	12-14.9	15-19.9	>20	P value
Cycle	238	27	16	9	4	
Nr. oocytes 7.0	4.7	1.9	1.2	0.8	<0.01	
Cycle cancellation (%)	7.6	11.5	56.3	88.9	75	>0.001

Table 3: Number of cycle,oocytes and percentage of cycle cancellation according to basal estradiol levels

Basal E2 pg/ml	<60	60-80	81-100	>100	P value
Cycle	177	68	38	11	
Nr. oocytes	7.9	5.2	1.3	0.8	<0.001
Cycle cancellation (%)	4.5	8.8	47.9	63.6	>0.001

Discussion

One of the factors which influences the success rate during IVF programmes is the ovarian response. In order to compare the ovarian response there are criterias such as the amount of gonadotrophin, number of aspirated follicles and number of oocytes, fertilization and cycle cancellation rates.[17,18] In our study cancellation rate was 16% for IVF cycles. In order to decrease the number of cycle cancellation it is important to evaluate the ovarian response.

Chronological age is proposed to be an important factor for the fertility rate.[3] But it is also reported that chronological age is not suitable for predicting the ovarian response. It could be used as a cofactor to FSH or E2.[19,20] In our study the number of the oocytes aspirated during IVF cycles was decreased as the age increased . Especially after 40 years of age this decrease was significant.

Basal FSH level is another important factor in the evaluation of ovarian response. It was reported that high basal FSH levels were correlated with poor prognosis.10,19,20 There are different cut-offs for FSH levels as 9,13,15 or 25 mIU/ml respectively.[19,11,21,20] In our study in the groups of 10mIU/ml and lower FSH levels the number of oocytes was the highest but the patients with basal FSH levels higher than 12mIU/ml were candidates for poor ovarian response. Bahceci et al determined the serum and intrafollicular concentrations of sex steroids in women demonstrating poor response to ovarian stimulation with gonadotropins and GnRH antagonists, and compared the results with age-matched women displaying normal ovarian response. Serum and follicular levels of E2 and progesterone were significantly lower in the poor responder group than the normoresponder group. Follicular level of testosterone was also lower in poor responders, but not to a level of statistical significance. The serum FSH level was higher in the poor responder group, but follicular levels of gonadotropins did not differ between the two groups.22 On the other hand, Cai et al reported that there were no significant differences in basal serum FSH levels among poor, moderate, and high responders. They concluded that, poor ovarian response to gonadotropin stimulation was associated with low expression of follicle-stimulating hormone receptor in granulosa cells.23 In our study it was found that FSH was more important than the chronological age for the evaluation of ovarian response. 12mIU/ml levels of FSH was accepted as our center's cut-off value.

Basal E2 levels were reported to be a secondary factor to FSH for evaluation of the ovarian response with a cut- off value of 60, 75 or 80 pg/ml.[24,25,12] In our study the group of ≤60pg/ml had the best results with a mean of 7.4 oocytes and 4.5% cancellation rate. As the basal E2 increased to be higher than 80pg/ml, the number of oocytes decreased and the cancellation rate increased. In this study if the basal FSH levels were normal but the basal E2 levels decreased it was found that the number of oocytes decreased.

In our study, it was found that cut-off of basal FSH levels ≤12mIU/ml was the most significant factor, secondary was E2 ≥80pg/ml and 3rd, chronological age ≥40 factors which influenced the ovarian response in IVF cycles. As a conclusion we say that combination of basal FSH and E2 is safer to use together for the evaluation of ovarian response.

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