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Research Article

Correlation of Antimullerian Hormone (AMH) and Follicle Stimulating Hormone (FSH)

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Abstract

The aim of this study is to find the correlations between anti-Mullerian hormone (AMH) and follicle stimulating hormone (FSH) where the most reliable marker could be indicated and adequate strategy for the initial stages of infertility treatment could be laid out.

Methods

Prospective study was done on sixty-one infertile women referred from prenatal clinic. Patients were divided into three age groups. I < 35 years (n = 27), group II 35 - 40 years (n = 21), and group III 41 - 46 years (n = 13) respectively. Blood samples were analyzed for follicle stimulating hormone (FSH) and anti-müllerian hormone (AMH) on days 2 - 3 of the patients' menstrual cycles.

Results

Significant negative correlation was observed between AMH level ($r_s = -0.51$, $p < 0.001$) and age however, moderate positive correlation was found between age and FSH ($r_s = 0.28$, $p < 0.001$). AMH negatively correlated with FSH ($r_s = -0.33$, $p < 0.001$). A statistically significant correlation between FSH and AMH was detected only in group I ($r = -0.53$, $p < 0.001$) and group II ($r = -0.61$, $p < 0.001$).

Conclusion

AMH should be considered as the more reliable indicator of the ovarian reserve assessment compared to FSH however, future study include AFC should be considered.

Keywords: *Antimullerian Hormone (AMH); Follicle Stimulating Hormone (FSH); Antral follicle count (AFC)*

Introduction

Anti-Müllerian Hormone (AMH), also known as Mullerian inhibiting substance (MIS) [1] is a homodimer glycoprotein produced by granulosa cells (GC) of the ovary [1,2]. It is virtually undetectable but increases gradually until puberty and remains relatively stable through the reproductive period [3,4]. It is widely accepted that the reduction of AMH levels in serum is the first indication for decline in the follicular reserve of the ovaries and can be measured in the blood at any time in the menstrual cycle due to its stability [5,6]. It is a marker for ovarian reserve and naturally lower in older women (> 40 year) and higher in women with Polycystic ovaries(PCO) and polycystic Ovary Syndrome (P OCS) [7,8]. It has been reported that Follicle stimulating hormone (FSH), Estradiol (E2) levels and antral follicle count (AFC) have been used for evaluation of ovarian reserve to determine the strategy for treatment of female infertility by age [1,8],

which becomes very essential in recent years. Traditionally, age, follicle stimulating hormone (FSH), (E2) levels and antral follicle count (AFC) at the early follicular phase have been used for evaluation of ovarian reserve. Levels of FSH and E2 were considered for assessment of low ovarian reserve for many years [1] where FSH level has been found above the norm only in cases when the ovary function is largely decreased [9] however, it is still the most commonly used test although its reliability is weak and association with significant inter- and intra-cycle variability is documented [10,11]. Opposing to FSH (AMH) is considered to be more specific marker of ovarian response to gonadotrophins [12] however, both AMH and FSH are still used as ovarian reserve tests [13] although FSH showed several obstacles where patients have been reported to show discordant values for their ovarian reserve and cycle outcome [8,14-16], poor response to gonadotrophin stimulation on day 3 [16], lower chances of pregnancy [17] except at high threshold level of ovarian response and it needs to be measured during early follicular phase [18-20]. In contrast AMH can be tested on any day of the menstrual cycle [21-23], although level variation between different blood samples for the same patient was reported during the same menstrual cycle especially in young patients [24-25] never the less AMH can still show 80% sensitivity and 93% specificity in predicting poor ovarian response at random blood test [26] and Its levels correlate with the number of oocytes retrieved and treatment can be individualized for optimal cycle [21-23]. The facts that AMH reported to show assays controversies [27], pregnancies even at undetectable levels [28] and intracycle variations level [25] raise question mark about the possible role of AMH in assisted reproduction. Although other studies showed that levels of FSH and E2 were used as biochemical markers for assessment of low ovarian reserve for many years, identification of AFC at later stage still considered more reliable marker in assessment of the ovarian reserve where, Follicle count can be determined easily using high resolution sonographic systems [19,29,30], although obtaining AFC reported to face some difficulties however, it has been recommended over basal FSH [31]. Thus, by some investigators AFC is considered as the first choice test [19,31]. FSH and AMH are two different hormones to predict ovarian reserve at two different stages of follicular development. It has been reported that FSH levels reflect antral and postantral follicular development while, AMH values are representative of post primordial preantral follicular pool [14]. Despite the use of both the hormones in parallel to determine ovarian reserve, there is not much literature about the frequency of discordance and concordance between them and its clinical significance [14]. Therefore, we conducted this study to determine the frequency of concordance and discordance between AMH and FSH levels in female infertility patients.

Materials and Methods

This was a prospective study's done on sixty one women referred from parental clinics. Patients were divided into three age groups: group I < 35 years (n = 27), group II 35 - 40 years (n = 21), and group III 41 - 46 years (n = 12). Blood samples were analyzed using (Tosoh A11, Japan) for FSH a chemiluminescent immunoassay. AMH levels were measured using the Generation II AMH (Gen II AMH assay) enzyme-linked immunosorbent assay kit (Beckman Coulter, Inc., USA).

Statistical Analysis

Results were statistically analyzed by SPSS 11.5 for Windows. The mean and the standard deviation (SD) for all the variables were calculated. Analysis of variance F test (ANOVA) was used to compare the results of all examined cases in all studied groups. Continuous variables are expressed as media ± standard deviation (SD). Categorical variables were presented as a percentage. We assessed the correlation between FSH and AMH hormones with the Pearson correlation coefficient. All data were considered statistically significant considered non-significant or significant when P > or < 0.05, respectively [32].

Results

Distribution of the study population according to age groups was as follows: group I (44.3%), group II (34.4%) and group III (21.3%). The two indicators of ovarian reserve significantly differed from each other in the different age groups (AMH: $\chi^2 = 50.585$, p = 0. 0.001; FSH: $\chi^2 = 15.566$. p = 0.0001. These indicators varied according to age. The differences between groups for the mean ± standard deviation AMH and FSH values are shown in (Table 1). There were significantly higher AMH levels in group I compared with groups II and III.

This value was also higher in group II compared to group III. There was a positive correlation between age and FSH. Negative correlation between AMH and FSH was observed. Significant correlation between FSH and AMH levels were detected in group I and II. According to regression analysis, age only explained the variation of AMH and FSH in 27%and 19% respectively.

Indicator	< 35.0	35-40	41-46
Age (Y)	24.4 ± 2.7	35.24 ± 1.54	41.7 ± 2.43
AMH (ng/ml)	2.1 ± 1.7	1.15 ± 1.16	0.41 ± 0.47
	p^*< 0.001	p^{**}< 0.001	p^{***}< 0.001
FSH (IU/L)	7.87 ± 3.46	10.23 ± 5.3	19.12 ± 17.67
	p^*< 0.456	p^{**}< 0.095	p^{***}< 0.001

Values are represented with means and ± SD

p; Between groups I and II, p**; Between groups II and III, p*** Between groups I and III, AMH; Anti-Mullerian hormone, FSH; Follicle stimulating hormone*

Table 1: *Deference between age groups FSH and AMH values.*

Discussion

The results obtained showed that ovarian reserve assessment tests in infertile women age group reflected age-specific changes which in agreement with the results of other researchers [15,16,26,33]. In the current study AMH values significantly differed in the three age groups while FSH levels showed a significantly higher result only in group III compared to group I. Therefore, AMH values reflected age-specific changes better than other indicators. Our findings agreed with other study [28] where serum AMH in infertile women declined significantly while FSH level remained unchanged. It is known that a woman's age alone is insufficient to determine ovarian reproductive potential and this potential can be affected by various pathologies conditions such as the diagnostic of infertile subjects. Other studies showed that regression analysis have shown that changes in AMH, FSH and AFC levels were due to other known or unknown factors and therefore not only to age and their data showed reduction in AMH and AFC levels by approximately one fourth was related to the increase in age. Approximately one sixth of the rate of change in FSH level could be attributed to age [8]. This is in a sense agreed with our results.

Studies indicated that when AMH and FSH are used in parallel, significant proportion of patients will have discordant values of these two hormones [34,45]. Until further AMH outcome data are available, should both FSH and AMH be assayed in parallel to have the greatest likelihood of detecting reduced ovarian reserve [27,34,36,37]. Our results shows the rate of change in FSH level could be attributed to age which agrees with other studies [1,2] where age had a highly significant negative correlation with AMH and a highly significant positive correlation with FSH level. Many studies revealed different results concerning correlation between AMH and FSH indicating the significant of changes in serum AMH levels associated with aging [15] and the of FSH level was not detected until cycles become irregular [28]. Therefore, AMH showed considerable change when the cycle is still normal and hence can be used as a marker with declining fertility and aging. On the contrary other studies showed that both FSH and AMH predict ovarian reserve independently and have been shown to correlate well [28]. While others indicated that patient showed discordant values of AMH and FSH when they used in parallel [34,35]. Therefore, until further AMH outcome data are available, both FSH and AMH should be assayed in parallel to have the greatest likelihood of detecting reduced ovarian reserve [27,34,36,37]. Many studies showed that AMH showed better correlation to AFC than FSH level and basal FSH [38-40]. Unfortunately, AFC was not included in our study however, it should be considered in future proposal.

Conclusion

Researchers showed that among ovarian reserve assessment tests used in modern practice, AMH levels should be considered as more reliable where they showed that serum AMH levels are strongly related with AFC levels and such relation is more significant than other ovarian reserve parameters [8] and serum AMH level is more indicative than compared to conventional hormone measurements. Measuring serum AMH levels in combination with AFC may improve the assessment of ovarian reserve for evaluating fertility potential and monitoring infertility treatment. Unfortunately, our study did not include AFC however our results for infertile women in this study showed that AMH levels should be considered as more reliable indicator over FSH for now however, further work must be done to include AFC parameter to detect significant of AFC levels and if it should be considered for future assessment as other ovarian reserve parameters which may improve the assessment of ovarian reserve for evaluating fertility potential and monitoring infertility treatment.

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