Nat. Volatiles & Essent. Oils, 2021; 8(6): 207-213

NVEO
Natural Volatiles &
Essential Oils

Anti-Mullerian Hormone, Antral Follicle Count, Follicle Stimulating Hormone As An Indicators Of The Ovarium Response In Stimulation

Vu Van Tam[1] , Duong Tho Quynh Huong[1] , Do Diem Huong[1*]

[1] Hai Phong hospital of Obstetrics and Gynecology

Corresponding author: Do Diem Huong

Abstract

Background: Gynecology treatment needs a personal approach to each patient, especially in conduction the controlled ovarian stimulation protocol. And control of the special hormones range can be a help to choose the correct cure protocol.

The main aim of the research was to compare the value of AMH, AFC and FSH for indentifying ovarian-response in in-vitro fertilization.

Materials and Methods. The research was conducted at Haiphong hospital of obstetrics and gynecology from 1/2017 to 1/2018. A prospective study was conducted 507 patients. On cycle day 2, each person had anti-mullerian hormone, antral follicle count and follicle stimulating hormone measured.

Results: Anti-mullerian hormone test was the most accurate in predicting poor and hyper response, followed by antral follicle count and the least one was follicle stimulating hormone. Anti-mullerian hormone rate 1.31ng/mL predicted poor response with sensitivity of 74% and specificity of 86.9%. Anti-mullerian hormone rate 3.31ng/mL predicted hyper-response with sensitivity of 85.6% and specificity of 71.9%.

Conclusions: Anti-mullerian hormone test has the best predictive value for predicting ovarian response.

Keywords: Assisted reproductive techniques; anti-mullerian hormone (AMH), antral follicle count (AFC), follicle stimulating hormone (FSH), ovarian response.

1. Introduction

Women's health is dependent on many factors: individual features and biomarkers; nutrition and lifestyle; the start of the sexual life and the first pregnancy happened. And very important to remember, that the mother's health causing great in the child one [1]. Must be said, women's health depends greatly on not only medical but also social problems. For example, it can be

associated with the development of chronic psychological stress, social and family insecurity [2]. All of this can make a great influence on the possible be pregnant.

The ovarian response is defined as the number of oocytes obtained following the above stimulation. The term ovarian response is used with both qualitative and quantitative meanings. The qualitative meaning is in determining whether or not ovulation is released. The quantitative value is mean the evaluation criteria of ovarian response are based on the number of oocytes retrieved.

Many studies have shown that the number of oocytes are closely associated with the clinical pregnancy rate of an ovarian stimulation cycle. So, most studies use oocyte retrieved to assess ovarian response. For the classification of ovarian response use several tags. **Poor ovarian response** means the retrieval of <4 oocytes following a standard in vitro fertilization (IVF) protocol. In the **normal ovarian response** in standard IVF protocol can be got the retrieval of 4-15 oocytes. **High ovarian response** meens the retrieval of more then 15 oocytes following a standard controlled ovarian stimulation (COS) protocol [3-5].

Individualized treatment is the current task of modern medicine. And the prognosis in each case - in the patient's ovarian response – is very meaningful for successful IVF in order both to save costs and reduce complications affecting the patient's health. Moreover, it improves the success rate for a cycle of ovarian stimulation.

The ovarian response prediction is mainly based on the tests including anti-mullerian hormone (AMH), antral follicle count (AFC) and follicle stimulating hormone (FSH). In Vietnam and other nations, there have been some studies comparing the value of the three tests, but the best method is still controversial [6-7].

1. Materials and Methods

We have conducted this study with goals to enhance the effectiveness of infertility examination and treatment at Hai Phong Obstetrics and Gynecology Hospital as well as provide additional data on the three tests. So, we have compared the value of AMH, AFC, and FSH for identifying ovarian response in in-vitro fertilization at Haiphong hospital of obstetrics and gynecology from 1/2017 to 1/2018.

1.1. Patient recruitment and counseling

Prospective study, a total of 507 IVF patients agreed to participate in the study and met the exclusion criteria (polycystic ovary syndrome, ovarian tumors, pituitary and thyroid pathologies) at Assisted Reproductive department of Hai Phong hospital of obstetrics and gynecology from January 2017 to January 2018.

1.2. Treatment protocol

Quantification of AMH, FSH, and AFC have been performed on the second menstrual cycle day. Quantification of FSH and AMH was performed by electrochemical luminescence immunization method on Cobas e411 automatic machine (Roche, Germany). The AFC count was performed on the Aloka 4100 ultrasound machine using a vaginal probe ultrasound of 7.5 MHz performed by the subject implementer following a standardized procedure.

Was conducted such stimulating ovaries method. The GnRH antagonist regimen was used. Induction of the FSH was made on 2nd menstrual cycles with an average dose of 150-300 IU/day.

The dosage was depended on each personal patient's case. After 5 days of rFSH, ultrasound reassessed oocyte development, if there is any follicle ≥14mm. At this time was start supplementing GnRHant daily with a dose of 0.25mg/day until at least 2 follicles ≥17mm, then cause maturity by injection of Human chorionic gonadotropin (HCG) 5000-10000 IU. Aspiration of oocyte has been conducted after injection HCG 34-36 hours and sperm preparation.

2. Results

2.1. Characteristics of patients before ovarian stimulation

The average age of patients in this study was 32.58±5.03 with an average infertility time of 4.25±3.09 years. The cause of infertility was mainly due to the husband prolems, accounting for 37.9%, unexplained (23%), and endometriosis with 3%. The average value of ovarian reserve test-results: AMH: 3.42±2.91 ng/mL, FSH 6.83±2.25 UI/L, AFC 11.56±5.23 follicles.

2.2. Characteristics and results of ovarian stimulation

The total dose of FSH used was 3159±609.69 IU with an average ovarian stimulation time of 9.23 ± 1.15 days. The number of oocytes obtained after aspiration was: 9.91 ± 6.45 (Fig. 1).

2.3. Correlation between the number of oocytes obtained and AMH, AFC and FSH tests

The largest Spearman correlation coefficient was of AMH 0.7, followed by AFC 0.6 and the lowest was FSH - 0.26. This showed that the AMH and the number of oocytes after aspiration had the strongest correlation, followed by AFC with r=0.6 and the lowest being FSH with r=-0.26.

2.4. Compare the predicted values of the AMH, AFC and FSH tests for poor and high ovarian responses

Analysis of the receiver operating characteristic (ROC) curve shows that all three tests had a predictive value of poor response. And area under curve (AUC) was respectively: AUC (AMH) = 0.88, AUC (AFC) = 0.85 and AUC (FSH) = 0.69 with p <0.01 (Table 2).

And the expected threshold response value of AMH was 1.31 ng/ml with sensitivity of 74% and specificity of 86.9%; AFC was <8 follicles with sensitivity of 74%, and specificity of 79.5%; FSH was 7.1 IU/L with a sensitivity of 67.1% and a specificity of 68.7%.

Analysis of the ROC curve shows that all three tests had a predictive value of high response, with AUC was respectively: AUC (AMH) = 0.85, AUC (AFC) = 0.81 and AUC (FSH) = 0.65 with p<0.01 (Table 3). And the expected threshold response value of AMH was 3.31 ng/mL with sensitivity of 85.6% and specificity of 71.9%; AFC was less 12 follicles with a sensitivity of 81.1% and a specificity of 64.3%; FSH was 5.72 IU/L with sensitivity of 52.2% and specificity of 70.3%.

3. Discussion

3.1. Correlation between AMH, AFC, and FSH with the obtained oocytes number

AMH and AFC were positively correlated with the number of oocytes, meaning that the higher the concentration of AMH and the AFC index, the higher the number of oocytes and vice versa, while the FSH value was less correlated with the number of oocytes collected (with r = -0.2). This result is similar to the study of Samuel Otto. Thus the combination of AFC and AMH can provide

additional data on the ovarian reserve of the subject and prognosis of the number of oocytes collected after aspiration [8].

3.2. Predictive values of AMH, AFC and FSH for high responses

In our study, three tests of AMH, FSH and AFC were all able to predict an excessive ovarian response, of which AMH had the best predictive value followed by AFC and FSH with poor predictive values. This result is similar to study of Vuong Thi Ngoc Lan et al (2016) and study of Nguyen Xuan Hoi et al (2015) [9-10]. The threshold value of AMH in this study was 3.31 ng/mL lower than other studies but the sensitivity and specificity in our study are better. The threshold value of AFC> 12 capsules is similar to that of Vuong Thi Ngoc Lan et al (2016) and is within the limits of other studies of 9-14 follicles [9-12].

3.3. Predictive values of AMH, AFC and FSH with poor ovarian response

In our study, three tests of AMH, FSH and AFC were all able to predict poor ovarian response, of which AMH had the best predictive value, followed by AFC and FSH with the least predictive value. This is similar to the studies of other several authors [9-12]

The AMH cutoff point in our study was 1.31 ng / ml with a high specificity of 86.9% and a sensitivity of 74%. This result is similar to the study of Polyzos et al (2013). The cut-off point of AFC was 8 which is similar to that of Polyzos et al (2013) with sensitivity and specificity more of 70% [14].

For FSH testing at the cutoff of 7.1 IU/L, it is similar to that of Hoi NX and coauthors but lower than the study of Vuong Thi Ngoc Lan et al. of 8.9 IU/L, sensitivity was only about 52% [9,10,15].

3.4. Application of research results to clinical practice

This study once again confirms the superiority of AMH over other ovarian reserve assessment tests, AFC and FSH, in predicting ovarian response.

This is the basis for selecting tests to assess ovarian reserve to reduce costs for patients in the specific conditions of each IVF center [16]. The use of FSH value should be considered because the ability to predict ovarian response is poor and high are not good.

When the results of tests are heterogeneous, we may prefer to select the value of the test with a better predictive value to provide appropriate treatment.

This study contributes to the overall data on AMH assay values in clinical practice of IVF towards the goal of individualizing treatment.

4. Conclussions

AMH had the best predictive value of poor and high ovarian response, followed by AFC and finally FSH. For poor ovarian response, the threshold values of the tests were AMH, respectively: 1.31 ng/mL (sensitivity 74%, and specificity 86.9%); AFC <8 capsules (sensitivity 74%, specificity 79%), FSH 7.1 IU/L (sensitivity 67.1%, specificity 68.7%). For high AMH ovarian response: 3.31 ng/mL (sensitivity 85.6%, specificity 71.9%); AFC> 12 capsules (sensitivity 81.1%, specificity 64.3%), FSH 5.72 IU/L (sensitivity 52.2%, specificity 70.3%).

Acknowledgments

The authors have made substantial equivalent contributions in the manuscript creation: the creation of the conception and design, acquisition of data, data analysis, and interpretation. All of the authors have taken part in drafting the article and revising it critically for important intellectual content; have given the approval of the final version, and agree to be accountable for all aspects of the work.

There are no potential conflicts with respect to the research, authorship, and publication of this article. The research has not been sponsored.

Referenes

1. Ayazbekov A, Nurkhasimova R, Kulbayeva S, Bolat K, Kurmanova AM et al. Features of Pregnancy, Childbirth and Postpartum Period of Young Mothers. Electronic Journal of General Medicine. 2020;17(6):em260. https://doi.org/10.29333/ejgm/8459

2. Ayazbekov, A., Uteuliyev, Y., Nurkhasimova, R., Ibrayeva, D., Khudaibergenova, S., & Kemelbekov, K. (2018). Evaluation of women's health with intrauterine fetal death in the city of Turkestan for the years of 2013-2017. Annals of Tropical Medicine and Public Health, 17(Special issue), S804-S804.

3. Peluso C, Oliveira RD, Laporta GZ, Christofolini DM, Fonseca FLA et al. Are ovarian reserve tests reliable in predicting ovarian response? Results from a prospective, cross-sectional, single-center analysis. Gynecological Endocrinology. 2021; 37(4), 358-366. https://doi.org/10.1080/09513590.2020.1786509

4. Nelson SM. Biomarkers of ovarian response: current and future applications. Fertility and sterility. 2013;99(4):963-969. https://doi.org/10.1210/jcem.85.9.6789

5. Nardo LG, Gelbaya TA, Wilkinson H, Roberts SA, Yates A, Pemberton P, Laing I. Circulating basal anti-Müllerian hormone levels as predictor of ovarian response in women undergoing ovarian stimulation for in vitro fertilization. Fertility and sterility, 2009;92(5):1586-1593. https://doi.org/10.1016/j.fertnstert.2008.08.127

6. Jang S, Kim KH, Jun JH, You S. Acupuncture for in vitro fertilization in women with poor ovarian response: a systematic review. Integrative medicine research. 2020; 9(2):100395. https://doi.org/10.1016/j.imr.2020.02.003

7. von Wolff M, Bruckner T, Strowitzki T, Germeyer A. Fertility preservation: ovarian response to freeze oocytes is not affected by different malignant diseases—an analysis of 992 stimulations. Journal of assisted reproduction and genetics. 2018;35(9):1713-1719. https://doi.org/10.1007/s10815-018-1227-0

8. Samuel O. I. Teil: Das Grundprinzip der Kulturontologie. Die Ontologie der Kultur. 2019:6-55. https://doi.org/10.1515/9783111537498-003

9. Lan VTN. The values of the AMH, FSH and AFC tests predict ovarian response in in vitro fertilization. Abstract doctor diss. in medicine, Ho Chi Minh University of Medicine and Pharmacy, Vietnam; 2016.

10. Hợi NX, Lâm TV. Evaluation of clinical pregnancy outcomes of recombinant FSH and highly purified urine FSH in intrauterine insemination. Journal of Obstetrics and Gynecology. 2015;13(2A), 64-67. [in Vietnam]

11. Themmen AP. Anti-Müllerian hormone: its role in follicular growth initiation and survival and as an ovarian reserve marker. JNCI Monographs, 2005;(34):18-21.

12. Arce JC, La Marca A, Klein BM, Andersen AN, Fleming R. Antimüllerian hormone in gonadotropin releasing-hormone antagonist cycles: prediction of ovarian response and cumulative treatment outcome in good-prognosis patients. Fertility and sterility. 2013;99(6):1644-1653. https://doi.org/10.1016/j.fertnstert.2012.12.048

13. Nguyen XH, Nguyen NNT, Nguyen TH. Current status and trends of mangroves and seagrasses in Nha Trang bay. Collection of Marine Research Works. 2015;21(2):201-211. http://113.160.249.209:8080/dspace/handle/123456789/18785

14. Polyzos NP, Tournaye H, Guzman L, Camus M, Nelson SM. Predictors of ovarian response in women treated with corifollitropin alfa for in vitro fertilization/intracytoplasmic sperm injection. Fertility and sterility. 2013;100(2):430-437. https://doi.org/10.1016/j.fertnstert.2013.04.029

15. Hợi NX. Comparison of effectiveness of HP-hMG and rFSH ovarian stimulation by antagonist regimen. Journal of Obstetrics and Gynecology. 2018;16(1):150-153. [in Vietnam].

16. Sfakianoudis K, Simopoulou M, Nitsos N, Rapani A, Pantou A et al. A case series on platelet-rich plasma revolutionary management of poor responder patients. Gynecologic and obstetric investigation. 2019;84(1):99-106. https://doi.org/10.1159/000491697

Tables

Table 1. Correlation between the number of oocytes obtained and AMH, AFC and FSH tests

Test	Spearman correlation coefficient	P
Anti-mullerian hormone	0.7	
Antral follicle count	0.6	<0.01
Follicle stimulating hormone	-0.26	

Table 2. Predictive values of AMH, AFC and FSH with poor ovarian response

Test	AUC (95% CI)	Threshold value	Sensitivity, %	Specificity, %	P
AMH	0.88 (0.84-0.92)	1.31ng/ml	74	86.9	
AFC	0.85 (0.8-0.9)	< 8 nang	74	79.5	<0.01
FSH	0.69 (0.62-0.76)	7.1 IU/L	67.1	68.7	

AMH anti-mullerian hormone; AFC - antral follicle count; FSH - follicle stimulating hormone; AUC - area under curve

Table 3. Predictive values of AMH, AFC and FSH with high ovarian responses

Test	AUC	Threshold value	Sensitivity,	Specificity,	P

	(95% CI)		%	%	
AMH	0.85 (0.81-0.88)	3.31ng/ml	85.6	71.9	
AFC	0.81 (0.77-0.85)	> 12 nang	81.1	64.3	<0.01
FSH	0.65 (0.59-0.71)	5.72 IU/L	52.2	70.3	

AMH anti-mullerian hormone; AFC - antral follicle count; FSH - follicle stimulating hormone; AUC - area under curve

Figures

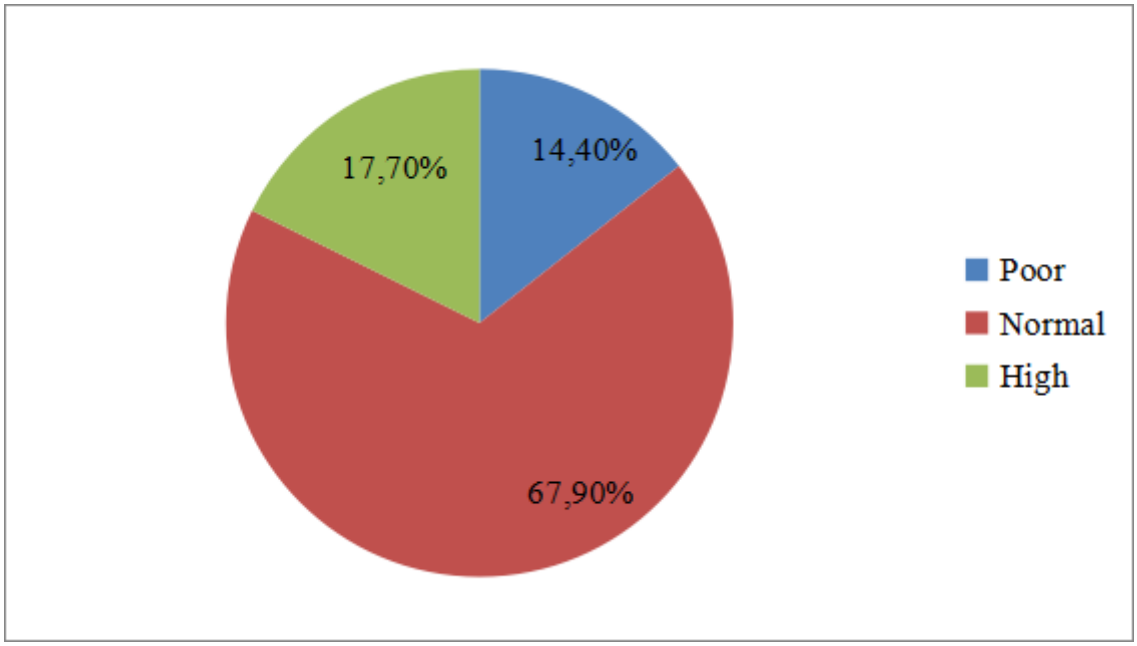

Figure 1. Results of ovarian response at the beginning of the experiment