Acta Scientific MICROBIOLOGY (ISSN: 2581-3226)

Volume 5 Issue 8 August 2022

Research Article

Anti-mullerian Hormone: A Significant Marker for Male Infertility

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DOI: 10.31080/ASMI.2022.05.1104

Received: May 04, 2022

Published: July 06, 2022

Abstract

A case study was carried to evaluate serum anti-Mullerian hormone (AMH) in men with normal, Oligospermic and Azoospermic sperm as a possible clinical marker for male infertility. The prospective study was conducted on eighty male participants, aged less than 50 years after obtaining ethical approval from the Jos University Teaching Hospital, Jos where the study took place. Infertile men were classified accordingly to their sperm count which was performed according to the World Health Organization (WHO) guidelines into Oligospermic (n = 27) and Azoospermic (n = 23). Thirty men were normal (n = 30). Serum concentrations of follicle stimulating hormone, Testosterone and Anti-Mullerian hormone were measured using ELISA. Results (mean ± SD) revealed that anti-Mullerian hormone (2.02 ± 0.52 ng/ml, $p < 0.001$) and the testosterone (6.9 ± 1.49 ng/ml, $P < 0.001$) of control participants were significantly higher than those in both Oligospermic (1.8 ± 0.34 ng/ml, 4.8 ± 0.8 ng/ml) and Azoospermic (1.55 ± 0.29 ng/ml, 2.3 ± 1.2 ng/ml) respectively. The mean serum of Follicle stimulating hormone was significantly reduced in controls (4.8 ± 2.0 miu/ml, $p < 0.001$) when compared with both Oligospermic (8.5 ± 3.2miu/ml) and Azoospermic (16.5 ± 5.5 miu/ml). anti-Mullerian hormone was negatively correlated with follicle stimulating hormone in both Azoospermic and Oligospermic. Anti-Mullerian hormone should be evaluated in patients with oligospermia and azoospermia. It may serve as a marker of infertility.

Keywords: Anti-Mullerian; Hormone; Marker; Male Infertility

Introduction

Anti-Mullerian Hormone (AMH) is a dimeric glycoprotein, a member of the transforming growth factor – beta super family which acts on tissue growth and differentiation. It was identified as a factor which is being synthesized by testicular Sertoli cells, and induces regression of the Mullerian ducts during male-fetal development [1,2]. It continues to be produced by the testes throughout life. AMH is thought to be involved in the inhibition of steroid hormone production in women of reproductive age [2]. In

males, AMH is the earliest Sertoli cells specific protein expressed by the gonad. It is secreted by the testes from the eight week of pregnancy and remain secreted at high level until puberty, when Sertoli cells maturation is characterized by decreased AMH production [4]. AMH has also been shown to inhibit production of pre-pubertal progenitor Leydig cells and prevent regeneration of Leydig cells after chemical ablation [5]. AMH is expressed only by immature Sertoli cells and by immunohistochemistry found only in tubules with spermatogenetic arrest of Sertoli-cell-only syndrome [6].

The aim of the study is to evaluate the role of AMH measurement in assessment of spermatogenesis in both Oligospermic patients and Azoospermic patients whether serum AMH would add any diagnostic advantage over other hormones.

Materials and Methods

This prospective case study was conducted at the Departments of Chemical Pathology, and Obstetrics and Gynecology of the Jos University Teaching Hospital (JUTH), Jos, Plateau State, North Central Nigeria. 50 diagnosed infertile male patients aged less than 50 years (having normal female partners) of which 27 were Oligospermics and 23 were Azoospermics who attended the infertility unit of Obstetrics and Gynecology Department of JUTH and 30-age matched fertile men (controls) participated in the study. Ethical clearance was obtained from the Research and Ethical committee of Jos University Teaching Hospital, Jos Plateau State, Nigeria. Patients that were included in this study was dependent on the confirmed seminal fluid analysis result according to the World Health Organization Manual (World Health Organization, 2000). Semen specimen were collected by masturbation after a period of 3-5 days of sexual abstinence, in which after liquefaction, semen analysis was performed to determine sperm concentration. Normal values for sperm concentration was $\geq 20\times10^6$/ml. Patients who had less than 20×10^6/ml were considered oligospermic and patients who had zero sperm concentration were considered as azoospermic patients.

Five milliliters of peripheral venous blood were collected from participants and controls. Blood samples were collected in plain tubes, allowed to clot and then centrifuged at 1500g for 5minutes. The serum was separated from the cells and transferred into samples bottles and then frozen at -20°C until the time for analysis. The hormonal studies in the present study were measurement of serum concentration of Follicle-Stimulating Hormone (FSH), Total Testosterone (TT) and Anti-Mullerian Hormone (AMH). The serum concentration of FSH, TT and AMH were measured by Enzyme Linked Immunosorbent Assay (ELISA) technique. Data Analysis was done using Statistical Package for Social Sciences (SPSS) Version 16 and Minitab program. Pearson correlation and unpaired T-test was used. P-value <0.001 was considered significant throughout the study.

Results

The study included 27 Oligospermic men, 23 Azoospermic men and 30 healthy fertile men. Table 1 showed the mean (± SD) values of serum concentrations of testosterone, FSH and AMH of infertile men and fertile control men. The mean values of serum AMH and Testosterone concentrations of fertile men (control) men (2.02 ± 0.52 ng/ml, 6.9 ± 1.49 ng/ml) was significantly higher than those of infertile men (1.67 ± 0.31 ng/ml, 2.3 ± 1.3 ng/ml; $p < 0.001$, $p < 0.001$ respectively). The mean value of serum FSH concentrations of fertile control men (4.8 ± 2.0 miu/ml) was significantly lower than that of the infertile men (14.9 ± 5.7 miu/ml; $p < 0.001$). Table 2 showed the mean (±SD) values of serum concentrations of testosterone, FSH and AMH of Azoospermic men and fertile control men. The mean values of serum AMH and testosterones concentrations of fertile control men (2.02 ± 0.52 ng/ml, 6.9 ± 1.4 ng/ml) were also significantly higher than those of azoospermic men (1.55 ± 0.29 ng/ml, 2.3 ± 1.2 ng/ml; $p < 0.001$, $p < 0.001$ respectively). The mean value of serum FSH concentrations of fertile control men (4.8 ± 2.0 miu/ml) was significantly lower than that of the azoospermic men (16.5 ± 5.5 miu/ml; $p < 0.001$). Table 3 showed the mean (±SD) values of serum concentrations of testosterone, FSH and AMH of oligospermic men and fertile control men. The mean values of serum AMH and testosterone concentrations of fertile control men (2.02 ± 0.52 ng/ml, 6.9 ± 1.4 ng/ml) were significantly higher than those of oligospermic men (4.8 ± 0.8 ng/ml, 1.80 ± 0.34 ng/ml; $p < 0.001$, $p < 0.001$ respectively). The mean value of serum FSH concentrations of fertile control men (4.8 ± 2.0 ng/ml) was significantly lower than that of the oligospermic men (8.5 ± 3.2 miu/ml; $p < 0.001$). Table 4 showed the mean (±SD) values of serum concentration of testosterone, FSH and AMH of Oligospermic and Azoospermic men. The mean values of serum AMH and testosterone concentrations of Oligospermic men (1.80 ±

0.34 ng/ml, 4.8 ± 0.8 ng/ml) was significantly higher than those of Azoospermic men (1.55 ± 0.29 ng/ml, 2.3 ± 1.2 miu/ml; p <0.001, p < 0.001 respectively). The mean value of serum FSH concentration of Oligospermic men (8.5 ± 3.2 miu/ml) was significantly lower than that of the Azoospermic men (16.5 ± 5.5 miu/ml; p < 0.001). The results of this study also revealed that there was a significant negative correlation between serum AMH concentration and serum levels of FSH in both oligospermic and azoospermic men (r = 0.443, p < 0.001, r = 0.852, p < 0.001 respectively). There was also a positive correlation between serum AMH and testosterone in both oligospermic and azoospermic men (r = 0.456, p < 0.001, r = 0.598, p < 0.001).

Hormone	Infertile men (n = 50)	Fertile controls (n = 30)	t-value	p-value
Testosterone(ng/ml)	2.3 ± 1.3	6.9 ± 1.4	14.4	<0.001
FSH (miu/ml)	14.9 ± 5.7	4.8 ± 2.0	-9.4	<0.001
AMH (ng/ml)	1.67 ± 0.31	2.0.2 ± 0.52	6.8	0.003

Table 1: Mean (±SD) Of Serum Hormones in Infertile and Controls.

Hormone	Azoospermic (n = 23)	Fertile controls (n = 30)	t-value	p-value
Testosterone(ng/ml)	2.3 ± 1.3	6.9 ± 1.4	13.9	<0.001
FSH (miu/ml)	16.5 ± 5.5	4.8 ± 2.0	6.2	<0.001
AMH (ng/ml)	1.55 ± 0.29	2.0.2 ± 0.52	1.8	<0.001

Table 2: Comparison of Serum Hormones in Azoospermic and Control Men using Unpaired T-Test.

Hormone	Oligospermic (n = 27)	Fertile controls (n = 30)	t-value	p-value
Testosterone(ng/ml)	4.8 ± 0.8	6.9 ± 0.14	6.9	<0.001
FSH(miu/ml)	8.5 ± 5.5	4.8 ± 2.0	6.2	<0.001
AMH (ng/ml)	1.55 ± 0.29	2.02 ± 0.52	1.8	0.007

Table 3: Comparison of Serum Hormones in Oligospermics and Control Men Using Unpaired T-Test.

Hormone	Azoospermic (n = 27)	Oligospermic (n = 30)	t-value	p-value
Testosterone(ng/ml)	2.3 ± 1.2	6.9 ± 0.8	9.1	<0.001
FSH (miu/ml)	16.5 ± 5.5	4.8 ± 3.2	5.3	<0.001
AMH (ng/ml)	1.55 ± 0.29	1.80 ± 0.34	2.8	0.008

Table 4: Comparison of Serum Hormones in Azoospermics and Control Men Using Unpaired T-Test.

Discussion and Conclusion

Several work with different results has been done depending on the possibilities of serum FSH and AMH being able to predict the states of spermatogenesis in the testis of men. In the present study we were able to compare some serum biomarkers in the Normospermic, Oligospermic and Azoospermic men. The results revealed significant difference in FSH, testosterone and AMH concentrations in both Azoospermic and Oligospermic men as compared to Normospermic men. This result is in agreement with that, reported by [8] who based their argument on indecision of detective spermatogenesis and as a result of feedback control probably by inhibin B or maybe a direct involvement of AMH. Serum AMH was also found to be significantly lower in Oligospermic and Azoospermic participants when compared with Normospermic participants. This is also in accordance with the results of previous work done by [7]. The regulation of AMH after birth is complex, basal levels of AMH is found to be independent of gonadotropin regulation, For example, during childhood and in patients with

hypogonadotropic hypogonadism [9]. The negative correlation between AMH and FSH in this study is also in line with previous work done by [11].

This might reflect an involvement in the signaling and regulation FSH and so the reproductive male system or must probably be a symptom of impaired or immature Sertoli cells [10]. In conclusion, AMH should be carefully evaluated in both azoospermic and oligospermic men since AMH is a marker of both Sertoli cell proliferation and protein synthesis activity in response to FSH before puberty and also a useful marker of FSH action in the assessment of testicular function in the prepubertal boys.

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