Anti Mullerian Hormone as an indicator for ovarian response in women receiving Long GnRH agonist protocol in Intracytoplasmic Sperm Injection cycles

Thesis

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Ahmed Mohammed Selim

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List of Abbreviations

AFC	:	Antral follicle count
AMH	:	Antimullarian hormone
ART	:	Assisted Reproductive technique
CC	:	Clomiphene citrate
CCCT	:	Clomiphene Citrate Challenge Test
COH	:	Controlled-ovarian-hyper-stimulation
COS	:	Controlled ovarian stimulation
DOR	:	Diminished ovarian reserve
EE	:	Ethinyl Estradiol
EFFORT	:	Exogenous FSH Ovarian Reserve Test
ESHRE	:	European Society of Human Reproduction and Embryology
FSH	:	Follicle-stimulating hormone
GnRH	:	Gonadotropin-releasing hormone
GnRH-a	:	Gonadotropin-releasing hormone agonist
HCG	:	Human chorionic gonadotrophins
hCG	:	Human chorionic gonadotropin
HMG	:	Human menopausal gonadotrophins
HS : P<0.01	:	Highly significant
ICSI	:	Intracytoplasmic sperm injection
IVF	:	in vitro fertilization
LBR	:	Pregnancy outcome and live birth rate
LH	:	Luteinizing hormone
NS : P>0.05	:	Non significant.
OCP	:	Oral contraceptive pills
OHSS	:	Ovarian hyperstimulation syndrome
OR	:	Ovarian reserve
PCOS	:	Polycystic ovarian syndrome
PGD	:	Preimplantation genetic diagnosis
POI/POF	:	Primary ovarian insufficiency or premature ovarian failure

List of Abbreviations (Cont.)

POR	:	Poor ovarian response
S : P< 0.05	:	Significant.
SERM	:	Selective Estrogen Receptor Modulator
SMAD	:	Small mothers against decapentaplegic
TGF-β	:	Transforming growth factor-hetero-dimeric-β
TVS	:	Trans-vaginal ultrasound scanning

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Anti Mullerian Hormone as an indicator for ovarian response in women receiving Long GnRH agonist protocol in Intracytoplasmic Sperm Injection cycles

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Abstract

Introduction

Fertility of females resides in the pool of primordial follicles, they are born with. Amongst these, 30 to 50 follicles are recruited with each menstrual cycle leading to decline in fertility after the age of 30 years. In cases of infertility, evaluation of ovarian reserve (OR) is essential to optimize protocol for assisted reproductive technique (ART) and prediction of response to counsel the couple**. Patients and Methods** ***Design:*** Prospective (cohort) study. ***Setting:*** This study was conducted in assisted reproductive technology unit of Ain Shams University Hospital after approval of the research ethical committee from April 2017 to April 2018. ***Population:*** Sixty six women undergoing ICSI were enrolled in and a written informed consent was obtained from each participant.`

Conclusion: In conclusion, in this study it was found that as the AMH level increases, the number of oocytes increases as well, but it is not a predictor of oocyte quality or pregnancy rate.
This might be because pregnancy is affected by many other factors such as embryo quality, transfer technique, and endometrial receptivity. Furthermore, treatment success is also affected by sperm properties in patients who receive the treatment due to the male factor.
Keywords: AFC: Antral follicle count; AMH: Antimullarian hormone; ART: Assisted Reproductive technique; CC: Clomiphene citrate.

Introduction

Fertility of females resides in the pool of primordial follicles, they are born with. Amongst these, 30 to 50 follicles are recruited with each menstrual cycle leading to decline in fertility after the age of 30 years ***(Broekmans, et al., 2007)***. In cases of infertility, evaluation of ovarian reserve (OR) is essential to optimize protocol for assisted reproductive technique (ART) and prediction of response to counsel the couple ***(Hansen, 2013).***

likelihood of satisfactory ovarian response is usually assessed on within comparable ages, wide variability has been reported ***(Zehra Jamil et al., 2016).***

The main indication for intracytoplasmic sperm injection (ICSI) is severe male infertility due to a limited number of spermatozoa or to a higher proportion of dysfunctional sperm cells (***Devroey and van Steirteghem, 2004).*** ICSI is used in couples with many other reproductive indications, even if clinical trials indicate that ICSI is no more effective in terms of clinical pregnancy rates than in vitro fertilization (IVF) ***(The ESHRE Capri Workshop Group, 2007).***

In turn, ICSI may be preferred in preimplantation genetic diagnosis (PGD) cycles because the higher fertilization rate with ICSI increases the number of embryos available for testing and the number of normal embryos available for transfer and especially because ICSI can avoid contamination by extraneous DNA ***(Jun et al., 2006).***

In recent years, mild stimulation protocols have risen in popularity. These protocols typically use lower

doses (≤150 IU/day), shorter duration of exogenous gonadotrophins, or both, compared with conventional protocols, with the goal of limiting the number of retrieved oocytes to less than eight
(Alper and Fauser., 2017).

It has been shown that ovarian reserve tests, such as basal FSH, antimullarian hormone (AMH), inhibin B, basal estradiol, antral follicular count (AFC), ovarian volume, ovarian vascular flow, ovarian biopsy and multivariate prediction models, have little clinical value in the prediction of a poor response. Although recent evidence points that AMH and AFC may be better than other tests but they still continue to be used and form the basis for the exclusion of women from fertility treatments. ***(Badawy et al., 2011).***

AMH, also known as Mullerian-inhibiting substance, is a dimeric glycoprotein that belongs to the transforming growth factor -β family. 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 ***(Battikhi, 2017).***

The European Society of Human Reproduction and Embryology (ESHRE) consensus defines poor ovarian response (POR) to ovarian stimulation as, "when at least two of the following three characteristics are present: (1) advanced maternal age (≥40 years) or any of the risk factors for poor ovarian responders, (2) a previous POR (≤3 oocytes with a conventional stimulation protocol), and (3) an abnormal ovarian reserve test result (i.e., antral follicle count [AFC] of <5-7 follicles or anti-Müllerian hormone [AMH] level of <0.5-1.1 ng/mL)," as in the Bologna criteria. Two episodes of POR after maximal stimulation

are sufficient to define a patient as a poor responder in the absence of advanced maternal age or an abnormal ovarian reserve test result ***(Bo Hyon Yun et al., 2017***).

The ovulatory menstrual cycle is the result of the integrated action of the hypothalamus, pituitary, ovary, and endometrium. Like a metronome, the hypothalamus sets the beat for the menstrual cycle by the pulsatile release of gonadotropin-releasing hormone (GnRH). GnRH pulses occur every 1-1.5 h in the follicular phase of the cycle and every 2-4 h in the luteal phase of the cycle. Pulsatile GnRH secretion stimulates the pituitary gland to secrete luteinizing hormone (LH) and follicle stimulating hormone (FSH). The pituitary gland translates the tempo set by the hypothalamus into a signal, LH and FSH secretion that can be understood by the ovarian follicle ***(Barbieri, 2014)***.

Recently, gonadotropin-releasing hormone agonist (GnRH-a) trigger has been used for the induction of final follicular maturation and ovulation with the aim of reducing the OHSS risk. Several studies have shown that the releases of endogenous follicular stimulating hormone (FSH) and LH after administration of GnRH agonist in in vitro fertilization (IVF) cycles are able to precede the final follicular maturation leading to removal of fertile oocyte with normal development of the embryo and ultimately pregnancy ***(Ashraf Alyasin et al., 2016)***.

Aim of the Work

Aim of the work is to assess the accuracy of AMH as a predictor of ovarian response in infertile women receiving long GnRH agonist protocol for ICSI cycles.