Cairo University

Faculty of medicine

Obstetrics and Gynecology Department

Evaluation of the role of follicular output rate (FORT) in the Prediction OF ICSI outcome

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By

Hosam Eldeen Metwally Mohammed

M B., B.CH, 2002 Assuit University

Registrar of Ob/Gyn at Assuit maternity hospital

Supervised by

Prof. Magdy Ibrahim Mostafa

Professor of Obstetrics and Gynecology

Faculty of Medicine - Cairo University

Dr. Abdelghany Mohamed Abdelghany

Lecturer of Obstetrics and Gynecology

Faculty of Medicine - Cairo University

Dr. Ayman Hani Ahmed

Lecturer of Obstetrics and Gynecology

Faculty of Medicine - Cairo University

Faculty of medicine
Cairo University

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Abstract

Using FORT to determine ovarian responsiveness to exogenous FSH has some limitations. FORT does not take into account the doses of COH drugs. If two groups of women had the same AFC and PFC but needed different FSH doses, they will have the same FORT implying that they have the same oocytes quality; however we believe that women needing less FSH have better oocytes quality. The use of FORT in women with polycystic ovarian syndrome (PCO) is limited by the high number of AFC, Zhang et al have found that moderate, rather than higher FORT values were correlated with better IVF/ICSI outcome in PCOS patients.

Key words

Evaluation of the role of follicular output rate (FORT) in the Prediction OF ICSI outcome

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List of Abbreviations

Abb.	*Full term*
ACTH	*Adreno-Corticotropic Hormone*
AFC	*Antral Follicle Count*
AMH	*Anti-Mullerian Hormone*
ART	*Assisted Reproductive Technology*
ATPase	*Adenosine Triphosphatase*
BMI	*Body Mass Index*
COH	*Controlled Ovarian Hyperstimulation*
DNA	*Deoxy Ribonucleic Acid*
E2	*Estradiol*
FORT	*Folliular Output Rate*
FSH	*Follicle stimulating hormone*
GnRH	*Gonadotropin Releasing Hormone*
GnRH-a	*Gonadotropin Releasing Hormone agonist*
GV	*Germinal Vesicle*
HCG	*Human Chorionic Gonadotropin*
hMG	*Human Menopausal Gonadotropin*
HOS	*Hypo-Osmotic Swelling*
ICSI	*Intra- cytoplasmic Sperm Injection*

IVF	*In Vitro Fertilization*
IVF-ET	*In Vitro Fertilization-Embryo Transfer*
LH	*Lutenizing Hormone*
MESA	*Microsurgical Epididymal Sperm Aspiration*
M I	*Metaphse I*
MII	*Metaphase II*
m-RNA	*messanger Ribonucleic Acid*
OC	*Oral Contraceptives*
OHSS	*Ovarian Hyperstimulation Syndrome*
OR	*Ovarian Reserve*
PCC	*Premature chromosomal condensation*
PCO	*Polycystic Ovaries*
PCOS	*Polycystic Ovary Syndrome*
PFC	*Preovulatory Follicular Count*
r-FSH	*recombinant Follicle Stimulating Hormone*
ROSI	*Round Spermatid Injection*
ROSNI	*Round Spermatid Nucleus Injection*
r-RNA	*Ribosomal Ribonucleic Acid*
SD	*Standard Deviation*
TEM	*Transmission Electron Microscopy*
TESE	*Testicular Sperm Extraction*
TNF- a	*Tumor Necrosis Factor -a*

TSH	*Thyroid Stimulating Hormone*
t-RNA	*Transfer Ribonucleic Acid*
u-FSH	*Urinary F ollicle Stimulating Hormone*

Introduction

Infertility affects approximately 10 -15 % of couples and is an important part of practice in Gynecology. Assisted reproduction technology has gained increasing importance lately and ovarian stimulation is a key procedure in assisted reproduction technology.

Ovarian stimulation is achieved by administration of exogenous gonadotrophins to increase follicular recruitment and oocyte yields. Although the regulatory mechanisms determining the extent of the sensitivity of individual antral follicles to FSH remain to be elucidated. The appropriate response of antral follicles to FSH and a high quality of oocytes may result in a good outcome after IVF/intracytoplasmic sperm injection (ICSI) ***(Zhang et al., 2013).***

There is no marker that can effectively predict both ovarian response and oocyte competence. The antral follicular count (AFC) comprises the number of follicles of 3–10 mm diameter measured in ovaries at the start of the menstrual cycle ***(de Carvalho et al., 2008).*** The AFC may reflect the size of the remaining primordial pool in women with proven natural fertility, and is highly correlated to the number of oocytes retrieved ***(Broer et al., 2009).***

Otherwise, AFC can be used in the prediction of ovarian response but not of oocyte/embryo quality or IVF outcome. The

number of preovulatory follicles (PFC) obtained at the end of ovarian stimulation is not a reliable reflection of antral follicle sensitivity to FSH, as it is greatly influenced by the number of small antral follicles available before treatment ***(Melo et al., 2009).***

To evaluate follicular responsiveness to exogenous FSH, the use of the follicular output rate (FORT) as an innovative measure has been suggested. FORT is assessed by the ratio of the preovulatory follicle count (PFC; 16–22mm) obtained in response to FSH administration on the day of human chorionic gonadotrophin (hCG) administration to the small antral follicle count (3–10 mm) ***(Genro et al., 2011)*** observed after the complete suppression of endogenous gonadotrophins by gonadotrophin-releasing hormone agonist(GnRHa) . (FORT = PFCx100/AFC) ***(Gallot et al., 2012).***

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Aim of work

To assess the accuracy of Follicular Output Rate (FORT) as a prognostic indicator of clinical pregnancy rate in women undergoing ICSI treatment.

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The ovary

Although Leonardo Da Vinci (1452 — 1519) drew accurately the anatomy of the uterus and the ovaries, the major advances in anatomic knowledge can be traced to the University of Padua, the famed Italian university where a succession of anatomists made important contributions ***(Motta et al., 1997)***.

Vesalius was the first to describe ovarian follicles and probably the corpus luteum. Fallopius (1523 - 1562***),*** was remembered for his description of the fallopian tubes. Fabricuis (a student of fallopius who in turn a student of Vesalius) was the first one to name the female gonad ovary **(*Motta et al., 1997*)**.

De Graaf was the first to accurately describe the corpus luteum and the graafian follicle which was named after him.

The process of fertilization was described by Newport in 1853, *bringing to a close the era of descriptive anatomy of the ovary and the* beginning of scientific explorations into physiology and endocrinology ***(Gougeon, 1986).***

The physiologic responsibilities of the ovary are the periodic release of gametes (eggs, oocytes) and the production of the steroid hormones (estradiol, progesterone). Both activities are integrated in the continuous repetitive process of follicle maturation, ovulation, and corpus luteum formation and regression ***(Motta et al., 1997).***

The ovary consists of three major portions: the outer cortex, the central medulla, and the retii ovary (the hilum). The hilum is the point of attachment of the ovary to the mesovarium. It contains nerves, blood vessels, and hilus cells. The outer most portion of the cortex is called tunica albuginea, topped on its surface by a single layer of cuboidal epithelum, referred to as the ovarian surface epithelium. The oocytes, enclosed in complexes called follicles, are in the inner part of the cortex ***(Motta et al., 1997)***.

Stages of Development of ovary:

The ovary starts development as early as intra uterine passing through the following stages (fetal, neonatal, children, adult ovary).

1-The fetal ovary:

During fetal life, the development of the human ovary can be traced through four stages:

a) The indifferent gonad stage
b) The stage of differentiation
c) The period of oogonal multiplication and oocyte formation, and finally
d) The stage of follicle formation.

a) The Indifferent Gonad Stage

At approximately 5 weeks of gestation, the paired gonads are structurally consolidated coelomic prominences overlying the