CONCENTRATION OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN FOLLICULAR FLUID IN RELATION TO DIAMETER, MATURITY OF OOCYTES AND FERTILIZATION RATE IN PATIENTS UNDERGOING INVITRO FERTILIZATION

THESIS

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GYNAECOLOGY AND OBSTETRICS

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في

تحت عنوان : باللغة الانجليزية : Concentration of Vascular endothelial Growth Factor in Follicular Fluid in relation to diameter maturity of oocytes and Fertilization rate in Patients undergoing ICSI

باللغة العربية : العلاقة بين تركيز عامل نمو الأوعية الدموية في السائل المحيط بالجويبة وقطرها ونضوج البويضة في المرضى الذين يخضعون لعلاج الحقن المجهري

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"قالوا سبحانك لا علما لنا الا ما علمتنا
انك أنت العليم الحكيم"

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LIST OF ABBREVIATIONS

AFC	Antral follicle count.
AMH	Anti mullirian hormone.
ART	Assisted Reproductive Technology.
Cb2	Cabergoline
COH	Controlled ovarian hyperstimulation.
DA	Dopamine agonists.
E2	Estradiol.
ECM	Extracellular matrix.
EGF	Epidermal growth factor
eNOS	Endothelial nitric oxide synthase.
ET	Embryo transfer.
FF	Follicular fluid.
FGF	Fibroblast growth factor.
FLK	Fetal liver kinase.
FSH	Follicular stimulating hormone.
GC	Granulosa cell.
GnRH	Gonadotropin releasing hormones.
GV	Germinal vesicle.
HSA	Human serum albumin.
HCG	Human chorionic gonadotropin.
HLA	Human leucocytic antigen.
HMG	Human memopausal gonadotropin.
ICM	Inner cell mass.
ICSI	Intracytoplasmic sperm injection.
IVF	In vitro fertilization.
IVM	In vitro maturation.
LH	Luteinizing hormone.
LMWH	Low molecular weight heparin.

LPS	Luteal phase support.
MCES	The mean cumulative embryo score.
MPR	Multiple pregnancy rates.
NIVF	Natural cycle IVF.
NRP1	Neuropillin 1.
NSAIDs	Non-steroidal anti-inflammatory drugs.
OHSS	Ovarian hyperstimulation syndrome.
OPU	Ovum Pick Up.
PAF	Platelets activating factor.
PCO	Polycystic ovary.
PCR	Polymerase chain reaction.
PGD	Preimplantation genetic diagnosis.
PN	Pronuclei.
PR	Pregnancy rate.
RCTs	Randomized controlled trials.
RIF	Recurrent implantation failure.
SART	Society for Assisted Reproductive Technology.
SBT	Single Blastocyst Transfer.
SEET	Stimulation endometrium embryo transfer.
SET	Single embryo transfer.
SVEGFR	Soluble VEGF receptor.
tPA	Tissue type plasminogen activator.
UPA	Urokinase type plasminogen activator.
VEGF	Vascular endothelial growth factor.
VP	Vascular permeability.
XO	Crossing over.
ZP	Zona Pellucida.

ABSTRACT

From this study we can conclude that locally produced growth factor, such as VEGF has significant important modulatory role in follicular growth and development by angiogenesis. Our study demonstrated that VEGF concentration in FF is positively correlated with follicular diameter and volume of FF r-0.885 (p-value 0.0001). HS VEGF is the major regulator of ovarian angiogenesis and may play a modulator role in the functional activity of GCs and follicular growth. Local production of VEGF may be important for mediating the GC-theca cell interaction required for antral follicle development. VEGF is associated with higher fertilization rate of mature oocytes. oocytes with positive fertilization had higher VEGF concentration (357.7±176.1) than negative fertilized oocytes 351.8±229.2 (*p*-value, 918) NS.

KEYWORDS:

Vascular endothelial growth factor
Follicular fluid
Oocytes and fertilization
In vitro fertilization

INTRODUCTION

INTRODUCTION

The development of an ovarian follicle from a small preantral follicle to a large preovulatory follicle, ovulation, and the formation of a corpus luteum (CL) after ovulation are key processes in the female reproductive cycle. These physiological processes are accompanied by marked changes in vasculature of the ovary (**Kanzaki H.,** *et al.,* **1982).**

The ovary is distinctive in that it is a site of active angiogenesis, and the development of follicular microvasculature is regulated by angiogenic factors in the ovary (**Robinson RS.,** *et al.*, **2009)**

A number of mediators induce angiogenesis, including members of the fibroblast growth factor (FGF) family, vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), tumor necrosis factor (TNF)-α, and members of the chemokine family (**Yancopoulos GD.,** *et al.*, **2000).**

Substances participating in angiogenesis are often secreted or transported into the follicular fluid (FF), and several factors detected in human FF are suggested to play roles in the human ovary (**Kawano Y.,** *et al.,* **2003).**

The VEGF acts as a key angiogenic factor in the regulation of ovarian vascularization; vascular endothelial growth factor is a 46-kDa disulfide-linked homodimeric glycoprotein that stimulates vascular endothelial cell proliferation, migration, organization into tubules, and permeability (**Ferrara N.,** *et al.,* **1998).**

All types of VEGF are produced by GCs, predominantly VEGF121 and VEGF165. The VEGF121 and VEGF165 promote the proliferation of vascular endothelial cells and permeabilization of blood vessels (**Kamat BR.,** *et al.,* **1995).**

It is produced by the theca interna and granulosa cells (GCs) in the human ovary in the preovulatory phase.

In view of pleiotropic functions of VEGF, we hypothesized that this angiogenic factor was involved in the development of human ovarian follicles. In this study, we will measure the concentrations of VEGF in individual human preovulatory follicles and related them to follicular diameter and volume to clarify the role of these molecules in folliculogenesis and assess relation between concentration of VEGF and maturity of oocyte and fertilization rate.

AIM OF THE WORK

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Aim of this work is to examine the relationship between VEGF concentration in FF and diameter of mature oocytes and fertilization rate in patients undergoing IVF.