

The Effect of Endometrial Injury on Pregnancy Rate in Women with Previous Intracytoplasmic Sperm Injection Failure/ a Randomized Clinical Trial

A thesis

Submitted for Partial Fulfillment of Master Degree
in Obstetrics and Gynecology

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سببنا انك لا تعلم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Dedication

For My Country

IRAQ

With Hopes To

Live In Peace



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List of Abbreviations

ART	: Assisted reproductive technique
ART U	: Assisted reproductive technique-unit
BMI	: Body mass index
CAM	: Cellular anti-adhesion molecules
CC	: Clomiphene citrate
CD	: Cluster of differentiation
CGH	: Comparative genomic hybridization
COH	: Controlled ovarian hyperstimulation
COX	: Cyclooxygenase
CSF-1	: Colony Stimulating Factor-1
DCs	: Dendritic cells
DNA	: Deoxyribonucleic acid
E2	: Estradiol 2
ECM	: Extracellular matrix
EC	: Early cleavage
EFT	: Endometrial Function Test
EGF	: Epidermal growth factors
EG-VEGF	: Endocrine gland-derived vascular endothelial growth factor
ENaCs	: Epithelial Na ⁺ channels
ERC	: Ethics and Research committee
ESHRE	: European Society of Human Reproduction and

List of Abbreviations

Embryology

ET	: Embryo transfer
FCP	: Fallopian tube sperm perfusion
FISH	: Fluorescence insitu hypridization
FSH	: Follicle-stimulating hormone
GnRH	: Gonadotropin releasing hormone
GRO-α	: Growth-regulated oncogene- α
HB-EGF	: Heparin binding-epidermal growth factor
HCG	: Human chorionic gonadotrophin
HEPS	: N-hydroxyethylpiperazin-N ethanolsulfonate
HLA-G	: Human leukocyte antigen G
sHLA-G	: Serum human leukocyte antigen G
HMG	: Human menopausal gonadotrophins
HSA	: Human serum albumin
HTF	: Human tubal fluid
ICSI	: Intracytoplasmic sperm injection
IGF	: Insulin like growth factor-II
IL	: Interleukin
INF	: Inferno
IVF	: In vitro fertilization
IVM	: Invitro maturation
IU	: International unit
LH	: Luteinizing hormone

List of Abbreviations

LIF	: Leukemia inhibitory factor
rLIF	: Recombinant Leukemia inhibitory factor
MCSF	: Macrophage colony stimulating factor
MHC	: Major histocompatibility complex
MIP-1B	: Macrophage inflammatory protein 1B
MUC	: Mucin
NCSs	: Nucleolar channel systems
NK	: Natural killer
OHSS	: Ovarian hyperstimulation syndrome
PB	: Polar body
PGE2	: Prostaglandin E2
PGS	: Pre implantation genetic screening
PGs	: Prostaglandins
PN	: Pronuclear
POF	: Premature ovarian failure
PCOS	: Polycystic ovarian syndrome
PZD	: Partial zonal dissection
RIF	: Recurrent implantation failure
RCT	: Randomized collecting trial
RNA	: Ribonucleic acid
SGK-1	: Serum-and Glucocorticoid-Regulated Kinase
SPP1	: Secreted phosphoprotein 1
SUZI	: Subzonal insemination

List of Abbreviations

TESA	: Testicular sperm aspiration
TGF	: Transforming Growth Factor
TNF-α	: Tumor necrosis factor- α
TSH	: Thyroid-stimulating hormone
UGET	: Ultrasound guided embryo transfer
WOI	: Window of implantation

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Introduction:-

Infertility is the inability to conceive after 1 year of unprotected intercourse. It is a common problem affecting approximately 13-14% in couple's reproductive age in other ward up to one in seven couples all over the world⁽¹⁾.

In vitro fertilization-embryo transfer (**IVF-ET**) and more recently, intracytoplasmic sperm injection (**ICSI**) are now commonly used treatment for infertility attributable to tubal factor, significant endometriosis, male factor and also used to treat persistent unexplained infertility⁽²⁾.

Intracytoplasmic sperm injection (ICSI) is one of the modalities of assisted reproductive technique which aims to the treatment of couples in whom the male partners has azoospermia or sever oligospermi. It can be used successfully in patients with fertilization failures after conventional IVf' and also in patients with too few morphologically normal and progressive, motile spermatozoa present in the ejaculate (<500,000) ⁽³⁾.

Analysis of data from National and Regional registers for trends in the use of ICSI and indications for assisted reproductive technology (ART) show that the use of ICSI has increased from 39.6% of ART cycles in 1997 to 58.9% in 2004⁽⁴⁾ relegating varicocele repair, vasectomy reversal, diagnosis and treatment of ejaculatory duct obstruction.

Implantation Failure:

Implantation failure is considered as the process by which an embryo cannot attaches to the uterine wall and cannot penetrates the epithelium. It has been postulated that the largest single cause of failed pregnancy is an error of implantation, the

rate of which may be as high as 78% in humans ⁽⁵⁾. Factors affecting success rate of implantation

Patient factor: including female age ,genetic factors as HOX genes that seem to play an important role in regulating differentiation of the endometrium in preparation for embryonic implantation , low parity, high body mass index and tubal disease⁽⁶⁾.

Embryo Factors: including number and quality of embryos transferred, assisted hatching, blastocyst culture ⁽⁷⁾ and embryo transfer ⁽⁸⁾.

Stimulation protocols factors: It has now been established that the routine use of GnRHa prior to IVF and gamete intrafallopian transfer “GIFT” increases the clinical pregnancy rate compared to the use of HMG alone ⁽⁹⁾.

Endometrial Factors: includes endometrial thickness and blood flow ⁽⁸⁾, endometrial mediators (cycle dependent substances) that increase adhesion of embryos to endometrium as mucins, Integrins, Trophinin and tastinand, growth factors and cytokines ⁽¹⁰⁾.

For implantation to occur, a genetically normal blastocyst should hatch, appose, adhere, penetrate, and finally invade a well-synchronized endometrium, under the influence of estrogens and progesterone. Recently, a number of locally acting molecules including growth factors, cytokines, matrix metalloproteinases (MMPs), adhesion molecules, extracellular matrix components, and homeobox element containing genes, which mediate the action of the steroids hormones on the endometrium, have been discovered ⁽¹¹⁻¹²⁾.