

No. 20 S
20
Ain Shams University
Faculty of Medicine
Department of Obstetrics & Gynaecology

**OVULATION INDUCTION WITH HUMAN MENOPAUSAL
GONADOTROPIN AFTER PITUITARY SUPPRESSION BY
GONADOTROPIN RELEASING HORMONE AGONIST
VERSUS CLOMIPHENE CITRATE AND HUMAN
MENOPAUSAL GONADOTROPIN IN
POLYCYTIC OVARIAN DISEASE**

MSA
THESIS

Submitted for the partial fulfillment of
The Master Degree in Obstetrics and Gynaecology

618.11
A. A
By
AZZA ALY MOHAMED
M.B., B.Ch.
Faculty of Medicine - Ain Shams University
Resident in El Mataria Teaching Hospital

52834
Under supervision of

DR. JEHAN ALLAM HAMED SAAD
Assistant Professor of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

DR. HASSAN AWWAD BAYOUMY
Lecturer of Obstetrics and Gynaecology
Faculty of Medicine
Ain Shams University

**Cairo
1994**



بسم الله الرحمن الرحيم

«لله ملك السموات والأرض يخلق ما يشاء يهب لمن يشاء
إناثاً ويهب لمن يشاء الذكور (٤٩) ، أو يزوجهم ذكرانا
وإناثاً ويجعل من يشاء عقيماً إنه عليم قدير (٥٠)»

صدق الله العظيم

سورة الشورى : الآيات ٤٩ ، ٥٠



To whom who give me

Love and kindness

To my Parents

and my Husband.

ACKNOWLEDGEMENT

Thanks to GOD to whom I am always indebted.

I wish to express my thanks and deepest appreciation to DR. JEHAN ALLAM HAMED, Assistant Professor of Obstetrics and Gynaecology, Faculty of Medicine, Ain Shams University, for her great help, continuous encouragement, unlimited support and constructive criticism and advise throughout the course of this study.

I also wish to express my sincere gratitude to DR. HASSAN AWWAD BAYOUMY, Lecturer of Obstetrics and Gynaecology, Faculty of Medicine, Ain Shams University, for his meticulous supervision, great interest, and generous help throughout the progress of this work.

I would like to have this opportunity to thank all those who helped me to reach the final form of this work.

Thanks to my patients, for without their help this work would not have come to light.

CONTENTS

	Page
Introduction	1
Aim of the Work	3
Review of Literature	4
• Physiology of Ovarian Function	4
• Polycystic Ovarian Disease (PCOD)	21
• Luteal Phase Dysfunction (LPD)	41
• Induction of Ovulation	55
• Gonadotropin Releasing Hormone (GnRH) Therapy and its Analogues (GnRHa)	84
• Monitoring of Ovulation	95
Materials and Methods	108
Results	116
Discussion	142
Summary and Conclusion	151
References	154
Arabic Summary	

LIST OF TABLES

	Page
Table (1): Mean $\pm$ SD of the size of follicles on 8th day of cycle after treatment in GI and G2.	115
Table (2): Mean $\pm$ SD of the number of follicles on 8th day of cycle after treatment in GI and G2.	116
Table (3): Mean $\pm$ SD of the size of follicles on 10th day of cycle after treatment in GI and G2.	117
Table (4): Mean $\pm$ SD of the number of follicles on 10th day of cycle after treatment in GI and G2.	118
Table (5): Mean $\pm$ SD of level of E ₂ on 10th day of cycle after treatment in GI and G2.	119
Table (6): Mean $\pm$ SD of size of follicles on 11th day of cycle after treatment in GI and G2.	120
Table (7): Mean $\pm$ SD of number of follicles on 11th day of cycle after treatment in GI and G2.	121
Table (8): Mean $\pm$ SD of level of E ₂ on 11th day of cycle after treatment in GI and G2.	122
Table (9): Mean $\pm$ SD of size of follicles on 12th day of cycle after treatment in GI and G2.	123

	Page
Table (10): Mean $\pm$ SD of number of follicles on 12th day of cycle after treatment in GI and G2.	124
Table (11): Mean $\pm$ SD of level of E ₂ on 12th day of cycle after treatment in GI and G2.	125
Table (12): Mean $\pm$ SD of size of follicles on 13th day of cycle after treatment in GI and G2.	126
Table (13): Mean $\pm$ SD of number of follicles on 13th day of cycle after treatment in GI and G2.	127
Table (14): Mean $\pm$ SD of level of E ₂ on 13th day of cycle after treatment in GI and G2.	128
Table (15): Mean $\pm$ SD of day of ovulation in GI and G2.	129
Table (16): Correlation between estradiol (E ₂), size of follicles and number of follicles in group I.	130
Table (17): Correlation between estradiol (E ₂), size of follicles and number of follicles in group II.	136

LIST OF FIGURES

	Page
Fig. (1): Steroidogenesis in the ovary.	5
Fig. (2): Development of the follicle.	12
Fig. (3): Dynamic changes of hormone concentration during the menstrual cycle.	19
Fig. (4): Showing pathophysiology of luteal phase dysfunction	46
Fig. (5): Drugs used in induction of ovulation.	110
Fig. (6): Ultrasound used in folliculometry (5 MHZ, Aloka 630, Japan).	112
Fig. (7): Correlation between E ₂ and size of follicles at day 10 in group 1.	132
Fig. (8): Correlation between E ₂ and No of follicles at day 10 in group 1.	133
Fig. (9): Correlation between E ₂ and and No of follicles at day 11 in group 1.	134
Fig. (10): Correlation between E ₂ and No of follicles at day 12 in group 1.	135
Fig. (11): Correlation between E ₂ and No of follicles at day 13 in group 1.	136
Fig. (12): Correlation between E ₂ and size of follicles at day 10 in group 2.	138
Fig. (13): Correlation between E ₂ and No of follicles at day 10 in group 2.	139
Fig. (14): Correlation between E ₂ and and No of follicles at day 11 in group 2.	140
Fig. (15): Correlation between E ₂ and No of follicles at day 12 in group 2.	141

LIST OF ABBREVIATIONS

ACTH	Adrenocorticotrophic hormone
BBT	Basal body temperature
CAH	Congenital adrenal hyperplasia
CASH	Cortical androgen stimulating hormone
CC	Clomiphene citrate
CNS	Central nervous system
DES	Diethylstilbesterol
DHEAS	Dehydroepiandrosterone sulfate
DHT	Dihydrotestosterone
E ₂	Oestradiol
FSH	Follicle stimulating hormone
GF	Growth factor
GnRH	Gonadotropin releasing hormone
GnRHa	Gonadotropin releasing hormone analogues
GnRIH	Gonadotropin releasing inhibitory hormone
HCG	Human chorionic gonadotropin
HIGFBP-1	Human insulin like growth factor-1 binding protein
HMG	Human menopausal gonadotropin

IGF-1	Insulin like growth factor
IVF-ET	In vitro fertilization and embryo transfer
LH	Luteinizing hormone
LHRH	Luteinizing hormone releasing hormone
LPD	Luteal phase dysfunction
OHSS	Ovarian hyperstimulation syndrome
P	Progesterone
PCOD	Polycystic ovarian disease
SHBG	Sex hormone-binding globulin
Sm-C	Somatomedin C

Introduction

INTRODUCTION

Polycystic ovarian disease (PCOD) is a condition with exaggerated steady state of tonic gonadotropin and estrogen function associated with persistent anovulation (*Rebar et al., 1976*).

Clinically, it is characterized by chronic anovulation which is the main hallmark of the disease, symptoms of this include amenorrhea, infertility and functional bleeding. There is a lot of theories regarding the pathophysiology of PCOD (*Rebar et al., 1976*).

Induction of ovulation whether medical or surgical is considered to be a management for chronic anovulatory state (*Hoult et al., 1981; Diamond et al., 1986*).

Clomiphene citrate has been used in different doses 50, 100, 150 mg per day for ovulation induction (*Hoult et al., 1981; Diamond et al., 1986*).

Treatment with clomiphene citrate alone or in combination with human menopausal gonadotropin (HMG) is probably the most popular superovulation regimen in current use in I.V.F. programs (*Quigley et al., 1983; Lopata, 1983*).

The use of HMG starting early in follicular phase and continued until satisfactory response is attained as judged by ultrasound and estradiol assay, then human chorionic gonadotropin (HCG) is injected to induce ovulation (*Laufer et al.*, 1983) when estradiol level ≥ 600 pg/ml and 2 follicles ≥ 18 mm.

In ovulation induction program to induce pharmacological hypophysectomy through suppression of pituitary function with the use of gonadotropins as an exclusive source of ovarian stimulation. Luteinizing hormone releasing hormone (LHRH) analogues were suggested to be used in different ways, to induce pituitary suppression and to enhance endogenous gonadotropin secretion using pulsatile LHRH infusion, also to replace HCG administration in midcycle (*Jones et al.*, 1985).

Aim of the Work