



Assessment of Ovulation in Polycystic Ovary Syndrome after Treatment with Tamoxifen

A Thesis Submitted to the Faculty of Medicine at Cairo University In final Fulfillment of Master Degree in Obstetrics and Gynecology

By

Maha Shaban Mohamed

M.B., B.Ch. (2004) – Faculty of medicine Misr University for science and technology

Supervised by

Prof. Dr. Sherif Abdel Rahman El Sharkawy

Professor of obstetrics and gynecology Faculty of Medicine-Cairo University

Dr. Ahmed Zakaria El Sheikhah

Associate Professor of obstetrics and gynecology Faculty of Medicine-Cairo University

Dr. Adel Mohammed Ali Nada

Assistant Professor of obstetrics and gynecology Faculty of Medicine-Cairo University

TABLE OF CONTENTS

LIST	Γ OF TABLES	
LIST	Γ OF FIGURES	
LIST	Γ OF ABBREVIATIONS	
ACK	KNOWLEDGMENTS	
ABS	STRACT	
INT	RODUCTION	1
POL	LYCYSTIC OVARIAN SYNDROME (PCOS)	
D	DEFINITION OF PCOS	3
P	PATHOPHSIOLOY OF PCOS	6
	Insulin Resistance	7
	Neuroendocrine Defect	10
	Ovarian Defect	12
	Increased Peripheral Cortisol Metabolism	15
	Genetic of pcos	18
\mathbf{D}	IAGNOSIS OF PCOS	21
	Clinical Features	22
	Differential Diagnosis	26
T	REATMENT OF PCOS	31
	General Measures	31
	Medical Induction of Ovulation	32
	Surgical Induction of Ovulation	38
TAN	MOXIFEN	
	Mechanism of action	42
	Uses	43
	Side effects	44

RESULTS	50
CONCLUSIONS AND FUTURE WORK	68
REFERENCES	70
ARABIC ABSTRACT	90

LIST OF TABLES

TABLE No.	DESCRIBTION	PAGE
Table 1:	Criteria for the diagnosis of polycystic ovary	22
	syndrome (PCOS)	
Table 2:	Possible biochemical features	25
Table 3:	Description of personal characteristics of study group	50
	1 (Tamoxifen 10mg)	
Table 4:	Description of clinical characteristics of study group 1	50
	(Tamoxifen 10mg)	
Table 5:	Description of complaints among study group 1	50
	(Tamoxifen 10mg)	
Table 6:	Description of outcome among study group 1	51
	(Tamoxifen 10mg)	
Table 7:	Description of personal characteristics of study group	51
	2 (Tamoxifen 20mg)	
Table 8:	Description of clinical characteristics of study group	51
	(Tamoxifen 20mg)	
Table 9:	Description of complaints among study group 2	52
	(Tamoxifen 20mg)	
Table 10:	Description of outcome among study group 2	52
Tubic 10.	(Tamoxifen 20mg)	32
Table 11:	Description of personal characteristics of study group	53
Table 11.	3 (control)	33
T. I.I. 12		5 2
Table 12:	Description of clinical characteristics of study group 3	53
	(control)	
Table 13:	Description of complaints among study group 3	53
	(control)	
Table 14:	Description of outcome among study group 3 (control)	54
Table 15:	Comparison between group 1 and 2 regarding age and	58
	other anthropometric measures.	

LIST OF TABLES CONT.

TABLE No.	DESCRIBTION	PAGE
Table 16:	Comparison between group 1 and 2 regarding complaints	59
Table 17:	Comparison between group 1 and 2 regarding lab outcome	59
Table 18:	Comparison between group 1 and 2 regarding clinical outcome	59
Table 19:	Comparison between tamoxifen groups and control group regarding age and anthropometric measures	60
Table 20:	Comparison between tamoxifen groups and control group regarding complaints	60
Table 21:	Comparison between tamoxifen groups and control group regarding lab and clinical outcome	61
Table 22:	Comparison between tamoxifen groups and control group regarding clinical outcome	62

LIST OF FIGURES

FIGURE NO.	DESCRIBTION	PAGE
Figure 1:	Ultrasound appearance of polycystic ovaries	13
Figure 2:	Cut section of pcos	16
Figure 3:	Description of age according to study group	54
Figure 4:	Description of weight according to study group	55
Figure 5:	Description of height according to study group	55
Figure 6:	Description of FSH according to study group	56
Figure 7:	Description of LH according to study group	56
Figure 8:	Description of DHEAS according to study group	57
Figure 9:	Description of progesterone according to study group	57
Figure 10:	Description of endometrial thickness according to study group	58
Figure 11:	Comparison between tamoxifen given patients group and control group regarding FSH, LH, progesterone levels, and endometrial thickness	61
Figure 12:	Comparison between tamoxifen given patients group and control group regarding DHEAS levels	62
Figure 13:	Comparison between tamoxifen given patients group and control group regarding ovulation	63
Figure 14:	Comparison between tamoxifen given patients group and control group regarding leading follicle	63

LIST OF ABBREVIATIONS

ACTH Adreno Cortico Trophic Hormone

ALT ALanine amino Transferase

BMI Body mass index

CAH Congential Adrenal Hyperplasia

CC Clomiphene citrate

CL Corpus luteum

CT Computed Tomography

CYP CYtochrome P

DHEAS Dihydroepiandrostenedione

DM Diabetes mellitus

DNA Deoxyribonuclear Acid

EGF Epidermal growth factor

ESHRE/ASRM European Society for Human Reproduction and

Embryology and the American Society for

Reproductive Medicine

ER Estrogen Receptor

FAH Functional Adrenal Hyperandrogenism

FDA Food and Drug Administration

FOH Functional Ovarian Hyperandrogenism

FSH Follicle Stimulating Hormone

GH Growth Hormone

GnRH Gonadotropin-Releasing Hormone

HCG human Chorionic Gonadotropin

HMG Human Menopausal Gonadotropins

HS High-Significant

LIST OF ABBREVIATIONS CONT.

IGF Insulin like Growth Hormone

LH Luteinising Hormone

LOD Laparoscopic Ovarian Drilling

MRI Magnetic Resonance Imaging

Nd-YaG Neodymium – Yttrium – Aluminnum – Garent laser

NIH National Institutes of Health

NS Non- Significant

OHSS Ovarian Hyperstimulation Syndrome

OWR Ovarian Wedge Resection

PAI Plasminogen Activator Inhibitor

PCOS Polycystic ovary syndrome

PKC Protein Kinase C

PRL Prolactin

S Significant

SD Standard Deviation

SHBG Serum sex Hormone-Binding Globulin

SPSS Statistical package for Social Science

TGF-α Transforming Growth Factor-α

TGF-β1 Transforming Growth Factor-β1

TSH Thyroid stimulating hormone

WHO World Health Organization

β HSD β Hydroxy Steroid Dehydrogenase

ACKNOWLEDGEMENTS

I would like to express my sincere thanks and deepest gratitude to Prof. Dr. Sherif Abdel Rahman El Sharkawy, Professor of obstetrics and gynecology, Faculty of Medicine Cairo University for his continuous interest, encouraging supervision, and valuable discussions during the process of this work.

I am greatly indebted to Dr. Ahmed Zakaria El Sheikhah, Associate Professor of obstetrics and gynecology, Faculty of Medicine Cairo University, for his precious help. I am very thankful for the time he devoted to the completion of this work. Also, I wish to express my deep thanks to Dr. Adel Mohammed Ali Nada, Assistant Professor of obstetrics and gynecology, Faculty of Medicine Cairo University, for his supervision, assistance, encouragement and valuable comments.

Finally, I want to thank all friends and colleagues, for their cooperation, help and support that was needed during the conduction of this study.

To my father, my mother, and All my family

Abstract

Polycystic ovary syndrome (PCOS) is an endocrine disorder that affects approximately 5% of all women. It occurs amongst all races and nationalities, is the most common hormonal disorder among women of reproductive age, and is a leading cause of infertility.

The principal features are weight problems, lack of regular ovulation and/or menstruation, and excessive amounts or effects of androgenic (masculinizing) hormones. The symptoms and severity of the syndrome vary greatly among women. While the causes are unknown, insulin resistance, diabetes, and obesity are all strongly correlated with PCOS.

Common symptoms of PCOS include: (i) Oligomenorrhea, amenorrhea (irregular, few, or absent menstrual periods). (ii) Infertility, generally resulting from chronic anovulation (lack of ovulation). (iii) Hirsutism (excessive and increased body hair, typically in a male pattern affecting face, chest and legs). (iv) Hair loss appearing as thinning hair on the top of the head. (v) Acne, oily skin, seborrhea. (vi) Obesity: one of two women with PCOS is obese. (vii) Depression and deepening of voice.

The use of tamoxifen for ovulation induction may be considered as an alternative to clomiphene citrate especially in cases resistant to clomiphene citrate. Sixty female patients with polycystic ovarian disease with mean age 30 years completed the study. All patients in the study were complaining of inability to conceive and menstrual irregularities in the form of oligomenorrhea or amenorrhea. These 60 patients are divided the three groups each group includes 20 patients. The three groups are namely: *Group A*: includes 20 patients who take 10 mg Tamoxifen per

day from 3-7 day of the menstrual cycle. *Group B*: includes 20 patients who take 20 mg Tamoxifen per day from 3-7 day of the menstrual cycle, and *Group C*: includes 20 patients were controlled.

The features of the three groups are described by, personal characteristics (age, weight, .. etc), the clinical characteristics (FSH, LH DHEAS level, ...etc), complaints (infertility, oligomenorrhea, and hirsutism), and finally compared regarding the clinical outcome (ovulation and presence of leading follicles). From our results we can conclude that: Tamoxifen 20 mg given patients group shows the success of ovulation by 30 %. Tamoxifen 10 mg given patients group shows the success of ovulation by 20 %. On the other hand, the Control group did not show any success.

Key Words:

Luteinising Hormone - Standard Deviation - Protein Kinase C.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age. The overall prevalence among women in this age group is between 4% and 8%, although the prevalence may be as high as 30% in women with secondary amenorrhea, 75% in women with oligomenorrhea, and 90% in women with hirsutism (*Pedersen et al. 2007*).

In 1935, Stein and Leventhal published their report of seven women with amenorrhea, hirsutism, obesity, and enlarged polycystic appearing ovaries. Since then, much has been learned about this complex disorder (*Stein and Levanthal* 1935).

It is now well recognized that women with this syndrome not only have reproductive health issues but their metabolic and cardiovascular health is also affected. Until recently, there has been no universally accepted definition for PCOS. In 2003, an international consensus group proposed that the diagnostic criteria for PCOS are ovarian dysfunction evidenced by oligomenorrhea or amenorrhea and clinical evidence of androgen excess (e.g., hirsutism and acne) in the absence of other conditions that can cause these same signs and symptoms.

Polycystic ovaries, as defined by ultrasonography (the presence of 12 or more follicles in each ovary measuring 2 to 9 mm in diameter, and/or ovarian volume > 10 mL) should also be considered as one of the possible diagnostic criteria for PCOS.

It is important to note that polycystic ovaries need not be present to make the diagnosis of PCOS. In fact, Clayton observed that 23% of normal women met the sonographic criteria for polycystic ovaries (*Clayton et al. 1989*).

Aim of the Work

The aim of the present work is to:

- Assess the effect of tamoxifen on the follicle growth & ovulation rate.
- Compare 10 mg vs. 20 mg tamoxifen as dose for induction.
- Compare tamoxifen vs. controlled.

DEFINTION OF PCOS

The classic syndrome originally was described in 1935 by Stein and Leventhal as the association of amenorrhea with polycystic ovaries in women, of whom about two thirds were hirsute, and one-half was obese.

The term PCOS was introduced upon recognition of a broader spectrum of clinical symptoms and ovarian histology, including stromal hyperplasia with multiple sub capsular follicles. (*Goldzieher et al.*, 1996)

Approximately two-thirds of patients with classic PCOS have hirsutism (or hirsutism equivalents, acne vulgaris or pattern alopecia), two-thirds have an ovulatory symptoms (manifested as amenorrhea, oligomenorrhea, dysfunctional uterine bleeding, or unexplained infertility), and one half are obese.

Thus, only about one-third of classic cases have the full-blown clinical picture. The laboratory diagnostic criteria for classic PCOS require biochemical evidence of Hyperandrogenism with either a polycystic ovary by ultrasound or an increased serum level of lutenizing hormone (LH) to follicle-stimulating hormone (FSH) ratio. These criteria have proven not to necessarily coincide (*Colleen et al.*, 2005).

In 1990, the National Institutes of Health (NIH) Conference on PCOS considered the implications of recent research findings for the diagnosis. Fifty percent to 60% of those present concurred that the criteria for PCOS should consist of chronic anovulation with clinical or biochemical signs of Hyperandrogenism that was not explained by other etiologies. This recognized the spectrum of the syndrome to include androgen excess in the absence of ultrasonographic and gonadotropic abnormalities (here termed non classic PCOS) (*Rosenfield*, 1999).