بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Laparoscopic Ovarian Drilling versus Letrozole in Clomiphene Citrate Resistant Polycystic Ovary: A Randomized Controlled Trial

Thesis

Submitted for Partial Fulfillment of Master Degree of Obstetrics and Gynecology

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Amro Ibrahim Abdel Rauof El-Tayeb

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List of Abbreviations

Abb.	Full term
A	*Androstenedione*
AFC	*Antral Follicle Counts*
AIs	*Aromatas Inhibitors*
Bio-T	*Bioavailable Testosterone*
BMI	*Body Mass Index*
C/C	*Clomiphene Citrate*
CI	*Confidence Interval*
COH	*Controlled Ovarian Hyper-stimulation*
DM	*Diabetes Mellitus*
E2	*Estradiol*
ERs	*Estrogen Receptors*
FAI	*Free Androgen Index*
FSH	*Follicle-Stimulating Hormone*
FT	*Free Testesterone*
HCG	*Human Chorionic Gonadotropin*
HTN	*Hypertension*
IGF-I	*Insulin Growth Factor 1*
IRB	*Institutional Review Board*
IVF	*In Vitro Fertilization*
LDL	*Low- Density Lipoprotein*
LE	*Letrozole*
LH	*Luteinizing Hormone*
LOD	*Laparoscopic Ovarian Drilling*
MD	*Mean Difference*
OHSS	*Ovarian Hyperstimulation Syndrome*
OR	*Odds Ratio*
PCOS	*Polycystic Ovary Syndrome*
PDR	*Physician's Desk Reference*
POF	*Premature Ovarian Failure*
RCTs	*Randomized Controlled Trials*
RR	*Risk Ratio*
SD	*Standared Deviation*
SHBG	*Sex Hormone Binding Globulin*
T	*Testosterone*
TSH	*Thyroid-Stimulating Hormone*
WHO	*World Health Organization*

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Introduction

Polycystic ovary syndrome (PCOS) is a common cause of reproductive endocrinopathy in women and is characterized by hyperandrogenism, chronic oligo-anovulation and insulin resistance ***(Tehrani et al., 2011).***

Previous studies have suggested that PCOS not only leads to disorders of the reproductive axis and reproductive function, but also contributes to the abnormal metabolism of glucose, increasing the risk of endometrial and breast cancers ***(Brown et al., 2009).***

For infertile woman with PCOS, clomiphene citrate (CC) remains the first line treatment; however, 15-40% of women do not resume ovulation following CC treatment, which is defined as CC-resistance ***(National Collaborating Centre for Women's and Children's Health, 2004).***

Currently, the most common treatments for CC-resistant PCOS are laparoscopic ovarian drilling (LOD) and gonadotropin treatment. Successful pregnancy outcomes for both treatments have been reported ***(Palomba et al., 2009).*** All meta-analysis confirmed that LOD is a second line treatment in PCOS patients, especially those with CC resistance ***(Farquhar et al., 2012).***

The main benefits of LOD are shorter time to pregnancy and less need to ovulation induction drugs. The other advantages of this technique are more comfort, cost-effectiveness, and possibility to be performed ambulatory. However, the results of LOD are not better than those of CC as a first-line treatment in PCOS. Also there’re disadvantages of LOD, as it requires hospitalization and general anesthesia and may lead to pelvic adhesions and decrease the ovarian reserve, which would hinder any subsequent pregnancies ***(Farquhar et al., 2012).***

Aromatase inhibitors (AIs) offer a new approach to the treatment of anovulation in women with PCOS. These agents selectively inhibit the aromatase enzyme, which catalyzes the rate-limiting step in the production of estrogens ***(Mitwally and Casper, 2003).***

Letrozole is a potent and selective third-generation aromatase inhibitor, which can effectively and highly selectively block the production of estrogen without disturbing other steroidogenic pathways. Letrozole was first used to treat breast cancer and was found to be superior to the previous gold standard, tamoxifen, and more effective than other AIs ***(Mitwally and Casper, 2001; 2003).***

Mitwally and Casper introduced letrozole to the ovulation induction field; since then, numerous investigations into letrozole induced ovulation have been performed ***(Wang and Zheng, 2015).*** Furthermore, letrozole has a short half-life (45 hours) and is therefore rapidly eliminated from the body ***(Okman et al., 2003).***

These potential benefits of letrozole inspired the performance of a randomized controlled trial to compare the reproductive outcomes after letrozole administration with those after LOD in women with CC-resistant PCOS.

Aim of the work

The aim of this study is to compare the reproductive outcomes of laparoscopic ovarian drilling with letrozole in women with clomiphene citrate resistant PCOS.

Study Question:

In women with clomiphene citrate resistant PCOS, is laparoscopic ovarian drilling effective as letrozole to improve reproductive outcome?

Research Hypothesis:

In women with clomiphene citrate resistant PCOS, laparoscopic ovarian drilling may be effective as letrozole in improving reproductive outcome.

Patients and methods

Study design:

A Randomized Controlled Trial.

Setting:

This study will be conducted in Ain Shams university maternity hospital.

Population of the study:

Ninety women will be recruited from those attending the outpatient clinic or the infertility clinic at Ain Shams university hospital with PCOS based on the revised 2003 Consensus diagnostic criteria for PCOS ***(Rotterdam ESHRE/ASRM-Sponsored PCOS consensus workshop group, 2004).***

A written informed consent will be obtained from each woman before participation in the study.

Inclusion criteria:

The criteria for inclusion in this study will be as follows:

Women diagnosed as PCOS according to Rotterdam (2003) diagnostic criteria for PCOS, two out of three of:

1. Clinical hyperandrogenism (Ferriman-Gallwey score >8) or Biochemical hyperandrogenism (Elevated Total/Free Testosterone).
2. Oligomenorrhea (Less than 6-9 Menses per year) or Oligo-Ovulation.