

Clomiphene Citrate Versus Aromatase  
Inhibitors In Treatment Of Unexplained  
Infertility

**Thesis**

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# علاج العقم غير المفسر بمثبطات الاروماتيز أو سيترات الكلومفين

رسالة

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## SUMMARY

Unexplained infertility is diagnosed when all of the standard elements of the infertility evaluation yield normal results. The incidence of unexplained infertility ranges from 10% to as high as 30% among infertile populations, depending on diagnostic criteria. At a minimum, the diagnosis of unexplained infertility implies a normal semen analysis, objective evidence of ovulation, a normal uterine cavity, and bilateral tubal patency (*Speroff, 2005*).

No uniform treatment protocol has been yet proposed for unexplained infertility. Woman often resist treatment undergoing in vitro fertilization (*Collins, 2003*).

In the absence of a correctable abnormality, the therapy of unexplained infertility is empiric (*Collins, 2003*).

Ovarian stimulation is a way of treatment that might be used as a first line of treatment in young woman with unexplained infertility (*Dankert et al., 2007*). Clomphine appears to be superior to no treatment or placebo (*Hughes et al., 2000*) however, the risk of clomiphene citrate therapy include an increase in multiple pregnancy rates and a slight risk of ovarian hyperstimulation syndrome (*Schenker et al., 1981*). In addition, clomphine citrate has a long half-life and may have a negative effect on the cervical mucus and endometrium

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## *List of Abbreviations*

<b>A.I</b>	<b>Aromatase inhibitors</b>
<b>ART</b>	<b>Assisted Reproductive Technologies</b>
<b>C.C</b>	<b>Clomphine citrate</b>
<b>CCCT</b>	<b>Clomiphine citrate challenge test</b>
<b>COH</b>	<b>Controlled ovarian hyperstimulation</b>
<b>ER</b>	<b>Empryo transfer</b>
<b>FSH</b>	<b>Fallopian tube sperm perfusion</b>
<b>FSH</b>	<b>Follicle stimulating hormone</b>
<b>GnGH-a</b>	<b>Gonadotrophine releasing hormone agonist</b>
<b>GnRH</b>	<b>Gonadotrophine releasing hormone</b>
<b>HcG</b>	<b>Human Chorionic gonadotrophines</b>
<b>HMG</b>	<b>Human menopausal gonadotrophines</b>
<b>ICSI</b>	<b>Interacytoplasmic sperm injection</b>
<b>IUI</b>	<b>Interauterine Insemination</b>
<b>IVF/ET</b>	<b>In vitro fertilization and embryo transfer</b>
<b>OHSS</b>	<b>Ovarian hyperstimulation syndrome</b>
<b>PCOs</b>	<b>Polycystic ovary syndrome</b>
<b>PGD</b>	<b>Preimplantation genetics diagnosis</b>

<b>PRs</b>	<b>Pregnancy rates</b>
<b>PZD</b>	<b>Partial zona dissection</b>
<b>RCTs</b>	<b>Randomized controlled Trials</b>
<b>SUZI</b>	<b>Subzonal Insemination</b>
<b>U.I</b>	<b>Unexplained infertility</b>
<b>WHO</b>	<b>World health organization</b>
<b>ZP</b>	<b>Zona pellucida</b>

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## INTRODUCTION

Infertility is defined as inability of a couple to conceive after one year of sexual Intercourse without the use of any contraceptive method (*Speroff et al, 2004*).

Infertility is said to be unexplained infertility when a couple doesn't conceive and no definite cause can be diagnosed after a complete standerd evaluation (*Aboulghar, 2002*).

The incidence of infertile population diagnosed with unexplained infertility ranges from 10% -15% and using normal findings on more invasive diagnostic techniques as laproscopy as a criterion, the prevelance may be less than 10% (*Crosignani et al, 1993 and speroff, 2005*).

Unexplained infertility refers to a diagnosis in couples in whom standerd investigation including semen analysis, test of ovulation and tubal patancy test are normal (*Siristatidis, 2008*).

No uniform treatment protocol has been yet proposed for unexplained infertility. woman often resist treatment undergoing in vitro fertilization (*Collins, 2003*).

In the absence of a correctable abnormality, the therapy of unexplained infertility is empiric (*Collins, 2003*).

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## Introduction and Aim of the Work

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Ovarian stimulation is a way of treatment that might be used as a first line of treatment in young woman with unexplained infertility (*Dankert et al, 2007*). Clomphine appears to be superior to no treatment or placebo (*Hughes et al, 2000*) however, the risk of clomiphene citrate therapy include an increase in multiple pregnancy rates and a slight risk of ovarian hyperstimulation syndrome (*Schenker et al, 1981*). In addition, clomphine citrate has a long half-life and may have a negative effect on the cervical mucus and endometrium (*Casper and Mitwally, 2006*).

Aromatase inhibitors have been used successfully in women with advanced breast cancer (*Mauri et al, 2006*).

Recently they are used to induce ovulation they suppress estrogen production, have a reduced half-life, lack the persistent antiestrogenic effect of clomiphene citrate in the late follicular phase, and may have less adverse effects compared to clomiphene citrate (*Casper and Mitwally, 2006* ).

Aromatase inhibitors in women with polycystic ovary syndrome might achieve pregnancy rates higher than clomiphene citrate (*Polyzos et al, 2007*). And are relatively safe agents regarding newborns (*Tulandi et al, 2006*).

## **AIM OF THE WORK**

To compare the effectiveness of aromatase inhibitors to clomphine citrate for ovulation induction in women with unexplained infertility.

## **CHAPTER (1)**

### **Initial Recommendations Concerning Infertile Couples**

#### **1. Frequency and timing of sexual intercourse:**

People who are concerned about their fertility should be informed that sexual intercourse every 2 to 3 days optimizes the chance of pregnancy. Timing intercourse to coincide with ovulation causes stress and is not recommended (*Guermandi, 2001*).

#### **2. Alcohol:**

Women who are trying to become pregnant should be informed that drinking no more than one or two units of alcohol once or twice per week and avoiding episodes of intoxication reduces the risk of harming a developing fetus. Men should be informed that alcohol consumption within the department of health's recommendations of three to four unit per day for men is unlikely to affect their fertility. Men should be informed that excessive alcohol intake is detrimental to semen quality (*Oldereid, 1992*).

#### **3. Smoking:**

Women who smoke should be informed that this is likely to their fertility should be offered referral to a smoking