بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

MONA MAGHRABY

Letrozole Prior to Misoprostol in Shortening Abortion time in the Second Trimester Abortion: A Randomized Controlled Trial

A Thesis

Submitted for partial fulfillment of master degree
in Obstetrics & Gynecology

By

Amira Said Hassan Hassan
M.B.B.Ch, 2008, Ain Shams University
Resident at Al-Sheikh Zayed Al-Nahian Hospital

Under Supervision of

Prof. Dr. Ahmed Mohammed Ibrahim
Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. Mohammed Saeed El-Din El-Safty
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Dr. Haitham Fathy Mohammed Gad
Lecturer of Obstetrics and Gynecology
Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2020

Acknowledgments

First and foremost, I feel always indebted to **Allah**, *the* ***Most Beneficent*** *and* ***Merciful*** *who gave me the strength to accomplish this work.*

My deepest gratitude to my supervisor, **Prof. Dr. Ahmed Mohammed Ibrahim,** *Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision.*

I would like to express my great and deep appreciation and thanks to **Prof. Dr. Mohammed Saeed El-Din El-Safty,** *Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his meticulous supervision, and his patience in reviewing and correcting this work.*

I must express my deepest thanks to **Dr. Haitham Fathy Mohammed Gad,** *Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for guiding me throughout this work and for granting me much of his time. I greatly appreciate his efforts.*

Special thanks to **My Parents, My Husband** *and* **all My Family** *members for their continuous encouragement, enduring me and standing by me.*

Amira Said Hassan Hassan

List of Contents

List of Abbreviations

Abbr.	Full-term
Acl	**:** Anticardiolipin antibodies
ACTH	**:** Adrenocorticotrophic hormone
APL	**:** Antiphospholipid antibodies
CDC	**:** Center for disease control and prevention
CI	**:** Confidence interval
DIC	**:** Disseminated Intravascular Coagulopathy
E2	**:** Estradiol
FHR	**:** Fetal heart
FPSTS	**:** False positive serological test for syphilis
LH	**:** Luteinizing hormone
RR	**:** Relative risk
SD	**:** Standard deviation
SE	**:** Standard error
SPSS	**:** Statistical package for social science
TSH	**:** Thyroid-stimulating hormone
WHO	**:** World Health Organization

List of Tables

List of Figures

Introduction

Abortion, spontaneous or induced, is a common complication of pregnancy. The World Health Organization reported that annually about 79 million unintended pregnancies excluding miscarriages are occurring worldwide ***(Sedgh et al., 2006).*** And annually, about 46 million induced abortions occur in the world ***(Sedgh et al., 2007).*** The estimation of the total number of abortions is quite difficult, especially in developing countries, and it is usually underreported due to the legal restrictions a huge number of the inducted abortions are performed in non-hygienic situations. The abortion might load an undesirable cost to the families and health care system. Serious complications such as maternal death, uterine rupture, and sepsis may occur after abortions that are not taken place under medical observation ***(Shaikh et al., 2010).*** The safety of the procedure has a dramatic importance in order to achieve a non-life threatening result ***(Naghshineh et al., 2015).***

Induced abortion can be performed by medical and surgical methods. Medical abortion is the induction of early abortion by consumption of special medications and is named successful if it is completed without the need of any surgical intervention. Also, the medical approach is a safe and effective alternative to surgical methods with a high level of patient satisfaction ***(Behjati; et al., 2005; Hosseini, 2007).***

Prostaglandins and their analogs are widely used for medical induced abortion. Misoprostol is a synthetic prostaglandin E1 analogue, manufactured as an oral preparation available as 200 mcg tablets used to prevent and treat gastro-duodenal damage induced by nonsteroidal anti-inflammatory drugs ***(Lee et al., 2011).*** The most common adverse effects of misoprostol are nausea, vomiting, diarrhea, abdominal pain, chills, shivering, and fever, all of which are dose-dependent. Misoprostol taken by pregnant women increases uterine tone and contractions ***(Mitwally and Casper, 2005).***

Misoprostol, a prostaglandin E1 analog, is used widely for early abortion and has been shown to be a better alternative to other prostaglandin substances due to feasibility, simple and easy administration, low price, stability at room temperature, and fewer systemic side-effects. Sublingual and vaginal are two common routes of misoprostol administration with different pharmacokinetics and effectiveness. Sublingual misoprostol reaches its peak concentration in a short time (20-40 minutes) and vaginal route has less adverse effects after administration. The range of reported successes rate of abortion induction with misoprostol is quite different in several studies (between 37% and 86%) depending on the regimen, route of administration, and dosage used. However, in combination with other drugs was more effective ***(Tanha et al., 2013).***

Letrozole is a non-steroidal competitive inhibitor of the aromatase enzyme system; it inhibits the conversion of androstenedione into estrone and the conversion of testosterone into estradiol. Letrozole acts differently from Tamoxifen in that it does not compete for the estrogen receptor but instead inhibits synthesis of estrogen ***(Kallner, 2012).***

Letrozole inhibits the aromatase enzyme by competitively binding to the heme of the cytochrome P450 subunit of the enzyme, resulting in a reduction of estrogen biosynthesis in all tissues. However, there were no data on the mechanism of action of letrozole in the context of termination of pregnancy ***(Kallner, 2012).***

There are two possible mechanisms of action for letrozole in termination of pregnancy. Letrozole may act directly on the corpus luteum in the early pregnancy or placenta in later gestation ***(Lee et al. 2011)a.***

Letrozole is capable of suppressing the estrogen biosynthesis very effectively up to 63 days. For more advanced gestations the percentage of suppression may not be satisfactory because of the higher basal E2 level ***(Lee et al., 2011)c.***

Letrozole did not affect uterine contractility or increase the sensitivity to misoprostol of the uterine myometrium ***(Chai and Ho, 2013).***

It has been demonstrated that letrozole markedly suppressed serum Estradiol (E2) concentration while it had no effect on the progesterone level ***(Chai and Ho, 2013).***

Estradiol induces differentiation of cytotrophoblasts into syncytiotrophoblasts through Estrogen receptors. The letrozole induced reduction of E2 may suppress trophoblast differentiation leading to delayed placental development ***(Chai and Ho, 2013).***

Another possible mechanism is through its effect on vascular endothelial growth factor and Ang-1 expression ***(Chai and Ho, 2013).***

Aim of the Work

The aim of this study is to evaluate efficacy of letrozole prior to misoprostol in comparison with misoprostol alone in shortening induction abortion time in the second trimestric abortion.

Chapter (1)
Abortion

Definition:

Abortion is the spontaneous or induced termination of pregnancy before fetal viability., some prefer the word miscarriage to refer to spontaneous fetal loss before viability. The national center for health statistics, the center for disease control and prevention (CDC), and the world health organization (WHO) define abortion as pregnancy termination prior to 20 weeks' gestation or a fetus born weighing less than 500 g **(Halvorson, 2008).**

Incidence:

Studies with ultrasound demonstrate that fetal viability ceases weeks before maternal symptoms occur; thus fetuses aborting clinically at 10 to 12 weeks gestation usually died weeks before.

Etiology

1) Chromosomal abnormalities:

Chromosomal abnormalitie is the major cause of clinically recognized pregnancy losses is s. At least a 50% of clinically recognized pregnancy losses result from a chromosomal abnormality **(Simpson, 2002).**