



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم



MONA MAGHRABY



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شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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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



The efficacy of Primrose oil with misoprostol in induction of second trimester miscarriage: Randomized Controlled Trial

Thesis

*Submitted for Partial Fulfillment of Master Degree in
Obstetrics and Gynecology*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبِّحْكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
AA.....	Arachidonic acid
ACOG	American College of Obstetricians and Gynecologists
cEBL.....	Calculated estimated blood loss
D&E	Dilatation and evacuation
D6D.....	D-6-Desaturase
DGLA.....	Dihomo- γ -linolenic acid
EFAs	Essential fatty acids
EPO	Evening primrose oil
FIGO.....	International Federation of Gynecology and Obstetrics (Fédération Internationale de Gynécologie et d'Obstétrique).
GLA	Gamma linoleic acid
HCT.....	Hematocrit
LA	Linoleic acid
MTL	Mid-trimester loss
NO donors.....	Nitric oxide donors
PG.....	Prostaglandin
PMS	Premenstrual syndrome
VAS.....	Visual analogue scale
VS.....	Versus

PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF
MASTER DEGREE IN OBSTETRICS & GYNECOLOGY

Title of the Protocol: The efficacy of Primrose oil with
misoprostol in induction of second
trimester miscarriage: Randomized
Controlled Trial.

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**What is already known on this subject? AND
What does this study add?**

Second trimester missed miscarriage is usually terminated by either medical or surgical methods.

Medical methods include the use of prostaglandins, oxytocin and mifepristone.

Evening primrose oil is a commonly used alternative therapy and a rich source of omega-6 essential fatty acids. It is best known for its use in the treatment of systemic diseases marked by chronic inflammation, such as atopic dermatitis and rheumatoid arthritis. It is often used for several women's health conditions, including breast pain (mastalgia), menopausal and premenstrual symptoms and cervical ripening.

In this study we will assess if adding primrose oil to misoprostol will shorten the duration of medical termination of 2nd trimester missed miscarriage.

1. INTRODUCTION

Second-trimester pregnancy loss has been defined as miscarriage diagnosed between the duration of gestation of 12–24 weeks (*McNamee et al., 2014*).

Most common causes of termination of pregnancy in the second trimester are congenital anomalies and missed miscarriage (*Ho et al., 2007*).

Termination of pregnancy by medications is one of the commonest methods. 90% of cases takes place in the first trimester, while in the second trimester medical termination constitutes 10-15% cases of induced miscarriage (*Laikumar et al., 2007*).

The optimal method of second-trimester miscarriage for fetal anomalies or fetal death is not well established. Worldwide, induction of miscarriage is used more often than dilatation and evacuation (D&E). Reasons given for preferring medical miscarriage include not requiring skilled providers, allowing for expulsion of intact fetus (*Kelly et al., 2010*).

Although complications of dilatation and evacuation (D&E) procedure are rare, morbidity and mortality related to abortion increase with gestational age. Beyond 12 weeks, the complications increase

approximately 20 percent per week of gestation (*Zane et al., 2015*).

Prostaglandins of E series are effective in dilatation and ripening of the cervix (*Batukan et al., 2008*). In recent years, misoprostol (a synthetic Prostaglandin E1 (PGE1)) is widely used in obstetrics and gynecologic conditions such as medical miscarriage, before dilatation and vacuum aspiration, treatment of post-partum hemorrhage and before hysteroscopy (*Waddell et al., 2008*).

Evening primrose (*Oenothera L.*) is a plant belonging to the family Onagraceae. Evening primrose oil (EPO) is extremely high in linoleic acid (LA) (70–74%) and γ -linolenic acid (GLA) (8–10%), which may contribute to the proper functioning of human tissues because they are precursors of anti-inflammatory eicosanoids. EPO supplementation results in an increase in plasma levels of γ -linolenic acid and its metabolite dihomo- γ -linolenic acid (DGLA) which is metabolized to series 1 prostaglandins (*Timoszuk et al., 2018*).

Evening primrose oil is widely used by many midwives to hasten cervical ripening in an effort to shorten labor and decrease the incidence of postdates pregnancies (*Dove et al., 1999*).

Evening primrose oil is effective in cervical ripening before hysteroscopy. It is used as an easy method without serious adverse effects (*Vahdat et al., 2015*).

2. AIM/ OBJECTIVES

The aim of this study is to assess the efficacy of evening primrose oil in shortening the duration of induction of miscarriage when added to misoprostol in women with 2nd trimester missed miscarriage.

Research hypothesis

Null hypothesis:

In women with second trimester missed miscarriage, adding primrose oil to misoprostol will have no effect in shortening the duration of induction of miscarriage.

Alternative hypothesis:

In women with second trimester missed miscarriage, adding primrose oil to misoprostol will shorten the duration of induction of miscarriage.

Research question

Does adding primrose oil to misoprostol will shorten the duration of induction of second trimester missed miscarriage?

Outcome:**Primary outcome:**

-Number of patients with complete miscarriage within the first 24 hours.

Which is defined as the expulsion of both the fetus and the placenta without operative assistance and ultrasound documented endometrial thickness of less than 10 mm(Esmaeillou et al., 2015)

Secondary outcome:

- Duration to achieve complete miscarriage.

- Amount of blood loss (calculated according to the following equation
Calculated estimated blood loss (cEBL) = Calculated pregnancy blood volume X Percent of blood volume lost

Where * Percent of blood volume lost = (HCT on admission- post abortion HCT) / HCT on admission.

* Calculated pregnancy blood volume = (0.75 ([maternal height (inches) X 50]+ [maternal weight in pounds X 25]) (Stafford et al.,2008)

- Pain (will be evaluated using visual analogue scale (VAS) **appendix 1** immediately prior to misoprostol administration and when women seek analgesia and the total needed doses of analgesics.

Misoprostol induced fever (defined as oral temperature >37.8 °C with exclusion of other causes of fever)

Other side effects: nausea, vomiting and diarrhoea, rupture uterus and allergy to prostaglandins or EPO.

3. METHODOLOGY:**Patients and Methods**

-Type of the study: Randomized controlled clinical trial, pilot study.

-Study setting: Ain Shams University

-Study population:

120 women with second trimester missed miscarriage.

Inclusion criteria:

- 1- Women aged 20-35 years old.
- 2- Singleton pregnancy.
- 3- Primigravida.
- 4- 13-24 weeks gestation.
- 5- Fetal life is negative.

Exclusion criteria:

- 1- Any contraindications for misoprostol use as:-
 - a- Previous uterine incisions(previous C.S, myomectomy or hysterotomy).
 - b- Hemodynamic instability or shock.
 - c- Hypersensitivity or allergy to prostaglandins.
 - d- Intrauterine contraceptive device in situ.
- 2- Any contraindications for primrose oil use:-
 - a-Women with heavy bleeding or any bleeding disorder.
 - b-Epilepsy.
- 3- Rupture of fetal membranes.
- 4- Evidence of low implanted placenta by ultrasound.
- 6- Evidence of clinical or subclinical chorioamnionitis.

Sample size justification:

Using STATA program, setting alpha error at 0.5 (confidence level = 95%) and beta error at 0.2 (power = 80%). According to the result from previous study (**Ting et al., 2015**) that showed the success rate for misoprostol for termination of second trimester missed miscarriage was 61% within first 24 hours ,while it is assumed to be 85% after adding primrose oil.

Based on this, to compensate for a 10% drop-out rate, we multiplied the sample size by 110%, giving a total sample size of 120 women.

Study Interventions: After taking informed written consent the recruited women will be subjected to the following:

History: