



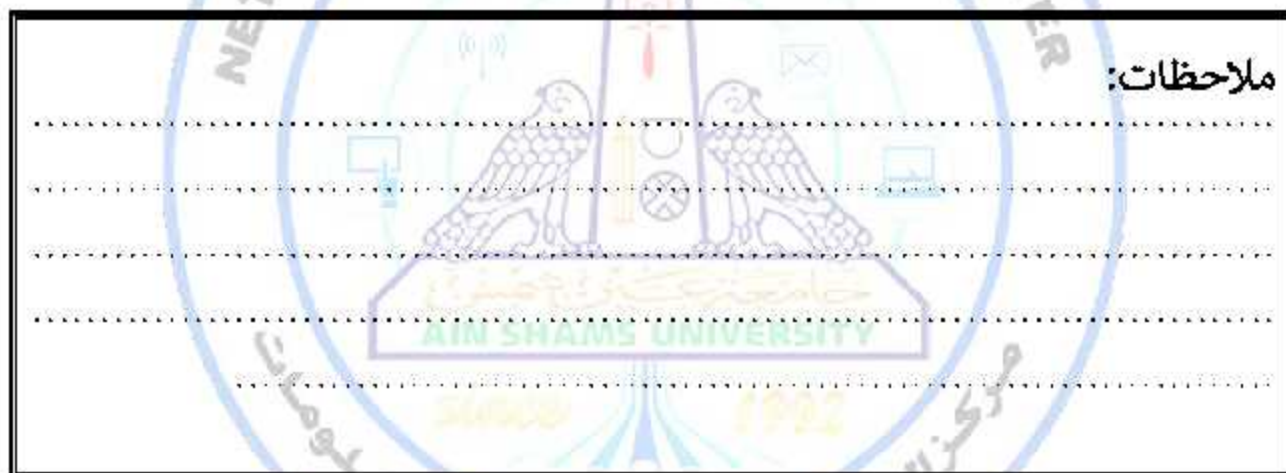
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تم رفع هذه الرسالة بواسطة / سنوي محمود عقل

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات:





Comparison of Duration Required for Expulsion with Misoprostol versus Misoprostol plus Isosorbide Mononitrate in First Trimester Missed Miscarriage

Thesis

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

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالَ

سَبِّحْ اِنَّكَ لَا تَعْلَمُ لَنَا
اِلَّا مَا عَلَّمْتَنَا اِنَّكَ اَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
ACL.....	Anti-cardiolipin
APS.....	Antiphospholipid syndrome
beta-hCG.....	Beta human chorionic gonadotropin
BPD	Bi- parietal diameter
CBC	Complete blood count
CRL.....	Crown lump length
CVS.....	Chorionic villus sampling
D & C.....	Dilatation and curettage
DM.....	Diabetes Mellitus
DNA.....	Deoxyribonucleic acid
EDRF	Endothelium-dependent relaxing factor
FDA	Food and drug administration
FIGO.....	Federation of Obstetrics and Gynecology
GDM	gestational diabetes
GTN	Glyceryl trinitrate
HC.....	Head circumference
ISMN	Isosorbide mononitrate
IUD	Intrauterine device
IVF.....	In vitro fertilization
LMP	Last menstrual period
MMP	Matrix metalloproteinases
MRI.....	Magnetic Resonance Imaging
MSD.....	Mean sac diameter
MTHFR	Methylenetetrahydrofolate reductase
NADPH	Nicotinamide adenine dinucleotide phosphate
NICE	National Institute for Health and Care Excellence
NO	Nitric oxide
NOS	Nitric oxide synthases

List of Abbreviations Cont...

Abb.	Full term
NSAIDs	Nonsteroidal anti-inflammatory drug
OGTT.....	Oral glucose tolerance test
PCOS	Polycystic Ovary Syndrome
PGs	Prostaglandins
PTL.....	Preterm labor
RCOG	Royal College of Obstetricians and Gynaecologists
RIF.....	Recurrent implantation failure
SIS	Saline sonohysterography
SNP.....	Sodium nitroprusside
TNF	Tumor necrosis factor
TPO-Ab.....	Thyroperoxidase antibodies

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PROTOCOL OF A THESIS FOR PARTIAL FULFILMENT OF
MASTER DEGREE IN OBSTETRICS AND GYNECOLOGY
Title of the Protocol:

**Comparison Of Duration Required For Expulsion
With Misoprostol Versus Misoprostol Plus
Isosorbide mononitrate In First Trimester Missed
Miscarriage**

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

Missed miscarriage in first trimester refers to spontaneous pregnancy loss before 12 weeks which need cervical ripening to ensure an uneventful surgical evacuation of uterine cavity. Misoprostol is a well-established cervical ripening agent with documented adverse effects. Isosorbide mononitrate (ISMN), a nitric oxide donor appears to emerge as a potential agent for uterine expulsion with lesser adverse effects.

1. INTRODUCTION/ REVIEW

Missed miscarriage is defined as an empty gestational sac or a pregnancy with an embryo or fetus without cardiac activity without spontaneous uterine expulsion. The diagnosis is usually made with ultrasound when women are asymptomatic or have vaginal bleeding (*Neilson et al., 2013*).

The incidence of clinically recognized miscarriages remains around 10-20%. Out of these miscarriages 80% occurs before 12 weeks of gestational age. Dilatation and curettage has been the standard treatment which unfortunately increases the cost and complications like uterine perforation, uterine infection, prolonged hospital stay and antibiotic prophylaxis. Moreover about 197,000 women are treated each year for complications of surgical termination of miscarriages (*Shauket et al., 2017*).

Prior to surgical evacuation of missed miscarriage, medications or mechanical dilators are often used to soften and dilate the cervix. The aim of cervical ripening is to reduce the possibility of injury to the uterus and cervix (*Webber and Grivell, 2015*).

As medical agent prostaglandins are the current pharmacological method of choice for the induction of cervical ripening and are usually administered into the posterior fornix of the

cervix. Prostaglandins act on the connective tissue stroma and lead to disintegration and dissolution of collagen as evidenced by proline uptake. However, prostaglandins are not free of adverse maternal and fetal effects, mainly because of their stimulatory effects on uterine contractions (*Arteaga-Troncoso et al., 2005*).

Misoprostol is a prostaglandin E1 analogue which is widely used for cervical ripening, termination of missed miscarriage and induction of labor while isosorbide mononitrate (ISMN), a newer and well tolerated drug, is NO donor which stimulate PGE2 alpha and is a major paracrine mediator of numerous biological processes including smooth muscle relaxation, host defense and inflammation and so help to soften the cervix and expel the products of conception (*Shauket et al., 2017*).

Using of combination of misoprostol with ISMN found to be more effective for cervical ripening than using of either IMN or misoprostol alone. (*Soliman, 2013*)

2. AIM/ OBJECTIVES

This study aims to compare the duration required for expulsion with misoprostol versus the duration required for expulsion with misoprostol plus isosorbide mononitrate in first trimester missed miscarriage

Outcome:

Primary outcome: induction to expulsion period (Interval measured from first dose of cervical ripening agent to start of expulsion).

Secondary outcome:

1. Uterine infection as defined by following criteria: fever more than 38 °C, offensive vaginal discharge and tender uterus.

2. Uterine perforation or Injury to bladder, bowel
3. Adverse effects of cervical ripening agents.
4. Intraoperative blood loss

3. METHODOLOGY

➤ **Type of the study:**

Randomized Control Trial, single-blind study

➤ **Randomization and blinding:**

Patients allocated into the study will be randomized into either of two groups using a computer-generated list at a 1: 1 ratio. Concealment will be achieved using opaque envelopes.

➤ **Study settings:**

Outpatient clinic and inpatient wards, Ain Sham University Hospital.

Study Period: 6 months

➤ **Study population:**

All women with first trimester missed abortion to be included in the study should fulfill the following criteria:

➤ **Inclusion criteria:**

1. Age 18- 40 years
2. First trimester gestational age missed abortion.
3. Confirmed intra uterine gestation non-viable pregnancy by (TVS)
4. Hemodynamic stable patient
6. Normal coagulation profile
7. Normal blood counts, urine analysis, liver and renal function

➤ **Exclusion criteria:**

1. Hemorrhagic disorders
2. Known allergy to the drugs
3. Cardiovascular and / or respiratory morbidity
4. Blood pressure less than 90 systolic and / or 60 diastolic at presentation
5. Patients on Aspirin or Heparin
6. Contraindications to the use of (ISMN) – severe anemia, head injury, malabsorption syndromes and methaemoglobinemia
7. Contraindications to the use of Misoprostol – seizure disorders, sickle cell anemia and glaucoma.

➤ **Sample Size:** 50 case

➤ **Methods:**

• **Full history:**

- ❖ Personal history
- ❖ Complete obstetric history (parity, previous CS, previous abortion, history of cervical cerclage).
- ❖ Past medical history including presence of organic disease or medical disease affecting coagulation profile as: Coagulopathy, Steroids treatment, Anticoagulant drugs.

• **Clinical examination:**

- ❖ General examination, abdominal & gynecological examination to exclude any gynecological diseases.
- ❖ TVS ultrasound will be held by expert doctor to identify missed abortion with following criteria:
 - If the crown rump length (CRL) is > 6 mm and there is no embryonic cardiac activity, this is defined as a missed miscarriage, or
 - If the mean gestational sac diameter is > 20 mm