A comparative study between the efficacy of vaginal versus sublingual misoprostol for medical treatment of second trimester medical termination of pregnancy Randomized controlled trial

Thesis

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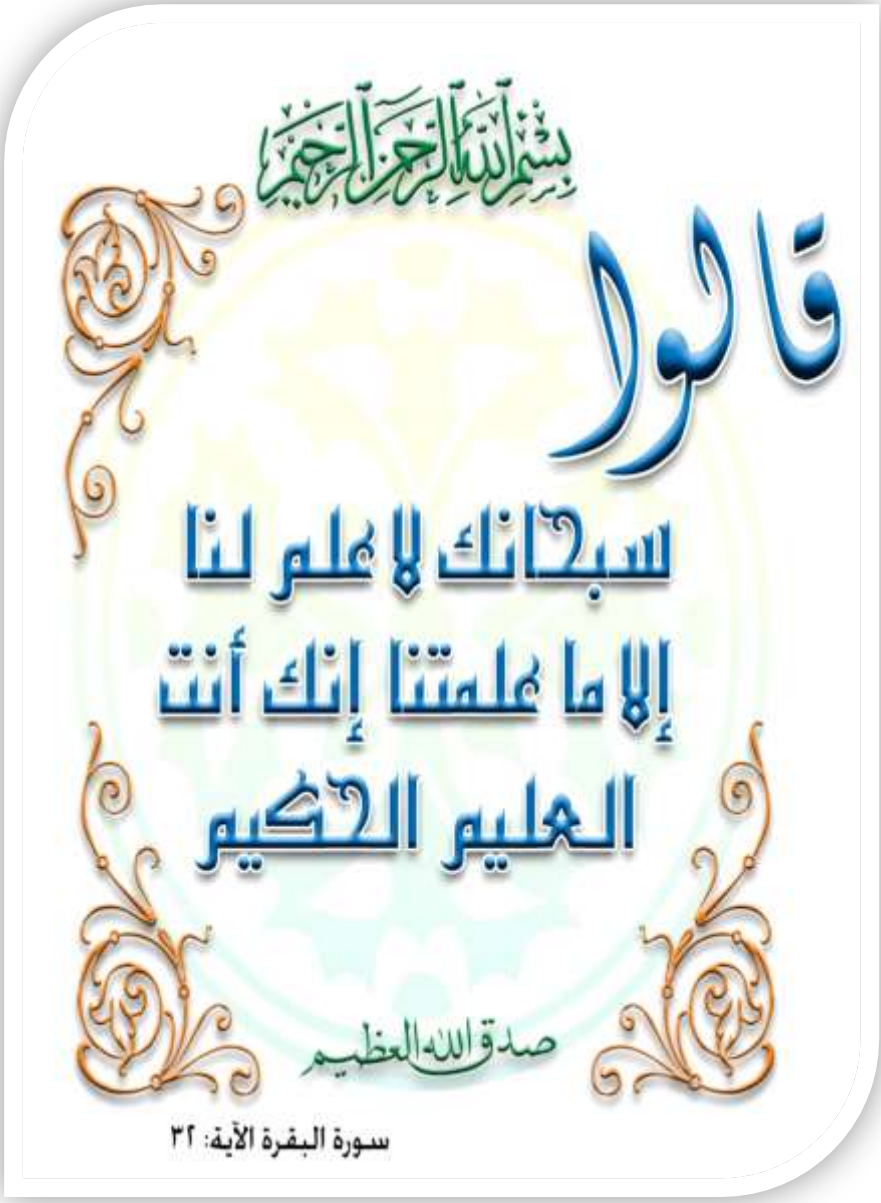
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Rana Moheb Soliman Ahmed

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List of Abbreviations

Abbr.	Full-term
ACR .....:	American College of Radiology
AUC.....:	Area under the curve
CDC .....:	Center for Disease Control and Prevention
CMV .....:	Cytomegalovirus
CRL .....:	Crown rump length
D&C .....:	Dilatation and curettage
D&E .....:	Dilatation and Evacuation
DES .....:	Diethylstilbestrol
DNA.....:	Deoxyribonucleic acid
EM .....:	Expectant management
FDA.....:	Food and Drug Administration
HbA1C.....:	Haemoglobin A1C
IDDM .....:	Insulin-dependent diabetes mellitus
IUCD .....:	Intrauterine contraceptive device
MSD .....:	Mean sac Diameter
NSAIDs.....:	Non-steroidal Anti-inflammatory drugs
PBLAC .....:	Pictorial Blood Loss Assessment Chart
PGE1.....:	Prostaglandin E_1
PGE_2.....:	Prostaglandin E_2
$PGF_{2\alpha}$.....:	Prostaglandin $F_{2\alpha}$
POC .....:	Products of conception
POC .....:	Products of conception
RCOG .....:	Royal College of Obstetricians and Gynecologists

RS .....: Retained sac

SD .....: Standard deviation

SLE .....: Systemic lupus erythromatosus

SPSS .....: Statistical package for social science

SRU .....: Society of Radiologists in Ultrasound

WHO.....: World Health Organization

NICE .....: National institute for Health and Care Excellence

ET.....: Endometrial thickness

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Abstract

Background: Medical treatment of second trimester miscarriage has been shown to be reasonable effective alternative to surgical evacuation. Aim of the Work: to compare the safety and efficacy aspect of sublingual versus vaginal misoprostol for medical treatment of second trimester miscarriage. **Patients and Methods:** This randomized controlled trial was conducted on 100 patients with previous miscarriage attending the outpatient clinic or reception room at Ain Shams University Maternity Hospital in the period from February to August 2018. The study group was divided into two groups: patients were randomly assigned to one of the two groups. Group A: 50 patients were given sublingual misoprostol, group B: 50 patients were given vaginal misoprostol. **Results:** The overall success rate in our study was 96% on in sublingual group and 98% in vaginal group). The route of misoprostol administration does not affect the induction abortion interval (P=0.475 or completeness of abortion (P=0.826)) Also, post-abortive drop in hemoglobin was the same among the vaginal group and sublingual group (p<0.968). The incidence of side effects in our study was more common among the sublingual group as compared to the vaginal group but most of patients consider it were tolerable, transient and decreased gradually after the first day of treatment. The risk of blood transfusion represents only 7% among both study groups due to significant blood loss affecting patient general condition causing marked drop in hemoglobin level. **Conclusion:** There is no difference between sublingual and vaginal misoprostol except in patient compliance.

Key words: vaginal, sublingual misoprostol, medical treatment, second trimester, pregnancy termination

Introduction

Miscarriage is the termination of pregnancy before the fetus has attained viability, i. e. becomes capable of independent extra uterine life ***(Kolte et al., 2014).***

Second trimester medical termination of pregnancy constitute 10-15% of all induced abortions worldwide ***(Desai et al. 2014).***

Therefore, Safe and legal medical termination of pregnancy is considered to be a key intervention for improving women's health and quality of life ***(Pandey et al., 2015).***

However, second trimestric medical termination of pregnancy are related to two-thirds of major abortion related complications. During the last decade, medical methods for second trimester medical termination of pregnancy had considerably improved and became safe and more accessible ***(Goyel et al., 2000).***

Although several methods have been tried over the years with varying success, the ideal method for mid-trimester medical termination of abortion remains elusive, as indicated by the constant search for new methods ***(Goldberg et al., 2001).*** Ethacridine lactate has a long history of use in our country and is recommended for use for mid-trimesteric termination of

pregnancy ***(FOGSI ICOG, 2005).*** However, its use has certain disadvantages such as a longer instillation abortion interval, a higher failure rate and more chances of incomplete abortion ***(Chaudhari et al., 2006).*** Prostaglandin Analogue is commonly used for termination of pregnancy in the second trimester ***(Lalitkumar et al., 2007).***

Reviews also shows that misoprostol in combination with mifepristone is an effective regimen for termination of second trimester medical termination of pregnancy up to 27 weeks. Mifepristone is, however, expensive and not approved in most countries of the world. Therefore, it is very important to develop a cost-effective regimen of medical abortion without mifepristone so that women particularly of developing countries can benefit from its advantages ***(Shail and Harleen, 2015).***

Misoprostol is the prostaglandin analogue commonly used, as it is cheap and stable at room temperature. It has been shown to be effective for second trimester medical termination of pregnancy ***(Chaudhari et al., 2006).***

Misoprostol is a synthetic prostaglandin E1 analogue it has several advantages over other forms of prostaglandin that made it the focus in obstetrics and gynecological research over the past two and half decades. Misoprostol is rapidly absorbed orally, sublingually, rectally and vaginally. It is substantially

less expensive than other preparations of prostaglandins and does not require refrigeration, simple to store and transport these characteristics make it particularly suitable to be used in developing countries ***(Khan et al., 2013).***

In this regard repeated doses of misoprostol have been used widely. Initially, misoprostol was used orally for medical termination of pregnancy. However, the use of vaginal misoprostol became a common practice for both medical termination of pregnancy and cervical priming for other indications. Many clinical trials have found that vaginal administration is more effective than oral administration. This was supported by pharmacokinetic study showing that systemic bioavailability after vaginal administration of misoprostol was three times higher than that after oral administration ***(Tang et al., 2007).***

However, there has been suggestive evidence showing that absorption through vaginal route is inconsistent and it is not uncommon to find the undissolved misoprostol tablets several hours after vaginal administration. Subsequently another route of giving misoprostol by sublingual administration has been developed ***(ACOG, 2009).***

The sublingual mucosa, being very vascular, serves the purpose of better absorption. Sublingual application also avoids the first pass effect through the liver. The misoprostol tablets,

when placed under the tongue, dissolve within 10-15 min. A pharmacokinetic study has demonstrated that sublingual administration could achieve the peak concentration in the shortest time and has the highest bioavailability ***(Tang et al., 2002).***

Aim of the Work

The aim of this work is to compare the efficacy of vaginal to sublingual misoprostol for medical treatment of second trimester miscarriage.

Chapter (1)
Miscarriage

While miscarriage is a term for early pregnancy loss, it is also frequently known in medical literature as spontaneous abortion ***(Oliver et al., 2014).***

Before the 1980s, health professionals used the phrase "spontaneous abortion" for a miscarriage and **"**induced abortion" for a willful termination of the pregnancy ***(Moscrop, 2013).***

Those born before 24 weeks of gestation rarely survive ***(Mohangoo et al., 2013).***

However, the designation "fetal death" applies variably in different countries and contexts, sometimes incorporating weight, and gestational age from 16 weeks in Norway, 20 weeks in the US and Australia, 24 weeks in the UK to 26 weeks in Italy and Spain ***(Li et al., 2012).***

A fetus that died before birth after this gestational age may be referred to as a stillbirth ***(Li et al., 2012).***

In the late 1980s and 1990s, doctors became more conscious of their language in relation to early pregnancy loss ***(Farquharson et al., 2005).*** Some medical authors advocated change to use of "miscarriage" instead of "spontaneous abortion" because they argued this would more respectful to women's feelings and help ease a distressing experience ***(Oliver et al., 2014).***