How useful is Oral Misoprostol Prior to IUCD Insertion in Women Who Delivered by CS?

Thesis

Submitted for partial fulfillment of the master degree of ***in Obstetrics and Gynecology***

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Doaa Saied Mohamed

Contents

List of Abbreviations

IUCD	:	The copper intrauterine device
IUCDs	:	The copper intrauterine devices
LNG	:	In addition, the levonorgestrel
NSAIDs	:	Nonsteroidal anti-inflammatory drugs
LNG	:	the levonorgestrel
NSAIDs	:	Nonsteroidal anti-inflammatory drugs
AUC	:	Area under the curve
T max	:	Time to peak serum level of MPA
Cmax	:	Peak serum levels of MPA
RBC	:	Red blood corpuscles
GTP	:	Guanonise tri phosphates
EP1&3	:	Prostaglandin E receptor
MLCK	:	Myosin Light Chain Kinase
PKA	:	Protin kinase A
MLCP	:	Myosin Light Chain phosphatase
MPA	:	Misoprostol acid
CYP-450	:	Cytochorom p 450
PTT	:	Parial thromboplastin time
STD	:	Sexual transimed disease
FDA	:	Food and drug administration
HIV	:	Human immunodeficiency virus
EC	:	Emergency contraceptive
WHO	:	World Health Organization
D&E	:	Dilatation and evacuation

List of tables

List of Figures

List of Figures (Cont.)

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Introduction

The copper intrauterine contaceptive device (IUCD) is a highly effective contraceptive method, also the ideal method for young, nulliparous women **(Guttmacher Institute Facts on Induced Abortion, 2010).**

The copper intrauterine devices (IUCDs) are safe, cost-effective in the long term and equally effective compared with tubal sterilization **(Grimes et al., 2007; Grimes and Mishell, 2008).**

In addition, the levonorgestrel (LNG)-releasing IUCDs (Mirena) provides noncontraceptive benefits, such as treatment for menorrhagia, dysmenorrhea and anemia **(Hurskainen et al., 2004; Milsom, 2007).**

However, a disadvantage in nulliparous women is that the insertion of an IUCD through a narrow cervix may be technically difficult and painful **(Farmer and Webb, 2003).**

Failed insertion, complications and side effects are significantly more common among women who have no previous vaginal delivery. The fear of painful insertion may make women to hesitate to use an IUCD **(Saav et al., 2007).**

Reported complications related to IUCD insertion are: 8.8% insertion failure, 2.8-11.5% cervical problems, 0.2% cervical perforation, 0.2% syncope and 5.8% expulsion **(Farmer and Webb, 2003).**

Insertion failures and cervical problems seem to occur more often among women who have never delivered vaginally **(Farmer and Webb, 2003; Li et al., 2005).**

By transvaginal ultrasound the cervix of women with a previous elective cesarean section may resemble the cervix of nulliparous women **(Kwee et al., 2004).**

In an attempt to facilitate IUCD insertion for nulliparous women, use of misoprostol has been promoted by several sources **(Hatcher et al., 2007; Association of Reproductive Health Professionals, 2008).**

Misoprostol is an inexpensive prostaglandin E1-analogue, which is associated with few side-effects **(Goldberg et al., 2001; Wing and Gaffney, 2006).**

Misoprostol commercially widely available and used to decrease the ulcerogenic effects of non-steroidal anti-inflammatory drugs (NSAIDs). Misoprostol is available in oral tablets and the dose used therapeutically is 400-800 microgram daily. PG analogues are used for cervical dilatation prior to surgical abortion in order to avoid damage to the cervix and uterus due to a rigid cervix and to decrease the bleeding **(Ngai et al., 1995, 1999; Lawrie et al., 1996).**

Priming with misoprostol prior to hysteroscopy and dilatation and curettage (D&C) in premenopausal women resulted in an increased cervical dilatation and a lower rate of cervical laceration **(Crane and Healey, 2006; Preutthipan and Herabutya, 2006).**

Misoprostol has been shown to be effective for cervical priming prior to IUCD insertion would reduce failure rates, complications and pain during insertion in non-pregnant women of fertile age especially in nulliparous with a narrow cervical canal **(Saav et al., 2007).**

Aim of the Work

The aim of the work is to evaluate the efficacy of the oral misoprostol to facilitate IUCD insertion in women who delivered only by cesarean section.

Research question:

Population: women with previous cesarean section and undergoing IUCD placement.

Intervention: participants will receive two tablets of 200 microgram misoprostol (total dose of 400 microgram misoprostol) orally 30 minute before IUCD insertion.

Comparison: compare with placebo.

Outcome: The primary outcome measure of this study is the proportion of difficulty of IUCD insertion.

Research hypothesis:

Null hypothesis: there is no difference in IUCD insertion before & after oral misoprostol.

Alternative hypothesis: there is difference in IUCD insertion before & after oral misoprostol.

Patients and Methods

Study Design:

Double blinded placebo randomized controlled clinical trial.

Setting:

The study will be conducted at Ain-Shams University Maternity Hospital.

Time:

June 2012 to June 2013.

Sample size calculation:

Using STATA® version 11 program, the sample size was Calculated based on the occurrence of complication following IUCD insertion, setting a type 1 error of 0.05 and a power of 0.80. We aimed at detecting a significant difference of expected complication 5 % among (misoprostol group) versus 19.1% among (placebo group). This was based on the 19.1% complication found in the retrospective study of (Dijkhuizen K et al, 2010); the calculated sample size was, therefore, 100 patients in each group.

Population of study:

Two hundred women candidate for T Cu 380A IUCD insertion will be Enrolled in the study. Half of them will receive 400 microgram of misoprostol oral and the other half will receive the placebo.

Inclusion Criteria:

- All women will be 18 to 45 years of age.

- Desires IUCD placement and able to participate.

- Negative pregnancy test.

- Willing to follow-up in 6-8 weeks for a standard IUCD follow-up visit.

- Previous delivery by cesarean section.

Exclusion Criteria:

- Active cervical infection.

- Current pregnancy.

- Uterine anomaly.

- Fibroid uterus.

- Copper allergy/Wilson's disease.

- Undiagnosed abnormal uterine bleeding.

- Cervical or uterine cancer.

- Allergy to misoprostol.

- Previous vaginal delivery.

Methodology:

All Participants will be subjected to the following:

History:

Full personal, obstetric, menstrual and medical history is taken. Data will be collected in a special form for each Participant.

Insertion of IUCD can take place from (The third day to the fifth day) during the menstrual cycle.

Ultrasound should be use prior insertion to detect uterine position (Anteverted or Retroverted) & any Intracavitary pathology (uterine anomaly &fibroid uterus)

A bimanual examination and sounding of the uterus are necessary to determine the uterine position and the depth of the uterine cavity.

Participants will randomly allocate to either the misoprostol or placebo group guided by a computer-generated randomization list.

We defined participants as women who never had a vaginal delivery and had undergone Cesarean section.

All participants will receive a numbered, blinded packet with either two tablets of 200 microgram misoprostol (total dose of 400 microgram misoprostol) or two tablets of placebo. The placebo is an adequate blind.

Participants will be instructed to administer the two tablets orally 30 minute before IUCD insertion.

The study will be conducted in a double-blind fashion: neither the clinician nor the participant knows whether placebo or misoprostol will be administered, the randomization list will