Comparative study of sublingual versus vaginal misoprostol in second trimester termination of pregnancy

Thesis

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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم
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ABSTRACT

Introduction: Clinical miscarriage constitutes approximately 12% of pregnancies ***(Blohm et. al., 2008).***Each year there are about 40-50 million abortions performed. Worldwide ***(World Health Organization, 2003).***and many of these are done in areas where facilities and expertise are lacking ***(Tang et. al., 2004).***

Objective: to compare the efficacy, side effects and acceptability of sublingual and vaginal misoprostol for second trimester medical abortion.

METHODS: Each patient will be given 200µg misoprostol (1 tablets Misotac®) every 4 hours and the maximum dose five doses per day either vaginally (group I) after wet of tablets by water or sublingually (group II) for 24 hours and if failed repeated for another 24 hours. Primary outcome: complete abortion rate at 24-48 hours. Secondary outcome Induction – abortion interval.

Results: The use of sublingual Misoprostol was as effective in termination of second trimestric abortion as vaginal Misoprostol. It was associated with induction of abortion in 55%of patients (22 patients from 40 total), versus in 60.0% of patients (24 patients from 40 total) with vaginal Misoprostol. Sublingual Misoprostol did not increase the side effects of misoprostol than vaginal route. Sublingual route is an effective and convenient alternative to vaginal administration of Misoprostol for termination of pregnancy in second trimestric abortion.

Conclusions: The use of sublingual Misoprostol is effective for termination of second trimestric abortion as vaginal Misoprostol without increasing the side effects. Sublingual Misoprostol can be conveniently self administered at home thereby decreasing hospital stay and cost. It also has a good patient acceptability rate.

Key words: second trimester\induced abortion\misoprostol\sublingual\vaginal

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ECM : EXTRACELLULAR MATRIX

FACIT : fibril associated collagens with interrupted triple helices

GAG : glycosaminoglycan side chains

TIMPs : tissue inhibitors of metalloproteinase

MMPs : MATRIXmetalloproteinase

TLRs : TOLL LIKE RECEPTORS

PAMPs: pathogen- associated molecular patterns

LPSs : lipopolysaccharides

NFκB : NUKLEAR FACTOR OF KAPPA LIGHT POLY PEPTIDE GENE ENHANCER IN B- CELL 1

IFN : INTERFERON

PGF2 : PROSTAGLANDINS F2

I.M : INTRAMASCULAR

D&C : DILATATION & CURRETAGE

H : HOURES

VA : Vacuum aspiration

D&E : Dilatation and evacuation

FDA : Food and Drug Administration

NSAIDs : Non steroidal anti-inflammatory drugs

B-hCG : B-SUBUNIT OF HUMAN CHORIONIC GONADOTROPHINS

MPA : misoprostol acid

GTP : guanosinetriphosphate

Introduction

Clinical miscarriage constitutes approximately 12% of pregnancies ***(Blohm et. al., 2008).***

Each year there are about 40-50 million abortions performed. Worldwide ***(World Health Organization, 2003).***and many of these are done in areas where facilities and expertise are lacking ***(Tang et. al., 2004).***

Reasons for procuring induced abortions are typically characterized as therapeutic. An abortion is medically referred to as therapeutic when it is performed to:

• Save the life of the pregnant woman ***(Roche, Natalie, 2004).***

• preserve the woman's physical or mental health

• terminate pregnancy that would result in a child born with a congenital disorder that would be fatal or associated with significant morbidity; or

•Selectively reduce the number of fetuses to lessen health risks associated with multiple pregnancies ***(Roche, Natalie, 2004).***

An abortion is referred to as elective when it is performed at the request of the woman "for reasons other than maternal health or fetal disease."***(Encyclopedia Britannica, 2007).***

There is a gradual increase in second-trimester abortion because of wide scale introduction of prenatal screening programs detecting women whose pregnancies are complicated by serious fetal abnormalities such as cardiovascular and skeletal malformation. In these cases, examination of the fetus could provide valuable information especially after medical abortion to confirm the congenital anomaly and further evaluate. The subsequent recurrence risk and provide information to help in counseling of these patients. ***(Boyd et al., 2004)***

Medical evacuation of missed abortion is an effective, safe and cost effective alternative to surgical evacuation of the uterus and is particularly suited to women not preferred hospital admission or surgical procedure under general anesthesia ***(Chia , Oqb, 2002).***

The standard treatment for missed miscarriage for the last 50 years has been dilatation and curettage which is typically done in an operating room, thus significantly increasing the costs ***(Creinin et al., 2006).***

Medical management of missed abortion has been shown to reduce the need for D&C, is less costly and is associated with a high level of patient satisfaction ***(Graziosi et al., 2005).***

More recent studies suggest sublingual route of misoprostol to be the most potent due to its highest bioavailability ***(Tang et al., 2002).***

However several problems have been identified with vaginal misoprostol like inconsistent absorption which may be improved by

dissolving the tablets in water and incomplete absorption of the tablet even after several hours of administration in addition to women finding vaginal administration uncomfortable ***(Ngai et al.,2000).***

Misoprostol has been proposed for a variety of other obstetrical and gynecological indications: induction of labor, preparation of the cervix for surgical procedures, prevention and treatment of postpartum hemorrhage, and pregnancy termination ***(Winikof et al., 2005).***

Carboprost, a 15(S)-15-methyl PGF2, was the first analogue to be tested clinically on a large scale for the termination of secondtrimester pregnancy. It is used either intra-amniotically (viable second-trimester pregnancy) or administered by I.M injection.It is of limited value as a primary method for abortion because of its association with high rates of gastrointestinal side effects but may be used when other methods have failed ***(Dickinson, Evans, 2005).***

Sublingual misoprostol was considered to be more convenient and more comfortable but associated with bad taste and a higher frequency of side effects ***(Tang et al., 2004).***

The most commonly encountered side effects were fever, shivering, vomiting and diarrhea. Another advantage with the oral/sublingual route is that the absorption of the drug is not affected if the woman starts to bleed. This is especially true when the repeated administration of misoprostol is required ***(Tang et al., 2004).***

Aim of work

The aim of this study is to compare the effect of sublingual versus vaginal administration of misoprostol in second trimester termination of pregnancy.

REVIEW OF LITERATURE

Physiological changes during pregnancy

Anatomy

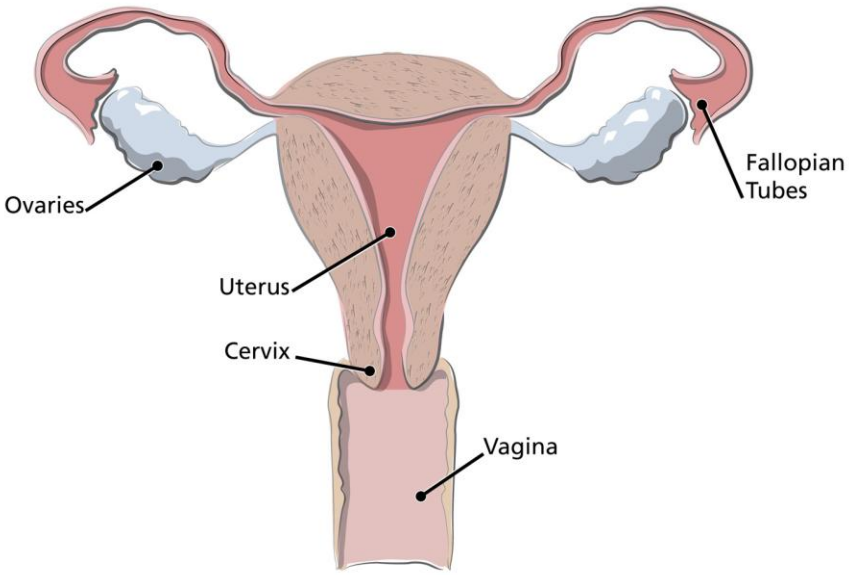

Figure 1: Anatomy of the human uterus.

Corpus uteri

Anatomically, the corpus uteri can be divided into the upper region, called the fundus, and the distal region close to cervix, called the isthmus. The uterus is mainly composed of smooth muscle cells, which constitute about 70% of the tissue. The uterus does not, however, only consist of smooth muscle cells: a substantial part of the tissue is made up of Extracellular Matrix (ECM). The ECM surrounds the muscle fibers, facilitating the cell-cell and cell-matrix communication that is crucial for achievement of effective contractions during labor ***(Cluff, 2006).***

Even though the proportion of muscle fibers is reduced gradually along the uterus, anatomical part of the corpus uteri the isthmus is still dominated by smooth muscle cells, making it an anatomical part of the corpus uteri ***(Granstrom et al., 1991).***

Cervix uteri

Cervix means neck in Latin, and this is the small, cylindrical narrow part that leads from the uterus to the vagina. It has a vital function in pregnancy, where it must stay closed and firm during most of the pregnancy but must undergo extensive remodeling at term to allow passage of the fetus through the birth canal.

The cervix is dominated by fibrous connective tissue, which gives it its tensile strength More than 85% of the non-pregnant cervix consists of ECM, where collagens are the major component. Only about 4-10% of the cervical tissue consists of smooth muscle cells ***(Anna Akerud, 2009).***

TISSUE REMODELING DURING PREGNANCY AND LABOUR

Connective tissue

The fibrous connective tissue of the uterus is a highly organized network of ECM molecules with cells sparsely distributed within it. The network provides tissues with mechanical support and tensile strength and forms the framework for the vertebrate body. The predominant cells in fibrous tissues are fibroblasts, but immune cells such as lymphocytes,