Misoprosotol and Isosorbide Mononitrate for Induction of Second Trimester Abortion

Randomized Controlled Trial

Thesis

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Foad Mahmoud

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List of Abbreviations

Abb.	Full term
AA	*Arachidonic Acid*
AP-1	*Activator Protein 1*
cGMP	*Cyclic Guanosine Monophosphate*
COX	*Cyclo-oygenase*
DHAS	*Dehydroepiandrosterone Sulfate*
DSPG II	*Dermatan Sulphate Proteoglycan II*
ECM	*Extra Cellular Matrix*
EDRF	*Endothelium Dependent Relaxing Factor*
eNOS	*Endothelial NOS*
GTN	*Glyceryl Trinitrate*
IMN	*Isosorbide Mononitrate*
iNOS	*Inducible NOS*
m RNA	*Messenger RNA*
MPA	*Misoprostol Acid*
NAPDH	*Nicotinamide Adenine Dinucleotide Phosphate*
nNOS	*Neuronal NOS*
NO	*Nitric Oxide*
NOS	*Nitric Oxide Synthases*
NSAIDs	*Non-steroidal Anti-inflammatory Drugs*
PG	*Prostaglandins*
PGDH	*Prostaglandin Dehydrogenase*
PGE1	*Prostaglandin E1*
PGE2	*Prostaglandin E2*
PGE2	*Prostaglandin E2*

List of Abbreviations (Cont...)

Abb.	Full term
PGFα	*Prostaglandin F2α*
PGs	*Prostaglandins*
PLA2	*Phospholipase A2*
PLC	*Phospholipase C*
RT-PCR	*Reverse Transcriptase-polymerase Chain Reaction*
SNP	*Sodium Nitroprusside*

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ABSTRACT

Within the first 24 Hours, 93.3% of cases group had successful induced abortion compared to 7O% of the controls and the difference was statistically significant.

The mean time needed for abortion was 10.4h in the drug group compared to 15.3h in the control group and difference was statistically significant.

In our study surgical evacuation was higher among group II (36.7%) than in group I (10%) but the difference was not statistically significant.

The number of women who complained of headache in the drug group was more than that of the control group. The difference was statistically significant.

Hospital stay was significantly shorter among group-I than among group-II.

Keywords: Non-steroidal Anti-inflammatory Drugs - Nicotinamide Adenine Dinucleotide Phosphate - Prostaglandin Dehydrogenase

INTRODUCTION

Abortion is defined as termination of pregnancy by any means before the fetus is viable.viability is now considered to be reached at 23-24 weeks of gestation.second trimester is aperiod ranging from 13-28weeks of gestation ***(Lalitkumar et al., 2007).***

There is still a gradual increase in second trimester abortion because of prenatal screening program dectecting pregnancies with fetal abnormalities as cardiovascular and skeletal malformation.

World wide mid- trimester abortion constitutes 10-15 of induced abortion but is responsible for two- third of major complication ***(WHO, 1997).***

Various cervical ripening agents have been evaluated and proven to be effective, such as laminaria and prostaglandins ***(Dabash et al., 2010).***

The most commonly used agents for ripening are prostaglandins analogues since they are convenient to administer. However, prostaglandins analogues have various adverse effects such as abdominal pain, nausea, vomiting, and diarrhea, therefore the ideal cervical ripening agent should be effective, and easy to adminsiter, with a low incidence of adverse effects ***(Diop et al., 2009).***

Isosorbide mononitrate is anitric oxide donar and vasodilator used primarily for patients with angina pectoris ***(Mousiolis et al., 2013).***

Nitric oxide is a free radical with a short half life. It exists in the body for at most 6-10 seconds before it reacts with oxygen and water to form nitrates and nitrites. Nitric oxide diffuses across cell membranes rapidly and is only synthesized on demand. It is a major chemical messenger in the human body, mainly in the central nervous system. Its first discovered function was as an endothelium –derived relaxing factor and a primary regulator of blood pressure ***(Sahafique et al., 2010).***

Many recent studies have shown that it is involved in various aspects of female reproductive physiology, including the process of cervical ripening ***(Kapp et al., 2010).***

A study with pregnant guinea pigs showed that local application of Nitric oxide effectively produced cervical ripening associated with ultra structural and functional changes, ***(Matsubara et al., 2010).***

In humans, nitric oxide donars cause myometrial relaxation and are used during external cephalic version, difficult vaginal or cesarean delivery, manual exploration of the uterus and for inhibiting uterine contraction ***(Aalberts et al., 2008).***

Studies have shown that nitric oxide donars can be used effectively for cervical ripening in term pregnancies ***(Chanrachakul et al., 2008).***

A study done in, Department of Obstetrics and Gynaecology, Government Thiruvannamalai Medical College and Hospital, Thiruvannamala, Showed that Vaginally administered isosorbide mononitrate seems to be safe and effective method in second trimester pregnancy termination. There is a reduction in hospital stay, manpower, economy spent on patient, and a sense of wellbeing from the patient also.

AIM OF THE WORK

Research Hypothesis

In pregnant women undergoing second trimester induction of abortion isosorbide mononitrate and misoprostol may be similar to misoprostol alone as regard induction termination interval.

Research Question

In pregnant women undergoing second trimester induction of abortion does isosorbide mononitrate and misoprostol simulates to misoprostol alone in effacicy and safety or in induction termination interval.

Chapter 1

CERVICAL CHANGES DURING PREGNANCY

The cervix is a fibrous organ composed principally of hyaluronic acid, collagen, and proteoglycan. Hyaluronic acid increases as pregnancy progresses, peaks after the onset of labor, and decreases rapidly after birth of the infant ***(Gabbe et al., 2007).***

The remarkable task of the cervix is to facilitate conception, retain the conceptus throughout pregnancy, dilate to allow safe delivery, and to repeat this process in subsequent pregnancies. These functions depend on regulation of the extracellular matrix, which is composed of collagen, elastin, and fibronectin. Collagen is the principal determinant of the tensile strength of the cervix. Cervical ripening occurs as the consequence of decreased total collagen content, increased collagen solubility, and increased collagenolytic activity by collagenase and leucocyte elastase.

Extracellular matrix turnover in the cervix is high, and thus, the mechanical properties of the cervix can change rapidly. Changes in extracellular matrix during cervical ripening include an influx of inflammatory cells (macrophages, neutrophils, mast cells, eosinophils, and so on) into the cervical stroma in a process similar to an inflammatory response. These

cells Produce cytokines and prostaglandins that affect extra cellular matrix metabolism ***(James et al., 2005).***

The extra cellular matrix (ECM) is considered to play an important role in the stability of tissues and in regulating the growth and differentiation of cells. Synthesis, accumulation, and catabolism of the ECM are involved in wound healing and in the initiation and progression of numerous diseases ***(Iwahashi et al., 2003).***

Histological changes in the cervix during pregnancy:

During pregnancy, normally uterine cervix rearranges its collagen fibers, the non pregnant cervix contains alienable collagen fibers that have a definite cable like structure and form fibril bundles. These fibrils appear wavy when viewed with a light microscope ***(James et al., 2005).***

Elastin fibers act as lubricant to allow the collagen fibers to slide by each others if stress is applied: Changes of the cervix during pregnancy cause a rearrangement of collagen fibrils so that the tissue assumes the characteristic of a soft easily distensible tissue ***(Myers et al., 2015).***

This occurs due to increased concentration of hyalouronic acid, which attracts water molecules and contributes to softening of the tissue ***(Sciscione, 2014).***