Sublingual versus Oral Misoprostol for Induction of Labour in Prelabour Rupture of Membranes at Term: RCT

Thesis

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By

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Amira Zohier Mohammed

Contents

List of Abbreviations

ACOG	**:**	American College of Obstetricians and Gynecologists
AFP	**:**	Alpha-fetoprotein
APH	**:**	Antepartum hemorrhage
cAMP	**:**	Cyclic adenosine 3, 5 monophosphate
DAO	**:**	Diamine oxidase
ECM	**:**	Extracellular matrix
ELISA	**:**	Enzyme-linked immunosorbent assay
FDA	**:**	Food and Drug Administration
FHR	**:**	Fetal heart rate
IDI	**:**	Induction-delivery interval
IGFBP-1	**:**	Insulin-like growth factor binding protein 1
IOL	**:**	Inducation of labour
IX	**:**	Glossopharyngeal nerve
MMPs	**:**	Matrix metalloproteinases
MPA	**:**	Metabolite misoprostol acid
onfFN	**:**	Oncofetal or fetal fibronectin
PGE	**:**	Being a prostaglandin E
PGE2	**:**	Prostaglandin E2
PROM	**:**	Premature rupture of membranes
PTT	**:**	Partial thrombin time
RCT	**:**	Randomized controlled trial

SLE	**:**	Systemic lupus erythematosus
TENS	**:**	Transcutaneous nerve stimulation
TIMPs	**:**	Tissue inhibitors of MMPs
VI	**:**	Abducens nerve
VII	**:**	Facial nerve
WHO	**:**	World Health Organization
XII	**:**	Hypoglossal nerve

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INTRODUCTION

Induction of labour is extensively used all over the world in cases in which continuation of pregnancy is hazardous to the mother and/or her fetus. In 2004 and 2005, one in every five deliveries in the United Kingdom was induced ***(NICE clinical guidelines, 2008)***. Unpublished data from the WHO Global Survey on Maternal and Perinatal Health, which included 373 health-care facilities in 24 countries and nearly 300 000 deliveries, showed that 9.6% of the deliveries involved labour induction. Overall, the survey found that facilities in African countries tended to have lower rates of induction of labour (lowest: 1.4% in Niger) compared with Asian and Latin American countries (highest: 35.5% in Sri Lanka**)** ***(WHO Global Survey on Maternal and Perinatal Health, 2010).***

Inducing labour when the cervix is ripe is not difficult, but complications increase significantly when the cervix is not ripe. There is a plethora of techniques available for induction of labour. However, prostaglandins remain the single most effective means of achieving cervical ripening and inducing labour when combined with a judiciously timed amniotomy, providing good clinical

effectiveness and patient satisfaction ***(Alfirevic, 2005).***

Prostaglandin E2 is registered for labour induction in many countries. However, it is expensive in developing countries and, because it is sensitive to temperature changes, it needs to be kept under refrigeration. In settings with high average parity, an induction regimen using only oxytocin without prostaglandin E2 is potentially dangerous. In Assiut University Hospital, for example, oxytocin was still the most widely used method of induction (62.9 %) in 1999; prostaglandin E2 was used in only 6.5% of cases. In such settings there is an urgent need for an affordable drug to optimize induction outcomes. Misoprostol (a prostaglandin E1 analogue) has several potential advantages: it is stable at room temperature, it is relatively inexpensive and it can be given via several routes (oral, vaginal, sublingual, buccal). These properties make misoprostol an ideal agent for induction of labour, particularly in settings where the use of prostaglandin E2 is not possible owing to lack of availability, facilities for storage, or financial constraints. Since the use of a powerful uterotonic such as misoprostol can lead to adverse maternal and perinatal effects, it is important to review the effectiveness and the side-effects of oral ***(Alfirevic and Weeks, 2006)*** and sublingual ***(Hofmeyr and Gulmezoglu,***

2003) misoprostol use in cervical ripining and induction of labour. Misoprostol is easily stored at room temperature and has only a few systemic side effects ***(Muzonzini and Hofmeyr, 2004)***.

There is no general agreement about the ideal management of the women with pre-labour rupture of membranes (PROM). Both expectant management and induction of labour are currently practiced in modern obstetrics ***(Svigos et al., 2000).***

The usual options for induction of labour in women with PROM are medical methods including oxytocin, prostaglandins and combination of both. Oxytocin only affects uterine contractions so is less likely to be effective in presence of unfavourable cervix. Prostaglandins especially PGE2 have been used successfully for cervical ripening and for induction of labour since early 1970's ***(Crane et al., 2003).***

Misoprostol, which is a methyl ester of prostaglandin E1 is a recent addition to the list of the prostaglandins. It was originally marketed for the treatment of duodenal ulcer but also has uterotonic properties and is useful for cervical ripening ***(Margulies et al., 1992).***

It is not licensed at present for the induction of

labour, but various groups successfully used the agent by oral or sublingual routes for the induction of labour on the basis of its effect on uterine contractions ***(Hofmeyr and Gulmezoglu, 2003; Alfirevic, 2005).***

AIM OF THE WORK

1- Research hypothesis:

In women presented with premature rupture of membrane at term, Sublingual Misoprostol is not superior to oral Misoprostol for induction of labour.

2- Research question:

In women presented with premature rupture of membrane at term, Is sublingual Misoprostol more efficient and safe than oral Misoprostol for induction of labour ?

3- Research aim:

The study aim to asses the safety and efficacy of sublingual versus oral Misoprostol to induce labour in women presented by premature rupture of membrane at term.

1. PROTOCOL OUTLINE

1.1 TITLE

Sublingual versus Oral Misoprostol for Induction of Labour in Women Presenting by Prelabour Rupture of Membranes at Term.

1.2 STUDY SITE

Ain Shams University Maternity Hospital.

1.3 Study phase

This study will be Randomized Controlled Trial (RCT).

2. OUTCOME MEASURES

2.1 PRIMARY OUTCOME

Achievement of successful vaginal delivery within 24 hours.

2.2 SECONDRY OBJECTIVES

Maternal outcome measures including: Induction delivery interval(time from start of medication till delivary), tachysystole (at least 6 contractions in 10 minutes during two consecutive 10 minutes), hyperstimulation (presence of tachysystole or prolonged

contraction > 2 minutes, accompanied with non-reassuring fetal heart pattern),need for analgesia, need for labor augmention by oxotocin, conversion to caesarean section, nausea, vomiting, pyrexia after administration of agent and in first post natal day, mode of delivery.

Fetal outcome measures including: Apgar score at one and five minutes of birth, admission to neonatal intensive care unit (NICU) and perinatal death.

3. STUDY DESIGN

It is aprospective, non-blinded randomized control study, comparing the safety and efficacy of sublingual with oral misoprostol for labor induction.

3.1 POPULATION

The current study will be conducted at Ain-Shams University Maternity Hospital during the period between March 2016 and December 2016.262 pregnant women planned for induction of labour will be recruited in this study according to inclusion and exclusion criteria.

3.1.1. Inclusion Criteria

1. Age: 18 – 35.

2. Live singleton pregnant women at term