Titrated Oral Misoprostol Compared to Vaginal Dinoprostone for induction of labor: A Randomized controlled trial

Thesis

Submitted in partial fulfillment of MD Degree
in Obstetrics and Gynecology

By

Sherif Essam Mostafa Daoud

M.B.,B.CH., MS (OBST. & GYNECOLOGY)
A. Lecturer in OB/GYN Department
Ain Shams University Hospital

Under Supervision of

Prof. Ihab Hassan Abd El-Fattah

Professor of Obstetrics and Gynecology
Head of the Obstetrics and Gynecology Dept.
Faculty of Medicine – Ain Shams University

Prof. Karam Mohamed Bayoumy

Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Dr. Amr Helmy Yehia

Assistant Professor in Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
2017

List of Contents

List of Abbreviations

ACOG	:	American college of Obstetricians and Gynecologists
AA	:	arachidonic acid
AROM	:	Artificial Rupture Of Membranes
BMI	:	Body Mass Index
CI		Confidence Interval
Cm	:	Centimeter
COX-2	:	Cycloxygenase-2
C.N.S		Central Nervous System
CS	:	Cesarean section
CTG	:	Cardio Tocography
FHR		Fetal Heart Rate
GTN	:	Glyceryl Trinitrate
hPGDS	:	Hematopoietic prostaglandin D synthases
HBsAg	:	hepatitis B surface antigen

hrs	:	Hours
IUGR	:	Intra Uterine Growth Restriction
lPGDS	:	lipocalin prostaglandin D synthases
μg	:	Microgram
Mg	:	Milligram
ml	:	Milliliter
mU	:	Milliunit
min	:	Minutes
NICU	:	neonatal intensive care unit
NADPH	:	Nicotinamide Adenine Dinucleotide Phosphate-Oxidase
NO	:	Nitric Oxide
NST	:	Non Stress Test
NSAIDs	:	non-steroidal anti-inflammatory drugs
PGF2α	:	α Prostaglandins F2
PROM	:	Pre-Labor Rupture Of Membranes
PGFS	:	Prostaglandin F synthase

PGFS	**:**	Prostaglandin F synthase
PGE1	**:**	Prostaglandins E1
PGE 2	**:**	Prostaglandins E2
RCT	**:**	Randomized controlled trial
ROM	**:**	Rupture Of Membranes
SD	**:**	Standard Deviation
t	**:**	Student t-test
TXA	**:**	Thromboxane
TxAS	**:**	Thromboxane A synthase
TENS	**:**	transcutaneous nerve stimulation
TNF	**:**	Tumor Necrosis Factor
U/S	**:**	Ultrasonography
wks	**:**	Weeks
yrs	**:**	Years

List of Tables

List of Tables *(Cont...)*

List of Figures

Introduction

Induction of labor is defined as the process of artificially initiating uterine contractions, prior to their spontaneous onset, with progressive effacement and dilatation of the cervix and ultimately, the delivery of the baby ***(Martin et al., 2005)***.

There are many indications for induction of labor in the obstetric practice, of which prolonged gestational age stands as the most common indication. It is well recognized that with an unripe cervix, induction may be difficult and often unsuccessful. The use of an agent to ripen the cervix prior to induction is acceptable in the modern practice ***(Josie, 2003)***.

Induction of labor in the third trimester of pregnancy may be considered beneficial in many clinical circumstances. The risks include ineffective labor (failed induction), or excessive uterine activity which may cause fetal distress or uterine rupture ***(Wing et al., 2006)***. Either problem may lead to an increased risk of caesarean section. Unsuccessful labor induction is most likely when the cervix is unfavorable, and in this circumstance prostaglandin, preparations have proved to be beneficial. Those prostaglandins, which have been registered for cervical ripening and labor induction, are expensive and unstable and require refrigerated storage ***(Weeks et al., 2006).***

Cervical ripening is associated with an increase in cyclooxygenase enzyme, which leads to local increase of prostaglandin production in the cervix. This in turn leads to a subsequent series of important changes associated with progressive cervical ripening ***(Dede et al., 2004)***.

Misoprostol, a prostaglandin E_1 analogue, is the most interesting alternative to Dinoprostone because of its effectiveness, low cost, and temperature stability. It ripens the cervix by inducing regular uterine contractions. However, it is associated with several adverse effects especially uterine hyperstimulation, which is painful and may result in fetal compromise. These adverse effects are infrequent, dose-dependent, and vary according to the route of administration ***(Hofmeyr et al., 2001)***.

Current experience with misoprostol used for labor induction has been reviewed. Although in most studies, misoprostol seems to be at least as effective as conventional methods, widely varying dosage regimens and small numbers of women studied do not allow for adequate assessment of safety ***(Shetty et al., 2005).*** The widespread use of misoprostol in clinical practice, using arbitrary dosages and without registration or proper surveillance for adverse events is a cause for concern, as are reports of complications such as uterine rupture. Although most researchers and clinicians have chosen

the vaginal route for misoprostol administration, oral administration may have several advantages ***(Kolderup et al., 1999)***. Administration is easier and may be more acceptable to women. Absorption is more rapid and possibly more predictable. The reported mean peak serum misoprostol acid level following oral administration was 227 pg/ml after 34 minutes compared with 165 pg/ml after 80 minutes for the vaginal route. Vaginally absorbed serum levels are more prolonged. The shorter half-life when given orally may be advantageous in the event of uterine hyper stimulation. On the other hand, the direct local effect of vaginal misoprostol on cervical softening may be advantageous ***(Hofmeyr et al., 2010).***

Based on the aforementioned facts, testing the efficacy and safety of titrated oral misoprostol versus vaginal dinoprostone may develop a new safe and effective method for labor induction.

Aim of the Work

To test the safety and efficacy of titrated oral misoprostol compared to vaginal dinoprostone for labor induction.