

Oral Misoprostol versus Vaginal Dinoprostone for Induction of Labour: a Randomized Controlled Clinical Trial

Thesis

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By

Marwan Osama Elkady

Assistant Lecturer of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Under Supervision of

Professor/ Maged Ramadan Abouseeda

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

Professor/ Walid Hitler Tantawy

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

Professor/ Adel Shafik Salah El-din

Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain shams University

Faculty of Medicine
Ain Shams University

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Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables	ii
List of Figures	iv
Protocol	
Introduction	viii
Aim of the Work	5
Review of Literature	
Misoprostol	6
Dinoprostone.....	37
Induction of Labour	47
Dinoprostone versus Misoprostol.....	67
Patients and Methods.....	74
Results	83
Discussion	112
Summary and Conclusion	121
Recommendations	125
References	126
Arabic Summary	—

List of Abbreviations

Abbr.	Full-term	.
ACOG	: American college of obstetricians and gynecologists	
APH	: Ante-partum hemorrhage	
ASUMH	: Ain Shams university maternity hospital	
AUC	: Area under the curve	
CC	: Cubic centimeter	
CS	: Caesarian section	
FIGO	: International federation of gynecologists and obstetricians	
IOL	: Induction of labour	
IUGR	: Intrauterine growth restriction	
mg	: Milligram	
ml	: Milliliter	
mmHg	: Millimeter mercury	
mu	: Milliunit	
NNH	: Number needed to harm	
NNT	: Number needed to treat	
NSAIDs	: Non steroidal anti-inflammatory drugs	
OMS	: Oral misoprostol in solution	
PG	: Prostaglandins	
PPROM	: Premature prelabour rupture of membranes	
RCT	: Randomized controlled trial	
U/S	: Ultrasound	
VDP	: Vaginal Dinoprostone	
WHO	: World health organization	

List of Tables

Table No.	Title	Page No.
Table (1):	Different routes of misoprostol administration	13
Table (2):	WHO recommendation for induction of labour, 2011	24
Table (3):	Intravaginal forms of dinoprostone	38
Table (4):	Recommended regimens for prostaglandin E2 administration.....	43
Table (5):	Bishop Score.....	51
Table (6):	Modified Bishop Scoring System.....	52
Table (7):	Initial Characteristics of Recruited Women.....	84
Table (8):	Indication for Induction of Labor in Recruited Women	86
Table (9):	Pre-Induction Data of Recruited Women.....	87
Table (10):	Difference between Groups regarding Initial Characteristics.....	89
Table (11):	Difference between Groups regarding Indication for Induction of Labor	91
Table (12):	Difference between Groups regarding Pre-Induction Data	92
Table (13):	Difference between Groups regarding Mode of Delivery.....	94
Table (14):	Difference between Groups regarding Delivery within 12 and 24 Hours	96

List of Tables (Cont.)

Table No.	Title	Page No.
Table (15):	Difference between Groups regarding No. of Doses and Duration of Labor	98
Table (16):	Difference between Groups regarding Maternal Adverse Effects	101
Table (17):	Difference between Groups regarding Fetal Adverse Effects	103
Table (18):	Difference between Groups regarding Apgar Scores	105
Table (19):	Difference between Groups regarding NICU Admission	107
Table (20):	Difference between Groups regarding Postpartum Complications	109
Table (21):	Difference between Groups regarding Maternal Satisfaction	111

List of Figures

Figure No.	Title	Page No.
Figure (1):	Structure of misoprostol	7
Figure (2):	Cytotec tablets	15
Figure (3):	Gymiso drug	15
Figure (4):	Vagiprost vaginal suppositories.....	15
Figure (5):	Misotac tablets	15
Figure (6):	Effects of misoprostol on uterine contractility following different routes of administration	16
Figure (7):	Safe single doses of vaginal misoprostol for producing uterine contractions at various gestations.....	26
Figure (8):	Misoprostol approval map	27
Figure (9):	Cervical ripening balloon	56
Figure (10):	Cervical ripening balloon	56
Figure (11):	Hygroscopic dilators dilapan	57
Figure (12):	Stripping of the Membranes	58
Figure (13):	Amniohook	59
Figure (14):	Amniotomy	59
Figure (15):	Oxytocin	61
Figure (16):	Syntocinon drug.....	64
Figure (17):	Mifeprystone.....	65
Figure (18):	Flow-Diagram showing Study Course	83

List of Figures (Cont.)

Figure No.	Title	Page No.
Figure (19):	Bar-Chart showing Age Distribution in Recruited Women	85
Figure (20):	Bar-Chart showing Gestational Age Distribution in Recruited Women.....	85
Figure (21):	Pie-Chart showing Indications for Induction of Labor in Recruited Women.....	86
Figure (22):	Box-Plot Chart showing Pre-Induction Bishop Score of Recruited Women	87
Figure (23):	Pie-Chart showing Pre-Induction Fetal Membranes Status in Recruited Women	88
Figure (24):	Box-Plot Chart showing Difference between Groups regarding Age.....	89
Figure (25):	Box-Plot Chart showing Difference between Groups regarding Gestational Age	90
Figure (26):	Bar-Chart showing Difference between Groups regarding Indications for Induction of Labor	91
Figure (27):	Box-Plot Chart showing Difference between Groups regarding Pre-Induction Bishop Score	92
Figure (28):	Bar-Chart showing Difference between Groups regarding Pre-Induction Fetal Membranes Status.....	93
Figure (29):	Bar-Chart showing Difference between Groups regarding Mode of Delivery	95

List of Figures (Cont.)

Figure No.	Title	Page No.
Figure (30):	Bar-Chart showing Difference between Groups regarding Indication for Cesarean Section	95
Figure (31):	Bar-Chart showing Difference between Groups regarding Delivery within 12 Hours.....	96
Figure (32):	Bar-Chart showing Difference between Groups regarding Delivery within 24 Hours.....	97
Figure (33):	Box-Plot Chart showing Difference between Groups regarding No. of Doses.....	99
Figure (34):	Bar-Chart showing Difference between Groups regarding Need for Oxytocin Infusion	99
Figure (35):	Box-Plot Chart showing Difference between Groups regarding Induction-to-Onset-of-Labor Duration	100
Figure (36):	Box-Plot Chart showing Difference between Groups regarding Induction-to-Delivery Duration	100
Figure (37):	Bar-Chart showing Difference between Groups regarding Maternal Adverse Effects	102
Figure (38):	Bar-Chart showing Difference between Groups regarding Fetal Adverse Effects	104

List of Figures (Cont.)

Figure No.	Title	Page No.
Figure (39):	Bar-Chart showing Difference between Groups regarding 1-min Apgar Score	106
Figure (40):	Bar-Chart showing Difference between Groups regarding 5-min Apgar Score	106
Figure (41):	Bar-Chart showing Difference between Groups regarding Incidence of NICU admission.	108
Figure (42):	Bar-Chart showing Difference between Groups regarding Postpartum Complications	110
Figure (43):	Bar-Chart showing Difference between Groups regarding Maternal Satisfaction.....	111

Oral Misoprostol Versus Vaginal Dinoprostone For Induction Of Labour: A Randomized controlled Clinical Trial

Maged Ramadan Abouseeda; Walid Hitler Tantawy; Adel
Shafik Salah El-Din and Marwan Osama Elkady

Department of Obstetrics and Gynecology, Ain Shams
University, Cairo, Egypt

Corresponding author: Marwan Osama Elkady

E-mail: marwan-elkady@hotmail.com

tel: +2 02 01205533315

Abstract

Background: Induction of labour is one of the most common obstetrical procedures. Methods for induction include mechanical and pharmacological options. Misoprostol and Dinoprostone are both prostaglandin analogues that are commonly used to induce labour.

Objective: The objective of this study was to compare the efficacy and safety of 2-hourly oral misoprostol in solution with dinoprostone vaginal tablets for labor induction.

Study Design: Subjects were randomized into oral misoprostol in solution or vaginal dinoprostone groups. Misoprostol was given as 25 µg orally every two hours until regular uterine contractions were achieved with a maximum of 4 doses. Dinoprostone was given as 3 mg vaginal tablets, 2 doses six hours apart was the maximum. The primary outcome variable was successful vaginal delivery in 24

hours. Safety assessment included incidence of maternal, fetal or neonatal adverse outcomes.

Patients and methods: 342 patients were recruited and randomized into two groups oral misoprostol in solution group (OMS) included 172 patients, and vaginal dinoprostone group (VDP) included 170 patients.

Results: Patients characteristics and indications for induction of labour were similar in both groups. Vaginal delivery was achieved within 24 hours in 106 of the OMS group and 109 of the VDP group ($P=0.297$). Incidence of caesarian section was comparable ($P=0.276$), incidence of operative vaginal delivery was comparable ($P=0.873$), need for oxytocin augmentation was similar in both groups ($P=0.964$), OMS was superior in initiating labour ($P<0.001$). Increased incidence of pyrexia ($P=0.001$) and shivering ($p<0.001$) with OMS, otherwise no difference as regards maternal adverse effects. Rates of fetal distress were comparable in both groups ($P=0.317$) as well as rates of NICU admission ($P=0.984$).

Conclusion: Oral misoprostol in solution in a dose of $25\mu\text{g}$ every 4 hours appears to be a safe and effective alternative to vaginal dinoprostone for inducing labour at term in primigravidas.

Key Words: Induction of labour, misoprostol, dinoprostone, safety and efficacy.

Introduction

Induction of labor is one of the most common obstetrical procedures performed, involving approximately 20% of all parturient women. As much as half of them are induced in the presence of an unfavorable cervix. Cervical conditions at initiation of induction of labor greatly affect the success rate of labor induction. It is well established that an unfavorable cervix is associated with a higher rate of induction failure and increased rate of operative vaginal delivery and cesarean delivery (*Ashwal et al., 2014*).

Indications for induction of labour include prolonged pregnancy as well as some complicated pregnancies such as prelabour rupture of the fetal membranes, pre-eclampsia, gestational diabetes mellitus and intrauterine growth restriction (IUGR) (*Thaisamboon et al., 2012*).

Methods for labor induction include both mechanical and pharmacologic options. Although oxytocin is an effective drug for the augmentation of labor in patients with favorable cervixes, in the patient with an unfavorable cervix, a ripening agent may be used (*ACOG, 2009*).

Two types of prostaglandin preparations, synthetic prostaglandin E1 (misoprostol) and natural prostaglandin E2 (dinoprostone) are approved for cervical ripening by the US

Food and Drug Administration. Dinoprostone, regardless of being used widely, has two disadvantages: it requires continuous refrigeration and is expensive. Therefore misoprostol, which is more stable at room temperature and less expensive, has been suggested as an alternative agent for induction of labour. However, misoprostol could lead to side effects such as disturbance in the gastrointestinal tract, uterine tachysystole, postpartum hemorrhage, and the most serious, uterine rupture. Those side effects are likely to be route and dose related (*Thaisamboon et al., 2012*).

In 1995, the Food and Drug Administration approved a dinoprostone vaginal insert (Cervidil; Forest Pharmaceuticals Inc, St. Louis, MO) for cervical ripening. This insert releases 10 mg of dinoprostone over 12 hours and was shown to shorten the interval between induction and vaginal delivery safely (*Witter et al., 1992*), (*Raburn et al., 1992*), (*Witter et al., 1996*). Other preparations in the form of vaginal tablets (2mg – 3mg) are now available.

Misoprostol, a synthetic prostaglandin E1 analog, can be administered orally, sublingually, buccally, intravaginally, or rectally and is used for both cervical ripening and labor induction. According to the American College of Obstetricians and Gynecologists (ACOG), there is extensive clinical experience with misoprostol, and a large body of published reports supports its safety and efficacy when used appropriately (*ACOG, 2009*).

Misoprostol has a short half-life (20- 40 minutes) following oral administration. It reaches peak serum concentration in 30 minutes, followed by a rapid decline to low levels by 120 minutes, with a more gradual decline thereafter (*Rouzi et al., 2014*).

Although misoprostol is not approved for labor induction, its comparative cost advantage over dinoprostone combined with greater satisfaction with oral administration contributed to its widespread off-label use for this indication. ACOG states that “no studies indicate that intrapartum exposure to misoprostol has any long-term adverse health consequences to the fetus in the absence of fetal distress, nor is there a plausible biologic basis for such a concern” (*ACOG, 2009*).

A Cochrane review of 56 randomized clinical trials (RCTs) of oral misoprostol with a total of 11,590 women concluded that this treatment is as effective as vaginal misoprostol for inducing vaginal delivery and results in fewer caesarean deliveries compared with vaginal dinoprostone (*Alfirevic et al., 2010*).

Women receiving oral misoprostol have a shorter interval to vaginal delivery and are more likely to deliver vaginally when compared to women receiving vaginal dinoprostone, also there is no increase in rate of caesarean section or adverse maternal or neonatal outcomes (*Faucett, 2014*).