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

Thesis

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Marwan Osama Saleh Elkady

Contents

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

List of Tables (Cont.)

List of Figures

List of Figures (Cont.)

Figure No.	Title	Page No.

List of Figures (Cont.)

Figure No.	Title	Page No.

List of Figures (Cont.)

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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 25µg 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 cervices, 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).***