

## Misoprostol Efficacy in Labor Induction

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### Abstract

<b>Background</b>	The process of normal human childbirth is categorized in three stages of labor: the shortening and dilation of the cervix, descent and birth of the infant, and delivery of the placenta. Oxytocin is the most commonly used agent for induction, and is used to induce uterine contractions.
<b>Objective</b>	To estimate the efficacy of oral misoprostol for labor induction.
<b>Methods</b>	This randomized, controlled trial study was comparing intravenous oxytocin to a 25-microgram dose of oral misoprostol every 3-4 hours. A woman who had cervical dilation of 0-2 cm then undergoes labor induction. Our outcome was recorded.
<b>Results</b>	we found when we used misoprostol the time duration was significantly less specially in primigravida and when os closed, the side effect approximately same as oxytocin.
<b>Conclusion</b>	Oral misoprostol is an effective agent for induction of labor.
<b>Keywords</b>	Induction of labor, misoprostol, oxytocin

**List of abbreviation:** ARM = artificial rupture of membrane, ACOG = American College of Obstetricians and Gynecologists, C/S = caesarean section, NICU = Neonatal intensive care unit.

### Introduction

Induction of labour can be defined as the artificial initiation of labour, before its spontaneous onset for the purpose of delivery of the fetoplacental unit. Prostaglandins and oxytocin are the principal hormones which can both be produced synthetically and be given to pregnant women to induce labour<sup>(1)</sup>.

Induction of labor is commonly performed in clinical practice, compared to spontaneous labor the main risks of induction are ineffective labor and excessive uterine activity, which may cause fetal hypoxia. In woman with previous cesarean sections or uterine scars there also appears to be higher incidence of uterine rupture. Labor may induced using medical methods (oxytocin or prostaglandins) or mechanical methods (e.g. extra-amniotic balloon catheters or artificial

rupture of membrane [ARM]) the most common methods in hospital practice worldwide are oxytocin (combined with ARM where possible) and vaginal prostaglandins<sup>(2)</sup>.

The naturally occurring prostaglandin E series was first discovered to inhibit gastric acid secretion in 1967 by Robert et al., and was first used for the induction of labor with a dead fetus in 1987<sup>(3)</sup>.

The uterotonic and cervical softening effects on the female genital tract were considered as side effects rather than therapeutic effects when misoprostol was first introduced. However, it is because of these effects that misoprostol is so widely used in obstetric and gynecological practice today<sup>(4)</sup>.

After a single dose of oral misoprostol there is increase in uterine tonus to produce regular contractions, however a sustained plasma level of misoprostol is required and this requires repeated oral doses<sup>(5)</sup>.

The American College of Obstetricians and Gynecologists (ACOG) guidelines recommend a full evaluation of the maternal-fetal status, the status of the cervix, and at least a 39 completed weeks (full term) of gestation for optimal health of the newborn when considering elective induction of labor. Induction is also considered for logistical reasons, such as the distance from hospital or psychosocial conditions, but in these instances gestational age confirmation must be done, and the maturity of the fetal lung must be confirmed by testing. The ACOG also note that contraindications for induced labor are the same as for spontaneous vaginal delivery, including vasa praevia, complete placenta praevia, umbilical cord prolapse or active genital herpes simplex infection<sup>(6)</sup>.

The objective of this study was to estimate the efficacy of oral misoprostol for labor induction

### Methods

Two hundred forty women with early labor were admitted to maternal and pediatrics teaching hospital in Al-Diwanyia city or labor induction between April 2011 to March 2012. A standardized data sheets were prepared for collection of information including name, age, body weight, height, maternal history. Cervical dilation of 0-2 cm. if decided to induce labor we approached any women with a full term pregnancy at least 40 weeks' gestation. We then obtained written informed consent. We excluded women with a "favorable" cervix (defined as a modified Bishop score of  $\geq 7$ ), any contraindication to vaginal birth, previous uterine surgery (including caesarean section), or ruptured membranes.

Those women divided into two groups: first group .121 patients started with misoprestol 25 microgram oral misoprostol every 3-4 hours (59 patients of them were primigravida) and second group 119 (60 patients of them primigravida) patients on oxytocin infusion and monitoring every patient by partogram and continuous cardiotography.

Our primary outcome measures duration of labor induction till delivery (including women

who achieved vaginal birth after 24 hours and those women who required a caesarean section), caesarean section (all and for heart rate tracing indicating fetal distress), and uterine hyperstimulation with changes in fetal heart rate.

We defined uterine hyperstimulation as uterine tachysystole (with five or more contractions in a 10 minutes period for two consecutive 10 minute periods) or uterine hypertonus (a uterine contraction lasting for more than two minutes). The changes in fetal heart rate that we considered abnormal included persistent late, or variable decelerations, fetal tachycardia (fetal heart rate  $> 160$  beats per minute), fetal bradycardia (fetal heart rate  $< 100$  beats per minute) and absent variability. A single investigator blinded to the treatment allocated reviewed all fetal heart rate tracings from an induced labour to maintain consistency in interpretation.

### Results

Two hundred forty cases of women with labor were admitted to the hospital. There were 121 (50.5%) patients started with misoprestol (59 patients (48.7%) of them were primigravida) and 119 (49.5%) (60 patients (50.4%) of them primigravida) patients on oxytocin infusion as shown in table 1.

**Table 1. Distribution of study groups**

Patients	Treatment	
	Misoprestol	Oxytocin
Primigravida	59 (48.7%)	60 (50.4%)
Multigravida	62 (51.2%)	59 (49.5%)
Total	121 (50.5%)	119 (49.5%)

The time duration for delivery with primigravida patients on misoprostol shown that 29 patient (49.1%) take about 8-10 hours and 2 patients (3.38%) take more than 14 hours. The primigravida patients on oxytocin shown that 38 patients (63.33%) take about 10-12 hours and 19 patients (31.66%) take more than 14 hours ( $p = 0.01$ ) . as shown in table 2.

The multigravida patients on misoprostol shown that 27 patients (43.5%) take about 8 - 10 hours for delivery while 1 patient take more than 14 hour ( 1.61%).The patients on oxytocin shown that 26 patients (44.06%) take about 10 - 12 hours and 7 patients (11.86%) take more than 14 hours. (p = 0.01) as shown in table 3.

**Table 2. Mean duration for delivery (primigravida)**

Misoprestol		Oxytocin	
No.	Time (hours)	No.	Time (hours)
10	<8	8	<8
29	8 - 10	14	8 – 10
21	10- 12	38	10 -12
2	>14	19	>14

**Table 3. Mean duration for delivery (more than one pregnancy)**

Misoprestol		Oxytocin	
No.	Time (hours)	No.	Time (hours)
14	<8	10	<8
27	8 - 10	16	8 – 10
20	10- 12	26	10 -12
1	>14	7	>14

Patients on the misoprostol group show uterine tachysystole and hypertonus compared with women on the oxytocin (76% compared with 63%, respectively; *P* = 0.01). There was no significant difference between two groups regarding non reassuring fetal heart rate (*P* = 0.20) or need a cesarean delivery. Patients on misoprestol shown meconium stained liquor (*P* = 0.02). No difference in need to admission to NICU (Table 4).

**Table 4. Maternal and perinatal outcome**

Outcome	Misoprestol	Oxytocin
Tachysystol & hypertonus	92 (76%)	75 (63%)*
Non-reassuring fetal HR	23 (19%)	22 (18.4%)
Required c/s	26 (21.8%)	27 (22.6%)
Meconium stained liquor	32 (26.44%)	20 (16.8%)+
Admission to NICU	27 (22.3%)	25 (21%)

\* *P* = 0.01, + *P* = 0.02, HR = heart rate

**Discussion**

Nowadays, induction of labor is more widely used than ever before <sup>(7,8)</sup>. Recent studies have shown that this increase is mainly due to a rise of inductions for marginal or elective reasons. Women may experience distress when labor has not started by the expected date <sup>(9)</sup> and obstetricians have to withstand pressure from these patients as well as the temptation to use prostaglandins earlier. Appropriate evaluation of the pregnancy and consultation with such patients will lead to the correct selection of those who will benefit most from a labor induction.

In this study, the time duration for delivery with primigravida patients on misoprostol shown that 29 patient take about 8-10 hours while the primigravida patients on oxytocin shown that 38 patients take about 10-12 hours. The multigravida patients on misoprostol shown that 27 patients take about 8-10 hours for delivery while patients on oxytocin shown that 26 patients take about 10-12 hours .This is in agreement with a study of Alfirevic <sup>(10)</sup>. Who done trial on 80 randomized women with prelabour rupture of membranes at term showed that, compared with placebo; oral misoprostol reduces the need for oxytocin infusion from 51 percent to 13 percent (relative risk 0.25, 95% confidence interval (CI) 0.1 to 0.6) and shortens delivery time by 8.7 hours.

To the best of our knowledge, Aalami-Harandi <sup>(11)</sup> estimates the efficacy of oral misoprostol for labor induction. He shows that misoprostol is a safe and effective drug with low complications for the induction of labor. Failure is seen less with misoprostol and caesarean sections are less frequently indicated as compared to oxytocin. Maternal and fetal complications were comparable between groups except gastrointestinal symptoms which were encountered more frequently in the misoprostol. Of particular concern are several reports of uterine rupture following misoprostol use in woman with and without previous caesarean section. Adverse effects were reduced, within lower rates of uterine

hyperstimulation and a tend to fewer admissions to neonatal intensive care unit<sup>(12, 13)</sup>.

The finding of a significantly more meconium stained liquor with misoprostol is of interest. Wing et al suggested the possibility of meconium passage in response to uterine hyperstimulation or a direct effect of absorbed misoprostol metabolites on the fetal gastrointestinal tract<sup>(14)</sup>.

They have previously observed an increased rate of meconium stained liquor in woman who has ingested castor oil, though causality was not proven, and suggested a possible direct effect of the castor oil metabolites on fetal bowel<sup>(15)</sup>. It is unlikely that the small amount of hydrogenated castor oil found in misoprostol tablets would have any pharmacological effect, but the possibility that misoprostol metabolites may directly stimulate fetal bowel is of interest<sup>(16)</sup>.

Attempting an explanation to the aforementioned side effects of misoprostol use and taking into account other reports, it appears that the increase in clinically relevant adverse effects is not only misoprostol related but it may be dose dependent<sup>(17,18)</sup>.

In conclusion, this study show oral misoprostol is an effective agent for induction of labor. We recommend use of misoprostol for induction of labor depend on selection of patient, like non scaring uterus and the compliance of the patients with good monitoring of ongoing process of labor and regarding its safety because of a relatively high rate of uterine hyperstimulation. Further studies needed regarding the dose, and use in scaring uterus.

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### Author contribution

Dr. Asma Z. Fadhil writes the article and the assistant Prof. Edwar Z. Khosho materially participated in the research and article preparation.

### Declaration of interest

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