



## Original Research Article

# Induction of labour with oral misoprostol solution 20 microgram versus vaginal misoprostol 25 microgram 6<sup>th</sup> hourly

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## ABSTRACT

**Background:** Induction of labour is the artificial initiation of labour before the spontaneous onset, and it is the common obstetric intervention.

**Aim:** To compare the potency of oral misoprostol solution with vaginal misoprostol to induce labour at term.

**Settings and Design:** This randomized control study was carried out from July 2020 to September 2020 at Government General Hospital, Kakinada.

**Materials and Methods:** 80 women requiring induction were recruited in the study. The women were randomized to receive 20 micrograms of oral misoprostol solution every 2<sup>nd</sup> hourly or vaginally 25 micrograms of misoprostol every 6<sup>th</sup> hourly until the labour sets in the active phase of labour. Delivery within 24 hours was the outcome in the study.

**Statistical Analysis:** Data were documented in Microsoft excel and analyzed using SPSS software.

**Results:** 82.5% of women in the oral group delivered by spontaneous vaginal delivery, whereas 75% in the vaginal group. In the oral group, 37.5% of delivery occurred within 6-12 hours, 40% delivered within 12-18hours duration, whereas in the vaginal group, 12.5% delivered within 6-12hours duration, 50% delivered within 12-18hours duration. Oxytocin augmentation was required in 25% of the oral group, whereas 42.5% in the vaginal group. Meconium stained liquor was 12.5% in the oral group, whereas 20% in the vaginal group. 12.5% underwent cesarean section in the oral group, 10% in the vaginal group.

**Conclusion:** Compared with vaginal misoprostol, oral misoprostol solution results in shorter induction delivery interval and less oxytocin augmentation required.

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## 1. Introduction

Induction of labour is the artificial initiation of labour before the spontaneous onset, and it is the common obstetric intervention. The ultimate aim of labour induction is uterine contraction stimulation before spontaneous onset resulting in vaginal delivery.<sup>1</sup>

Misoprostol is unique prostaglandin E1 analog. Misoprostol was introduced by Sanchez-Ramos et al. in 1993.<sup>2</sup> Misoprostol can be administered by various oral, buccal, sublingual, rectal, and vaginal routes. Misoprostol is available at low cost, stable at room temperature, and

easy availability of the drug.<sup>3,4</sup>

### 1.1. Oral misoprostol

The oral route of misoprostol solution is better tolerated by women as it involves less vaginal examination.<sup>5</sup> Oral misoprostol solution has a short half-life of 20-40 minutes, plasma concentration reaches an optimal level around 30 minutes after administration, within 120 minutes drug being cleared from the blood.<sup>6,7</sup>

### 1.2. Vaginal misoprostol

Vaginal administration of 25 micrograms of misoprostol is considered safe with fewer uterine tachysystole rates,

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uterine hyperstimulation, and cesarean section due to meconium. It reaches peak concentration after 70-80 minutes of administration, and the drug is eliminated 6 hours following administration.<sup>7,8</sup>

## 2. Materials and Methods

This study was conducted at Government general hospital, Kakinada, from July 2020 to September 2020. Patients recruited in the study were primigravida and second gravida with the obstetric or medical indication for termination of pregnancy. These patients were either booked case or emergency admission in the labor room.

A total of 80 patients at term randomly selected for the study, grouped into 40 primigravidas and 40 second gravida. Out of 40 primigravida, 20 primigravidas for oral misoprostol solution, and the remaining 20 primigravidas for vaginal misoprostol. Out of 40 second gravida, 20 women for oral misoprostol, and the remaining 20 for vaginal misoprostol. The method of induction was explained to patients and their relatives, and informed consent taken from them.

### 2.1. Inclusion criteria

1. Primigravida and second gravida
2. Pregnancy between 37-42 weeks of gestation
3. Clinically adequate pelvis
4. Single live fetus in cephalic presentation
5. No prior uterine surgery
6. Bishop score of  $\leq 5$
7. Reactive NST

### 2.2. Exclusion criteria

1. Patient refusal to consent
2. Known hypersensitivity to misoprostol
3. Non-reactive NSTa
4. Placenta previa
5. Previous cesarean section
6. Multiple pregnancy

### 2.3. Procedure

History is taken in detail and examined thoroughly. The last menstrual period and the expected date of delivery was calculated. General examination, systemic examination, per abdomen, and per vaginal examination was done. Bishop's score was calculated. Ultrasound is done to know the gestational age, amount of liquor, placental maturity, and location and severity of IUGR. Nonstress was done.

### 2.4. Methods

Women were given 20ml (20 micrograms) of misoprostol solution every second hourly until adequate uterine contractions obtained (3 contractions per 10 minutes lasting

for 30-40 seconds) until the patient landing in the active phase of labour. The artificial rupture of the membrane was done at the active phase. Uterine contractions were monitored. If inadequate, then oxytocin augmentation was used.

For correct dosage, 200 micrograms of misoprostol tablets are dissolved in 200ml of water (1microgram per ml), shaking the solution before each administration. The solution is stored at room temperature for 24 hours in a sterile glass bottle.

### 2.5. Equipment

1. Measuring jug
2. Spoon
3. Clean drinking water
4. Misoprostol tablet of 200 microgram
5. Clean glass bottle

Uterine contraction is assessed by regular abdominal palpation. The fetal heart rate is monitored by intermittent auscultation every 15 minutes in the first stage of labour and every 5 minutes in the second stage of labour. Cardio topography was done. The patient reassessed every 2<sup>nd</sup> hourly for uterine contraction, and per vaginal examination was done after 6 hours of the first dose. Repeat per vaginal examination was done when the contraction was adequate in the oral group. In the patient with an active phase of 4cm dilatation, amniotomy is done, the liquor's color noted, and partograph was plotted. If the subsequent contraction is inadequate, then oxytocin augmentation was started. Oxytocin 5 units for primigravida and 2.5 units for the second gravida started at 15 drops per minute, escalated by another 15 drops per minute if contractions are inadequate till a maximum of 60 drops per minute. The progress of labour was monitored.

Vaginal misoprostol is administered every 6<sup>th</sup> hourly till the active phase of 4cm dilatation; then, the oxytocin augmentation is decided based on the adequacy of uterine contraction.

### 2.6. Failed induction

If a woman is not in an active phase of labour after ten doses of solution or failed to deliver within 24 hours of misoprostol administration, patients who require LSCS, who failed to progress categorized as failed induction.

### 2.7. Successful induction

Women who delivered vaginally within 24 hours from the initial induction of misoprostol were considered as successful induction.

### 2.8. Outcome

1. Induction delivery interval

2. Rate of LSCS
3. The requirement of oxytocin augmentation
4. Fetal heart rate abnormality
5. Incidence of meconium stained liquor
6. Neonatal outcome- birth weight, NICU admission, morbidity/ mortality.
7. Drug adverse effects.

Data entry, data checking and analysis were done.

### 2.9. Statistical analysis

Data entered in MS excel and analyzed by using SPSS software. Qualitative data were represented as frequencies or percentages and quantitative data was represented as mean and median. Unpaired t-test was used to know the statistical significance between quantitative variables. P-value <0.05 was considered as statistically significant.

### 3. Results

The number of patients randomized was 80. The age group of patients belong to 21-25 years of age of about 50%. 31.2% belong to 26-30 years of age (Table 1). Of the patients (Table 2), premature rupture of the membrane of 50%, 37.5% of non-severe preeclampsia, 32.5% of oligohydramnios, 25% of post-dated pregnancy was the most common indication for induction of labour.

Table 3 and Table 4 indicate the induction delivery interval. In the oral misoprostol solution group, 87.5% delivered vaginally within 24 hours and 12.5% delivered by cesarean section, whereas in the per-vaginal group, 90% delivered vaginally within 24 hours and 10% delivered by cesarean section. P-value <0.01 hence significant.

Oxytocin augmentation is listed in Table 5. In the oral misoprostol solution group, 75% of patients do not require oxytocin to augment labour; 25% required oxytocin augmentation. In per vaginal group patients, 57.5% required oxytocin augmentation, 42.5% does not require oxytocin to augment labor.

Table 6 and Table 7 shows the mode of delivery and oxytocin augmentation based on bishop score. In the oral misoprostol solution group, 22.5% had a bishop score of 0-2, 37.5% had a bishop score of 3-4, 40% had a bishop score of 5. In per vaginal misoprostol group, 22.5% had bishop score of 0-2, 27.5% had bishop score of 3-4, 50% had bishop score of 5. (P-value <0.001- very significant)

The neonatal outcome is listed in table 8. In the oral misoprostol group, 12.5% had meconium stained liquor, 2.5% had meconium aspiration syndrome, Apgar <=7 at 1min of 10%, 5% had NICU admission of duration < 5 days. In per vaginal misoprostol group, 20% had meconium stained liquor, 7.5% had meconium aspiration syndrome, Apgar <=7 at 1min of 10%, Apgar <=7 at 5min of 2.5%, 12.5% had NICU admission of duration < 5 days. The mean birth weight in each group is 3 kg. Take home baby rate was

100%.

shows the side effect of the drug misoprostol. In both groups, there was no severe side effect. In the oral misoprostol group, 7.5% had nausea, and in per vaginal group, 12.5% had fever. In the oral misoprostol group, the number of per vaginal examination is reduced, making the patient comfortable.

**Table 1:** The age group of patients in the study group

Age	Number of patients	Percentage
<20 years	10	12.5%
21-25 years	40	50%
26-30 years	25	31.2%
>=31 years	5	6.25%

Mean age – 22.5 years; Median: 25 years; age range- 18-35 years  
Maximum age - 35 years; minimum age- 18 years

**Table 2:** Indication of labour induction

Indication	Oral solution	Per vaginal
Post-dated pregnancy	8 (20%)	2 (5%)
Severe preeclampsia	2 (5%)	5 (12.5%)
Non severe preeclampsia	7 (17.5%)	10 (25%)
Gestational hypertension	3 (7.5%)	5 (12.5%)
PROM	10 (25%)	10 (25%)
Oligohydramnios	7 (17.5%)	6 (15%)
IUGR	3 (7.5%)	2 (5%)
Total	40 patients	40 patients

**Table 3:** Induction delivery interval in oral misoprostol solution group

Induction delivery interval	Oral solution (primigravida)	Oral solution (second gravida)
6-12 hours	-	15 (37.5%)
12-18 hours	12 (30%)	4 (10%)
18-24 hours	4 (10%)	-
>24 hours (LSCS)	4 (10%)	1 (2.5%)
Total	20 patients	20 patients

**Table 4:** Induction delivery interval in per vaginal misoprostol group

Induction delivery interval	Per vaginal (second gravida)	Per vaginal (second gravida)
6-12 hours	1 (2.5%)	4 (10%)
12-18 hours	8 (20%)	12 (30%)
18-24 hours	7 (17.5%)	4 (10%)
>24 hours (LSCS)	4 (10%)	-
Total	20 patients	20 patients

**Table 5:** Oxytocin augmentation requirement

Oxytocin	Oral	Per vaginal
Required	10 (25%)	17 (42.5%)
Not required	30 (75%)	23 (57.5%)
Total	40 patients	40 patients

**Table 6:** Mode of delivery based on Bishop score in oral misoprostol solution group

Oral solution	Oxytocin		Mode of delivery	
	Required	Not	Vaginal	LSCS
Bishop score				
0-2	8 (20%)	1 (2.5%)	5 (12.5%)	4 (10%)
3-4	2 (5%)	13 (32.5%)	14 (35%)	1 (2.5%)
5	-	16 (40%)	16 (40%)	-
Total	10 (25%)	30 (75%)	35	5 (12.5%)

**Table 7:** Mode of delivery based on Bishop score in per vaginal misoprostol group

Per vaginal	Oxytocin		Mode of delivery	
	Required	Not	Vaginal	LSCS
Bishop score				
0-2	9 (22.5%)	-	6 (15%)	3 (7.5%)
3-4	6 (15%)	5 (12.5%)	10 (25%)	1 (2.5%)
5	2 (5%)	18 (45%)	20 (50%)	-
Total	17 (42.5%)	23 (57.5%)	36 (90%)	4 (10%)

**Table 8:** Neonatal outcome

	Oral solution	Per vaginal
MSAF	5 (12.5%)	8 (20%)
MAS	1 (2.5%)	3 (7.5%)
Apgar <=7 at 1min	3 (7.5%)	4 (10%)
Apgar <=7 at 5 min	-	1 (2.5%)
NICU admission	2 (5%)	5 (12.5%)
NICU Duration <5 days	2 (5%)	5 (12.5%)
Neonatal death	-	-
Mean birth weight	3 kg	3 kg

**Table 9:** Drug side effect

Side effect	Oral solution (n=40)	Per vaginal (n=40)
Nausea	3 (7.5%)	-
Vomiting	-	-
Fever	-	5 (12.5%)
Diarrhea	-	-
Uterine hypersensitivity	-	-
Uterine tachysystole	-	-
Hyper tonus	-	-

#### 4. Discussion

Low dose misoprostol solution for the induction of labour is equally effective in achieving vaginal delivery within 24 hours as compared to per vaginal group with less cesarean rate and less need of oxytocin augmentation, less fetal distress with good safety to the mother in this study. This study is consistent with a study done by Dodet et al. in 2006,<sup>9</sup> Chang et al. in 2008,<sup>10</sup> Alamin Harandi et al. in 2012,<sup>11</sup> Varsha et al. in 2016,<sup>12</sup> O Lapuente- Ocamica et al. study 2016.<sup>13</sup>

Low dose misoprostol induces low-frequency contraction and decreases the myometrial acidemia.<sup>14</sup> The oral solution gives dose accuracy and patient satisfaction positively. Compared to per vaginal group, 42.5% required oxytocin, only 25% required oxytocin augmentation in the oral misoprostol group. Safety is associated with the rapid clearance of the drug in oral misoprostol.

## 5. Conclusion

Misoprostol is used as a promising agent in labour induction after being approved by the FDA. Misoprostol is cost-effective, readily available, and cheap, and stable at room temperature can be safely used in developing countries. It has an excellent uterotonic and cervical ripening effect in both groups. Low bishop score requires oxytocin augmentation and increased cesarean rate in misoprostol in both groups. Compared with vaginal misoprostol, oral misoprostol solution results in a shorter induction delivery interval and less oxytocin augmentation required.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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