10.5005/jp-journals-10045-0071

ORIGINAL ARTICLE

# Comparison of 50 µg Oral and Vaginal Misoprostol Tablets in Induction of Labor at Term

[1]Vineeta Yadav, [2]Rangaiah Nagaratnamma, [3]Nagendra Prasad


## ABSTRACT

**Objective:** To compare efficacy and safety of 50 µg misoprostol administered vaginally, with oral route for induction of labor at term.

**Materials and methods:** One hundred women at term gestation, Bishop score ≤ 4, with various indications for labor induction were randomized. Fifty women received 50 µg misoprostol orally and 50 women received 50 µg vaginally, fourth hourly (maximum six doses) or till the women went into active labor.

**Results:** In vaginal misoprostol group, induction delivery interval was significantly less (8.70 *vs* 17.47 hours) and successful induction was significantly higher (70 *vs* 60%) than oral group, within 24 hours of induction. In vaginal group, 46% women needed two doses for delivery compared with 8% in oral group. A maximum of six doses were required.

**Conclusion:** Vaginal route of misoprostol is more effective in inducing labor than oral administration.


**Keywords:** Induction of labor, Oral misoprostol, Vaginal misoprostol.

**How to cite this article:** Yadav V, Nagaratnamma R, Prasad N. Comparison of 50 µg Oral and Vaginal Misoprostol Tablets in Induction of Labor at Term. J Med Sci 2018;4(1):1-4.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Induction of labor at term is a common obstetric intervention, and cervical ripening in these cases is considered to be of importance. Literature review and meta-analysis have shown that there are advantages in using vaginal prostaglandins (PGs) when compared with oxytocin alone in the presence of an unripe cervix, with regard to a shorter induction to delivery time and a lower cesarean section rate.[1] Induction of labor at term with unfavorable cervix is associated with increased risk of failed induction and cesarean sections. Various methods for cervical ripening include oxytocin, Foley's catheter, and others. All these methods have their own advantages and disadvantages. Hence, there is a need for more efficient inducing agent with less limitations. Till today no ideal agent has been found. Prostaglandins are new drugs of interest in this field. Out of all PGs, PGE1 and PGE2 have been tried for induction of labor. Prostaglandin E2 is being used as gel and tablet, has the advantage of being used intracervical or vaginally,[2-4] is expensive, and needs refrigeration.

Synthetic analog of PGE1, misoprostol, is originally used as gastro protective agent[5]; its use for cervical ripening and labor induction is upcoming[6] and is being tried enthusiastically by obstetricians worldwide. It has advantage of being cheap, stable at room temperature, and easy to be administered by various routes, i.e., vaginal, oral, sublingual, or rectal.[7] When administered orally absorption of the drug is erratic, and at the same time, it is more rapid than vaginally administered misoprostol, reaching peak serum concentrations within 30 minutes compared with 1 hour with vaginal route. Oral misoprostol is eliminated rapidly (2–3 hours)[5] than vaginal (4 hours).[5] Hence, vaginal route seems to be more efficacious than oral one and should result in shorter induction–delivery interval and reduced need for oxytocin augmentation,[6] but at the cost of little more complications.

There have been only few trials looking at the use of oral misoprostol for the induction of labor. Bennett et al[8] found that 50 µg of oral misoprostol effectively induced labor and Windrim et al[9] showed that at this dose misoprostol was as effective as the other more commonly used methods of induction. Misoprostol was found to be safe and effective in patients with prerupture of membranes at term.[10]

We have taken up this study to compare administration of 50 µg misoprostol through vaginal and oral routes for cervical ripening in induction of labor.

## MATERIALS AND METHODS

### Research Setting

Department of Obstetrics and Gynecology, RajaRajeswari Medical College & Hospital, Bengaluru, Karnataka, India, a tertiary care teaching hospital in southern India.

### Study Population

Cases are pregnant women with gestational age between 37 and 40 weeks.

[1]Postgraduate Student (Third Year), [2]Professor and Head [3]Associate Professor

[1-3]Department of Obstetrics and Gynecology, RajaRajeswari Medical College & Hospital, Bengaluru, Karnataka, India

**Corresponding Author:** Vineeta Yadav, Postgraduate Student (Third Year), Department of Obstetrics and Gynecology RajaRajeswari Medical College & Hospital, Bengaluru, Karnataka India, Phone: +918700703095, e-mail: Vineetayadav136@gmail.com

### Sampling Frame

One hundred pregnant women were randomly assigned in the study, of which 50 cases received misoprostol orally and other 50 were given vaginally, fourth hourly, with a maximum of six doses.

### Sample Size

One hundred pregnant women included in the study received misoprostol orally or vaginally.

### Inclusion Criteria

Patients at term gestation, singleton pregnancy, cephalic presentation, without fetal congenital malformation, reactive fetal heart rate pattern, and Bishop score ≤ 4 were included in the study.

### Exclusion Criteria

Patients with Bishop score > 4, cephalopelvic disproportion, placenta previa or unexplained vaginal bleeding, previous cesarean section or other uterine surgery, with active herpes simplex, carcinoma cervix, chorioamnionitis and contraindication to use of prostaglandins like hypersensitivity acute pelvic inflammatory disease were excluded from the study.

After detailed history of the patient, systemic and local examination were done. Blood investigations included complete blood count, human immunodeficiency virus, hepatitis B virus surface antigen, Venereal Disease Research Laboratory test, blood grouping, and Rh typing. Ultrasound of the abdomen and pelvis was conducted to rule out congenital and acquired anomalies.

After obtaining informed consent, study groups were allotted. All the enrolled parturient were divided into two groups as follows:

1. *Group I (n = 50):* Parturient who were given 50 µg misoprostol orally.
2. *Group II (n = 50):* Parturient in which 50 µg misoprostol was inserted vaginally in posterior fornix.

Both oral and vaginal tablet were repeated every fourth hourly till either patient went into active labor or maximum dose of six tablets have been consumed. Progress of labor was monitored using partogram. The uterine contractions were monitored for its frequency, intensity, and duration. Fetal heart rate and other maternal complications like nausea, vomiting, diarrhea, distress, etc., were monitored closely. Side effects of the drug like nausea, vomiting, diarrhea were treated symptomatically.

Woman was said to be in "active labor" if she had four uterine contractions per 10 minutes, lasting for 40 seconds and of good intensity which was judged subjectively.

During the course of induction, uterus was said to be hypertonic if uterine contractions lasted for >120 seconds, tachysystole if >6 contractions per 10 minutes for two consecutive 10 minutes or hyperstimulation if either or both hyper tonus tachysystole associated with abnormal fetal heart rate pattern occurred, then vaginal tablet was removed from the posterior fornix and no further dose oral or vaginal due was given.

Following data were collected.

### Baseline Data

- Maternal age
- Socioeconomic status
- Parity
- Gestation
- Indication for induction and preinduction cervical score
- Mode of delivery
- Intrapartum and postpartum maternal and fetal complications.

### After Delivery

- Both mother and the neonate hospital stay and complication

### Measures of Efficacy

- Successful induction (i.e., number of women who achieved active labor within 24 hours of induction and their induction delivery interval)
- Number of deliveries within 24 hours
- Total dose of misoprostol/oxytocin required for mode of delivery.

### Measures of Safety

- Uterine tachysystole
- Uterine hyper tonus
- Abnormal fetal heart tracings
- Incidence of meconium passage
- Neonatal outcome.

## RESULTS

Of a total of 100 women recruited for the study, 50 women had received 50 µg misoprostol orally and 50 women received it vaginally. None of the women recruited requested to be withdrawn after enrollment. Maternal demographic characteristics and indications for induction were comparable in both the groups (Table 1). Common indication for induction of labor was hypertensive disorders in both vaginal and oral groups.

The successful induction rate was 70% in vaginal group and 60% in oral group (Table 2). Induction delivery interval was 8.70 hours (3.24–26.32) *vs* 17.47 hours (5–28). Also greater number of women (32/50) delivered within

**Table 1:** Demographic characteristics and indications for labor induction

| | *Oral misoprostol group (n = 50)* | *Vaginal misoprostol group (n = 50)* |
|---|---|---|
| *Demography* | | |
| Age (years) | 26 (20–35) | 25 (20–35) |
| Primigravida | 35 (70%) | 30 (60%) |
| Gestation (weeks) | 39 (37–40) | 39 (37–40) |
| Initial Bishop's score | 4 (0–7) | 3 (0–6) |
| *Indication for induction* | | |
| Hypertensive disorder | 20 (40%) | 24 (48%) |
| Mild intrauterine growth restriction | 5 (10%) | 2 (4%) |
| Oligohydramnios | 1 (2%) | 1 (2%) |
| Postdated | 18 (36%) | 16 (32%) |

Values are expressed as median (range or percentage)

**Table 3:** Misoprostol dose requirement

| *Total dose of misoprostol* | | *Oral group* | | *Vaginal group* | |
|---|---|---|---|---|---|
| *No. of tablets* | *µg* | *Delivered No. (%)* | *Not delivered No. (%)* | *Delivered No. (%)* | *Not delivered No. (%)* |
| 1 | 50 | 2 (4) | | 6 (12) | |
| 2 | 100 | 14 (28) | | 23 (46) | |
| 3 | 150 | 8 (16) | | 9 (18) | |
| 4 | 200 | 6 (12) | | 8 (16) | |
| 5 | 250 | 6 (12) | | 2 (4) | |
| 6 | 300 | 4 (8) | 10 (20) | | 2 (4) |
| Total | | 50 (100) | | 50 (100) | |

**Table 2:** Comparison of outcomes in labor in women who delivered vaginally, after random allocation to oral or vaginal misoprostol

| | *Oral group (n = 50)* | *Vaginal group (n = 50)* |
|---|---|---|
| Successful induction | 30 (60%)[a] | 35 (70%)[a] |
| Failures | 20 (40%)[a] | 15 (30%)[a] |
| Induction delivery interval | 17.47 (5–28)[b] | 8.70 (3.24–26.32)[b] |
| No. delivered within 24 hours | 28 (56%)[a] | 32 (64%)[a] |
| Maximum dose required | 5 (1–6)[b] | 2 (1–6)[b] |
| Tachysystole | 7 (14%)[a] | 9 (18%)[a] |
| Hyper tonus | 0 | 0 |
| Hyperstimulation | 2 | 0 |
| Uterine rupture | 0 | 0 |

[a]Percentage; [b]Range

**Table 4:** Mode of delivery

| *Mode of delivery* | *Oral group (n = 50)* | *Vaginal group (n = 50)* |
|---|---|---|
| Vaginal | 40 | 48 |
| Normal | 38 | 46 |
| Forceps | 2 | 2 |
| Lower segment cesarean section for fetal distress | 10 (20%) | 2 (4%) |

**Table 5:** Neonatal outcome

| | *Oral group (n = 50)* | *Vaginal group (n = 50)* |
|---|---|---|
| Birth weight (kg) | 2.8 (1.5–4) | 2.8 (1.5–4) |
| Apgar at 1 min | 8 (0–10) | 8 (0–10) |
| Apgar at 5 min | 9 (0–10) | 9 (0–10) |
| Meconium staining of liquor | 4 | 1 |
| Uterine contractile abnormality | 5 | 7 |
| Fetal heart abnormality | 8 | 2 |
| Admission to NICU | 2 | 0 |
| Live birth | 50 | 50 |
| Still birth | 0 | 0 |

24 hours of induction with vaginal misoprostol than with oral misoprostol (28/50; Table 2). In the oral group, 22/50 women did not achieve active labor within 24 hours of induction as compared with 18/50 in vaginal group, and these were labeled as "failures" (Table 2).

Greater number of women delivered with two doses of vaginal misoprostol (46 *vs* 28%). In the oral group, 4/50 (8%) required six doses to go into active labor, while no woman in vaginal group (Table 3) required this maximum dose, and the highest dose required in vaginal group was five tablets in 2/50 women (4%).

The majority of women in both the groups (88/100) delivered vaginally (Table 4) but overall incidence of vaginal births was significantly greater in vaginal group 48/50 *vs* 40/50 in oral group. However, cesarean section rate was significantly more in oral group (20 *vs* 4%) and commonest indication for cesarean section was fetal distress in both the groups.

Lesser fetal heart rate abnormalities (Table 5) were observed with vaginal misoprostol than with oral misoprostol (2/50 *vs* 8/50). Incidence of uterine contractile abnormalities was more with vaginal misoprostol (7/50 *vs* 5/50; Table 5). Neonatal outcome in both groups was good as all the neonates were born alive with median Apgar score of 8 and 9 at 1 and 5 minutes respectively (Table 5). Two neonates from oral group required neonatal intensive care unit (NICU) admission, one for low birth weight with tachypnea and other for respiratory distress syndrome (Table 5).

## DISCUSSION

Misoprostol is a wonderful drug in the armamentarium of obstetricians for induction of labor. Vaginal misoprostol is an effective cervical ripener and labor-inducing agent.[11]

In our study, successful induction with 50 µg vaginal misoprostol was higher (70 *vs* 60%). Shetty et al[6] reported lower failure (2.4 *vs* 6.76%, relative risk 2.7, 95% confidence interval 0.7–10.0) with 50 µg vaginal misoprostol as compared with oral misoprostol, and at the same time, reported shorter induction delivery interval by 10.1 hours.[6]

Latika and Biswajit[2] observed 100% success rate with 50 µg vaginal misoprostol[2] and 100 µg oral misoprostol.[12] In our study, induction delivery interval was shorter with 50 µg vaginal misoprostol (8.70 *vs* 17.47 hours). While

comparing 50 µg vaginal misoprostol with Foley's catheter/oxytocin, successful induction was 90.61 *vs* 78.44% and induction delivery interval shorter by 7.87 hours in vaginal misoprostol group.[13]

As vaginal misoprostol is absorbed rapidly and eliminated slowly from body making, it is available to act for a longer time as compared with oral misoprostol,[5] resulting in rapid progression of labor and leading to greater number of women delivering within 24 hours of induction (69.5 *vs* 56.4%).[6] In our study, more women (64 *vs* 56%) in vaginal group delivered within 24 hours. Main fear with this drug is excessive uterine contractions and uterine rupture in both scarred and unscarred uterus. These complications are dose-related. The higher the dose, the more is the uterine stimulation but shorter is the induction delivery interval.[7] With 50 µg vaginal misoprostol, incidence of uterine contractile abnormalities has been reported to be 4.9,[6] 9,[13] 12,[2] and 12%. Ewert et al[14] observed these complications as 3, 6.25, 10% with 25, 100, and 200 µg controlled release vaginal inserts of misoprostol. While with 50 and 100 µg oral misoprostol, uterine hyperstimulation incidence of 0.8[6] and 6.4%,[15] respectively, are reported. Oxytocin, which has been considered safer than misoprostol,[13] is also not without uterine abnormalities, with incidence being 19.2%.[16] Apart from this, PGE2 also has lesser complications (12%[2]) than misoprostol. One case of uterine rupture was reported in scarred[13] and one in unscarred[17] uterus with vaginal misoprostol. One case with dinoprostone[3] has also been reported.

In our observation, despite high incidence of uterine contractile abnormalities with vaginal route, it does not increase cesarean section rate. In our study, oral group cesarean section rate was significantly more compared with vaginal group (20 *vs* 4%). In Shetty et al[6] study, cesarean section rate was 24.6 *vs* 22.8% and in How et al,[7] it was 33 *vs* 17%. Common indication for cesarean section in our study was fetal distress. Misoprostol and its use by vaginal and oral route does not adversely affect neonatal and maternal outcome.[6,7,13]

## CONCLUSION

Vaginally administered 50 µg of misoprostol is a highly effective cervical ripener and labor-inducing agent than oral misoprostol.

Misoprostol when administered vaginally has a faster onset of action than the oral route in equivalent doses. But its use demands close monitoring for uterine contractile abnormalities.

## REFERENCES


1. Keirse MJ. Vaginal prostaglandins for cervical ripening (revised 1995 Apr 3). In: Keirse MJ, Renfrew MJ, Neilson JP, Crowther C, editors. Pregnancy and childbirth module of the Cochrane pregnancy and childbirth database, the Cochrane Collaboration. Vol. 2. Oxford: Update Software; 1995.
2. Latika S, Biswajit C. Comparison of prostaglandin E1 (misoprostol) with prostaglandin E2 (dinoprostone) for labour induction. J Obstet Gynecol Ind 2004 Mar-Apr;54(2):139-142.
3. van Gemund N, Seherjon S, LeClassie S, van Leeuwen JH, van Roosmalen J, Kanhai HH. A randomized trial comparing low dose vaginal misoprostol and dinoprostone for labour induction. Br J Obstet Gynaecol 2004 Jan;111(1):42-49.
4. Chuck FJ, Huffaker BJ. Labour induction with intravaginal misoprostol versus intracervical PGE2 gel (prepidil gel): randomized comparison. Am J Obstet Gynaecol 1995 Oct;173(4):137-142.
5. More B. Misoprostol: an old drug, new indications. J Postgrad Med 2002 Oct-Dec;48(4):336-339.
6. Shetty A, Danielian P, Templeton A. A comparison or oral and vaginal misoprostol tablets in induction of labour at term. Br J Obstet Gynaecol 2001 Mar;100(3):238-243.
7. How HY, Leasebevrge L, Khoury JC, Siddiqi TA, Spinnato JA, Sibai BM. A comparison of various routes and dosages of misoprostol for cervical ripening and the induction of labour. Am J Obstet Gynaecol 2001 Oct;185(4):911-915.
8. Bennett KA, Butt K, Crane JMG, Hutchens D, Young DC. A masked randomised comparison of oral and vaginal administration of misoprostol for labour induction. Obstet Gynecol 1998 Oct;92(4 Pt 1):481-486.
9. Windrim R, Bennett K, Mundle W, Young DC. Oral administration of misoprostol for labour induction: a randomised controlled trial. Obstet Gynecol 1997 Mar;89(3):392-397.
10. Ngai SW, To WK, Lao T, Ho PK. Cervical priming with oral misoprostol in prelabour rupture of membranes at term. Obstet Gynecol 1996 Jun;87(6):923-926.
11. Wing DA, Paul RH. A comparison of different dosing regimens of vaginally administered misoprostol for preinduction cervical ripening and labour induction. Am J Obstet Gynaecol 1996 Jul;175(1):158-164.
12. Ngai SW, Chan YM, Lam SW, Lao TT. Labour characteristics and uterine activity: misoprostol compared with oxytocin in women at term with pre labour rupture of membranes. Br J Obstet Gynecol 2000 Feb;107(2):222-227.
13. Promila J, Bhupinder Kaur G, Bala T. A comparison of vaginal misoprostol versus Foley's Catheter with oxytocin for induction of labour. J Obstet Gynaecol India 2007 Jan-Feb;57(1):42-47.
14. Ewert K, Powers B, Robertson S, Alfirevic Z. Controlled release misoprostol vaginal insert in parous women for labour induction. Obstet Gynaecol 2006 Nov;108(5):1130-1137.
15. Wing DA, Fasett MJ, Guberman C, Tran S, Parrish A, Guinn D. A comparison of orally administered misoprostol to intravenous oxytocin for labour induction in women with favourable cervical examinations. Am J Obstet Gynaecol 2004 Jun;190(6):1689-1696.
16. Abramovici D, Goldwasser S, Mabie BC, Mercer BM, Goldwasser R, Sibai BM. A randomized comparison of oral misoprostol versus Foleys catheter and oxytocin for induction of labour at term. Am J Obstet Gynaecol 1999 Nov;181(5 Pt 1):1108-1112.
17. Blanchette HA, Nayak S, Erasmus S. Comparison of the safety & efficacy of intravaginal misoprostol (prostaglandin E1) with those of Dinoprostone (prostaglandin E2) for cervical ripening and induction of labour in a community hospital. Am J Obstet Gynaecol 1999 Jun;180(6 Pt 1):1551-1559.