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Original Article

# Comparative Study of Oral Mifepristone and Endocervical Prostaglandins E2 Gel as Preinduction Cervical Ripening Agent in Parturition

**B Arumugaselvi[1], S Sujathasenthil[1], Heber Anandan[2]**

[1]Assistant Professor, Department of Obstetrics and Gynaecology, Tirunelveli Medical College Hospital, Tamil Nadu, India, [2]Senior Clinical Scientist, Department of Clinical Research, Dr. Agarwal's Healthcare Limited, Tirunelveli, Tamil Nadu, India

## Abstract

**Introduction:** The present day obstetrics calls for induction of labor for a myriad of obstetrical, medical, and fetal indications. We should only induce labor when we are sure that we can do better. The prostaglandins (PGs) and antiprogesterones have major role in labor induction.

**Aim:** The aim is to evaluate the efficacy and safety of oral mifepristone and endocervical PGE2 gel in labor induction.

**Methods:** To compare the efficacy of oral mifepristone and endocervical PGE2 gel as preinduction cervical ripening agents. 100 antenatal women were selected among which 50 women received 200 mg oral mifepristone and 50 women received 0.5 mg endocervical PGE2 gel.

**Results:** Mean increase in Bishop score in mifepristone group is 5, whereas 36 in PGE2 gel group. Oxytocin requirement for augmentation in mifepristone group is 66%, whereas 78% in PGE2 gel group. Duration of 2nd and 3rd stage of labor was shorter in mifepristone group. Cesarean section rate was higher in PGE2 gel group 24% whereas in mifepristone was 6%. Maternal complications were similar in both groups. Neonatal intensive care unit admission was 18% in PGE2 gel group whereas 10% in mifepristone group.

**Conclusion:** Oral mifepristone is very safe and an effective drug for preinduction cervical ripening. It is more effective in multigravida than primigravida.

**Key words:** Bishop score, Cervical ripening, Favorability, Induction of labor, Mifepristone, Oxytocin, Prostaglandin E2 gel

## INTRODUCTION

Successful labor induction is clearly related to the state of the cervix. Women with an unfavorable cervix, who have not experienced cervical ripening phase before labor, present the greatest challenge with regard to labor induction. In addition, the duration of labor induction is affected by parity and to a minor degree by baseline uterine activity and sensitivity to oxytocic drugs. Many investigators have identified the importance of assessing cervical status before induction of labor.[1] Mifepristone is a steroidal compound that has antiglucocorticoid and antiprogesterone properties. It increases uterine activity and causes cervical effacement and dilatation for pregnancy termination. The pharmacokinetics of mifepristone are characterized by rapid absorption and a long half-life of 25-30 h.[2] In late pregnancy, the uterus is sensitized by mifepristone to prostaglandins (PG) and promotes cervical ripening which induces labor. Various studies conducted on induction of labor in live term pregnancies with mifepristone in doses of 200-400 mg have shown an improvement in cervical ripeness and increased rates of spontaneous labor with no serious maternal or fetal side effects.[3] PGs are most commonly used pharmacological agents for ripening of cervix and PGE2 is the agent of choice for this purpose.[4]

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### Aim

The aim is to compare the safety and efficacy of oral mifepristone and endocervical PGE2 gel for the preinduction cervical ripening.

**Corresponding Author:** S Sujathasenthil, Assistant Professor, Department of Obstetrics and Gynaecology, Tirunelveli Medical College Hospital, Tamil Nadu, India. Phone: +91-9894570136. E-mail: draselvi@gmail.com

## MATERIALS AND METHODS

This comparative study was conducted in Department of Obstetrics and Gynecology at Tirunelveli Medical College Hospital to compare the efficacy of oral mifepristone and endocervical PGE2 gel as preinduction cervical ripening agents in term gestation and prolonged pregnancies and was done in uncomplicated antenatal women who had clear indication for the induction of labor. 100 antenatal women were selected for the study among which 50 women received oral mifepristone 200 mg and 50 women received endocervical PGE2 gel 0.5 mg.

### Inclusion Criteria

Inclusion criteria were singleton pregnancy in cephalic presentation, post-dated uncomplicated pregnancy, term uncomplicated pregnancies with unfavorable cervix (Bishop-score < 4), intrauterine fetal death, congenitally anomalous babies, term or post-term pregnancies with no contraindications for vaginal delivery, no contraindications for PGs or mifepristone, primigravida <35 years and uncomplicated multigravida up to three pregnancies, and intact membranes during the time of induction.

### Exclusion Criteria

Exclusion criteria were premature rupture of membranes, malpresentations, cephalopelvic disproportion, bad obstetric history or history of previous abortions, previous history of cesarean section or any uterine surgery, associated medical complications, multiple pregnancy, elderly primigravida (age >35 years), oligohydramnios, Rh-negative mother, placental complications such as abruption or placenta previa, abnormal fetal heart rate patterns, intrauterine growth retardation, parity >3, active herpes infection, contraindication for PGs, chorioamnionitis, and any febrile morbidity.

On admission, a detailed history and complete general and obstetric examination were carried out. Vaginal examination was done under strict aseptic precautions and the cervical status and fetal station were assessed. Gestational age calculated by Naegele's rule and a routine obstetric scan for fetal maturity and well-being were done. Once the inclusion criteria were fulfilled and cephalopelvic disproportion was ruled out, the patient was prepared and transferred to the labor ward. Indication for induction was noted after reaffirming that there was no contraindication for induction.

Group - 1: 50 pregnant women were given tablet mifepristone 200 mg orally on day 1. They were observed for maternal vitals, uterine activity bleeding or draining pv, and fetal heart rate. After the wait period of 24 h or when the Bishop score was ≥6 or when the cervical dilatation was >2 cm or when the membranes ruptured or when the patient was well in labor whichever is earlier labor was accelerated with oxytocin drip.

Group - 2: 50 pregnant women pregnant were instilled endocervical PGE2 gel 0.5 mg on day 1. They were observed for maternal vitals, uterine activity, bleeding, draining pv, and fetal heart rate. After the wait period of 6 h or when the Bishop score was ≥6 or when the cervical dilatation was >2 cm or when the membranes ruptured or when the patient was well in labor whichever is earlier labor was accelerated with oxytocin drip.

Maternal vitals, uterine activity, and fetal heart rate were monitored clinically. Partogram was maintained for all patients and used to record all the clinical events during the course of labor. A watch for the rupture of membranes was done. If membranes not ruptured, ARM was done at 3 cm cervical dilatation. Pre-vaginal examination was done if there was rupture of membranes or once in 2 h in active phase of labor. The pulse rate, blood pressure, temperature, and urine output were recorded. Delivery particulars, duration of each stage of labor, blood loss at the third stage of labor, and baby particulars were recorded. Mother and baby were observed for postnatal complications if any.

Data were analyzed and all the values were expressed as mean ± standard deviation or as percentages. Statistical comparison was performed by Student's paired and unpaired *t*-test and Chi-square test.

## RESULTS

Age and parity distribution of women included in this study were comparable in both mifepristone and PGE2 gel group. All the mothers in both groups had initial Bishop score of 0-3 before preinduction cervical ripening. Mean increase in Bishop score in mifepristone group is 5 whereas 3.6 in PGE2 gel group. *P* value for Bishop score at start is 0.864, which is not significant. *P* value for Bishop score at augmentation is 0.001, which is significant. *P* value for Bishop score difference is 0.000, which is significant (Figure 1).

In the mifepristone group, among the six primigravida who were not in need of oxytocin augmentation 4 (8%) had vaginal delivery within 24 h of oral mifepristone administration. Shortest drug administration to delivery interval was 12 h and 5 min. Among the 11 multigravida who were not in need of oxytocin augmentation in the mifepristone group, 9 (18%) had vaginal delivery with in 24 h of oral mifepristone, of which 4 (8%) had delivery

within 10 h. Shortest drug administration to delivery interval was 5 h 54 min.

Whereas in PGE2 gel group, 11 antenatal women that include 8 primigravida and 3 multigravida who were not in need of oxytocin augmentation were those delivered by cesarean section. In other words, in PGE2 gel group, all women who had vaginal delivery were in need of oxytocin augmentation (Figure 2).

Duration of 2nd and 3rd stage of labor was shorter in mifepristone group with statistical significance. Duration of 1st stage was shorter in PGE2 gel group which is not statistically significant. Drug administration to delivery interval was shorter with PGE2 gel group with statistical significance. Statistically significant was shorter duration of 1st and 3rd stage of labor in multigravida in mifepristone group whereas no statistical difference in duration of labor among primigravida and multigravida in PGE2 gel group (Table 1).

Cesarean section rate was higher in PGE2 gel group which was 24% when compared to mifepristone group in which it was 12%. Mean blood loss in mifepristone group was less when compared to PGE2 gel group. In PGE2 gel group 1 (2%), primigravida had atonic PPH - blood loss of 1250 ml which was controlled with uterotonics. Maternal complications were similar in both groups (Table 2).

Neonatal intensive care unit admission was 18% in PGE2 gel as compared to 10% in mifepristone group. In PGE2 gel group, one neonate was admitted for low birthweight. Apgar score at 1 min and 5 min were similar in both groups.

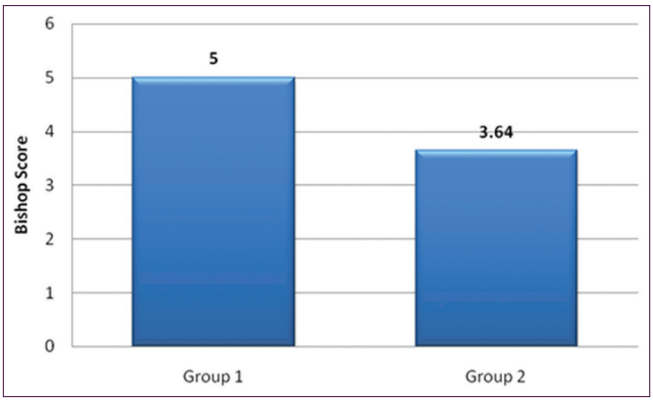


**Figure 1: Distribution of Bishop score**

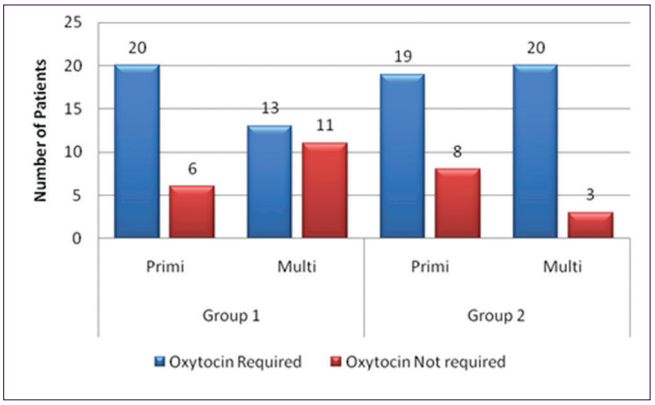


**Figure 2: Augmentation with oxytocin**

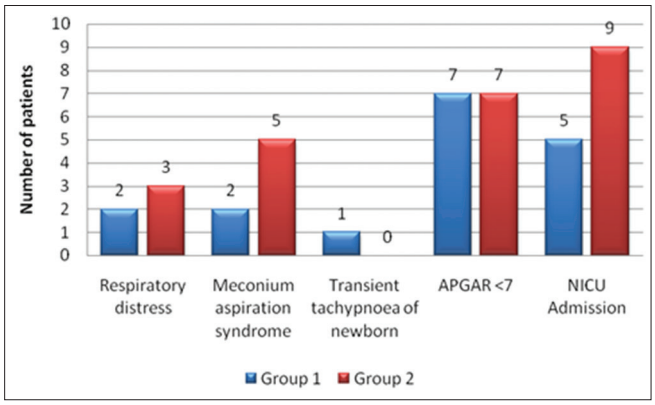


**Figure 3: Distribution of neonatal complications**

**Table 1: Distribution of duration of labor**

| Duration of labor | Group | Mean±SD | *P* value |
|---|---|---|---|
| Duration of 1st stage (h) | Group - 1 | 6.8867±2.12457 | 0.951 |
| | Group - 2 | 6.8618±1.41495 | |
| Duration of 2nd stage (min) | Group - 1 | 22.4222±5.19829 | 0.001 |
| | Group - 2 | 26.9474±6.40501 | |
| Duration of 3rd stage (min) | Group - 1 | 4.0659±1.20309 | <0.0001 |
| | Group - 2 | 5.4408±1.30596 | |
| DD interval | Group - 1 | 18.7341±10.04693 | <0.0001 |
| | Group - 2 | 11.4784±3.85563 | |

SD: Standard deviation

**Table 2: Distribution of mode of delivery**

| Mode of delivery | Group - 1 (%) | | | Group - 2 (%) | | |
|---|---|---|---|---|---|---|
| | Primi | Multi | Total | Primi | Multi | Total |
| Labor natural | 22 (44) | 21 (42) | 43 (86) | 18 (36) | 18 (36) | 36 (72) |
| Outlet forceps delivery | 1 (2) | - | 1 (2) | - | 1 (2) | 1 (2) |
| LSCS | 3 (6) | 3 (6) | 6 (12) | 9 (18) | 3 (6) | 12 (24) |
| Spontaneous expulsion of fetus | - | - | - | 1 (2) | - | 1 (2) |
| Total | 26 (52) | 24 (48) | 50 (100) | 27 (54) | 23 (46) | 50 (100) |

LSCS: Lower segment cesarean section

**Table 3: Comparison of dosage schedule**

| Study | Year | Dosage schedule | Control | Wait period |
|---|---|---|---|---|
| Wing *et al.*[5] | 2002 (180) | 200 mg of mifepristone oral dose followed by intravaginal misoprostol 25 micrograms every 4th hourly or IV oxytocin[5] | Placebo | 24 h |
| Li *et al.*[6] | 1996 | 150 or 200 mg mifepristone in the 1st 2 or 3 days and on the 4th day misoprostol was added successively in 100-300 mg dosage | - | 3 days |
| Su *et al.*[7] | 1996 (124) | 50 mg mifepristone 12th hourly for 2 days followed by PG or oxytocin | - | 48 h |
| Frydam *et al.*[8] | 1992 (120) | 200 mg mifepristone on days 1 and 2 followed by augmentation with PG on day 4 | Placebo | 4 days |
| This study | 2010 | 200 mg mifepristone as a single oral dose | PGE2 | 24 h |

PGE2: Prostaglandin E2

7 (14%) neonates in each group had Apgar score <7 at 5 min following birth (Figure 3).

## DISCUSSION

In this study, mifepristone given as 200 mg single dose orally and observation period of 24 h similar to the Wing *et al.,*[5] in which mifepristone was compared with placebo whereas PGE2 gel in this study (Table 3).

In this study, 66% required oxytocin; this was consistent with prior studies. In our study, mean duration of the 1st stage was <8 h and 2nd stage duration was <30 min. These results were consistent with the World Health Organization standards. In this study, 36 (72%) women, 32% primigravida and 40% multigravida, delivered vaginally within 24 h and totally 44 (88%) women, 46% primigravida and 42% multigravida, delivered vaginally within 48 h which was consistent with Wing *et al.* study (Table 4).[5]

In our study, vaginal delivery rate was 88% (46% primigravida and 42% multigravida) the results were consistent with above-mentioned studies. In this study, the success of induction was vaginal delivery within 48 h. Success rate was 88% which was consistent with 87.5% success rate in Wing *et al.* study (Table 5).[5]

In our study, success of induction in relation to change to favorable Bishop score of 6 or more was seen in 90% (42% in primigravida and 48% in multigravida) which was consistent with Wing *et al.* and Frydman *et al.* study.[5,8]

In this study, failed induction in terms of cesarean section or vaginal delivery after 48 h of ripening was seen in 12% among which one primigravida underwent cesarean section for failed induction. These results were consistent with Giacalone *et al.*[9] study and Wing *et al.* study in which failed induction rate was 9.2%.

## CONCLUSION

This study reveals that oral mifepristone is very safe and an effective drug for preinduction cervical ripening. It has an added advantage of ease of administration, better patient compliance and acceptance, reduced oxytocin requirement, shorter duration of 2nd, 3rd stages of labor, and less blood loss with an overall success rate of 88%. The drug has no untoward side effects on uterine contraction and no major maternal complications. This drug has safe nenatal outcome. This drug is more effective in multigravida when compared to primigravida. Hence, mifepristone offers advantages over PGE2 gel which is currently used for preinduction cervical ripening. Mifepristone is administered orally which is very convenient and antenatal mothers can be ambulant when compared to cumbersome PGE2 gel administration which has to be instilled endocervically with strict asepsis by technically skilled personnel and needs observation in the left lateral position.

**Table 4: Comparison of need of augmentation**

| Study | Year | Need for augmentation (%) |
|---|---|---|
| Wing *et al.*[5] | 2002 | 67 |
| Li *et al.*[6] | 1996 | 80 |
| Su *et al.*[7] | 1996 | Decreased |
| Frydam *et al.*[8] | 1992 | Decreased |
| This study | 2010 | 66 |

**Table 5: Comparison of incidence of vaginal delivery**

| Study | Year | Incidence of vaginal delivery |
|---|---|---|
| Wing *et al.*[5] | 2002 | 87.5 |
| Li *et al.*[6] | 1996 | 80.88 |
| Su *et al.*[7] | 1996 | 22.58 (vs. 4.84% of control group) |
| This study | 2010 | 88 |

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