

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Comparative Analysis of Safety, Efficacy and Fetomaternal Outcome of Induction of Labour with Mifepristone versus Intracervical Dinoprostone Gel.

Vidya Gaikwad, Bilsa Mittal, and Mangal Puri*

Department of Obstetrics and Gynaecology, Dr. D.Y. Patil Medical College and Hospital and Research Center, Pune 411018, Maharashtra, India.

ABSTRACT

Mifepristone and Dinoprostone used in inducing labour in late pregnancy by acting as cervical ripening drugs. Present study was done to compare and portrair the beneficial effects of both the drugs for induction of labour. The objective was comparative analysis of safety, efficacy and fetomaternal outcome of induction of labour with Mifepristone versus intracervical Dinoprostone gel. 100 patients were included after taking their informed consent. 50 patients were placed in each group A and B. Tablet Mifepristone 200mg orally was given in group A patients and intracervical gel induction was done in group B patients. Pre induction Bishop's score was noted at beginning to compare improvement in Bishop's score after induction, mode of delivery and induction-delivery interval in both the groups. Rate of successful IOL or vaginal delivery was 84% with Mifepristone and 56% with Dinoprostone. After induction with Mifepristone 94% women had cervical ripening as compared to 80% with Dinoprostone. 20% Mifepristone treated group required Oxytocin for augmentation as compared to 56% in Dinoprostone. Among the babies, 6% and 14% belonging to Mifepristone and Dinoprostone group respectively, required NICU admissions. In the present study, women who were induced with Mifepristone showed significantly more improvement in Bishop's score than Dinoprostone. Although overall average induction- delivery interval was more in Mifepristone group (29hours) than Dinoprostone group (21hours), vaginal mode of delivery with Mifepristone was more, decreasing the incidence of caesarean section with lesser need for augmentation with Oxytocin. Lesser NICU admissions and maternal complications were noted with Mifepristone. Thus, Mifepristone is a better drug for successful induction of labour as compared to Dinoprostone with a better fetomaternal outcome.

Keywords: Mifepristone, Dinoprostone, Induction of labour.

**Corresponding author*

INTRODUCTION

Induction of labour is one of the most common interventions practiced in modern obstetrics. Overall, throughout the world, up to 20 per cent of women have labour induced by one method or the other [1].

Augmentation is the process of stimulation of uterine contractions that are already present but found to be inadequate [2].

Indications for induction [3]

- Pregnancy induced hypertension (PIH)
- Eclampsia
- Intrauterine fetal death (IUFD)
- Prolonged pregnancy
- Suspected fetal anomalies
- Intrauterine growth restriction (IUGR)
- Medical problems like chronic hypertension and diabetes mellitus

Mifepristone (RU 486)

Mifepristone, an antiprogestin, causes blockage of progesterone receptors, results in vascular damage, decidual necrosis and bleeding. It will soften the cervix, increase the sensitivity to prostaglandins and convert the quiet pregnant uterus into organ of spontaneous activity. It is characterised by rapid absorption and half life of 24 to 30 hours.

Dinoprostone

Is a naturally occurring prostaglandin E₂ (PGE₂). Prostaglandins allow for an increase in intracellular calcium levels, causing contraction of myometrial muscle. Dinoprostone Gel (cerviprime gel) is a prostaglandin E₂. Fetal membranes (amnion) produce prostaglandin E₂. It acts mainly on the cervix due to its collagenolytic property and has an oxytocic effect on the pregnant uterus when used in appropriate dose, stimulates labour and delivery and thus terminates pregnancy. Dinoprostone also is capable of stimulating the smooth muscles of gastrointestinal tract.

Aims and Objectives

- To study the efficacy of Mifepristone and Dinoprostone as a cervical ripening / priming agent for induction of labour.
- To study improvement in Bishop's Score.
- Necessity for augmentation of labour with Oxytocin.
- To study induction delivery interval.
- To study maternal and fetal outcome in terms of mode of delivery, fetal heart rate and Neonatal Natal intensive Care Unit admissions (NICU).

MATERIALS AND METHODS

A randomised controlled study was carried to investigate the safety, efficacy and fetomaternal outcome of induction of labour with Mifepristone comparing with the commonly used agent Dinoprostone gel. Augmentation required or not was noted. Period of study was from July 2011 to September 2013.

The study was approved by the institutional ethics committee.

Inclusion criteria

- Patients in third trimester of pregnancy 28 to 41 weeks
- Pregnancy induced hypertension (PIH)
- Gestational diabetes mellitus patients
- Post-dated pregnancy
- Intrauterine fetal death (IUFD)
- Fetal congenital malformations

Exclusion criteria

- Previous cesarean section patients
- Malpresentation
- Cephalopelvic disproportion
- Premature rupture of membranes (PROM)
- Oligohydramnios

Out of 100 patients in the study group, 50 patients (group A) were given one tablet of 200mg Mifepristone orally and remaining 50 patients (group B) received single dose of intracervical dinoprostone gel for induction and post induction improvement in Bishop's score was noted after 12, 24, 48 and 72 hours or whenever the patient went in active labour.

A detailed analysis was carried out in both the groups regarding the efficacy of the drugs in terms of

- Improvement in Bishop's score
- Necessity of augmentation of labour with Oxytocin
- Induction to delivery interval
- Mode of delivery: normal vaginal/ caesarean section
- No. of cases with failed induction
- Maternal and fetal outcome

DISCUSSION

Post induction improvement in Bishop's score was seen to be significantly more in Mifepristone (96.6%) induced group than Dinoprostone (76.6%) group as shown in Table 1.

20% of patients in group A (Mifepristone) and 56% in group B (Dinoprostone) required augmentation as in Table 2. Thus, Mifepristone induced patients required less need for augmentation. In both the groups, induction to delivery interval was more in primigravida than multigravida patients. Not much statistical difference was noted in induction delivery interval of multigravida patients of both the groups. Overall average induction to delivery interval in Mifepristone group was 29 hours and 21 hours in Dinoprostone group (Table 3), but the percentage of vaginal deliveries seen with Mifepristone was 84%, decreasing the incidence of caesarean section. Dinoprostone group showed 56% vaginal deliveries (Table 4). With more number of vaginal deliveries maternal outcome was better in Mifepristone group. No case of hyperstimulation or meconium stained liquor was noted with Mifepristone. Mifepristone induced patients had lesser rate of failed induction (6%) as compared to Dinoprostone (28%) Out of the 4 fetal distress cases in group A, 3 neonates had 1 or 2 tight loops of cord around neck as noted during intra operative period. 1 neonate in group B had a tight loop of cord around neck during intra operative period as shown in Table no. 5.

As shown in Table 6, 14% of group B(Dinoprostone) neonates required NICU admission due to fetal distress as compared to group A (Mifepristone) neonates.

These results were quite consistent with the study conducted by Wing DA. Fasset M J, Mishell DR and Stenlund et al.

Wing DA.Fasset M J,Mishell DR [3] did a randomized controlled trial with tablet Mifepristone for preinduction cervical ripening beyond 41 weeks and concluded that Mifepristone had a modest effect on cervical ripening when given 24hrs before labour induction appearing to reduce the need for Misoprostol and Oxytocin compared with placebo.

Stenlund P M; Ekman G; Aedo A R; Bygdeman M [5] did a prospective double blind study to evaluate efficacy of Mifepristone in induction of labour in women with unripe cervix .He found that during first 48 hrs following treatment,79.2% of women treated with Mifepristone went in labour. The overall success rate was 83.3% for Mifepristone. The result shows that Mifepristone is a simple and effective treatment for inducing labour in post term pregnant women with an unripe cervix.

Hapangama D, Neilson JP [6], in their study of Mifepristone for induction of labour compared to placebo observed that Mifepristone treated women were more likely to have a favourable cervix at 48 hours. Effect persisted at 96 hours. Less need of augmentation with Oxytocin was required. They were less likely to undergo caesarean section or failure of induction and more likely to have an instrumental delivery. A single dose of 200 mg Mifepristone appears to be the lowest effective dose for cervical ripening. Abnormal fetal heart rate patterns were more common but there was no evidence of differences in the other neonatal outcomes. The present study showed no abnormal fetal heart rate patterns and had results similar to the above study.

Dr. Warke et al [7] did a study in 75 patients with unripe cervix who underwent induction of labour with PGE2 gel.The commonest indications were postdatism, intrauterine

growth retardation and pregnancy induced hypertension. All patients were primigravidae with singleton pregnancy and beyond 35 week pregnancy. 68.1% patients required augmentation of labour and 31.9% did not require augmentation of labour with Oxytocin drip. The incidence of vaginal delivery was 81.33% and that of caesarean was 17.33%. The commonest indication of caesarean section was fetal distress.

Table 1: Post induction improvement of Bishop’s score

Group A (Mifepristone)

| Post induction | Primi (%) | Multi (%) | Total |
|---------------------------------------|------------|-----------|-----------|
| No. of Patients | 30 (100%) | 20 (100%) | 50 (100%) |
| Patients with improved Bishop’s score | 29 (96.6%) | 18 (90%) | 47 (94%) |

Group B (Dinoprostone)

| Post induction | Primi (%) | Multi (%) | Total |
|---------------------------------------|------------|-----------|-----------|
| No. of Patients | 30 (100%) | 20 (100%) | 50 (100%) |
| Patients with improved Bishop’s score | 23 (76.6%) | 17 (85%) | 40 (80%) |

Table 2: Comparison of augmentation required with Oxytocin in both study groups (n= 100)

| Parameter | Group A (Mifepristone) | Group B (Dinoprostone) |
|--------------------------------|------------------------|------------------------|
| Oxytocin augmentation required | 10 patients (20%) | 28 patients (56%) |

Table 3: Comparison of induction to delivery interval in both study groups

| Induction to delivery interval (Hours) | GroupA (Mifepristone) | GroupB (Dinoprostone) | Z Value | P Value |
|--|-----------------------|-----------------------|---------|---------|
| | Mean ± SD | Mean ± SD | | |
| Primi (n=30) | 33 ± 14.81 | 20.93 ± 9.72 | 3.74 | <0.0001 |
| Multi (n=20) | 23.6 ± 14 | 22.1 ± 10.9 | 0.36 | >0.05 |
| Overall (n=50) | 29.2 ± 15.1 | 21.4 ± 10.1 | 3.04 | <0.005 |

Table 4: Mode of delivery in study groups

| Mode of delivery | Group A | Group B | Total |
|------------------|-----------|-----------|-------|
| LSCS | 8 (16%) | 22 (44%) | 30 |
| Vaginal | 42 (84%) | 28 (56%) | 70 |
| Total | 50 (100%) | 50 (100%) | 100 |

Chi-square = 9.33, P<0.0001

Table 5: Indication of operative delivery wise distribution of cases in study groups

| Indication | Group A (%) | Group B (%) | Total |
|----------------------|-------------|-------------|-------|
| Failure of induction | 3 (6%) | 14 (28%) | 17 |
| Fetal distress | 4 (8%) | 5 (10%) | 9 |
| Hyperstimulation | 0 | 1 (2%) | 1 |
| Persistent ROP | 1 (2%) | 0 | 1 |
| Thick MSL | 0 | 2 (4%) | 2 |
| Total | 50 (100%) | 50 (100%) | 100 |

Table 6: NICU admission required in study groups (n= 100)

| NICU admission | Group A | Group B |
|----------------|---------|---------|
| Required | 3 (6%) | 7 (14%) |

CONCLUSION

In conclusion after conducting this research is, Mifepristone when compared with routinely used intracervical Dinoprostone gel, acts as a better cervical ripening agent and requires lesser need for Oxytocin augmentation. Though, mean induction delivery interval was more with Mifepistone, the incidence of successful vaginal delivery was higher as compared to Dinoprostone with good neonatal outcome. Thus Mifepristone is an effective inductive agent for cervical ripening and initiation of labour in term pregnancy and can improve the outcome of labour induction. However, further trials with bigger sample size are required.

REFERENCES

- [1] The Management of Labour, 3rd edition, Chapter 23. Induction of labour; P.368.
- [2] DC Dutta. Text book of Obstetrics.^{6th} edition. New Delhi: New Central Book Agency; 2000. P.98.
- [3] Williams Obstetrics, 23rd edition, Chapter 22. Labour Induction; 500.
- [4] Wing DA, Fassett MJ, Mishell DR. In Obstet Gynecol 2000;96(4):543-8.
- [5] Stenlund PM; Ekman G; Aedo A R; Bygdeman M. Acta Obstetricia et Gynecologica Scandinavica 1999;78(9):793.
- [6] Hapangama D, Neilson JP. Cochrane Database Syst Rev 2009(3):CD002865.
- [7] Warke H S, Saraogi R M, Sanjwalla S M. J Postgrad Med 1999;45:105.