

# Role of Mifepristone in Pre - Labor Cervical Ripening and Induction of Labour

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**Abstract:** *Objective:* To assess the efficacy of Mifepristone for pre labor cervical ripening and induction of labor. *Material and methods:* This study was conducted in the department of OBG in DDUZH, Shimla, 200 nulliparous women at term were divided into two groups based on inclusion and exclusion criteria. Pre - labor assessment of Bishop score was done. Group A received 400mg Mifepristone while group B was kept under expectant management. All women were reassessed after 48 hours. *Result:* 75 women in group A and 48 women in group B went into spontaneous labor within 48 hours ( $p=0.048$ ). 20 women in group A and 50 women in group B still had a Bishop score of  $< 6$  which was statistically significant ( $p<0.001$ ). *Conclusion:* Mifepristone is highly effective, safe, cheap, convenient and economical method for pre induction cervical ripening and induction of labor. Pre induction ripening of cervix further helps in increasing the rate of vaginal delivery and mifepristone can be considered as an attractive method of pre induction cervical ripening and labor induction.

**Keywords:** Mifepristone, cervical ripening, labor, induction

## 1. Introduction

Induction of labor is defined as an intervention designed to artificially initiate the uterine contractions leading to progressive dilatation and effacement of cervix and birth of the baby. Induction of labor is indicated only when it is agreed that mother or fetus will benefit from higher probability of a healthy outcome than if birth is delayed. The state of cervix is a major contributor for successful labor. Cervical ripening is a physiological process occurring throughout the latter weeks of pregnancy and is completed with onset of labor. When delivery is necessary and ripening has not had time to occur this natural process has to be accelerated.<sup>1</sup>

Labor induction in unfavourable cervix is a difficult and lengthy procedure, extenuating both mother and child. So when labor induction is performed favourable cervix is fundamental to a good outcome.<sup>2</sup> The state of cervix can be assessed by Bishop pelvic scoring system. Bishop score of less than 6 usually requires cervical ripening agent.<sup>3</sup>

The female steroid sex hormone, progesterone, inhibits contractility of the uterus. A new class of pharmacological agents (antiprogesterin) has been developed to antagonize the action of progesterone. Of these, mifepristone (also called RU 486) is best known. Mifepristone is a 19 nor - steroid which has greater affinity for progesterone receptors than does progesterone itself. It thus blocks the action of progesterone at the cellular level. The pharmacokinetics of mifepristone are characterized by rapid absorption and a long half - life of 25 to 30 hours (Heikinheimo 1997)<sup>4</sup>. Key metabolites also have high affinity to progesterone receptors. Mifepristone now has an established role in termination of pregnancy (in combination with prostaglandins) during the

early first, and the second trimesters (Van Look 1995)<sup>5</sup>. Mifepristone is an orally active drug with 70% absorption rate and 40% bioavailability after the first pass through the liver.<sup>6</sup> It is 98% protein bound. Peak plasma level occurs within 1 - 2 hours and the drug is slowly excreted. Side effects include nausea, vomiting, headache, sweating, dizziness, fatigue, abdominal pain, diarrhoea and fever.<sup>7</sup>

Animal studies have suggested that mifepristone may also have a role in inducing labor in late pregnancy. Hapangama and Neilson in Cochrane collaboration published in 2009 are of the opinion that there is insufficient information available from clinical trials to support the use of mifepristone to induce labor.<sup>8</sup> Hence this study is carried out to study the effects of mifepristone in cervical ripening and induction of labor.

### Aims and objectives

- 1) To evaluate the efficacy of mifepristone in improving the Bishop's score at term
- 2) To evaluate the efficacy of mifepristone for induction of labor at term

## 2. Material and Methods

This study was carried out in the Department of Obstetrics and Gynecology, DDUZH, Shimla for a period of one year from January to December, 2022. 200 pregnant females scheduled for planned delivery for various indications were included in the study after informed consent. The women were randomly divided into two groups. Group A was given 400mg mifepristone and group B was not given mifepristone. Women who had not gone into spontaneous labor were reassessed after 48 hours to check for improvement in Bishop score.

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Inclusion criteria were singleton nulliparous women with cephalic presentation at term with maternal or fetal indication of labor induction, in whom labor could be deferred for 48 hours and had a Bishop score of  $<6$ .

Exclusion criteria were: non vertex presentation, previous cesarean section, multiple pregnancy, multipara, contraindication to vaginal delivery, medical disorders including renal, hepatic or adrenal insufficiency, women on anticoagulant therapy, blood clotting disorder, hypersensitivity to prostaglandins or mifepristone, Bishop score  $>6$

The statistical difference between two groups was evaluated by using student t test and Chi square test. The p value of  $<0.05$  was considered statistically significant.

### 3. Results

The age group in both groups ranged from 19 - 35 years. Mean age in group A was 25.54 and in group B was 25.75 ( $p=0.572$ ). The period of gestation in the study ranged from 37 - 42 weeks. The mean gestational age at induction was 39.9 weeks in group A and 40.07 in group B ( $p=0.561$ ).

**Table 1:** Mean demographic characteristics of both groups

	Group A	Group B	p value
Age (years)	25.54	25.75	0.572
Gestational age (weeks)	39.9	40.07	0.561

Commonest indication of induction was post date pregnancy for which 76 patients in group A and 77 patients in group B were induced. Eleven patients in group A and 10 patients in group B were induced for IUGR, 9 and 8 patients were induced for PIH in group A and group B respectively. Four patients in group A and five patients in group B were induced for intrahepatic cholestasis of pregnancy. The difference between both groups were comparable. The mean Bishop score prior to induction in both groups was 3 with score ranging from 2 - 5 in both groups.

**Table 2:** Bishop score prior to induction

Bishop score	Group A	Group B
2	12	10
3	33	36
4	35	29
5	20	25

During the first 48 hours following treatment, 75 women in group A and 48 women in group B went into labor. The statistical difference was significant ( $p=0.048$ ). Five and 2 women in group A and group B respectively had a ripe cervix (Bishop score  $\geq 6$ ) at the end of 48 hours ( $p=$ ). Bishop score of less than 6 even after 48 hours was found in 20 women in group A and 50 women in group B which was highly significant ( $p=$ ).

**Table 3:** Outcome in both the groups

Outcome	Group A (n=100)	Group B (n=100)	p value
Spontaneous labor	75	48	0.048
Bishop score $\geq 6$	5	2	
Bishop score $< 6$	20	50	0.000

There were minimal side effects in both the groups like nausea, vomiting and dizziness. No serious side effects were reported.

### 4. Discussion

Induction of labor for maternal or fetal indication at or near term is not an uncommon procedure. If labor is induced in the presence of unripe cervix, the failure rate is high and the overall incidence of instrumental deliveries and cesarean section is increased. The synthesis of Mifepristone and other antiprogesterin has opened up new therapeutic perspectives, not only for termination of pregnancy but also for labor induction. The present study was conducted to evaluate the safety and efficacy of Mifepristone as a cervical ripening agent and induction agent in term pregnancies.

Our study showed that Mifepristone 400mg is significantly effective for pre labor cervical ripening and for induction of labor as compared to expectant management. This is in comparison to previous studies conducted. The earliest studies on the use of mifepristone for induction of labor were done by Frydman and colleagues in 1990's.<sup>9</sup> Also, it was reported in previous studies that mifepristone is better than a placebo in ripening the cervix and there is evidence of a possible reduction in the incidence of caesarean section rates following mifepristone treatment. In the study conducted by Kanan Y et al in 2014, 100 women with prolonged pregnancy beyond 40 weeks and Bishop score  $<6$  were recruited and 50 women received 200mg Mifepristone and 50 women received placebo. Their study also demonstrated significant efficacy of Mifepristone as a cervical ripening agent after 24 hours of administering Mifepristone.<sup>10</sup> Hapangama D, Neilson JP in May 2009, in their study of "Mifepristone for induction of labour" compared to placebo (108 women), mifepristone treated women were more likely to have a favourable cervix at 48 hours [risk ratio (RR) 2.41, 95% confidence intervals (CI) 1.70 to 3.42].<sup>11</sup> Li L, Gao W, Chen S5 did a study at Beijing Tian Tan Hospital, Capital University of Medicine on Labour induction in women at term with mifepristone and misoprostol. Results of their study women who were given mifepristone: the cervical length was 1 - 3 cm shorter and Bishop score was 4 - 5 higher than those before treatment. The cervical ripening ratio was 100.00%. Incidence of the onset of labor was 93.00%. Incidence of vaginally delivery was 80.88% after misoprostol was given for augmentation.<sup>12</sup>

### 5. Conclusion

The present study shows that treatment with Mifepristone is a simple and effective method of inducing labor in women with term pregnancy and unripe cervix. The use of Mifepristone provides an interesting new alternative to classic uterotonic agents when induction of labor is necessary. Mifepristone combined with or without augmentation is a safe, efficient, economical and convenient induction agent for initiation of labor in women at term. It also has potential advantages over prostaglandins and oxytocin, mainly in which these are contraindicated and further study is warranted in such cases.

## References

- [1] Mackenzie IZ. Induction of labour at the start of the new millennium. *Reproduction*.2006 Jun; 131 (6): 989 - 98. doi: 10.1530/rep.1.00709. PMID: 16735538.
- [2] Surita FG de C, Cecatti JG, Kruppa F, Tedesco RP, Parpinelli MÂ. Cervical ripening methods for labor induction. *Rev Bras Saude Mater Infant* [Internet].2004Apr; 4 (2): 125–33. Available from: <https://doi.org/10.1590/S1519-38292004000200002>
- [3] Tenore JL. Methods for cervical ripening and induction of labor. *Am Fam Physician*.2003 May 15; 67 (10): 2123 - 8. PMID: 12776961.
- [4] Heikinheimo O. Clinical pharmacokinetics of mifepristone. *Clinical Pharmacokinetics* 1997; 33: 7 - 17
- [5] Van Look PF, von Hertzen H. Clinical uses of antiprogestogens. *Human Reproduction Update* 1995; 1: 19 - 34.
- [6] Van Look P, Bygdeman M. Antiprogestational steroids: a new dimension in fertility regulation. *Oxf Rev Reprod Biol*.1989; 11: 1 - 60
- [7] Mifepristone [internet] 2009 Dec 20. Available from: <http://www.drugs.com/ppa/mifepristone.html>
- [8] Dharani H, James PN. Mifepristone for induction of labour (review). *Chochrane Database Syst Rev*.2009; 3, Art. No. CD002865.
- [9] Frydman R, Lelaider C, Baton - Saint - Mleux C, Fernandez H, Vial M, Bourget P. Labour induction in women at term with mifepristone (RU 486): a doubleblind, randomized, placebo - controlled study. *Obstetrics&Gynecology*.1992 Dec 1; 80 (6): 972 - 5.
- [10] Yelikar K, Deshpande S, Deshpande R, Lone D. Safety and Efficacy of Oral Mifepristone in Pre - induction Cervical Ripening and Induction of Labour in Prolonged Pregnancy. *J Obstet Gynaecol India*.2015 Jul; 65 (4): 221 - 5. doi: 10.1007/s13224 - 014 - 0584 - 6. Epub 2014 Jul 11. PMID: 26243986; PMCID: PMC4518014.
- [11] Hapangama D, Neilson JP. Mifepristone for induction of labour. *Cochrane Database Syst Rev* 2009; (3): CD002865. doi: 10.1002/14651858. CD002865. pub2.
- [12] Li L, Gao W, Chen S. Labour induction in women at term with mifepristone and misoprostol. *Zhonghua Fu Chan Ke Za Zhi* 1996; 31: 681 - 4.