



EFFICACY OF ORAL MIFEPRISTONE 200MG IN PRE - INDUCTION CERVICAL RIPENING FOR INDUCTION OF LABOUR IN TERM PREGNANCY

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ABSTRACT

INTRODUCTION: Mifepristone is a steroidal compound that has antiglucocorticoid and antiprogesterone properties. It increases uterine activity and causes cervical effacement and dilatation for pregnancy termination. A ripe or favorable cervix is a prerequisite for successful vaginal birth. Cochrane collaboration published in 2009 are of the opinion that there is insufficient information to support the use of mifepristone to induce labor. The present study was undertaken to find out the safety and efficacy of mifepristone for preinduction cervical ripening and labor induction in term pregnancy and to assess improvement in bishop score.

AIMS AND OBJECTIVES:

1. To study efficacy of oral tab mifepristone 200mg as a cervical ripening agent for induction of labor.
2. To study improvement in bishop's score.

METHOD(S): One hundred women with single live fetus, term gestation, cephalic presentation, reactive fetal heart pattern and Bishops score <6 were included in the study. After detailed history, examination, confirmation of diagnosis, investigations and after written informed consent, The participant will receive Tab. mifepristone 200 mg orally. In all women, at the end of 24 hr and 48 hrs., Bishop's score was assessed. Once the patient's bishop score has improved or gone into active labour further management will be according to the hospital protocol.

When the women entered in active labor, ARM was done and if required Oxytocin drip was started for augmentation of labor, If fetal heart rate pattern remained normal with satisfactory progress of labor, these women were kept for vaginal delivery. If progress was unsatisfactory or variable fetal heart pattern, these women underwent cesarean section. The efficacy of mifepristone was assessed on the basis of improvement in Bishop score.

RESULTS: After induction with mifepristone for cervical ripening in this study, 71% primigravida and 12% multigravida who had bishop score <3 on admission had cervical score improved to >6 within 24 hours, at the end of 48 hours, bishop score had improved to >6 in 64% primigravida and 14% in multigravida.

CONCLUSION : Our study concludes that there was drastic improvement in bishop score within 24 - 48 hours of oral mifepristone and it is a safe and efficient agent for cervical ripening and for initiation of labor when given 24h - 48 hours prior to labor induction.

KEYWORDS : Bishops score, mifepristone

INTRODUCTION:

According to **Williams, 25th edition**, Induction implies stimulation of contractions before the spontaneous onset of labor, with or without ruptured membranes. When the cervix is closed and uneffaced, labor induction will often commence with cervical ripening, a process that generally employs prostaglandins to soften and open the cervix.¹

Watchful expectancy had been the rule from ancient times, with regard to delivery.. Although most patients experience spontaneous labor at term, induction of labor is the option of modern day obstetrics when indicated. induction of labor has become a common obstetric practice referring to the process of labor where the uterine contractions are initiated by medical and surgical means before the onset of spontaneous labor (**Norwitz, et al., 2002**).²

In current obstetric practice, induction of labor is often carried out for various maternal, fetal, or logistic reasons. Induction of labor is the artificial initiation of uterine contractions prior to their spontaneous onset with natural, mechanical or medical drugs leading to progressive dilatation and effacement of the cervix culminating in the process of birthing.

Historical perspective

Hippocrates' original descriptions of mammary stimulation and mechanical dilation of the cervical canal. Moshion was the first to describe manual dilation of the cervix.³

Induction of labor is still controversial. The need to time delivery has been recognized and practiced for centuries. Although the indications have clearly changed during the past 200 years from a need to expel a dead fetus to pre-emptive action to reduce the threat to fetal or maternal health, effective and safe methods of achieving delivery must always have been the primary objectives. the possibility to prevent intrauterine fetal morbidity and mortality of known or unknown cause and the possibility to apply intra partum fetal surveillance and monitoring from the beginning of labor are put forward as arguments in favor of induction of labor. Techniques for inducing labor have also changed from dietary delicacies and verbal threats giving way to

physical stimulation mainly achieved by cervical stretching and amniotomy to pharmacological manipulation using oxytocin and prostaglandins, Thus to initiate the artificial means for initiation of labor we need to understand the parturition cascade with the biophysio-chemical changes to evolve and establish normal labor and thus the impact of induction of labor on achieving it.

OBJECTIVES

1. To study the efficacy of mifepristone as a cervical ripening agent for induction of labour.
2. To study improvement in bishop's score.

MATERIALS AND METHODS:

Source of data: Patients attending OBG department at Kempegowda Institute of Medical Sciences Hospital & Research centre. Bengaluru.

Method of collection data:

Sampling method: Purposive sampling.

Sample size: 100.

Study duration: 18 months.

Place of study : In KIMS Hospital, Department of obstetrics and gynaecology, in patients, over a period of 18 months, after meeting the inclusion criteria and taking informed consent

Inclusion criteria:

1. Women with term pregnancy with maternal age >18 years,
2. Singleton gestation,
3. Cephalic presentation,
4. Reactive FHR pattern in live fetus,
5. Intact membranes,
6. Bishop score <6

Exclusion criteria:

1. Estimated fetal weight >4,500 or <2,000 g,
2. Antepartum hemorrhages,

3. Previous cesarean section,
4. Chorioamnionitis,
5. Parity >4,
6. Oligoamnios

Method :

After detailed history, examination, confirmation of diagnosis, investigations and after written informed consent, The participant recieved Tab. mifepristone 200 mg orally, In all women, at the end of 24 hr and 48 hrs., Bishop's score was assessed.

Once the patient's bishop score has improved or gone into active labour further management will be according to the hospital protocol.

When the women entered in active labor, ARM was done and if required Oxytocin drip was started for augmentation of labor, If fetal heart rate pattern remained normal with satisfactory progress of labor, these women were kept for vaginal delivery. If progress was unsatisfactory or variable fetal heart pattern, these women underwent cesarean section. The efficacy of mifepristone was assessed on the basis of improvement in Bishop score.

STATISTICAL ANALYSIS:^{4,5,6,7}

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

Continuous data was represented as mean and standard deviation. **Independent t test** was used as test of significance to identify the mean difference between two quantitative variables. **Paired t test** is the test of significance for paired data for quantitative data. ANOVA **test** was used as test of significance to identify the mean difference between more than two quantitative variables

Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

Table 1:- Distribution of the patients according to age group

Age group	patients	Percent
19-23yrs	42	42.0
24-28yrs	52	52.0
29-33yrs	6	6.0
Total	100	100.0

In my study group, majority of patients(52%) belong to 24-28yrs age group, the youngest being 19 years and oldest is 33 years.

Table 2:- Distribution of the patients according to parity

	patients	Percent
Multigravida	15	15.0
Primi gravida	85	85.0
Total	100	100.0

Out of 100 study group women, 85 were primigravida and 15 were multi gravida, the majority recruited for the study were primigravida, to study the effect of cervical ripening.

Table 3:- Distribution of the patients according to Gestational Age

Gestational Age	No. of patients	%
37weeks-38weeks +6days	19	19.0
39weeks-40weeks+6days	81	81.0
Total	100	100.0

According to our hospital protocol, induction of labor was carried out at 40 weeks-40 +3 weeks in low risk women, hence, majority of the women(81) were in the gestational age of 39- 40+6 weeks.

Table 4:- Distribution of the patients according to indication for induction

Indication	No. of patients	Percent
Decreased FM	6	6.0
GDM	11	11.0
Hypertension	17	17.0
IUGR+doppler changes	4	4.0
Past dates	55	55.0
Bad obstetric history	3	3.0
Prolonged latent phase	4	4.0
Total	100	100.0

Most common indication for induction was past dates(55 of patients)at 40-40⁺³ weeks as per our hospital protocol, followed by 17 hypertension cases, and then by GDM

Table 5: BISHOP Score distribution of patients studied

Bishop score	No. of patients, At 0 hours	percent
<3	61	61.0
4-5	39	39.0
6	0	0
Total patients	100	100

In our study, (61%) of patients belong to bishop score of less than 3.

Table 6: Bishop's score distribution of patients at 24 hours

Improvement in Bishop's score	No. of patients, At 24 hours	percent
<6	24	24
>6	76	76
Total	100	100

After a wait period of 24 hours, maximum number of patients(76%) had improvement in bishop score, hence, 61% of patients who had bishop score <3 had improved to >6.

Table 7: Bishop's score distribution of patients at 48 hours

Improvement in Bishop's score	No. of patients, At 48 hours	percent
<6	11	12.5
>6	77	87.5
total	88	100

At the end of 48 hours, it was observed that 77% of patients had improved bishop score (implies success of tab mifepristone).

*12 patients went into spontaneous labor, after 24 hours of giving mifepristone tablet. 4 patients delivered vaginally with mifepristone alone, 5 patients were augmented with oxytocin and delivered vaginally, 3 patients underwent lscs for fetal distress and CPD.

Table 8:- Distribution of the patients according to mode of delivery

Mode of delivery	No. of patients (n=100)	%
Vaginal	61	61.0
LSCS	39	39.0
Instrumental	0	0.0

In our study, 61% of patients had vaginal delivery.

Amongst the 39% of patients who underwent LSCS for various other indication, bishop score had improved to >6 in 28% of patients.

Table 9:- Distribution of the subjects according to indication for LSCS

Indication	number	Percent
CPD	9	23.07
failed induction	5	12.82
Fetal distress	18	46.16
maternal request	1	2.56
NPL	6	15.39
Total	39	100.0

In my study, most common indication for patient to undergo lscs was fetal distress(18%).

Table 10:- Distribution of the subjects according to colour of liquor

	Frequency	Percent
Clear	89	89.0
MSAF	11	11.0
Total	100	100.0

In our study, 89 patients had clear liquor, and MSAF was found in only 11 patients

Table 11:- Distribution of the new born babies according to NICU admission

Nicu admission	No of babies	Percent
Not required	92	92.0
Required	8	8.0
Total	100	100.0

92 newborn did not require NICU admission, 8 new born required NICU admission for various other reasons.

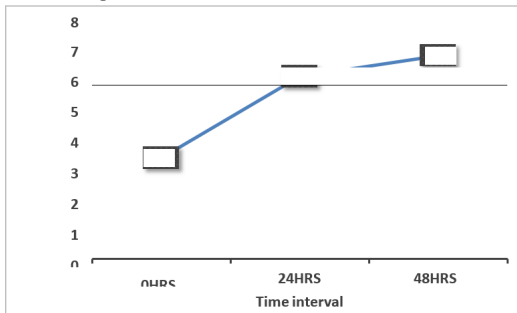
Table 12:- Mean Bishop's Score at various time interval

	Mean	Std. Deviation	P value
0hrs	3.42	0.572	<0.001
24hrs	6.18	1.167	
48hrs	6.89	1.226	

When we compared mean bishop's score at 0hr and 24hrs There was statistically significant difference found at these time interval with respect to Bishop's score with P value <0.001.

When we compared mean bishop's score at 0hr and 48hrs There was statistically significant difference found at these time interval with respect to Bishop's score with P value <0.001.

When we compared mean bishop's score at 24hrs and 48hrs There was statistically significant difference found at these time interval with respect to Bishop's score with P value <0.001

**Figure 12:- Graph showing Mean Bishop's Score at various time interval**

DISCUSSION

We have observed the impact of tablet Mifepristone for pre-induction cervical ripening and improvement of Bishop's score after 24hrs and 48 hours, and outcome of study is compared with few similar studies recently done by others authors.

71 primigravida and 12 multigravida patients who had Bishop's score was <6 on admission, had cervical score >6 within 24 hours of administration of mifepristone 24% of patients went into spontaneous labor. Similar observations are with Wing⁸, D.A Fassett, Michael J where Bishop's score before administration of mifepristone were unfavorable (<5) and almost 20% pts went in spontaneous labor with favorable Bishop's score (>7).

Frydman⁹ et al. reported 3 % women went into labor within 24 h of ingestion of mifepristone. Hapangama and Neilson¹⁰ reported that mifepristone-treated women were more likely to be in labor or to have a favorable cervix at 48 h (risk ratio (RR) 2.41, 95 % confidence interval (CI) 1.70–3.42), and this effect persists at 96 h (RR 3.40, 95 % CI 1.96–5.92). In the present study, 19 women in Study Group went in labor and delivered vaginally without any need of other agents within 24- 48 hrs of ingestion of mifepristone. This was found to be significant.

After 48 hours of administration, improvement of bishop score 64% of

patients bishop score was >6, signifying that waiting period of 48 hours was more helpful in improvement of bishop score, consistent with other studies.

Shanitha Fathima¹¹ et al observed the significant difference in Bishop's score pre and post administration of mifepristone as well as dianoprostone in their study as mean pre induction score 2.32±0.76 and mean post induction score as 7.25±1.75 at 48 hrs

Athawale R¹² et al also observed pre induction Bishop's <3 in 84% as compared to 58% in placebo group, where Bishop's score improved 24hrs after mifepristone up to >8 in 72% as compared to placebo where Bishop's score remain between 4- 8 in 86% pts.

Yelikar¹³ K et al observed Mean Bishop's Score at 0 hour (Mean± SD) in study group with mifepristone 2.02±0.749 and 2.16±0.77 with placebo which improved up to 5.0408±1.90 with mifepristone administered group and 3.26±1.15 in placebo group.

In this study, 61% had vaginal delivery, 48 (out of 85 primigravida) and (13 out of 15 multigravida) and these results were consistent with study by manoj¹⁴ et al. Rate of LSCS with mifepristone and with addition of misoprostol/dinoprostone/combination in this study was 39%. When mifepristone used alone, lscs was 5 (20.8%) and mifepristone and dinoprostone was used, lscs was 20 (41.7%) Similar findings were noted by Shanitha F et al. Gaikwad V¹⁵ et al also found high rate of LSCS in dinoprostone group. In their study 16% rate of LSCS was in mifepristone group and 44% in dinoprostone group. They found significant difference in rate of LSCS amongs two groups (P=0.001).

In this study the most common indication for LSCS was fetal distress, it was 46.5%. Fetal distress was also the most common indication for LSCS in the study of Fathima Shanitha et al. Gaikwad V et al in their study found that the most common indication for LSCS was fetal distress in Mifepristone group (8%) and the most common indication for LSCS was failed induction in dinoprostone group (28%).

CONCLUSION

From our study we finally conclude Mifepristone (RU 486) is a safe and efficient agent for cervical ripening and for initiation of labor when given 24h-48 hours prior to labor induction.

It is easy to administer, better patient compliance and acceptance

The drug has no untoward side effects on uterine contraction and no major maternal complications. Mifepristone provides a new alternative for induction of labor at term and can be considered as a simple and safe method of labor induction. It can be administered safely with no increase in adverse events on the fetus or mother.

After analyzing the different observations in the study, we summarize the following results.

There was significant improvement in the Bishop's score after administering Mifepristone to the patients. This comparative drug therapy has got no difference on mode of delivery and perinatal outcome.

REFERENCES

- Williams obstetrics 25th Edition, F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, John C. Hauth, Larry C. Gilstrap III, Kotharine D. Wenstrom, Section II – Chapter 6 Parturition.
- Arulkumar, Leonie K. Penna K. Bhasker Rao, The management of Labour Second edition, Chapter 1, Physiopharmacology of labour Pg. 11, 12, 14, chapter 18 Induction of labour 281, 292 – 296, 2007.
- E. Norwitz, J. Robison, and J Repke, —Labor and delivery, I in S.G. Gabbe, J.R. Niebyl, J.L. Simpson, eds. Obstetrics: normal and problem pregnancies, 4th ed., (New York: Churchill Livingstone, 2002) pp. 353-94.
- Bernard Rosner (2000), Fundamentals of Biostatistics, 5th Edition, Duxbury, page 80-240
- Robert H Riffenburg (2005), Statistics in Medicine, second edition, Academic press. 85-125.
- Sunder Rao P S S, Richard J (2006): An Introduction to Biostatistics, A manual for students in health sciences, New Delhi: Prentice hall of India. 4th edition, 86- 160
- Suresh K. P. and Chandrasekhar S (2012). Sample Size estimation and Power analysis for Clinical research studies. Journal Human Reproduction Science, 5(1), 7-13.
- Wing DA, Fassett Michael J, Mishell Daniel R. Mifepristone for preinduction cervical ripening beyond 41 weeks' gestation: a randomized controlled trial. Obstet Gynecol. 2000;96:543-548. doi: 10.1016/S0029-7844(00)00947-9
- Frydman R, Lelaider C, Baton-Saint-Mieux C, et al. Labour induction in women at term with mifepristone (RU 486): a double-blind, randomized, placebo-controlled study. Obstet Gynecol. 1992;80:972-975
- Hapangama D, Neilson JP. Mifepristone for induction of labour. The Cochrane database of systematic reviews. 2009 Jul 8(3):CD002865.

11. Fathima S, Nayak SR, Rao B, et al. Mifepristone in induction of labour at term. *Int J of Pham Biomed Res.* 2013;4(3):164–166.
12. Athawale R, Acharya N, Samal S, et al. Effect of mifepristone in cervical ripening for induction of labour. *Int J Reprod Contracept Obstet Gynecol.* 2013;2(1):35– 38. doi: 10.5455/2320- 1770.ijrcog20130206
13. 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;65(4):221-5
14. Manandhar R, Saha R, Bajracharya J, Malla R. Mifepristone versus oxytocin for cervical ripening prior to induction of labour. *Journal of Kathmandu Medical College.*;6(3):90-5.
15. Gaikwad V, Mittal B, Mangal P. Comparative analysis of safety, efficacy and feto maternal outcome of induction of labour with mifepristone versus intracervical dinoprostone gel. *RJPBCS.* 2014;5(2):611.