

The role of mifepristone in labor induction and its impact on fetomaternal outcomes in term pregnancies

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Abstract

Background: Mifepristone is a steroid-based drug that blocks glucocorticoid and progesterone effects. It enhances uterine contractions and promotes cervical changes necessary for childbirth. This study evaluates how effective a single oral dose of mifepristone is for cervical preparation during labor induction in the third trimester, examining both mother and baby outcomes, along with any side effects.

Method: The study involved 120 women at full term (37-40 weeks) with unfavorable cervical scores (Bishop score <6). They were divided equally into two groups: 60 women received 200mg oral mifepristone (Study Group), while 60 received a placebo (Control Group). After 24 hours, cervical changes were evaluated using the Bishop's score. Subsequently, 25µg misoprostol was given vaginally every 4 hours, up to 6 times, to start or strengthen labor. The study analyzed both maternal and fetal outcomes to assess the drug's safety and effectiveness.

Results: Bishop score improvement was noted in 64% of participants. The study group showed faster progression from induction to delivery, with a notable 46% of patients not requiring any misoprostol after mifepristone treatment, suggesting mifepristone alone might suffice for future labor inductions. Neonatal intensive care admission rates were lower in the study group (4%) compared to the control group (12%).

Conclusion: The study demonstrated that women receiving 200mg oral mifepristone showed significant cervical Bishop score improvement within 24-48 hours. This resulted in reduced cesarean sections, decreased need for additional labor-inducing medications (misoprostol or oxytocin), fewer NICU admissions, and reduced maternal complications.

Keywords: Mifepristone, induction of labor, bishop's score

Introduction

Labor induction refers to artificially starting uterine contractions before they begin naturally, with the goal of gradually dilatation and effacement of the cervix to deliver the baby [1]. In certain cases, inducing labor becomes necessary when continuing the pregnancy poses greater risks to mother or baby than the intervention itself [2]. The American College of Obstetricians and Gynecologists (ACOG) stated in 2009 that labor induction aims to achieve vaginal delivery by artificially stimulating uterine contractions before natural labor begins [3]. Successful vaginal delivery depends strongly on having a soft, ripened cervix. Therefore, cervical ripening must be evaluated before choosing an induction method.

Mifepristone, also known as RU-486 (named after Roussel Uclaf), is a 19-nor steroid that strongly competes with and blocks progesterone action while also significantly inhibiting glucocorticoid activity. It's used preliminarily to prepare the cervix. Research shows that mifepristone effectively alters cervical consistency, demonstrably improving cervical dilation. Its mechanism involves blocking progesterone receptors and preventing progesterone's cellular effects through its antiprogesterone, antiglucocorticoid, and mild antiandrogenic properties, ultimately promoting cervical softening.

While mifepristone has limited direct effects on uterine contractions, it enhances the uterus's response to prostaglandins and transforms the normally quiet pregnant uterus into an actively contracting organ. However, Hapangama and Neilson's 2009 Cochrane review [4], concluded that current clinical trial evidence is insufficient to definitively support mifepristone use for labor induction.

Aim: To evaluate mifepristone's role in cervical preparation for labor induction

Objectives

1. To evaluate mifepristone's effectiveness and safety for cervical preparation in full-term pregnancies, focusing on achieving positive maternal and fetal outcomes while reducing cesarean rates.
2. To compare maternal and fetal outcomes between mifepristone-treated and control groups.
3. To assess and compare cervical score improvements between study and control groups.
4. To determine the need for additional labor augmentation measures.

Materials and methods

This prospective, randomized comparative study was conducted at RNT Medical College attached Hospital of

Department of Obstetrics and Gynaecology from January 2022 to November 2023. The study included 120 participants who provided written informed consent.

Inclusion criteria

Participants were included if they had:

1. Full-term pregnancy (37-40 weeks)
2. Cephalic presentation
3. Intact amniotic membranes
4. Adequate pelvic measurements

Exclusion criteria

Patients were excluded if they had:

1. Previous C-section
2. Fetal growth restrictions
3. Low amniotic fluid
4. Abnormal fetal positioning
5. Medical conditions (including hypertension, diabetes, heart problems, anemia, thyroid disorders, epilepsy, or asthma)
6. Premature membrane rupture
7. Known allergies to prostaglandins or mifepristone
8. Placental insufficiency
9. Cephalo-Pelvic Disproportion

A detailed history was obtained at admission, covering relevant medical, surgical, and obstetrical details. Gestational age was assessed using both the last menstrual period and ultrasound evaluation.

- Informed consent was secured from the patient. An obstetric examination was performed to confirm the fetal lie, gestational age, and fetal heart rate. A pelvic examination was conducted to assess the Bishop's score and evaluate the pelvis.
- Those participants who received 200 mg of mifepristone tablets were assigned to the Study Group (n = 60). Participants who received the placebo were assigned to the Control Group (n = 60).
- For all the women, the Bishop's score was evaluated at the end of 24 hours. If the score was less than 6, then 25 µg of misoprostol tablets were administered vaginally every 4 hours (up to a maximum of 6 doses, totaling 150 µg) until the Bishop's score reached 6 or higher, or the woman went into active labor.
- When the women progressed to active labor, artificial rupture of membranes (ARM) was performed. If needed, an oxytocin infusion was initiated to augment labor, but not until at least 4 hours after the last dose of misoprostol was administered.
- If the fetal heart rate pattern remained normal and labor was progressing satisfactorily, these women were allowed to continue towards a vaginal delivery.
- If the labor progress was unsatisfactory or the fetal heart rate pattern became variable, these women underwent a cesarean section. The efficacy of mifepristone was evaluated based on improvements in the Bishop's score, the average dose of misoprostol required, and the duration from induction to the active phase of labor.
- The observed results were subjected to appropriate statistical analysis, and a p-value less than 0.05 was considered statistically significant.

Observation

A detailed analysis was conducted for both the study group and the control group regarding

1. Drug Efficacy in terms of:
 - Changes in Bishop's score
 - Misoprostol dosage requirements
 - Failed induction rates
2. Maternal Outcomes in terms of:
 - Mode of delivery.
 - Cesarean section rates
 - Drug side effects
3. Fetal Outcomes in terms of:
 - APGAR scoring
 - NICU admission requirements

Table 1: Modified Bishop's score

	0	1	2	3
Dilatation(cm)	1	1-2	2-4	>4
Effacement(cm)	4	2-4	1-2	<1
Station(cm)	3	-2	-1/0	+1/+2
Consistency	Firm	Average	Soft	
Position	Posterior	Central	Anterior	

Result

Table 2: Distribution of cases according to age

Age Groups (in years)	No. of cases in Control Group		No. of cases in Study Group	
	N=60	%	N=60	%
<20	2	4%	3	6%
21-25	42	70%	40	64%
26-30	10	16%	10	18%
31-35	4	6%	5	8%
>35	2	4%	2	4%
Mean age with SD	24.5+4.13		24.78+3.92	

The majority of women enrolled in both groups were in the 21-25 age range. Only up to 8% of patients in each group were over 30 years old.

Table 3: Distribution of patients according to gestational age in weeks

Gestational Age in weeks Percentage	Control Group		Study Group	
	N=50	%	N=50	%
37-38	19	32%	22	36%
39-40	39	64%	36	60%
>40	02	4%	02	04%

Most of the patients were between 39-40 weeks (64% in the control group and 60% in the study group), indicating a nearly equal distribution across both groups.

Table 4: Bishop's score in both the groups

Bishop Score	Control Group		Study Group	
	N=60	%	N=60	%
<3	20	34%	25	42%
>3	40	66%	35	58%
Mean Bishop Score	4.02±1.09		3.84±1.03	
After 24 hours				
<3	25	42%	1	02%
4-8	29	48%	20	34%
>8	6	10%	39	64%
Mean dose required	3.84±1.03		8.54±2.06	

Significant improvement in the Bishop’s score was observed after administering Mifepristone to the patients; the mean Bishop’s score 24 hours post-administration was 8.54±2.06. This improvement was statistically significant, with a p-value of <0.0001.

Table 5: Subsequent dosages of Misoprostol in both the groups

Dose of Misoprostol	Control Group (Group 1)		Study Group (Group 2)	
	N=60	%	N=60	%
0	0	0%	28	46%
1	8	14%	23	38%
2	35	58%	6	10%
3	17	28%	3	06%
Mean dose required	2.14+0.63		1.4+0.8	

As shown in the table, the control group had a higher frequency of repeated Misoprostol doses than the study group. The difference in the need for subsequent Misoprostol doses between the two groups was statistically significant (p < 0.0001). A striking observation is that 46% of patients did not require any Misoprostol after cervical ripening with Mifepristone, implying that Mifepristone alone might be sufficient for future inductions.

Table 6: Mode of delivery in both the groups

Mode of delivery	control Group		Study Group	
	N=60	%	N=60	%
VD	47	78%	52	86%
LSCS	10	16%	07	12%
Instrumental VD	03	06%	01	02%

The majority of patients in both groups delivered vaginally, with 78% in Group 1 and 86% in Group 2. While a 4% reduction in LSCS was observed in the study group, this difference was not statistically significant.

Table 7: apgar score and NICU admission in relation to study and control group

Apgar Score	Control Group		Study Group	
	≤ 7	≥ 7	≤ 7	≥ 7
1 minute	20(34%)	40(66%)	10(16%)	50(84%)
5 minute	7(12%)	53(88%)	2(04%)	58(96%)
Admission to NICU				
Yes	7(12%)		02(04%)	
No	53(88%)		58(96%)	
Total	60(100%)		60(100%)	

At one minute, 66% of neonates in the control group and 84% in the study group achieved an Apgar score of 7 or higher. By five minutes, only 12% of neonates in the control group and 4% in the study group had an Apgar score below 7, a difference that was not statistically significant.

Maternal complications were evaluated, excluding cases of failed induction. The majority of patients in both groups experienced no major complications, including sepsis, fever, and postpartum hemorrhage. While a few minor genital tract injuries were noted, there was no statistically significant difference between the study and control groups.

Discussion

The purpose of our investigation was to determine the effectiveness of mifepristone tablets in cervical preparation prior to induction and labor initiation at term pregnancy. The research participants were selected from qualifying patients at the RNT Medical College's affiliated Zanana Hospital in Udaipur, based on specific inclusion and exclusion parameters. This prospective research study examined 120 cases. The outcomes revealed that while 86%

of participants delivered through vaginal birth, emergency cesarean sections were necessary for 12%. Twenty-four hours post-mifepristone administration, significant improvements were observed in the Bishop score. Notably, 46% of participants successfully delivered vaginally with mifepristone alone, requiring no additional induction methods. When Bishop scores remained under 6 after 24 hours, seen in 38% of cases, one dose of tab misoprostole was used for induction. Several studies have demonstrated significant findings regarding mifepristone use in labor induction. Fathima and colleagues reported higher rates of spontaneous vaginal deliveries with fewer cesarean sections and instrumental deliveries [6]. Research by Byrne and Wing revealed elevated cortisol levels within 18 hours following mifepristone administration and labor induction [5].

A Beijing-based study at Tian Tan Hospital by Li, Gao, and Chen evaluated mifepristone and misoprostol for term labor induction. Their findings showed mifepristone administration resulted in cervical shortening by 1-3 cm and Bishop scores increasing by 4-5 points compared to pre-treatment measurements [7]. Similarly, our research demonstrated statistically meaningful improvements in mean Bishop scores after 24 hours, suggesting effective progesterone withdrawal.

Wing's research team also observed favorable Bishop scores 24 hours post-mifepristone administration [8]. These findings were further supported by both Atwale's and Fathima's studies, which noted significant Bishop score improvements with oral mifepristone [9]. Our findings aligned with existing literature showing reduced prostaglandin requirements for term induction.

According to Hapangama and Neilson's research, women receiving mifepristone treatment showed lower rates of cesarean sections due to failed induction (RR 1.43, 95% CI 0.20-0.80) and reduced need for oxytocin augmentation (RR 0.80, 95% CI 0.66-0.97) [10]. Our study's induction success rates were comparable to these findings.

Yelikar Kanan's team studied 100 patients with late-term pregnancies beyond 40 weeks and Bishop scores below 6. Their research concluded that administering mifepristone 24 hours before induction effectively promoted cervical ripening and labor initiation in late-term pregnancies [10].

Conclusion

Our findings indicate that Mifepristone (RU 486) is a safe and effective method for cervical ripening and labor induction when administered 24 hours before induction. This approach may reduce the need for Misoprostol augmentation. Mifepristone presents an appealing new alternative for labor induction at term, offering obstetricians a simple and safe method.

As a progesterone antagonist, Mifepristone can soften and dilate the cervix and increase uterine activity in pregnant women. Whether used alone or with augmentation, Mifepristone is a safe, efficient, cost-effective, and convenient method for inducing labor in women at term, without posing additional risks to the fetus or mother.

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Conflict of interest: None declared

Ethical Approval

Ethical approval for the study was obtained from the Institution.

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