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Original Research Article

Is mifepristone a game changer in induction of labour..?

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ABSTRACT

Introduction: Induction of labor is defined as artificially stimulating the uterus to start labor. Mifepristone is a synthetic steroid hormone analog that has both anti-progesterone and anti-glucocorticoid activities. This study aimed to study the efficacy of mifepristone in the induction of labor and cervical ripening.
Materials and Methods: This study was conducted in Gandhi Hospital from August 2022 to November 2022. A total of 100 antenatal cases were admitted for safe confinement after 37 completed weeks and given oral mifepristone 200 mg and assessed for cervical ripening and need for further augmentation and the outcome was studied based on improvement in bishops score assessed after 24 hours of intake of oral mifepristone.
Results: It was observed that there was a significant improvement in the bishop's score 24 hours after giving mifepristone. Out of 100 women who were given mifepristone, 79% delivered vaginally and 21% delivered through emergency cesarean section. The major indication for emergency cesarean section was fetal distress. The majority of patients had good neonatal outcomes and there were no serious maternal complications.
Conclusion: Mifepristone is an effective and safe method of induction of labor with significant improvement in Bishop's score within 24 hours of administration.

1. Introduction

Mifepristone RU-486 was discovered by Roussel Uclaf of France in 1980 while they were studying glucocorticoid receptor antagonists.[1] Mifepristone is established for the termination of first and second-trimester pregnancy.[2] Mifepristone is a steroid compound, which has anti-progesterone and anti-glucocorticoid activity. It increases uterine activity and causes cervical effacement and dilatation. It has rapid absorption and a long half-life of 25 to 30 hours.[3] This study aimed to study the efficacy of mifepristone in the induction of labor and cervical ripening.

2. Materials and Methods

This study was conducted in Gandhi Hospital over a period of 3 months from August 2022 to November 2022. A total of 100 antenatal cases were admitted for safe confinement at 37 completed weeks, given oral mifepristone 200 mg, and assessed for cervical ripening. The need for further augmentation and outcome was studied.

2.1. Design

Prospective observational study; single-blind study.

After written informed consent, 100 women with a Bishop score <6 were recruited. Tab. Mifepristone 200mg single dose per oral was given at term gestational assessed for cervical ripening and the need for further augmentation and the outcome was studied based on improvement of

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Bishop's score which was assessed at 24 hours from the time of induction.

2.2. *Inclusion criteria*

1. Singleton live gestation
2. Fetus in cephalic presentation
3. Age between 18-40 years
4. EFW between 2-4 kg
5. Gestational age between 37 weeks 0 days 42 weeks 0 days.
6. Patients who are not in labor with intact membranes
7. Patients with no contraindications for vaginal delivery (placenta previa, vasa previa, active genital herpes)
8. Patients with Bishops score <6 at the time of randomization
9. Patients with no contraindications for mifepristone (chronic adrenal failure, concurrent long-term corticosteroid therapy, H/O hemorrhagic disorders).

2.3. *Exclusion criteria*

1. Multiple gestations.
2. Non-vertex presentation,
3. Age <18 years and >40 years
4. EFW >4kgs,
5. EFW <2kgs,
6. Severe oligohydramnios,
7. Previous cesarean section,
8. Mal-presentation,
9. Significant cardiac, renal, or hepatic maternal complications,
10. Premature rupture of membranes with signs and symptoms of chorioamnionitis,
11. Non-reassuring fetal heart rate pattern,
12. Antepartum hemorrhage,
13. Contra indications for vaginal delivery.

3. Results

It was observed that there was a significant improvement in the bishop's score 24 hours after giving mifepristone. Out of 100 women who were given mifepristone, 79% delivered vaginally and 21% delivered through emergency cesarean section. The major indication for emergency cesarean section was fetal distress. The majority of patients had good neonatal outcomes and there were no serious maternal complications

The statistical analysis mainly comprises the induction delivery time, mode of delivery, and maternal and fetal outcomes.

In our study group, the majority of patients (64%) belong to the 18-24 yrs. age group, the youngest being 18 years and the oldest being 36 years.

Out of the total study group women, 58 were Primigravida (58%) and 42 were Multigravida (42%).

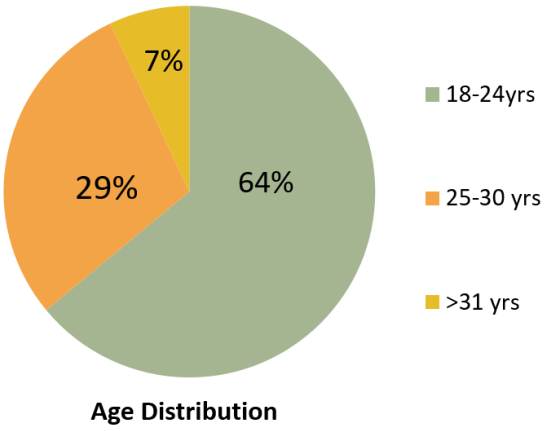

Fig. 1: Distribution of the patients according to age group

Table 1: Distribution of the patients according to parity

Parity	No. of patients (n=100)	Percentage
Primi	58	58%
Multi	42	42%
Total	100	100%

Table 2: Progression in bishop score

	Bishop's score (>6) 24 hours after mifepristone	Total % (n=100)
Primi	34	58.6%
Multi	22	52.3%

34 primigravida and 22 multigravida patients who had Bishop's score <6 on admission, had an improvement in bishops score >6 after 24 hours of administration of mifepristone.

Table 3: Augmentation methods

Augmentation	Primi	Multi	Total (n=100)
Misoprostol	40%	17%	57%
Stripping	0	4%	4%
Oxytocin	11%	6%	17%
None	7%	15%	22%
Total	58%	42%	100%

In our study, a total of 88 study subjects needed augmentation and the mode of augmentation more commonly used was T. Misoprostol given to patients after a time period of 24 – 48 hours according to bishop score.

Table 4 depicts that induction to delivery time is considerably shorter in multi gravidas (35.7%) than primi gravidas (17%). About 45% of the total patients were delivered within 24 to 48 hrs of mifepristone induction. About 30% of patients delivered after 48 hrs. About 25% of the patients had an induction to the delivery interval of less than 24hrs. In this study the time duration from induction to

Table 4: Distribution of the patients according to induction to delivery interval

Induction to delivery interval	Parity	Patients	Total %	p value
< or equal to 24hrs	Primi	10%	25%	
	Multi	15%		
24-48 hrs	Primi	28%	45%	0.1
	Multi	17%		
>48 hrs	Primi	20%	30%	
	Multi	10%		
Total			100%	

delivery was found to be statistically not significant among primi and multi gravidas.

Table 5: Distribution of the patients according to the mode of delivery

Mode of delivery	Primi N=58	Multi N=42	No. of patients (n=100)	p value
Vaginal delivery	35 (60.35%)	40 (95.23%)	75 (75%)	0.01
	4 (6.89%)	0 (0%)	4 (4%)	
Cesarean section	19 (32.76%)	2 (4.77%)	21 (21%)	

Table 5 depicts the modes of delivery. Out of 100 patients, 79% of the patients were delivered by normal vaginal delivery, and out of them, 4 patients had instrumental delivery. 21% of the total patients delivered by cesarean section. In this study the cesarean section rate was statistically significantly higher among primi gravidas as compared to multi gravida.

Table 6: Indication for cesarean sections

Indication	Primi	Multi	Total%
Fetal distress	9	0	42.9%
Non-progression of labor	8	0	38.1%
Cord prolapse	0	2	9.5%
CPD	1	0	4.75%
Abruption	1	0	4.75%
Total	19	2	100%

In our study the most common cause for cesarean section was fetal distress (42.9%), the other cause being a non-progression of labor (38.1%). Abruption in 1 patient, CPD in one patient, and cord prolapse in two patients.

In our study group, only 13% of the total babies born needed NICU admissions all of them were discharged healthy indicating better fetal outcomes.

In our study group majority of babies had a good APGAR score at birth and 5^{th} minute.

Table 7 and Figure 1 depict better perinatal outcomes in general due to lower NICU admissions, better APGAR, and

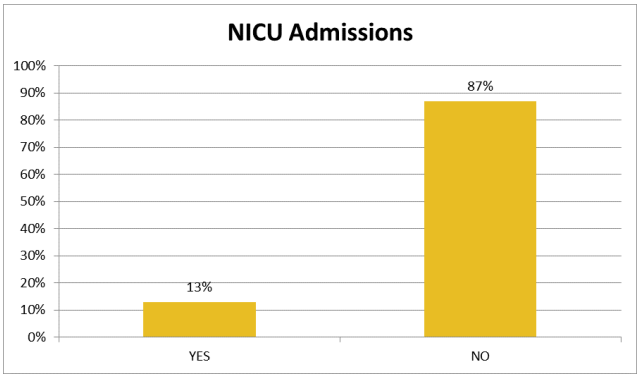

Fig. 2: Distribution of the newborn babies according to NICU admission

Table 7: Distribution of the newborn babies according to APGAR

APGAR	Primi	Multi	Total
>or = 7/1, 9/5	51	36	87%
<7/1, 9/5	7	6	13%

better birth weight.

4. Discussion

Mifepristone (RU486) has a specific high affinity to the progesterone receptor and thus compete with progesterone at the level of their respective binding site as the result of the withdrawal of the inhibitory effect of progesterone there is an increase in the synthesis of prostaglandins.[4] The sensitivity of the myometrium to the contraction-inducing activity of prostaglandins markedly increases after mifepristone administration[5] and labor often starts without additional inductors.

In the present study, we assessed the ages of the study subjects. 64% of the study subjects belonged to the age group of 18 to 24 years. Kanan Yelikar et al. in their study observed that the mean age of the study subjects is 22.98 years.[6]

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

34 primigravida and 22 multigravida patients who had Bishop's score was <6 on admission, had a bishop score of>6 within 24 hours of administration of mifepristone. These observations are consistent with Wing[7] D.A Fassett Michael J where Bishop's score before administration of mifepristone was unfavorable (<5) and almost 20% pts went in spontaneous labor with favorable Bishop's score (>7).

Shanitha Fathima et al. observed a significant difference in Bishop's score pre- and post-administration of mifepristone as well as dinoprostone in their study as a mean pre-induction score of 2.32±0.76 and mean post-induction score as 7.25±1.75 at 48 hrs.[8]

Out of 100 patients, 79% of the patients delivered by normal vaginal delivery, 4 of these patients delivered by instrumental delivery, and 21% of the patients delivered by cesarean section. A study was done by Ravi Karad et al. successful Induction of labour[9]– natural labor was maximum in Mifepristone group-68% and had 4% instrumental deliveries in their study which is comparable with our study.

Ghimire et al[10] also found in their study that vaginal delivery was 66.0% in the test group and 42% in the control group. Whereas cesarean was 58.0% vs. 34.0% in the test and control group with a p-value of 0.01.

The most common indication for the patient to undergo cesarean section was fetal distress. Similar results were obtained in the study of M.H.Jasiya Afreen and P. Sudha C et al.

In the present study, 19 multigravidas in the group went into labor and delivered vaginally without any need for other agents within 24-48 hrs of ingestion of mifepristone.

Frydmann et al.[11] reported 3% of women went into labor within 24 h of ingestion of mifepristone. Hapangama[12] and Neilson 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. Kayastha et al[9] reported similar benefits in post-cesarean pregnancies where labor induction was indicated.

A randomized controlled trial was done by Baev O et al. in 2017 to evaluate the efficacy and safety of mifepristone for cervical ripening and induction of labor versus expectant management in a full-term pregnancy, the induction-delivery interval was shorter in the mifepristone group than in the expectant group.[13]

Our study also depicts that there are reduced NICU admissions (13%) and all were discharged healthy indicating good perinatal outcomes in newborns. Similar results in a study done by B. Arumugaselvi et al[14] depicted neonatal intensive care unit admission was 18% in the PGE2 gel group whereas 10% in the mifepristone group.

5. Conclusion

From our study, we finally conclude Mifepristone is an efficient agent for cervical ripening and initiation of labor with significant improvement in Bishop's score without any labor pains, repeated p/v examination with extreme patient satisfaction decrease in induction to delivery interval, and reduced need for further doses of misoprostol for augmentation, shorter instrumental delivery rate and significantly improved perinatal outcome. Mifepristone provides an interesting new alternative for induction of labor at term and can be considered by obstetricians as a simple and safe method of labor induction.

6. Source of Funding

None.

7. Conflict of Interest

None.

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