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# Comparative Study of Efficacy and Safety of Mifepristone and Foley's Catheter in Induction of Labour

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**Abstract:** ***Background: Labour Induction the most common Obstetric intervention done all over the world and where many methods are experimented for the same. Mifepristone, an antiprogestin effectively used for labour induction in term pregnancies is an upcoming area of interest. Foley's bulb induction is an ancient and effective method as inducing agent, Misoprostol (PGE1) has been in use more effectively from 1990's for Induction of labour. Since there is no single novel drug for induction, which is more effective and universally accepted, there is always scope for research. Hence this is a study undertaken to compare Mifepristone and Foley's bulb in induction of labour. Objectives: 1) To compare the efficacy and safety of mifepristone and Foley's catheter insertion in induction of labor. 2) To compare the maternal and fetal outcome in both the groups. Methodology: Prospective Randomised Control Trial undertaken in 100 Pregnant women undergoing labour induction for various indications meeting the inclusion and exclusion criteria. Group A received Mifepristone 200mg PO, followed by 25mcg vaginal misoprostol 4th hourly for maximum of 4 doses and oxytocin accordingly deciding on Bishop's score, In Group B Foley's bulb inserted intracervically and inflated with 30ml of distilled water and followed similarly with misoprostol and oxytocin. Change in Bishop's score, progress of labour induction to delivery interval, successful IOL and neonatal outcome noted. Results: The primary outcomes were -1) The improvement in Bishop's score was similar in Mifepristone and Foley's bulb group, i. e. 2.80 and 2.88 respectively 2) Mean induction to delivery interval which is comparatively short in Mifepristone group (20.50 hrs) compared to Foley's bulb group (19.47 hrs) and was found to be not statistically significant(P<0.001). 3) Successful IOL - Labour natural was maximum in Mifepristone group-68% compared to 62% in Foley's group. Conclusion: Foley's catheter & Mifepristone are effective agents for cervical ripening which have comparable efficacy and negligible fetomaternal side effects.***

**Keywords:** Induction of labour, Mifepristone, foley's catheter, Misoprostol, Induction delivery interval, Bishop's score

## 1. Introduction

Over the past many years, obstetricians are enticed with the process and the timing of the complex process called "Human labour". Thus, the concerns for maternal and fetal well-being related to timing of birth have been extensively studied to generate many approaches to initiate labor.

A common obstetric procedure - Induction of labour (IOL) is the artificial initiation of labour before its spontaneous onset for the purpose of delivery of feto-placental unit. It is indicated when the benefits to the mother or fetus outweigh the benefits of continuing the pregnancy[1].

The rate of IOL varies by region and institution. It is well established that labour will be induced in approximately 20 % of pregnancies. However, induction fails in 20 % of induced pregnancies . It is well recognized that the success of induction of labour which ultimately aims at achieving vaginal delivery depends to a great extent on the favourability of the cervix and also precisely the maternal and fetal outcome.[2]

Since antiquity, various methods and pharmacological drugs have been used in attempt to bring on labor , but the effectiveness and safety of a range of induction methods or drugs, still in an open field of future research in search of a novel method.

When the cervix is 'unfavorable' a ripening process is generally used before labour induction. Single agent and combination methods are being tried to achieve vaginal delivery. In our study well established Foley's catheter and misoprostol combination is compared with Mifepristone, antiprogesterone in combination with misoprostol is compared with respect to their efficacy and safety of the methods in induction of labour.

## 2. Materials and Methods

Prospective Randomised Control Trial undertaken in 100 women undergoing labour induction for various indications meeting the inclusion and exclusion criteria.

After taking an informed written consent, detailed history will be taken and clinically evaluated .The enrolled women are randomized using Block randomization into group A and group B.

In group A, women are given 200 mg of mifepristone orally and monitored, she is then reassessed after 24 hours, If the Bishop's score is ≥6, Artificial rupture of membranes is Performed and oxytocin started. Even after 24h, if Bishop's score is <6, 25µg of misoprostol is administered vaginally every 4th hourly to a maximum of 4 doses till women enters to active stage of labour. Even after 4 doses of misoprostol, if the Bishop's score has not changed, the induction attempt is categorized as failed.

The women in Group B, Foley's catheter no-16 with all aseptic precautions is inserted intracervically under direct vision and bulb inflated with 30ml of sterile water and left in situ for maximum of 18hrs, time of expulsion of the bulb noted and if Bishop's score ≥ 6, ARM is performed and

oxytocin started, if Bishop's score is < 6, 25µg of misoprostol is administered vaginally every 4th hourly to a maximum of 4 doses. If cervix remains unfavorable, induction is categorized as failed. In both group A and group B, progress of labour is monitored as per institutional protocol. Maternal and fetal outcome in both groups are recorded and compared and statistically analysed using analysed using SPSS software Version 20.0. Various descriptive and inferential statistics are calculated and expressed as mean ± SD and in percentage with P value of <0.05 considered statistically significant.

Inclusion and Exclusion Criteria: Inclusion ofwomen of ≥18years due for various indications willing to participate in the study in third trimester with Singleton cephalic presentation , reactive FHR pattern, Intact membranes, Bishop's score < 5 ,adequate pelvis and Exclusion of women of Parity > 4 / Estimated fetal weight >4 Kg / <2Kg / APH /Fetalcongenital anomaly/ previously scarred uterus /severe oligohydramnios / polyhydramnios, / chorioamnionitis/ known hypersensitivity to prostaglandins or mifepristone/ any maternal medical disorders (Hepatic / renal/ heart diseases ,adrenal insufficiency)

**Outcomes Measured**: Improvement in Bishop's score, Necessity of augmentation of labour with misoprostol/oxytocin, Mode of delivery: normal vaginal/ caesarean section, Induction to delivery interval, Neonatal outcome (Birth weight, APGAR score, NICU admission), Maternal side effects.

## 3. Results & Analysis

**Table 1:** Requirement of misoprostol dosage in the study subjects among the two groups

| Doses | Group A | | Group B | | P value |
|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | |
| 0 doses | 35 | 70.0 | 24 | 48.0 | 0.188 |
| 1 dose | 5 | 10.0 | 13 | 26.0 | |
| 2 doses | 6 | 12.0 | 7 | 14.0 | |
| 3 doses | 1 | 2.0 | 2 | 4.0 | |
| 4 doses | 3 | 6.0 | 4 | 8.0 | |
| Total | 50 | 100.0 | 50 | 100.0 | |
| Mean ± SD | 0.64 ± 1.15 | | 0.98 ± 1.24 | | 0.159 |

**Table 2:** Mode of delivery in the study subjects among the two groups

| Mode of delivery | Group A | | Group B | | P value |
|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | |
| Vaginal | 33 | 66.0 | 31 | 62.0 | 0.391 |
| Instrumental delivery | 3 | 6.0 | 1 | 2.0 | |
| C section | 14 | 28.0 | 18 | 36.0 | |
| Total | 50 | 100.0 | 50 | 100.0 | |

**Table 3:** Indications for C section in the study subjects among the two groups

| Indications | Group A | | Group B | | P value |
|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | |
| Arrest of descent | 3 | 21.4 | 2 | 11.1 | 0.697 |
| Cephalopelvic disproportion | 1 | 7.1 | 1 | 5.6 | |
| Fetal distress | 10 | 71.4 | 15 | 83.3 | |
| Total | 14 | 100.0 | 18 | 100.0 | |

**Table 4:** Comparison of mean induction to vaginal delivery interval with respect to parity

| Parity | Group A (n=36) | Group B (n=32) | P value |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | |
| Primigravida | 22.32 ± 10.47 | 19.92 ± 9.89 | 0.501 |
| Multigravida | 19.24 ± 9.12 | 18.90 ± 9.81 | 0.921 |
| Total Mean | 20.50 ± 0.71 | 19.47 ± 9.64 | 0.662 |

**Table 5:** Maternal side effects and complications among the two groups

| Side effects | Group A (n=50) | | Group B (n=50) | | P value |
|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | |
| Fever | 1 | 2.0 | 1 | 2.0 | 0.245 |
| Headache | 0 | 0.0 | 4 | 8.0 | |
| Nausea | 1 | 2.0 | 0 | 0.0 | |
| Dizziness | 0 | 0.0 | 1 | 2.0 | |
| Vomitting | 1 | 2.0 | 0 | 0.0 | |
| Puerpeural pyrexia | 3 | 6.0 | 2 | 4.0 | |
| Mild PPH | 2 | 4.0 | 3 | 6.0 | |
| Severe PPH (atonic) | 1 | 2.0 | 0 | 0.0 | |
| Wound gaping | 0 | 0.0 | 1 | 2.0 | |
| Uterine hyperstimulation | 0 | 0.0 | 1 | 2.0 | |

**Table 6:** NICU admission of neonates among the two groups

| NICU | Group A | | Group B | | P value |
|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | |
| Yes | 9 | 18.0 | 14 | 28.0 | 0.181 |
| No | 41 | 82.0 | 36 | 72.0 | |
| Total | 50 | 100.0 | 50 | 100.0 | |

In our study majority of subjects were to the age group 21-25 years in both the groups withmean age in Mifepristone group 23.06 ± 2.85years & Foley's group 23.04 ± 2.72 , Age distribution among the two groups were comparable and of normal ranged BMI in both the groups.

The obstetric profile of both groups are comparable ,with 52% of the subjects in Mifepristone group and 64% in Foley's group were nullipara with no statistically significant difference.

Period of gestation for termination of pregnancy were comparable in both the groups with more than 60% of the subjects who required IOL belong to gestational age 39-41wks in both the groups.

The Indication of IOL is HDP (mild pre-eclampsia)and postdatism inmajority of cases with comparaple distribution among both the groups.

Mean pre induction Bishop score in Mifepristone group is 2.90 ± 1.02 &2.62 ± 1.12 in foley's group, which is comparable in both the groups statistically.

In our study >63% of the subjects in Mifepristone group and >51% of the subjects in Foley's group had favourable cervix at the end of 24hrs , which was not of statistically significant outcome, and hence mifepristone was of equal potency as that of Foley's bulb induction.

More requirement of misoprostol dose in Foley's group comparatively, which is not statistically significant, 70% of the subjects in mifepristone and 48% in foley's group did not require dose of misoprostol.

The commonest mode of delivery is vaginal which amounts to >60 % in both the groups. Slightly higher rate of instrumental delivery in Mifepristone group which is of negligible difference statistically.

Majority of the cases were taken up for C-section for fetal distress in both the groups 71.4% and 83.3% respectively). 2 cases in each group had no favourable cervical changes even after the complete dose of misoprostol and were categorised as failed induction and were followed up as per institutional protocols, where as 2 cases in Group A and 1 case in group B delivered vaginally, where as 1 case in Group B was taken for Emergency LSCS with indication of arrest of descent.

Mean duration of labour was 12.16 hrs , 1.03 hrs , 6.95 min in I, II, III stages of labour in Mifepristone group, whereas 10.42hrs , 0.90hrs , 7.06 mins which is comparable.

The mean induction to delivery interval in Primigravida is 22.32 ± 10.47 hours and 19.92 ± 9.89 hours in Foley's group and 19.24 ± 9.12 and 18.90 ± 9.81 in Multigravida , whereas the mean induction to delivery interval irrespective of the parity is 20.50 ± 0.71 and 19.47 ± 9.64 in respective groups which are of comparable values .

The maternal adverse effects were noted in 18% of subjects in Mifepristone group considered individually whereas 12% in Foley's group, Headache took major place in Foley's group which amounts to 8%, side effects were overlapping, and there was no significant difference in side-effects with p value of 0.245 , and no major events were noted such as puerperal sepsis /severe PPH.

In our study group, majority of the babies born were of normal range of birth weight (2.5-4kg) , with good APGAR scores and none of the babies were having severe birth asphyxia, 9 newborns among Group A and 14 among group B were admitted in NICU, with common cause for NICU admission in both the groups was MAS (Meconium Aspiration Syndrome) which accounts for 66% in Mifepristone group and 50% with Foley's group among the total NICU admissions.

## 4. Discussion

Mechanical and Pharmacological cervical ripening agents have differentmechanisms of action, it is plausible that using these methods simultaneously couldproduce synergic effects. Combination methods typically use Foley's catheter withsequential administration of either Prostaglandins or Oxytocin infusions, Mifepristone combined with subsequent prostaglandins is also being commonly used for labour induction after fetal death. The data from women undergoing termination of early pregnancy have shown that Mifepristone is more effective in nulliparous women.

Since Foley's and misoprostol is an accepted combination method we have compared our study with studies done using Mifepristone as inducing agent.

There is thus reason to anticipate that Mifepristone might prove an effective method of inducing labour in late human pregnancy within the safety profile.

Hapangama D (2009) study where Ten trials (1108 women) of Mifepristone were included, and stated that mifepristone treated women were more likely to be in labour or to have a favorable cervix at 48 hours and this effect persisted upto 96 hours Compared to placebo.They were less likely to need augmentation with oxytocin. Mifepristone treated women were less likely to undergo caesarean section but more likely to have an instrumental.[3]

There is insufficient evidence to support a particular dose but a single dose of 200 mg mifepristone appears to be the lowest effective dose for cervical ripening (increased likelihood of cervical ripening at 72 hours.

Not all studies reported on fetal outcome, although abnormal fetal heart rate patterns were more common after mifepristone treatment ,although there was no evidence of differences in admission to a neonatal intensive care unit ( NICU or of neonates having APGAR scores less than seven at five minutes. There was no evidence that neonatal hypoglycaemia might be more common after exposure to mifepristone (it antagonises the action of glucocorticoids as well as progesterone.

The incidence of all reported adverse events was higher in women receiving mifepristone than placebo, however, these seem to be mainly minor gastro-intestinal upsets (nausea, diarrhoea and vomiting). A further study (Wing 2003) has compared the use of mifepristone to oxytocin in inducing labour in pregnancies beyond 36 weeks with prelabor rupture of membranes and women after mifepristone were less likely to have a vaginal delivery within 24 hours and their babies had an increased likelihood of neonatal adverse outcomes with more NICU admissions and abnormal fetal heart rate patterns.[4]

In our study, majority are of nullipara, Parity plays a major role in cervical softening, as parity increases, the cervical length and the fibrosity decreases and has influence on prelabormechanism.

In our study mean BMI in Mifepristone group was 23.97 ± 3.33 and 24.99 ± 3.60 in Foley's group which is comparable with other studies. BMI is one of the non-modifiable factor which affects success of IOL, BMI of 40Kg/$m^2$ has a negative predictive value on success of IOL, otherwise no much difference noted regarding BMI influence on success of IOL.

In our study Mean pre induction Bishop's Score in Mifepristone group was 2.90 ± 1.02 & 2.62 ± 1.12 in Foley's group with p-value 0.194. According to Kanan Y et al[5] study mean pre induction Bishop score in Mifepristone group was 2.02 ± 0.749 and 2.16 ± 0.77 in placebo group which was comparable in both the studies.

In our study Bishop's Score after 24hrs in Mifepristone group was 5.72 ± 1.42 and 5.50 ± 1.03 in Foley's group. As per Kanan Y et al[5], post induction Bishop's score in Mifepristone group was 5.0408 ± 1.90, which is comparable with our study, improvement in Bishop's score was 2.80 ± 1.34 in Mifepristone group and 2.88 ± 1.17 in Foley's group, which is comparable to each other and can be stated Mifepristone is almost of equal efficacy that of Foley's bulb. In KananY et al[5] study statistically significant improvement was observed in mean Bishop's score in Mifepristone Group at the end of 24 h. Wing et al[3]demonstrated more women had favourable Bishop score after 24 h of mifepristone than placebo though the difference was not found to be statistically significant. Athawaleet al[6] and Fathima et al[7] also noted the significant change in Bishop score with the use of oral mifepristone. Another study by ArchanaA et al[8] study suggests improvement in the Bishop's score was significant in Group A with T. Mifepristone with T. Misoprostol than only with T. Misoprostol in Group B which was statistically significant. Mean pre-induction Bishop's score was 4.50 in Group A. It was increased by 6.80 in 6 hrs and 8.22 after 12 hrs. The mean pre induction Bishop's score was 4.72 in Group B. It was increased to 5.94 in 6 hrs and 7.81 after 12 hrs. Other studies mentioned above and also our study is of the opinion that mifepristone will definitely improve the Bishop's score favouring vaginal delivery either when used alone or in combination with misoprostol.

In our study, Mifepristone subjects did not require misoprostol when compared to Foley's (70% and 48% respectively). There is definite decrease in the misoprostol requirement in Mifepristone group compared to Foley's but not statistically significant. Study of Kanan Y et al[5] found statistically significant decrease in the requirement of misoprostol with prior use of mifepristone, there results were consistent with the literature that shows decreased prostaglandin requirements when Mifepristone is given.

Frydmannet al[9] also reported 3 % women went into labor within 24 h of ingestion of Mifepristone. Hapangama and Neilson[3] 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 our study majority delivery is vaginal in both the groups, that is 72% in Mifepristone group 64% in Foley's group, 6% instrumental delivery in Mifepristone and 2% in Foley's. In Kanan Y et al[5] thirty-four (68 %) women delivered vaginally between 24 and 48 h, there were 6 (12 %) caesareans and 2 (4 %) instrumental deliveries in Study Group, which is comparable with our study. Similar results were reported by Wing et al[4].Hapangama and Neilson[3] reported that mifepristone treated women were less likely to undergo caesarean section as a result of failure of induction. Sailathaet al[10] found that chances of failure of induction was lesser with mifepristone than dinoprostone and mifepristone did not increase the incidence of fetal distress.

All these studies including ours indicates successful vaginal delivery, which is more with mifepristone when compared with placebo or Foley's catheter, though in some cases it is yet statistically significant.

In our study, the mean induction delivery interval in Mifepristone group is 20.50 ± 9.71 hours and 19.47 ± 9.64 hours in Foley's group. The induction delivery interval in Mifepristone group is slightly greater than the Foley's group which is comparable.

Similar to our study Sailatha et al[10] stated that The mean I-D internal was 20.3 h (±15) h in Mifepristone group which was compared to Dinoprostone gel which accounts to 11.5 h study(±8.7 ), with significant difference.

In our study most common indication for LSCS is Fetal distress , mainly meconium stained liquor in early labour ,which accounts for 71.4 %(10 cases) in Mifepristone group &83.3%(15 cases) in Foley's. 21.4% and 11.1% done for arrest of descent in Mifepristone and Foley's group respectively. Similar results are seen with the study by Sailatha et al[10].

In our study group adverse neonatal outcome as MSAF, BA leading to RDS and HIE for which NICU admission needed were noted. 18% in Mifepristone group and 28% in Foley's group needed NICU admission. The common cause for NICU admission in both the groups is MSAF which accounts for 66.7% in Mifepristone group and 50% with Foley's group probably because of the association of majority cases with posdatism. Birth asphyxia (BA) accounts for 22% in Foley's group and 0% in Foley's group with perinatal death cause being sepsis. Hapangama and Neilson[3] reported abnormal fatal heart rate pattern, common after mifepristone treatment (RR 1.85, 95 % CI 1.17–2.93), but there was no difference in other neonatal outcome .We did not have much of abnormal fetal heart rate pattern in mifepristone group compared to this.Mifepristone did not pose any risk to the fetus in the observations of our study.

Maternal complications such as puerperal pyrexia is seen in 6% cases with Mifepristone group and 4% cases with Foley's group. PPH is 6% in Mifepristone group and 6% in Foley's group.2% in Foley's group presented with episiotomy wound infection. In Athawale et al[6] study the majority did not have any major complications in either of the group like sepsis, pulmonary embolism and PPH, just few minor genital tract injuries but the difference was not significant statistically in the study group.

Combination of mifepristone and misoprostol is more effective method of achieving vaginal delivery with minimum requirement of misoprostol, decreasing the C-section rates when compared to combination of Foley's catheter and misoprostol. Foley's catheter though safe, effective, simple, low cost method in unfavorablecervix, it fails to gain women/ caregiver's satisfaction. Mifepristone pretreatment in attaining the same, with dual role as a cervical ripening and labor inducing agent has definite comparable efficacies with Foley's induction. A similar larger study and inference about the safety profile of mifepristone would make it more applicable in daily obstetric care.

## 5. Conclusion

This prospective and comparative study depicted comparable efficacy and fetomaternal outcome in terms of pregnancy who were induced with Mifepristone and Foley's catheter. Foley's catheter & Mifepristone are effective agents for cervical ripening, Mifepristone an antiprogestin is more effective agent in minimizing the need for misoprostol dosages in achieving vaginal delivery, and decreasing the C-section rates when compared to Foley's induction. Foley's catheter though safe, effective, simple, low cost method for Induction in unfavorable cervix, it fails to gain woman's satisfaction/caregiver's satisfaction.

Combination of mifepristone and misoprostol is more effective method of achieving vaginal delivery with minimum requirement of misoprostol, decreasing the C-section rates when compared to combination of Foley's catheter and misoprostol.

A similar larger study and inference about the safety profile of mifepristone would make it more applicable in daily obstetric care.

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