Original Article

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# Enlightening a Novel Dimension- Mifepristone in Pre-Induction Cervical Ripening in Term Pregnancy

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**Abstract**

*Introduction:* Mifepristone is a 19-nor steroid that binds to the progesterone receptor and inhibits the activity of progesterone at cellular level. It ripens cervix with minimal effect on uterine contractility, favouring pre-induction cervical ripening to enhance the rate of spontaneous labour without apparent maternal and neonatal side effects.

*Aims and Objectives:*

- To determine the efficacy and safety of Mifepristone to prime the cervix and induce labour at term.
- To compare the effect of Mifepristone with placebo on cervical ripening before labour induction in term pregnancy.

*Material and Methods:* 100 patients with singleton pregnancy of 37-42 weeks with Modified Bishop's score ≤ 5 were included in the study after their informed consent.

*Exclusion Criteria:* Cephalopelvic disproportion

- Previous LSCS
- Hypersensitivity to Prostaglandins and Mifepristone

Patients were given either oral Tablet Mifepristone 200mg (n=50) or Placebo (n=50) after assessing Modified Bishop's score. Change in Modified Bishop's score is assessed after 24 hrs and 48 hrs. Even after 48 hrs if labour had not begun or Modified Bishop's score ≤ 5 induction with Prostaglandin E2 0.5mg gel or Prostaglandin E1 tablet 25 μg done.

*Results:* Out of 100 patients, 29 patients entered spontaneous labour within 48 hrs, of which 19 were treated with Mifepristone (38%) & 10 with placebo-(20%). 9 of Mifepristone treated (18%) & 3 of placebo treated (6%) patients required only oxytocin for labour augmentation. 59 patients required Prostaglandins for induction, of which 22 were Mifepristone treated (44%) & 37 Placebo treated (74%). Mifepristone treated patients had 72% vaginal delivery rate with reduced induction-delivery interval while it was 46% with placebo. Cesarean rate was 14% in those treated with Mifepristone while 42% with placebo. There was no statistical difference in instrumental delivery. There was no significant difference in intrapartum uterine contractile abnormality and fetal heart rate pattern. There was no significant difference in neonatal outcome measured by APGAR score and NICU admission.

*Conclusion:* Mifepristone is safe & efficient in cervical ripening and initiation of labour at term with increased chance of vaginal delivery in 48hrs.In this era of high primary cesarean rates, Mifepristone provides a new milestone to enhance vaginal delivery rates with safe maternal and neonatal outcome. Theme: "Let Mifepristone unveil the curtains to a new era with drastically decreased primary cesarean rates"

**Keywords:** Mifepristone; Term Pregnancy; Cervical Ripening; Vaginal Delivery; Cesarean Rate.

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## Introduction

Mifepristone (RU 486) is a 19-nor steroid that strongly binds to the progesterone

receptor and inhibits the activity of progesterone at cellular level [1]. It also has potent anti-glucocorticoid and weak anti-androgenic actions [1]. It has the ability to ripe cervix with additional effect on uterine contractility. It sensitizes the uterus to prostaglandins and oxytocin. It also blocks the progesterone receptors in the placenta, resulting in termination of pregnancy. Hence it can be used for pre-induction cervical ripening to enhance the rate of spontaneous labour without apparent maternal and neonatal side effects [1-3].

*Aims and Objectives*

- To determine the efficacy and safety of Mifepristone to prime the cervix and induce labour at term.
- To compare the effect of Mifepristone with placebo on cervical ripening before labour induction in term pregnancy

## Material and Methods

A prospective, simple randomised study was conducted on 100 patients with term pregnancy with Modified Bishop's score ≤ 5, after their informed consent at Adichunchanagiri Institute of Medical Sciences, B.G. Nagara, Karnataka.

*Inclusion Criteria*

- Singleton pregnancy of 37-42 weeks of gestation in cephalic presentation
- Modified bishop's score ≤ 5

*Exclusion Criteria*

- Cephalopelvic disproportion
- Previous LSCS
- Hypersensitivity to Prostaglandins and Mifepristone
- Medical disorders like renal, cardiac, hepatic disorders

Patients were given either oral Tablet. Mifepristone 200 mg (n=50) or Placebo (n=50) after assessing Modified Bishop's score. The change in Modified Bishop's score was assessed after 48 hrs. Incase even after 48 hrs if labour had not begun or Modified Bishop's score ≤5, induction with Prostaglandin E2 0.5mg gel or Prostaglandin E1 tablet 25 µg was done.

## Results

Those 50 patients who received Mifepristone were in the study group and 50 patients who received placebo were in the control group. The characteristics of the two groups were matched with similar maternal age, gestational age and gravidity.

In our study, out of the 100 patients, 58 were primigravida and 42 were multigravida. Modified Bishop's score at the time of admission was ≤3 in 56 patients, of which 27 were in study group and 29 in control group. Modified Bishop's score was 4-5 in 44 patients, of which 23 were in study group and 21 in control group. After 48 hrs the Modified Bishop's score were re-assessed and results are in table. 29 patients entered spontaneous labour after or within 48 hrs, of which 19 were given Mifepristone (38%) and 10 were placebo treated (20%). 9 of those treated with Mifepristone (18%) and 3 of those treated with placebo (6%) required only oxytocin augmentation to deliver. 59 patients required Prostaglandins for further induction of which 22 belonged to Mifepristone group (44%) and 37 were from Placebo group (74%). Mifepristone treated patients were associated with an increased chance of vaginal delivery 72% when compared to 46 % in placebo treated patients. The induction to delivery interval was 2874 min in the study group and 3326 min the control group. There is no significant difference in the rate of instrumental delivery.

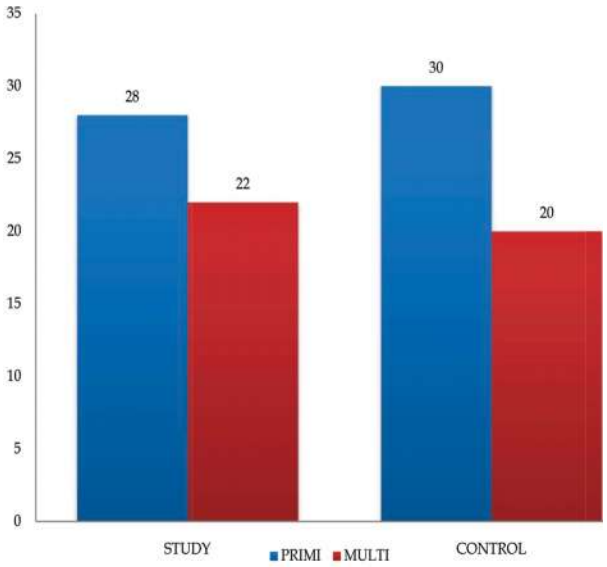
In the study group, caesarean rate was significantly lower in those treated with Mifepristone (14%) when compared to control group (42%). The rate of failed induction was also low in Mifepristone group(4%) when compared to Placebo group(24%).There is no statistical difference with regard to intra-partum abnormal foetal heart rate patterns and intra-partum uterine contractile abnormalities. There was no statistical difference in Meconium stained Amniotic Fluid. There was no statistical difference in neonatal outcome of both groups with regard to Apgar score and admission to NICU.

**Table 1:** Comparison of parity

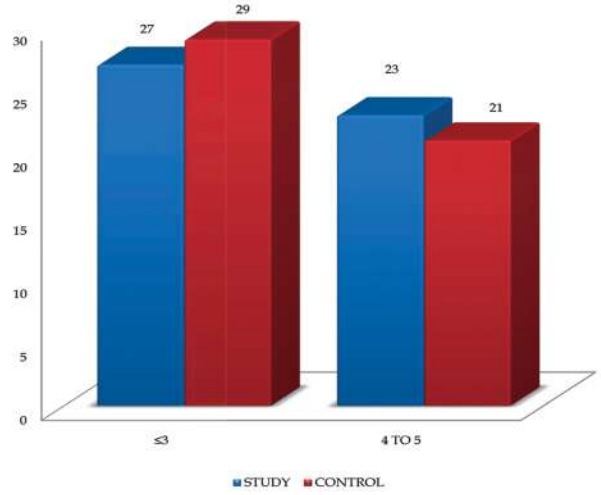
| | Study (n=50) | Control (n=50) |
|---|---|---|
| Primi Gravida | 28 (56%) | 30 (60%) |
| Multi Gravida | 22 (44%) | 20 (40%) |
| Total | 50 | 50 |

**Table 2:** Modified bishop's score at admission

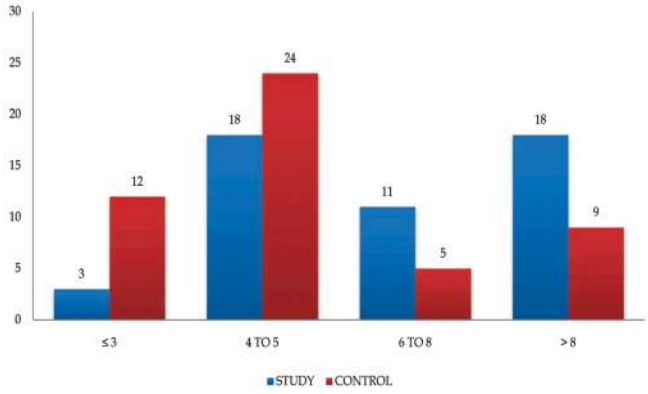
| Modified Bishop's Score At Admission | Study (n=50) | Control (n=50) |
|---|---|---|
| ≤3 | 27 (54%) | 29 (58%) |
| 4-5 | 23 (46%) | 21 (42%) |



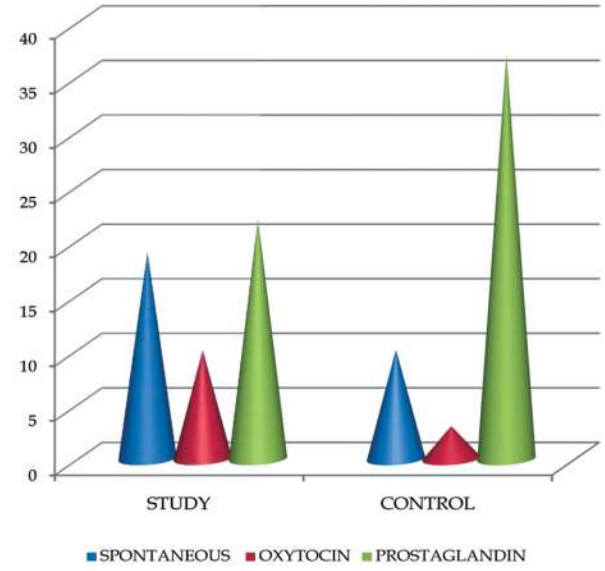

**Graph 1:** Comparison of parity




**Graph 2:** Modified bishop's score at admission




**Graph 3:** Modified bishop's score after 48 hrs




**Graph 4:** Requirement of oxytocin & prostaglandin

**Table 3:** Modified bishop's score after 48 hrs

| Modified Bishop's Score After 48 Hrs | Study (N=50) | Control (N=50) |
|---|---|---|
| ≤3 | 3 (6%) | 12 (24%) |
| 4-5 | 18 (36%) | 24 (48%) |
| 6-8 | 11 (22%) | 5 (10%) |
| >8 | 18 (36%) | 9 (18%) |

The chi-square statistic is 11.5071. The *p*-value is 0.009277. The result is significant at $p < 0.05$.

**Table 4:** Requirement of oxytocin & prostaglandin

| | Study (N=50) | Control (N=50) |
|---|---|---|
| Spontaneous Labour | 19 (38%) | 10 (20%) |
| Oxytocin | 9 (18%) | 3 (6%) |
| Prostaglandins | 22 (44%) | 37 (74%) |

The chi-square statistic is 9.6067. The *p*-value is 0.008202. The result is significant at $p < 0.05$

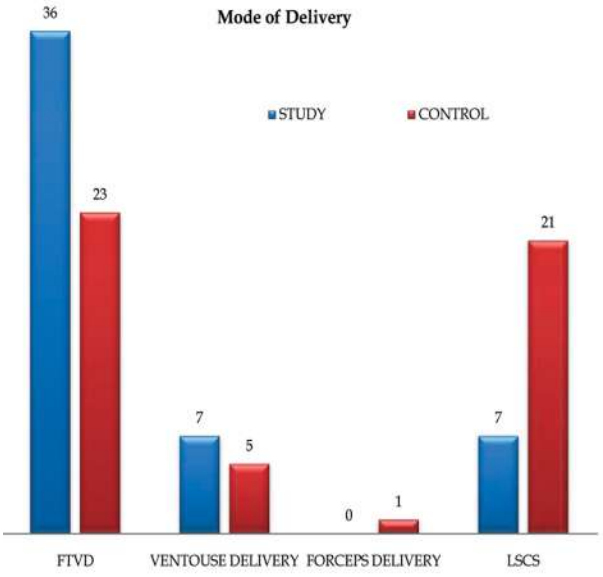
**Table 5:** Mode of delivery

| Mode of Delivery | Study (N=50) | Control (N=50) |
|---|---|---|
| FTVD | 36 (72%) | 23 (46%) |
| Vento use Delivery | 7 (14%) | 5 (10%) |
| Forceps Delivery | 0 | 1 (2%) |
| LSCS | 7 (14%) | 21 (42%) |

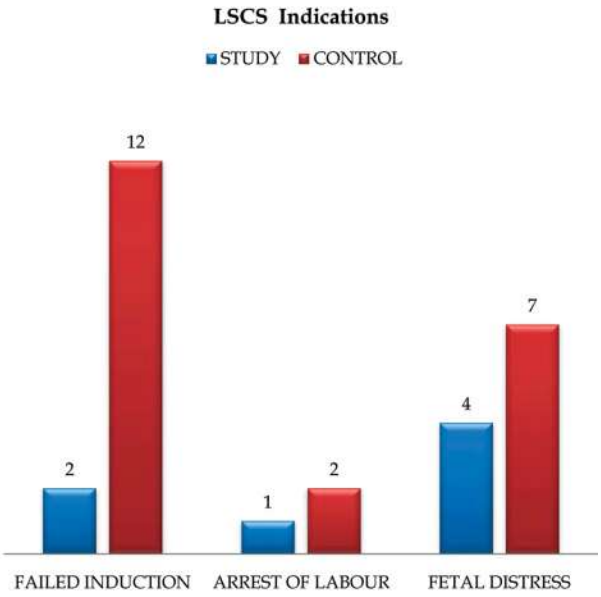
The chi-square statistic is 9.9413. The $p$-value is 0.006939. The result is significant at $p < 0.05$.

**Table 6:** Indications for LSCS

| Indications for LSCS | Study (N=50) | Control (N=50) |
|---|---|---|
| Failed Induction | 2 (4%) | 12 (24%) |
| Arrest of Labour | 1 (2%) | 2 (4%) |
| Fetal Distress | 4 (8%) | 7 (14%) |
| Total | 7 (14%) | 21 (42%) |



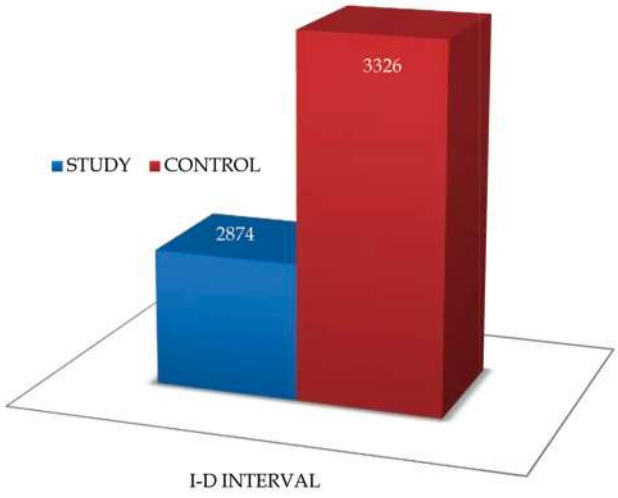

**Graph 5:** Mode of delivery




**Graph 6:** Indications for LSCS

**Table 7:** Mean induction to delivery time

| | Study (N=50) | Control (N=50) |
|---|---|---|
| Mean Induction-Delivery Interval | 2874 min | 3326 min |




**Graph 8:** Intrapartum uterine contractile abnormality

**Table 8:** Intrapartum uterine contractile abnormality

| Uterine Contractile Abnormality | Study (N=50) | Control (N=50) |
|---|---|---|
| Tetanic Uterine Contractions | 0 | 0 |
| Tachysystole | 0 | 1 (2%) |

**Table 9:** Comparison of meconium stained amniotic fluid

| Meconium Stained Amniotic Fluid | Study (N=50) | Control (N=50) |
|---|---|---|
| Thin | 6 (12%) | 5 (10%) |
| Moderate | 2 (4%) | 2 (4%) |
| Thick | 3 (6%) | 4 (8%) |
| Total | 11 (22%) | 11 (22%) |

The chi-square statistic is 0.2338. The *p*-value is .889689. The result is *not* significant at $p < .05$.

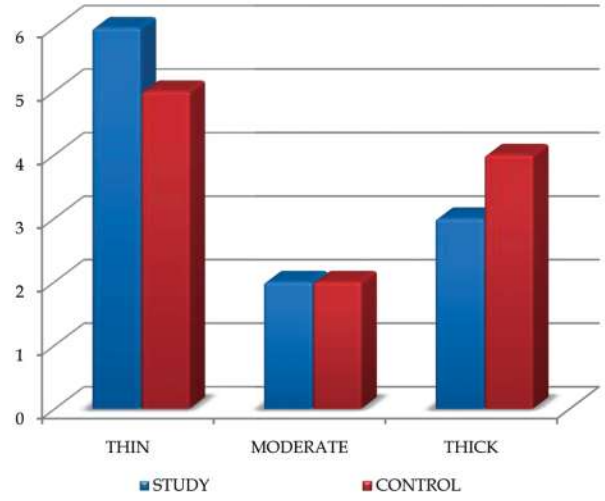
**Table 10:** Comparison of apgar score of <7 at 1 min & 5 mins

| APGAR <7 | Study (n=50) | Control (n=50) |
|---|---|---|
| 1 Minute | 4 (8%) | 6 (12%) |
| 5 Minutes | 0 | 2 (4%) |

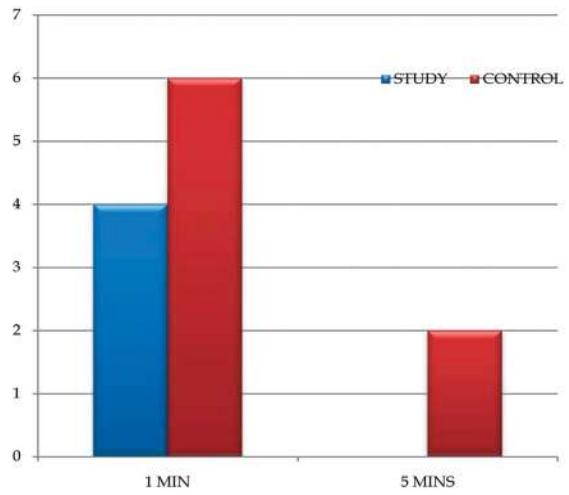
The fisher exact test statistic value is 0.515152. The result is *not* significant at $p < 0.05$.

**Table 11:** Comparison of NICU admission

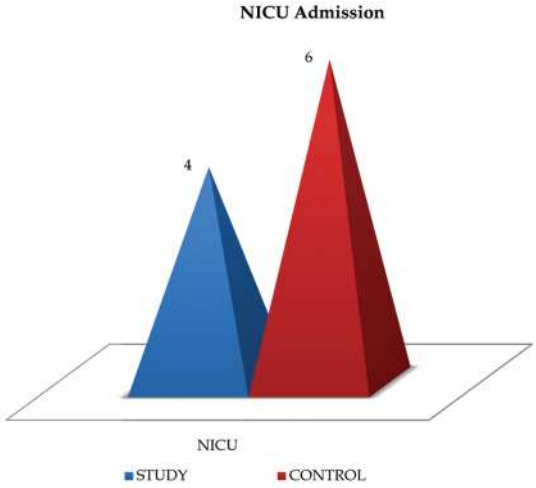
| | Study (n=50) | Control (n=50) |
|---|---|---|
| NICU Admission | 4 (8%) | 6 (12%) |




**Graph 9:** Comparison of meconium stained amniotic fluid




**Graph 10:** Comparison of apgar score of <7 at 1 min & 5 mins




**Graph 11:** Comparison of nicu admission

## Discussion

In our study of 100 patients, 29 patients entered spontaneous labour after or within 48 hrs, of which 19 were given Mifepristone (38%) and 10 were placebo treated (20%). This was in accordance to the study by Lelaidier et al [2], where the rate of spontaneous labour after 48 hrs was 33% with those given Mifepristone. 9 of those treated with Mifepristone (18%) and 3 of those treated with placebo (6%) required only oxytocin augmentation to deliver. 59 patients required Prostaglandins for further induction of which 22 belonged to Mifepristone group (44%) and 37 were from Placebo group (74%). These results were correlating with the studies conducted by Yelikar et al [3], Frydman et al [4] and Athawale R et al [5]. Mifepristone treated patients were associated with an increased chance of vaginal delivery 72% when compared to 46% in placebo treated patients with reduced induction to delivery interval. These results were in accordance to the study conducted by Athawale R et al where the rate of vaginal delivery was 76% compared to 36% in placebo treated [5]. However the study conducted by Berkane N et al in 2005 concluded that Mifepristone, even up to the dose of 600mg does not induce labour within 54 hrs in unfavourable cervix [6].

In the study group, caesarean rate was significantly lower in those treated with Mifepristone (14%) when compared to control group (42%). Mifepristone was better than placebo in reducing the likelihood of Caesarean sections performed for failed induction of labour. This result was in accordance to the studies of Gallot D et al [7], Wing et al [8] and Stenlund et al [9]. There is no significant difference in the rate of instrumental delivery.

There is no statistical difference with regard to intra-partum abnormal foetal heart rate patterns and intra-partum uterine contractile abnormalities. In the study by Wing et al revealed higher uterine contractile abnormalities and non-reassuring FHR patterns in Mifepristone treated patients, most of which were during active phase of labour, though they were not statistically significant [8]. There was no statistical difference in neonatal outcome of both groups with regard to APGAR score and admission to NICU. These were in accordance to various studies of Lelaidier et al [2], McGill et al [10], Elliott CL et al [11] Shanitha Fathima et al [12].

## Conclusion

Mifepristone is a safe, efficient agent for cervical ripening and initiation of labour at term. It is associated with increased chance of vaginal delivery in 48 hrs with decreased incidence of Caesarean section without increase in maternal and neonatal complications. In this era of increased primary Caesarean section rates Mifepristone provides a new milestone to enhance vaginal delivery with safe maternal and neonatal outcome.

*"Let Mifepristone Unveil the Curtains to a New Era with Drastically Decreased Primary Caesarean Rates!! "*

*Ethical Approval*

The study was approved by the Institutional Ethical Committee. Informed consent was obtained from all the women before including in the study.

*Conflict of Interest*

No conflict of interest to declare.

*Funding*

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