International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Lata G et al. Int J Reprod Contracept Obstet Gynecol. 2018 Dec;7(12):5041-5044
www.ijrcog.org

pISSN 2320-1770 | eISSN 2320-1789

DOI: http://dx.doi.org/10.18203/2320-1770.ijrcog20184963

Original Research Article

Mifepristone for cervical ripening and induction of labour

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Received: 02 October 2018
Accepted: 22 October 2018

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ABSTRACT

Background: The study was aimed to evaluate the efficacy of Mifepristone for induction of labour and in improving the Bishop score at term. The study also aimed to assess induction delivery interval and maternal and fetal outcomes with Mifepristone.
Methods: The study was carried out on 200 pregnant females with 2 study groups of 100 each. Group A females received tablet Mifepristone 400mg and Group B females received placebo.
Results: Time interval between induction to onset of labour was 28 hours 54 min and 42 hours 18 min respectively in cases and control group. Mean induction delivery interval was 35 hours 38 min and 49 hours 52 minutes respectively in cases and control group. LSCS rate was less with Mifepristone group.
Conclusions: This study showed that treatment with Mifepristone is a simple and effective method of inducing labour in women with term pregnancy with unripe cervix. The use of Mifepristone provides an interesting new alternative to classic uterotonic agents when induction is necessary. The potential advantage of Mifepristone over PGs or oxytocin requires further evaluation in scarred uterus.

Keywords: Lower segment caesarean section, Mifepristone, Prostaglandins

INTRODUCTION

In an ideal world all pregnancies would go to term and labour would begin spontaneously. The progress of Medicine in general and of Obstetrics has allowed the termination of pregnancy at term or close to term for high risk pregnancies with maternal or foetal indication.

Induction of labour is defined as an intervention designed to artificially initiate the uterine contractions leading to progressive dilation and effacement of cervix and birth of the baby. It is indicated only when it is agreed that mother or foetus will benefit from healthy outcome than if birth is delayed. The state of cervix is a major contributor for successful labour. When delivery is necessary, and ripening has not had time to occur this natural process has to be accelerated. [1] The status of cervix can be assessed by Bishop pelvic scoring system. Bishop score of less than 6 usually requires cervical ripening agent.[2] A number of folkloric or old wives´ tales are still used today.

Among the more common approaches are frequent walking, vaginal intercourse, heavy exercise, consumption of laxatives, spicy foods, nipple stimulation and administration of enema.[3,4]

But techniques of inducing labour have changed to physical stimulation mainly achieved by cervical stretching and amniotomy and more recently to oxytocin and prostaglandins, antiprogestins, nitric oxide (NO), relaxin and other complementary methods.[1,5] Oxytocin

has been safely used for decades and the results are satisfactory for labour induction.[5] By the mid 1980s the prostaglandins (PG) had become established as the most effective pharmacological agent for inducing labour when cervix is unripe.

Mifepristone (RU-486) was discovered by Roussel Uclaf of France in 1980 while they were studying glucocorticoid receptor antagonists. The drug was first licensed in France in 1988, for use in combination with a prostaglandin, under the name Mifegyne.

It is used as an abortifacient in the first two months of pregnancy, and in smaller doses as an emergency contraceptive.[6] As it is a 19 nor - steroid which has greater affinity for progesterone receptors than does progesterone itself, it blocks the action of progesterone at the cellular level. It antagonizes progesterone and thus increases sensitivity of the uterus to prostaglandins and initiates the labour.[7]

Mifepristone has been recently used in post-term pregnancies in comparison with a group receiving placebo. When compared to placebo, there is evidence that risk of C-section is lower with Mifepristone.[8]

It probably is a new field for future research on cervical ripening and labour induction in viable pregnancies. But more research is needed to establish the optimal application, safety and efficacy of Mifepristone as an agent for cervical ripening and labour induction.

METHODS

The study was carried out in Department of Obstetrics and Gynaecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla, on 200 pregnant females scheduled for planned delivery for various indications. Subjects were divided into 2 groups with 100 each. Group A received tablet Mifepristone 400mg and Group B received placebo in form of vitamin C.

Inclusion criteria

Singleton pregnancy with

- Cephalic presentation
- Term pregnancy
- Maternal or foetal indications for labour induction
- Women in whom labour induction could be deferred for 48 hours
- Unfavourable cervix with Bishop's score < 6.

Exclusion criteria

- Non-vertex presentation
- >1 previous caesarean section
- Multiple pregnancy
- Parity 5 or more
- Contraindication to vaginal delivery
- Diabetes Mellitus, renal failure, hepatic disorder, adrenal insufficiency
- Women on aspirin or NSAIDS for last 15 days
- Women on anticoagulant therapy or corticosteroids
- Blood clotting disorders.
- Known hypersensitivity to prostaglandins or Mifepristone.

In all women, history, general physical examination, systemic and obstetrical examination including per vaginum was done and all investigations were carried out. Informed written consent was taken. Bishop's score was assigned before medication. Number of women going in spontaneous labour within 48 hours of administration of the drug was noted. If the labour did not start within 48 hours, vaginal examination was repeated, and Bishop's score was calculated.

If Bishop's score was ≥6, amniotomy was done and oxytocin was started. If Bishop's score still remained unfavourable (<6) then the female was induced with intracervical prostaglandin E2 gel (0.5mg).

Women with previous caesarean section were induced with Foley's catheter. Subjects were assessed after 8 hours and second dose of prostaglandinE2 was instilled if Bishop's score did not improve.

Examination was repeated again after 6 hours of second dose of PGE2 gel and if Bishop's score still remained unfavourable, caesarean section was performed for failed induction.

If at any stage Bishop's score was 6 or more amniotomy was done and oxytocin infusion was started. Active stage of labour was monitored partographically.

Mode of delivery was noted down. Apgar score was recorded. Efficacy of the drug was assessed by the number of women who went into spontaneous labour with-in 48 hours of Mifepristone administration or by Bishop's score of 6 or more at 48 hours.

The statistical difference between two groups was evaluated by using student t test and Chi square test. The p value of <0.05 was considered as statistically significant.

RESULTS

In both groups, age, parity and indication of induction were comparable (Table 1).

Mean age was 25.54 and 25.75 in Mifepristone and control group respectively. Most of the females were primipara in both groups (58 and 52). In both groups most, common indications were postdate pregnancy, PIH and IUGR.

Table 1: Comparison of baseline characteristics expressed as mean values (±standard deviation) or numbers with % in parentheses.

Characteristic	Mifepristone (n=100)	Control (n=100)	p-value
Mean Age (years)	25.54	25.75	0.572
Parity primipara (n)	58	52	0.102
Indications			
Post-term	76	77	0.992
PIH	9	8	
IUGR	11	10	

It was observed that majority of the females had Bishop score 3 before induction. Cervical ripening and onset of spontaneous labour was earlier in Mifepristone group (Table 2).

Table 2: Comparison of characteristics among cases and controls.

Characteristic	Cases	Control	p value
Bishop score before induction	3	3	-
Time interval b/w induction to onset of labour	28 hours 54 min	42 hours 18 min	0.000
Mean induction delivery time	35 hours 38 min	49 hours 52 min	0.000
Unfavourable cervix at 48 hours	20	50	0.000
Mode of delivery by LSCS	10	20	0.124

The mean time interval between induction to start of labour pains was 28 hours 54 min in cases and 42 hours 18 min in control group. This difference was highly significant statistically (p=0.000). During the first 48 hours following treatment, 75 women treated with Mifepristone and 48 treated with placebo went into labour.

Table 3: Comparison of adverse effects of Mifepristone and neonatal outcome among cases and controls.

Characteristic	Cases	Control	p value
Nausea and vomiting	6	2	0.732
Hyperthermia	2	0	
Tahysystole	0	1	
Hypertonicity	0	1	
Neonatal Outcome			
Birth weight	2.75	2.74	
Meconium	8	12	

The statistical difference between the two groups was significant (p=0.048). The mean induction to delivery interval in Mifepristone group was 35.38 hrs and 49.52hrs in placebo group. Induction to delivery interval between the 2 groups was highly significant (p=0.000) (Table 2). There were no significant adverse effects of the drug Mifepristone. Neonatal outcome was comparable in both groups (Table 3). In Mifepristone group 6 patients had nausea and vomiting as compared to 2 in control group. That difference was not significant(p=0.732). Birth weight was comparable in both groups i.e. 2.75 and 2.74kg. There were 8 neonates in Mifepristone group and 12 in control group who had meconium and the difference was not significant.

DISCUSSION

Induction of labour on maternal and fetal indication at or near term is not an uncommon procedure. Various studies have been conducted on Mifepristone for its effect on cervical ripening and labour induction. In Stenlund study, time interval between induction to onset of spontaneous labour is comparable to present study.[9] But results are not exactly comparable to Frydman study because most of the females were around full term in Frydman study as compared to post term in present study (Table 4).[10]

Table 4: Time interval between induction to onset of spontaneous labour.

Mean time interva	Study Group	Control Group
Present Study	28 hours 54 min	42 hours 18 min
Frydman study	51 hours 45 min	74 hours 30 min
Stenlund study	24 hours 10 min	52 hours

During the first 48 hours after the treatment was started 75% women who were given Mifepristone and 48% who were given placebo went into labour. Elliot et al evaluated 2 doses of Mifepristone and compared to placebo for their effect on cervical ripening and induction of labour in women whose cervices were initially unfavorable. In their study, 17 (68%) and 7 (23.3%) patients in the study and control group respectively had labour pains within 48 hours of treatment.

Number of women with onset of labour within 48 hours was significantly more in Mifepristone treated group than in placebo group.[11] Giacolone conducted a study in post term pregnant females with Bishop score less than 6. In their study, 28 (68.3%) patients in study group and 14 (33.3%) patients in control group had onset of labour pains within 48 hours.[12]

In Frydman study, spontaneous onset of labour occurred in 31 (54%) patients in study group but only in 10 (18%) patients in placebo treated females. The number of patients with onset of labour pains within 48 hours of induction was less than the present study. As Mifepristone success is known to increase with gestation age in late pregnancy and especially after 40 weeks, the difference in gestation age at inclusion in present study and Frydman et al study could partly explain our positive result (Table 5).

Table 5. Percentage of women who had labour pains within 48 hours.

%	Study group	Control group
Present study	75	48
Frydman[10]	54	18
Elliot[11]	68	23.3
Giacolone[12]	68.3	33.3

In present study, mean induction delivery time was 35 hours 38 min in study group and 49 hours 52 min in control group. It was significantly more in control group indicating that Mifepristone is an efficient inducing agent at term pregnancy (p=0.000).

In Stenlund and Wing study, the interval between tablets to delivery was significantly shorter in those who had Mifepristone as compared to placebo.[13] It is almost comparable to the present study (Table 6).

Table 6: Mean induction delivery time.

Mean	Study group	Control group
Present study	35 hours 38 min	49 hours 52 min
Stenlund study[9]	36 hours 23 min	53 hours 17 min
Wing study[13]	36 hours 11 min	41 hours 14 min

In present study caesareans were performed in 10% women in group A and 20% in group B. In Stenlund study, 4 (17%) caesareans were performed in Mifepristone group as compared to 3 (25%) in placebo group. It is almost comparable to present study (Table 7).

Table 7: Mode of delivery: LSCS.

Percentage	Study Group	Control Group
Present study	10	20
Stenlund study[9]	17	25

CONCLUSION

The present study showed that treatment with Mifepristone was a simple and effective method of inducing labour in women with term pregnancy and unripe cervix. Cervical ripening was successful in 80% patients in study group as compared to 50% patients in control group.In Mifepristone group 70% patients delivered within 48 hours as compared to 38% patients in control group . Mean induction delivery interval was 35 hours 38 min in study group and 49 hours 52 min in control group.

The use of Mifepristone provides an interesting new alternative to classic uterotonic agents for induction of labour. The potential advantages of Mifepristone over prostaglandins or oxytocin requires further evaluation, mainly for situations in which these are contraindicated as in scarred uterus.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Lata G, Rana N, Mittal R, Kumar S. Mifepristone for cervical ripening and induction of labour. Int J Reprod Contracept Obstet Gynecol 2018;7:5041-4.