Original Article

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Efficacy and safety of oral mifepristone in induction of labour in prolonged pregnancy

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Abstract

Background: Induction of labour implies, achieving vaginal delivery by stimulating uterine contractions before spontaneous onset of labour. Prolonged pregnancy exceeding duration of expected date of delivery is associated with increased risk to foetus and most common indication for induction of labour.

Objectives: To study the safety and efficacy of oral mifepristone in induction of labour in prolonged pregnancy.

Methods: This experimental study was carried out in Universal College of Medical Sciences Teaching Hospital, Bhairahawa between June 2016 to June 2017 after ethical clearance. Total 102 women were included in the study with 51 participants in the study group (mifepristone) and 51 in the control group (misoprostol). Data were expressed in frequency and mean ± SD and analysed using Independent "t" test and Chi-square test. A p-value of <0.05 was considered significant. Safety and efficacy of the drug was analysed with regards to maternal and perinatal outcome.

Results: Single dose of mifepristone was sufficient enough for successful induction in 40 (78.43%) women in study group. Time interval from induction to delivery had maximum frequency of 6-12 hours in both groups (p-value 0.13). The active phase of labour lasted for 2-6 hours in 38 (74.5%) women of the study group. Around 27 (42.9%) women of study group required augmentation of labour and 49 (96.1%) women had vaginal delivery. There was no significant difference in perinatal outcome between both the groups.

Conclusion: Mifepristone combined with or without augmentation is safe, efficient, economical, and convenient induction agent for initiation of labour in prolonged pregnancies.

Key words: Induction of labour; Mifepristone; Misoprostol; Prolonged pregnancy.

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INTRODUCTION

Induction of labour (IOL) implies artificial initiation of regular uterine contractions after 28 weeks of gestation, before spontaneous onset, resulting in progressive effacement and dilatation of cervix, with aim to secure vaginal delivery.[1] Labour is induced when risk of continuing pregnancy outweighs risk of delivery.[1] Prolonged pregnancy is considered indication for IOL as it is associated with increased risk to foetus, including increased perinatal mortality rate, low APGAR scores, and increased risk of death within first year of life.[2]

Mifepristone (RU 486) is 19-norsteroid with specific high affinity binding to progesterone receptor and inhibits activity of progesterone at cellular level with potent antiprogestogenic, antiglucocorticoid, and weak antiandrogenic action.[3] In late pregnancy, uterus is sensitised by mifepristone to prostaglandins and promotes cervical dilatation.[4] Mifepristone is absorbed rapidly after oral administration, reaching maximum

serum levels within two hours and has half-life of about 25 hours.[3,5] Mifepristone has been emerging as newer agent for IOL at term pregnancy. Fewer studies have been conducted on effect of mifepristone on IOL at term with live foetus.

Objective was to study the safety and efficacy of oral mifepristone in induction of labour in prolonged pregnancy and to evaluate its role in cervical ripening along with misoprostol.

METHODOLOGY

An experimental study was conducted in the Department of Obstetrics and Gynaecology, Universal College of Medical Sciences (UCMS) Teaching Hospital, Bhairahawa from June 2016 to June 2017after ethical clearance. Ethical approval was received from the institutional review committee of Universal College of Medical Sciences and Teaching Hospital (Ref. UCMS/IRC/008/16). Informed written consent was obtained from all the participants. Patients with post-dated pregnancy admitted in the labour room who were willing to participate were included in the study by convenience sampling. The majority of participants were in the age group of 20-30 years in both the groups. The women admitted in the labour room meeting the following inclusion criteria were enrolled in the study: Singleton pregnancies with vertex presentation, gravida (one to four), Clinically adequate pelvis, Bishop score of less than six, prolonged pregnancy. Patients with any medical or obstetric contraindication like pregnancy associated with high risk or chronic illness or previous history of caesarean section were excluded.

Total 113 participants who came to the study site during that period were included in the study but 11 of them did not come for follow-up thus complete data could not be collected from them. Therefore, a total of 102 patients were the final participants in the study who were randomly allocated in the two groups: study group and control group, with 51 in each group. The participants in the study group received tab mifepristone and in the control group, they received tab misoprostol. Study participants did not know about the randomisation and group assignment. The participants were asked to randomly pick up the paper chit from the box in which it was written mifepristone and misoprostol and mixed together. After a detailed history, examination, confirmation of diagnosis, investigations, and after informed written consent, women were allocated into two groups. Thus, the participants receiving mifepristone 200 mg tablets were assigned in the study group (n = 51) and those receiving misoprostol 25 µg tablets alone were assigned in the control group (n = 51). All data were collected in a Proforma prepared for this study. The data collected were entered in Microsoft Excel sheet and statistical analysis was done using IBM SPSS Statistics for Windows, version 20 (IBM Corp., Armonk, N.Y., USA). Chi-square and Independent t-test were used to find out the association and differences between two groups.The p-value was calculated under predetermined level of significance set at <0.05.

Oxytocin infusion was started in the active phase of labour, in the absence of adequate uterine contractions: meaning, three uterine contractions for 10 minutes lasting for >30 seconds (secs), four hours after the last dose of tab misoprostol 25 µg administered intravaginally. Maternal pulse rate, blood pressure, and foetal heart rate were monitored every 30 minutes from the time of induction. Once the patient entered into the active phase of labour, partograph plotting was started to monitor the progress of labour. Efficacy of the treatment was compared in terms of Bishop Score, augmentation of labour required or not, duration of the active phase of labour, mode of delivery, baby's outcome, and postpartum complications.

RESULTS

Both the groups were compared for maternal age, parity, and gestational age (Table 1). The mean age of participants in the study group was 23.66 ± 0.78 years whereas that of the control group was 24.29 ± 0.67 years. Both in the study and control group majority of participants were primigravida.

Mean Bishop score prior to cervical ripening and its improvement after 24 hours in both groups are shown in Table 2. In the study group 49 (96.1%) women had normal vaginal delivery and only two (3.9%) women had to undergo LSCS. The indications for LSCS were: foetal distress with meconium stained liquor and non-progress of labour secondary to arrest of descent of head respectively. And in the control group 48 (94.1%) women had normal vaginal delivery whereas three (5.9%) women had undergone LSCS. The operative delivery was performed for failed induction in two women and for foetal distress in one woman. None of the women in both the groups developed any complications in the postpartum period.

Table 3 represents the frequency of requirement of single or multiple doses of drugs for IOL in the study and the control group. In the study group, 40 (78.43%) women achieved successful IOL with single dose of mifepristone whereas seven (13.72%) women required additional

single dose of misoprostol and four (7.84%) women required mifepristone with two doses of misoprostol for successful induction of labour. No women required more than two doses of misoprostol after 24 hours of taking mifepristone in the study group. Similarly, in the control group 31 (60.78%) women achieved successful IOL with single dose of misoprostol but rest of the women required multiple doses of misoprostol. The p-value was 0.68 and was considered as statistically not significant.

In the study group, 27 (42.9%) women required the augmentation of labour with Injection Oxytocin whereas in the control group, 23 (45.1%) women required the augmentation of labour. It was statistically significant with p-value of 0.014.

In the study group, all babies (100%) had an APGAR score of more than 7/10 and 8/10 in one minute and five minutes respectively whereas in the control group 47 (92.2%) babies had 7/10 and 8/10 of APGAR score and two (3.9%) babies had 6/10 and 7/10 of scoring. The remaining two (3.9%) babies had APGAR scoring of 5/10 and 6/10 at one minute and five minutes respectively and required NICU admission. After two days, both the babies were given to their mothers.

Table 1: Baseline characteristics, parity, and gestational age on admission

Characteristics	Study group (*n* = 51)	Control group (*n* = 51)	p-value
Age (years)	23.66 ± 0.78	24.29 ± 0.67	0.155
Parity	1.48 ± 0.64	1.62 ± 0.44	
Primigravida	27 (52.9%)	31 (60.8%)	0.033
Multigravida	24 (47.1%)	20 (39.2%)	
Gestational age (weeks)	40.33 ± 0.73	40.17 ± 0.78	0.046

Table 2: Improvement in Bishop Score with increase in induction duration time in the study and the control group

Variable	Study group (*n* = 51)	Control group (*n* = 51)	p-value
Mean Bishop score at 0 hour	2.02 ± 0.74	2.16 ± 0.77	
Score <3	24 (47.1%)	16 (31.4%)	0.159
Score 3-5	27 (52.9%)	35 (68.6%)	
Mean Bishop score at the end of 24 hours	8.52 ± 1.90	8.11 ± 1.15	0.688
Mean induction to active stage interval (hours)	9.45 ± 0.85	9.61 ± 0.94	0.539
Mode of delivery			
Vaginal delivery	49 (96.1%)	48 (94.1%)	0.051
LSCS	2 (3.9%)	3 (5.9%)	
Mean induction delivery interval (hours)	15.85 ± 0.51	16.14 ± 0.58	0.135

Table 3: Frequency of requirement of single or multiple doses of drugs for IOL, n (%)

Variables	Study group (*n* = 50)	Control group (*n* = 50)	p-value
Single dose (Mifepristone or Misoprostol)	40 (78.43)	31 (60.78)	
Double dose (Mifepristone+ Miso)/ (Misoprostol+Misoprostol)	7 (13.72)	10 (19.60)	0.68
Three doses (Mifepristone+Misoprostol+Misoprostol)/ (Misoprostol+Misoprostol+Misoprostol)	4 (7.84)	10 (19.6)	

Table 4: Augmentation of labour in the study and the control group, n (%)

Augmentation of labour	Study group (n=51)	Control group (n=51)	p-value
Not done	24 (47.1)	28 (54.9)	0.014
Done (Inj. Syntocin)	27 (42.9)	23 (45.1)	

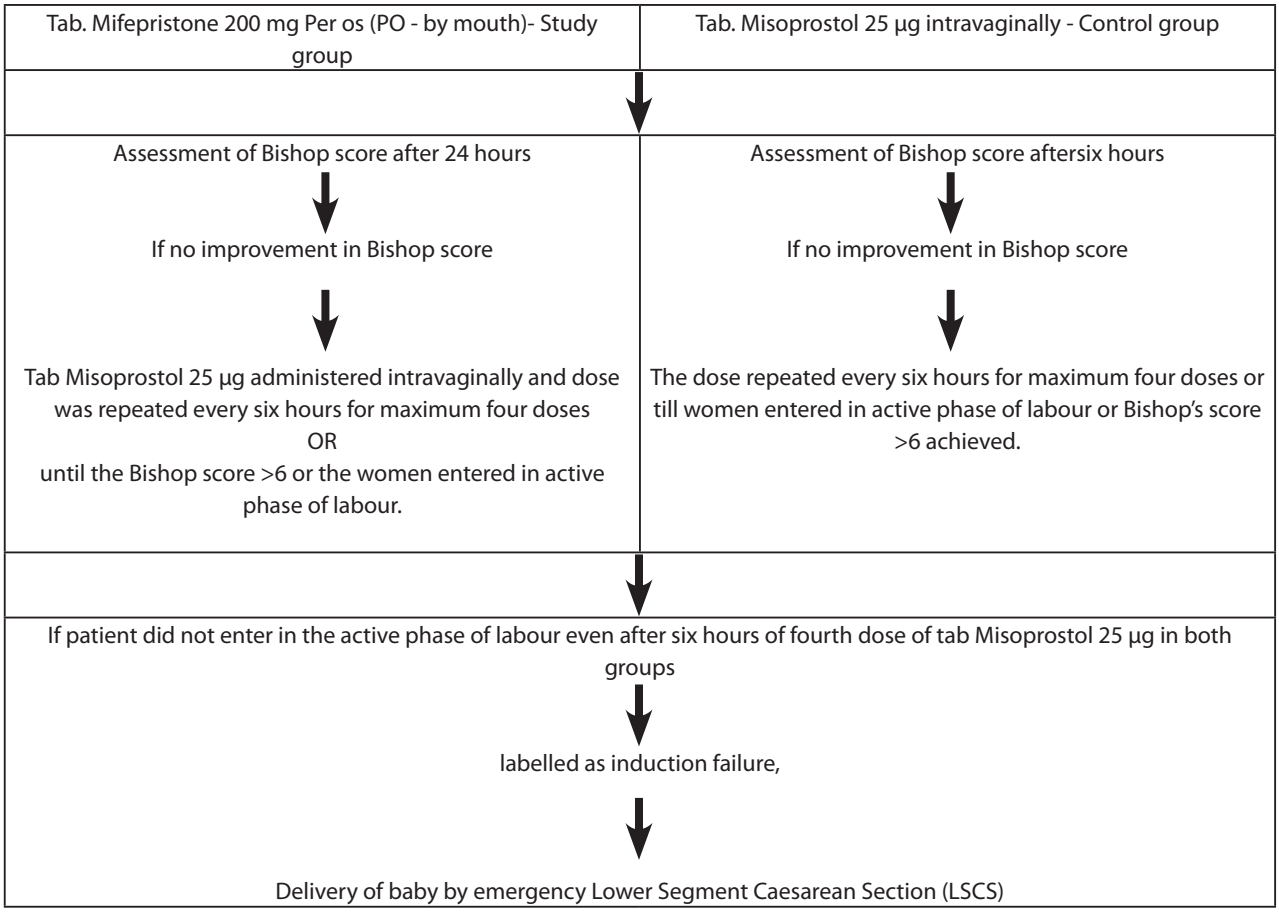

Figure 1: On the day of IOL

DISSCUSSION

This study evaluated 102 cases (with singleton pregnancy with >40 weeks gestational age) who participated in this research for IOL in the maternity unit of UCMS. The result revealed that women who were induced with mifepristone 200 mg orally showed drastic improvement in Bishop score within 24hours with decreased rate of LSCS in the study group which is similar with the study conducted by Frydman et al.[2]

In this study, 27 (52.9%) women were primigravida and 24 (47.1%) women were multigravida in the study group which is statistically significant (p-value 0.033). This is similar to findings of the study conducted by Athawale et al. with 34 (68%) women as primigravida and 16 (32%) women were multiparas.[8] In this study there was a significant improvement in Bishop score in both groups. In the study group all 51 (100%) women went into the active phase of labour with 49 (96.1%) women delivered vaginally whereas in the control group only two (3.92%) women had no improvement in Bishop score and was categorised into failed induction. This result was similar with the study conducted by Yelikar et al. which showed, a significant improvement in mean Bishop score in the study group (5.04082 ± 1.90) compared with the control Group (3.26 ± 1.15).[9] Also similar with the study conducted by Wing et al. which demonstrated more women had favorable Bishop score after 24 hours of oral intake of mifepristone than placebo though the difference was not found to be statistically significant.[10] The cervical ripening ratio was 100%. Athawale et al. and Fathima et al. also noted the significant change in Bishop score with the use of oral mifepristone.[8,11]

The authors found a significant decrease in the requirement of misoprostol with prior use of mifepristone (Table 3). This was found to be statistically not significant with p-value of 0.68 and may be correlated that the women with prolonged pregnancy may have more chances to go in labour with cervical ripening with induction of labour. Yelikar et al. and Wing et al. also reported the reduced need of prostaglandin/oxytocin in the mifepristone group.[9,10] Also Hapangama and Neilson reported that mifepristone treated women were more

likely to be in labour or to have a favourable cervix at 48 hours (risk ratio (RR) 2.41, 95 % confidence interval(CI) 1.70–3.42), and this effect persists at 96 hours (RR 3.40, 95 % CI 1.96–5.92).[4]

In this study, 39 (76.46%) women in study group delivered vaginally within 24hours of induction of labour with single dose of mifepristone as compared to 31 (60.87%) women in the control group, which was similar with findings conducted by Yelikar et al.[9] This was not found to be statistically significant with p-value of 0.135. Incidence of the onset of labour was 100% in the study group which was similar with findings of the study conducted by Athawale et al.[8]

In this study, 49 (96.1%) women had normal vaginal delivery (NVD) and only two (3.9%) women had LSCS in the study group as compared to control group with 48 (94.1%) women having NVD and three (5.9%) women had LSCS. Similar results were reported by Wing et al. and Fathima et al. whereas contrast results were reported by the study conducted by Yelikar et al. which revealed higher incidence of LSCS with 12% in the study group and 16% in the control group underwent LSCS.[9-11] Thus literature supports this finding that women induced with mifepristone are less likely to undergo caesarean section.

Hapangama and Neilson reported that mifepristone treated women were less likely to need the augmentation with oxytocin (RR 0.80, 95 % CI 0.66–0.97) which was similar to this study that revealed 24 (47.1%) women in the study group and 28 (54.9%) women in the control group did not require augmentation with oxytocin which was found to be statistically significant (p-value 0.014).[4] The rate of successful induction of labour in the study conducted by Yelikar et al. was 94%, which was comparable with this study and the study conducted by Wing et al.[9,10] Yelikar et al and Hapangama and Neilson reported abnormal foetal 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.[4,9] In this study, there was no significant impact on foetal heart rate and difference in APGAR score of the baby after delivery as all 100% of babies had APGAR sore of 8/10 or more at five minutes in the study group and did not require NICU admission.

CONCLUSION

In this study it was observed that mifepristone is an effective agent for induction of labour when given 24 hours prior in prolonged pregnancy with reduced need for prostaglandins and can be administered safely with no increase in adverse effect on the foetus or mother. It appears to reduce the need for the augmentation with oxytocin after cervical priming. Mifepristone is also associated with an increase in the chance of vaginal delivery within 24-48 hours with decreasing incidence of LSCS. Thus, mifepristone can be successfully used for cervical ripening and inducing labour in prolonged (post-dated) pregnancies.

Conflict of interest: None
Source(s) of support: None

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