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Induction of labour with mifepristone versus misoprostol and pregnancy outcomes at a rural teaching hospital: A comparative study

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Abstract
Introduction: Induction of labour is mainly attempted when continuation of pregnancy may harm either mother or foetus or both. Different methods of labour induction in full term pregnancy are widely practiced to prevent these complications. There are not enough studies on comparision of mifepristone and misoprostol for induction of labour in full term pregnancy. The present study compared the effectiveness and safety of induction of labour with mifepristone and with misoprostol.
Methods: A hospital based, comparative study on hundred pregnant women admitted with term gestation at Mediciti Institute of Medical Sciences, Ghanpur was carried out from April 2018 to September 2019. Women were divided alternatively into 2 groups with 50 in each group (group 1 mifepristone 200 mg was given & in group 2 misoprostol was given). The primary outcome measures were successful vaginal delivery, induction to delivery interval (first dose of misoprostol / mifepristone to complete delivery of fetus and placenta) and secondary outcome measures were failed induction, mode of delivery, birth weight, meconium stained liquor, fetal distress, NICU admission, primary postpartum haemorrhage.
Results: The mean age of women in group 1 and group 2 was 23 years and 27.8 years respectively. The mean BMI in both the groups was similar (22.63kg/m^2 and 22.27kg/m^2). The mean induction to delivery was 31.34hours in group 1 and in group 2, it was 15.79 hours. This was statistically significant in both groups with favourable and unfavourable cervix (p= 0.00001).
Conclusion: Women induced with misoprostol had higher rates of successful vaginal delivery, shorter induction to delivery interval and better neonatal outcomes when compared to mifepristone.

Keywords: Induction, labour, mifepristone, misoprostol

Introduction
Induction of labour is mainly attempted when continuation of pregnancy may harm either mother or foetus or both. Prolonged pregnancy is associated with significantly increased risk of postpartum hemorrhage, perineal lacerations, oligohydramnios, fetal birth injury, fetal distress in labour, increased rates of cesarean delivery [1]. Different methods of labour induction in full term pregnancy are widely practiced to prevent these complications.
Previous studies have shown that prevention of progestogenic effect by mifepristone promotes cervical ripening owing to action of estrogens such as increase in cervical collagenase and prostaglandin synthetase activity and vaginal misoprostol appears to be safe and effective for cervical ripening in 3rd trimester [2]. It helps vaginal delivery within 24 hours, does not increase incidence of caesarean section and has no adverse effect on foetal outcome [3].
There are studies on comparing effectiveness of oral versus vaginal misoprostol in induction of labour, misoprostol versus combination of mifepristone and misoprostol in induction of labour but there are not enough studies on comparision of mifepristone and misoprostol in induction of labour in full term pregnancy [6]. The present study compared the effictiveness and safety of induction of labour with mifepristone and with misoprostol.

Materials and Methods
A hospital based, comparative study on hundred pregnant women admitted with term gestation at Mediciti Institute of Medical Sciences, Ghanpur was carried out from April 2018 to September 2019. Women presenting to outpatient department/Labour room with term gestation were interviewed & examined clinically. Gestational age at presentation was determined preferably by first trimester scan.

If first trimester scan was not available, then menstrual dating and/or a second trimester scan was considered. Complete blood picture, random blood sugar, blood grouping & typing, complete urine examination, viral screening, serum TSH were done as part of antenatal profile. Dating scan, anomaly scan and growth scan were done routinely. Women of 18 to 35 years age, gestational age 40 weeks and above, singleton, live pregnancy with cephalic presentation with intact membranes were included in the study. Parity greater than 3, women with obstetric complications like hypertension/preeclampsia, prior caesarean deliveries, gestational diabetes mellitus, overt DM, fetal malformations, any medical indications for caesarean section were excluded from the study.

Eligible women were informed regarding details of the study protocol, alternative methods, and the adverse effects of the drugs. Written informed consent was taken from willing participants.

A total of 100 pregnant women with term gestation were included in the study. Women were divided alternatively into 2 groups with 50 in each group (group 1 mifepristone was given & in group 2 misoprostol was given).

Group I (Mifepristone): Women received 200 mg mifepristone rally followed by mifepristone 2nd dose when required after 24 hrs.

If induction of labour was not achieved with 2 doses of mifepristone, such cases were labelled as failed induction and in these cases cerviprime or misoprostol was used.

Group II (Misoprostol): Misoprostol 25micrograms was kept in posterior fornix every 4th hourly for a maximum of 4 doses. Assessment of cervix was based on Bishop scoring.

Induction was considered failed with misoprostol, when vaginal delivery was not achieved with six doses of misoprostol.

Subsequent to induction of labour, vital signs and progress of labor were recorded in modified World Health Organization (WHO) partographs. Active management of third stage of labor was performed. Oxytocin was used for augmentation of labour in active labour if required. Successful treatment was defined as delivery within 48 hours of 1st misoprostol / mifepristone dose in both the groups.

The primary outcome measures were successful vaginal delivery, induction to delivery interval (first dose of misoprostol / mifepristone to complete delivery of fetus and placenta) and secondary outcome measures were failed induction, mode of delivery, birth weight, meconium stained liquor, fetal distress, NICU admission, primary postpartum haemorrhage.

Results

In the present observational study, 100 pregnant women with term gestation were divided alternatively into two groups of 50 each. Group 1 patients received tablet mifepristone and Group 2 patients received only tablet misoprostol.

The age of the women ranged from 24 to 32 years. The mean age of women in group 1 was 23 years and 27.8 years in group 2. Ninety five percent of women belonged to low socioeconomic status. Majority of women were booked in both the groups (96% and 94% respectively). The mean BMI in both the groups was similar (group 1 – 22.6kg/m^2 and 22.27kg/m^2 respectively). Primigravida constituted 52% in group 1 and 60% in group 2. Bishop score was 4-6 in 64% and 70% in group 1 and 2 respectively. The mean induction to delivery interval in women who received mifepristone was 31.3 hours and only 15.79 hours in women who received misoprost. In mifepristone group, 3 out of 50 women needed misoprostol and one women needed cerviprime gel after failed induction with mifepristone. The mean induction to delivery interval was statistically significant in both women with favourable and unfavourable cervix (p= 0.00001). In group 1, 60% of women required only one dose of oral mifepristone. A second dose of oral mifepristone was needed in 40 % of women. In group 2, 32% of women delivered after induction with one dose of misoprostol and 20% of women needed 3 doses of misoprostol.

With respect to mode of delivery, 74% and 66% in group 1 and 2 delivered vaginally. Instrumental delivery was required in 6% and 10% of women in group 1 and 2 respectively. Emergency caesarean section was done in 20% and 24% of women in group 1 and 2 respectively for reasons like non progress of labor and fetal distress. APGAR scores did not vary much in both the groups. NICU admissions were required for 12 % of babies in women who received mifepristone and 4% of babies in women induced with misoprostol. However, this was not statistically significant. There were no cases of uterine tachysystole, hypertonicity primary postpartum haemorrhage observed in both the groups. However, fever was the only side effect noticed in women induced with misoprostol.

Table 1: Demographic details of women from both groups

Age in years	**Group 1 (n= 50)**	**Group 2 (n=50)**	P value
< 20	14 (28%)	15 (30%)	
21-29	34(68%)	35(70%)	
≥ 30	2 (4%)	-	
Mean± SD	23.52±3.48	22.72±2.82	0.2
Booking status			
Booked	44 (88%)	49(98%)	
BMI(kg/m^2)			
< 18.5	9 (18%)	8 (16%)	
18.5-22.9	17 (35%)	23(46%)	
23- 24.9	12 (24%)	7 (14%)	
25- 29.9	10 (20%)	9 (18%)	
≥ 30	2 (4%)	3 (6%)	
Mean±SD	22.63±3.41	22.27±3.93	0.3
Gravida status			
Primigravida	26 (52%)	30 (60%)	0.4
Multigravida	24 (48%)	20 (40%)	

Table 2: Labour characteristics of women from both groups

Bishop Score	**Group 1**	**Group 2**	
< 4	11(22%)	6 (12%)	
4-6	32(64%)	35 (70%)	
>6	7 (14%)	9 (18%)	
Mean±SD	4.68±1.72	5.26±1.61	0.08
Induction to delivery interval (hours)			
1-8	11	7	
9-16	8	24	
17-24	8	12	
25-32	1	5	
33-40	6	1	
41-48	2	1	
49-56	3	-	
>56	11	-	
Mean±SD	31.86±22.93	16.11±8.34	0.00001
Induction to delivery interval in relation to Bishop score	In hours	In hours	
1-2	80	36	
3-4	35.96	18.97	
5-6	24.7	14.43	
7-8	35.1	15.42	

Table 3: Delivery and neonatal outcomes of women from both groups

Sex of baby	Group 1	Group 2	P value
Female	25 (50%)	27 (54%)	
Male	25(50%)	23(46%)	
Birthweight (kg)			
<2.5	1(2%)	5(10%)	
2.5-3	15(30%)	23(46%)	
3-3.5	23 (46%)	20 (40%)	
3.5-4	11 (22%)	2 (2%)	
Mean±SD	3.13±0.39	2.94±0.30	0.06
Mode of Delivery			
Vaginal delivery	37 (74%)	33 (66%)	0.6
Instrumental Delivery	3 (6%)	5 (10%)	
Emergency LSCS	10 (20%)	12 (24%)	
APGAR score at 1 min			
<7	3 (6%)	-	
>7	47(94%)	50 (100%)	
NICU admissions			0.15
Yes	6 (12%)	2 (4%)	
No	44 (88%)	48 (96%)	

Discussion

The present study was conducted in a rural tertiary teaching hospital where majority of women belonged to low socio economic status & usually get married around the age of 20 years and conceive soon. Hence the mean maternal age in the present study was 23.52 years in group 1 & 22.72 years in group 2, which was comparable with Lata G [21] study (mean maternal age in group 1 & 2 was 25.54 yrs & 25.75 yrs respectively) & Nasreen *et al.* [20] study (22±5.2) and Yelikar 2 study (21.36 ± 2.048) but in Oleg R. Baeva [6] study, the mean maternal age was 28.72 ± 4.98yrs.

How close a woman to the onset of spontaneous labour will influence the likelihood that induction of labour will be successful. This is assessed by vaginal examination and cervical status measured using the bishop's score. The five characteristics of Bishops score cervical dilatation, length, consistency, position, and fetal station were assessed. The score was commonly used to predict labour induction outcome. Bishop score of 6 or less identifies an unfavourable cervix and may be an indication for cervical ripening. Bishop score of more than 6 is considered as favourable cervix. Eighty six percent of women in group 1 and eighty two percent in group 2 had unfavourable cervix prior to induction. In the present study, group 1 patients had favourable bishop score when compared with group 1 though the difference was statistically not significant (p=0.08). In Lata G *et al.* [21], Nasreen *et al.* and Yelikar *et al.* [2] studies, the pre induction bishop score was less than 6.

In the present study, the mean induction to delivery interval in group 1 was 31.86 hours and in group 2 was 16.11 hours which was statistically significant (p=0.00001). The reasons for the prolonged induction to delivery interval being 48% of women in group 1 were primigravida and had mean Bishop score of 4.68 when compared to group 2. Primigravida were 40% and mean bishop score was 5.26. In Lata G [21] study shorter induction to delivery interval was seen in women induced with 400 milligrams of Mifepristone when compared to placebo. But in Oleg R Baeva [6], enrollment-induction to delivery interval was shorter in mifepristone group (p<0.001). In Yelikar *et al.* [2] study, the mean induction delivery interval was significantly less in vaginal group (P=0.0001, highly significant). In group 1, caesareans section was required in 20% of the cases, the reasons being fetal distress was seen in 40% of cases, CPD was encountered in 30% and meconium stained liquor was seen in 20% of the cases, non progress of labour in 10% of the cases). In group 2, the caesarean section rate was 24% of the cases, reasons being fetal distress was seen in 60% of the cases, meconium stained liquor was seen in 30% of the cases, non progress of labour was seen in 20% of the cases.

Similarly, rate of caesarean sections in Lata G [21] was lower in cases (mifepristone) when compared to controls who received placebo, the reason being meconium stained liquor. But in Oleg R. Baeva [6] study caesarean rate was more when mifepristone was used for induction of labour when compared to expectant management. Indications for cesarean delivery before labour were: failed induction/expectant management (4 and 2 women) and placenta abruption (2 women). Intrapartum indications for operative delivery by cesarean in induction and expectant management were, respectively: cephalopelvic disproportion in 9 and 2 cases; abnormal fetal heart rate patterns in 4 and 7 cases; protracted/ arrest of active phase in 8 and 6 cases.

In Nasreen [20] *et al.* study, caesarean section was done in 103 (10.8%) cases. The indications for caesarean section were foetal distress in 42 cases (40%), occipito-posterior position in 8 women (7.7%), abruption placentae in 2 cases (1.9%), cord around the neck in 9 women (7%), uterine hyperstimulation in 6 cases (5.8%) and failure to progress in 20 (19%) cases.

In Yeliker *et al.* study, in oral group 26% patients required caesarean section of which 18% were due to fetal distress and one due to impending eclampsia. These cannot be attributed to failure of drug. Three patients in Group A (oral misoprostol) had caesarean section due to non progress of labour due to unforeseen cephalopelvic disproportion. Only three patients in oral group had undergone caesarean section due to failed induction. In vaginal group, out of 17 caesarean sections, 14 patients required LSCS for fetal distress which cannot be attributed to failure of drug, three patients had non progress of labour due to unforeseen cephalopelvic disproportion. None of the patients in vaginal group had caesarean section for failed induction. Overall, caesarean section rate was higher in women induced with mifepristone when compared to expectant management but lesser when compared to induction with misoprostol.

In the present study birth weight was higher in group 1 than in group 2 which was not statistically significant (p=0.06), as in group 1, 46% of the women were multigravidae. The babies tend to weigh heavier as parity increases. Mean birth weight was same in both groups of Lata G [21] study. Similarly, mean birth weight in expectant group was more in Oleg R. Baeva [6] study when compared to mifepristone group but was not significant (p=0.7).

NICU admissions were needed in 12% in group1. Fetal distress was seen in 66%, meconium stained liquor was seen in 33% of the neonates in group 2. Four percent of neonates required NICU admissions and all babies had meconium stained liquor. In Lata G *et al.* study [21], there were 8 neonates in mifepristone group and 12 in control group who had meconium and the difference was not significant. In Oleg R. Baeva [6] study, there were no differences in main neonatal outcomes (weight, height, Apgar score, NICU admission). In Nasreen *et al.* [20] study, NICU admissions were only in 2.95% cases, reasons being meconium stained liquor and prematurity. In Yeliker [2] study, neonatal outcome data showed no significant difference between two groups with respect to birth weights (Group A 2,820 ± 377 g, Group B 2730 ± 447 g t = 1.53, P = 0.12, not significant), meconium aspiration syndrome (6 % in Group A and 11 % in Group B), 1 min APGAR score 7 (30 in Group A, 28 in Group B), NICU admissions (30 in Group A, 28 in Group B).

Conclusion

Women induced with misoprostol had higher rates of successful vaginal delivery, shorter induction to delivery interval and better neonatal outcomes when compared to mifepristone.

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Conflict of interest

The authors declare they have no conflicts of interest.

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