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Comparative Analysis of Safety, Efficacy and Fetomaternal Outcome in Term Live Pregnancy for Induction of Labour with Oral Mifepristone and Intracervical Dinoprostone Gel

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Abstract
Objective*: To compare the efficacy of Mifepristone and Dinoprostone as a cervical ripening agent for induction of labour and also on the status of newborn.*
Methods: *It is a single blind prospective randomized comparative study.One hundred antenatal cases as per the inclusion and exclusion criterias selected. Fifty women received 200mg oral mifepristone as cases and fifty women received 0.5mg dinoprostone gel intracervically as control. Pre induction Bishop's score was assessed just before administration of the drug. Post induction Bishop's score was assessed after 6 hr. in dinoprostone group and after 24 hr. in mifepristone group or with onset of labour, whichever was earlier. Oxytocin augmentation was started in cases with unsatisfactory progress of labour. The newborn was examined immediately after birth, the Apgar score being determined at 5 minutes. Any fetal abnormalities occurring in hospital were noted. All maternal side-effects were recorded.*
Results: *In mifepristone group mean ± S.D of pre induction Bishop's score was 5.04 ± 0.81 and in dinoprostone group it was 5.06 ± 0.71. Post induction Bishop's score in mifepristone group mean ± S.D was 7.96 ±1.01 and in dinoprostone group it was 8.32 ± 1.08. Induction delivery interval in Mifepristone group (mean 28.72 hr.) was more than in dinoprostone group (mean 10.30hr). In mifepristone group 36 out of 50 needs oxytocin augmentation and in dinoprostone group 41 out of 50 needs oxytocin. So there was less oxytocin needed in mifepristone group. There were 11 cases of failed induction in mifepristone group and 13 cases of failed induction in dinoprostone group. Mifepristone group shows less number of failed induction. 2 cases of fetal distress in mifepristone group and 4 cases in dinoprostone group found. There was no significant statistical difference between the two groups (p value = 0.678). There were 36 vaginal delivery in mifepristone group and 31 in dinoprostone group. 13 cases need caesarean section in mifepristone group whereas 17 cases need in dinoprostone group. The number of instrumental delivery in mifepristone group was 1 and in dinoprostone group were 2. There was no significant statistical difference between the two groups (p value = 0.534). two babies in each group had an Apgar score of <7 at 5 minutes and there was no significant statistical difference between the two groups (p value =1.000).There were also two babies in each group need NICU admission and no significant statistical differences seen between the two groups (p value =1.000). The results of the present study show that mifepristone is a simple and effective treatment for inducing labour*
Conclusion: *The results of the present study show that mifepristone is a simple and effective treatment for inducing labour. Mifepristone and Dinoprostone gel are comparable in fetomaternal outcome. Thus, mifepristone can be a safe alternative to dinoprostone gel in induction of labour, especially when prostaglandins are contraindicated.*
Key Words: *Mifepristone, Dinoprostone, Induction of labour.*

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I. Introduction

Induction of labour means initiation of uterine contractions (after the period of viability) by any method (medical, surgical or combined) for the purpose of vaginal delivery. Generally induction of labour is indicated when the benefits of early delivery are greater than the risks of continuing the pregnancy (1) .There are several methods of labour induction, including administration of prostaglandins, prostaglandin analogues, oxytocin and smooth muscle stimulants such as herbs or, castor oil, or mechanical methods such as digital stretching of the cervix and sweeping of the membranes (2) .A successful induction is primarily dependent on the pre-induction Bishop's scoring of the cervix. When the cervix is favorable the usual method of induction is amniotomy and oxytocin, whereas with an unfavorable cervix vaginal prostaglandins are commonly used (3).Dinoprostone is a

synthetic analogue of ProstaglandinE2 (PGE2).Mifepristone is also called as RU (RousselUclaf) - 486.It is 19 norsteroid with potent competitive anti progesterone and significant antiglucocorticoid activity. Mifepristone is used as a pretreatment to prime thecervix adequately(4).Various studies conducted on induction of labor in live term pregnancies with mifepristone in doses of 200-400 mg has shown to improve cervical ripening and rates of spontaneous labor with no apparent maternal or fetal side effects(5).

Aims and objectives: The objectives of this study areto compare the efficacy of Mifepristone and Dinoprostone as a cervical ripening agent for induction of labour, to study improvement in Bishop's score, need for oxytocin in augmentation of labour or not, also to study induction delivery interval, modes of delivery and Neonatal Intensive Care Unit admissions (NICU).

II. Materials and methods

The study was conducted in the Department of Obstetrics and Gynaecology in Burdwan Medical College and Hospital, West Bengal after taking approval from the ethical committe**.**It is asingle blind prospective randomized comparative Study.

One hundred antenatal cases as per the inclusion and exclusion criterias admitted under OBG department, BMCH from December 2015 to November 2016.Antenatal women admitted in labour ward through antenatal OPD werequestionnaired and examined with predesigned and pretested schedule and was selected for study population with certain inclusion and exclusion criteria. Postdatedprimigravida mother aged 18-25 years having singleton live pregnancy with cephalic presentation and mild pre eclampsia (BP140/90 mm Hg but 160/110mm Hg) with Bishop's score<6, were the inclusion criterias. Previous cesarean section,malpresentation, cephalopelvic disproportion, premature rupture of membranes (PROM), severeoligohydramnios, IUFD, multigravidamother, severepreeclampsia (BP160/110 mm Hg) are the exclusion criterias. After proper counselling and taking informed consent from each antenatal mother selected in study population, detailed history and clinical examination was performed. The two groups were matched according to age, gravida, parity, maternal weight, trimester.100 women with above inclusion criteria were divided into two groups, group A and groupB, each having 50 subjects. Group A women received 200mg oral mifepristone as cases and group B women received 0.5mg dinoprostone gel intracervically as control. Pre induction Bishop's score was assessed just before administration of the drug. Post induction Bishop's score was assessed after 6 hr. in dinoprostone group and after 24 hr. in mifepristone group or with onset of labour, whichever was earlier. The dinoprostone gel was administered into thecervical canal just below the level of internal os. The mother was instructed to remain recumbent or lying down on one side for at least 30 minutes after application of gel. Oxytocin augmentation was started in cases with unsatisfactory progress oflabour. Oxytocin was not started for 6 hours following administration of vaginal prostaglandins. If cervix remains unfavorable induction is categorized as failed. If at any time, in either of the groups, progress of labour was unsatisfactory or variable fetal heart pattern was observed, the participants underwent Caesareansection.

The newborn was examined immediately after birth, the Apgar score being determined at 5 minutes. Any fetal abnormalities occurring in hospital were noted. All maternal side-effects were recorded.

A detailed analysis was carried out in both groups regarding efficacy of drugs interms of change in Bishop's score after 24hours in Mifepristone group and after 6 hour in Dinoprostone group or whenever the patient went into labour, whether there is oxytocin augmentation required or not.

Induction delivery interval, mode of delivery, maternal and fetal outcome, fetal distress,APGARscore, NICU admission.All women were followed until delivery and early postpartum period andbabies till early neonatal period. Categorical variables are expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes/ Fisher's Exact Test as appropriate. Continuous variables are expressed as Mean ± Standard Deviation and compared across the 2 groups using Mann-Whitney U test. The statistical software SPSS version 20 has been used for the analysis.

An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

III. Results & Analysis

Table: 1

	Mifepristone Group(Mean±SD)	Dinoprostone Group(Mean±SD)	p Value	Significance
Preinduction Bishops score	5.04 ± 0.81	5.06 ± 0.71	0.873	Not Significant
Postinduction Bishops score	7.96 ± 1.01	8.32 ± 1.08	0.082	Not Significant
Induction delivery interval	28.72 ± 3.24	10.3 ± 2.42	<0.001	Significant

Table: 2

	Mifepristone Group	Dinoprostone Group	p Value	Significance
Need for oxytocin	Yes36	41	0.235	Not Significant
	No 14	9		
Fetal Distress	Yes 2	4	0.678	Not Significant
	No48	46		
Failed Induction	Yes 11	13	0.640	Not Significant
	No 39	37		
Mode of delivery	SVD 36	31	0.534	Not Significant
	IVD 1	2		
	Cs13	17		
Maternal side effect	Vomiting 1	1	1.000	Not Significant
	No side effects 49	49		

Table: 3

	Mifepristone Group	Dinoprostone Group	p Value	Significance
APGAR score < 7 at 5 minutes	Yes 2	2	1.000	Not Significant
	No 48	48		
NICU admission	Yes 2	2	1.000	Not Significant
	No 48	48		

IV. Discussion

Baseline characteristics like age, parity, period of gestation, indication for induction were comparable in both groups. Table No. 1 shows pre induction and post induction Bishop's Score between both groups. In mifepristone group mean ± S.D of pre induction Bishop's score was 5.04 ± 0.81 and in dinoprostone group it was 5.06 ± 0.71.Post induction Bishop's score in mifepristone group mean ± S.D was 7.96 ±1.01 and in dinoprostone group it was 8.32 ± 1.08. Though there was more improvement of Bishop's score in dinoprostone group but no significant statistical difference between the groups found.In their study Sailatha R. et al shows there was statistically significant improvement in Bishop score in favor of dinoprostone (Mean 4.7) than mifepristone (Mean 4.0).(6).VidyaGaikwad, et al showed after induction with Mifepristone 94% women had cervical ripening as compared to 80% with Dinoprostone(7). Our study also resembles those presented by Wing DA.et al where they also found that mifepristone had a modest effect on cervical ripening (8).It had been shown that induction delivery interval in Mifepristone group (mean 28.72 hr.)was more than in dinoprostonegroup (mean 10.30hr). There was significant statistical difference between the two groups (p value =<0.001).The median time from the start of treatment to delivery was 36 hours (Stenlund PM et al, 1999) (9). Mifepristone treated women were have a favorable cervix or in labour at 48 hours risk ratio RR 2.41, 95% CI 1.70 to 3.42 (Hapangama et al) (10). Also,Sailatha R et al (11) in their study showed the induction delivery interval wassignificantly less (Mean 11.5 hrs.) with dinoprostone than mifepristone (Mean20.3 hrs.). In a study conducted by VidyaGaikwad et al (7) rate of successful IOL or vaginal delivery was 84% with mifepristone and 56% with dinoprostone.In their study ShanithaFathima et al demonstrated significant efficacy of mifepristone for cervical ripening and induction of spontaneous labor after drug administration as more women had favorable Bishop's scores at the end of 48hr. (12).In their study YELIKAR K et al showed that themean induction to delivery interval was 1,907 ± 368.4 min for study group and the improvement in mean Bishop score was 5.0408 ± 1.90 for study group.16 % women in study Group delivered vaginally within 24 h without any need of augmentation. YELIKAR K et al (13).

Table 2 shows number of patient requiring oxytocin augmentation in both groups. In mifepristone group 36 out of 50 needs oxytocin augmentation and in dinoprostone group 41 out of 50 needs oxytocin. So there was less oxytocinneeded in mifepristone group. But there was no significant statistical differencebetween the two groups (p value = 0.235).Also mifepristone treated group were less likely to need augmentation with oxytocin RR 0.80, 95% CI 0.66 to 0.97 (Hapangama et al) (10). 20% Mifepristone treated group required Oxytocin for augmentation as compared to 56% in Dinoprostone (VidyaGaikwad et al) (7). There were 11 cases of failed induction in mifepristone group and 13 cases of failed induction in dinoprostone group. Mifepristone group shows less number of failed induction. But there was no significant statistical difference between the two groups (p value = 0.640). Also, Sailatha R et al (11) in their study showed number of cases undergoing LSCS for failed induction was less in mifepristone group (4%).

Table 2 also shows the number of post induction fetal distress in both groups. 2 cases of fetal distress in mifepristone group and 4 cases in dinoprostone group found. There was no significant statistical difference between the two groups (p value = 0.678). There were 36 vaginal delivery in mifepristone group and 31 in dinoprostone group. 13 cases need caesarean section inmifepristone group whereas 17 cases need indinoprostone group. The number of instrumental deliveryin mifepristone group was 1 and in dinoprostone

group were 2. There was no significant statistical difference between the two groups (p value = 0.534).Mifepristone treated women were less likely to undergo caesarean section RR 0.74, 95% CI 0.60 to 0.92, but more likely to have an instrumental delivery RR 1.43, 95% CI 1.04 to 1.96 (Hapangama et al) (10). YELIKAR K et al 16 % women in study group delivered vaginally within 24 hr. without any need of augmentation. There were 6 (12 %) caesareans and 2 (4 %) instrumental deliveries in study Group, YELIKAR K et al (13). Rate of successful IOL or vaginal delivery was 76% in study group, After induction with mifepristone for cervical ripening in study group 76% patient who had cervical score <3 on admission had cervical score improved to>8 within 24 hours RutujaAthawaleet al.(14).The rate of vaginal delivery, caesarean sections, instrumental delivery and overall fetal outcome was comparable in both groups. Sailatha R et al(11).

Table 2 shows the occurrence of maternal side effects (vomiting) between the study and the control group. Both the groups show one case of eachvomiting as a maternal side effect. There was no significant statistical difference between the two groups (p value = 1.000).

Table 3 shows two babies in each group had anApgar score of <7 at 5 minutes and there was no significant statistical difference between the two groups (p value =1.000).There were also two babies in each group need NICU admission and no significant statistical differences seen between the two groups (p value =1.000).The median Apgar score was slightly lower at 1 minute ($p<0.05$) following mifepristone treatment, but did not differ at 5 and 10 minutes (Stenlund PM, et al, 1999) (9).In their study VidyaGaikwad et al (7)among the babies, 6% and 14% belonging to mifepristone and dinoprostone group respectively, required NICU admissions. Among the babies, 36% required baby unit admission in mifepristone groupRutujaAthawale et al(14).Abnormal fetal heart rate patterns were more common after mifepristone treatment RR 1.85, 95% CI 1.17 to 2.93, but there was no evidence of differences in other neonatal outcomes (Hapangama et al).

V. Summary

There was more improvement of Bishops score in Dinoprostone group though statistically it was not significant.
Induction delivery interval less in Dinoprostone group.
There was more incidence of vaginal delivery in Mifepristone group whereas more incidence of caesarean section in Dinoprostone group.
Oxytocin augmentation was more needed in Dinoprostone group.
There was less incidence of failed induction in Mifepristone group.
Less incidence of post induction fetal distress in Mifepristone group.
Maternal complications and NICU admission were same in both the groups.

VI. Conclusion

The results of the present study show that mifepristone is a simple and effective treatment for inducing labour. There is insufficient information available from clinical trials to support the use of mifepristone to induce labour. However the studies suggest that mifepristone is better than placebo in reducing caesarean sections for failed induction of labour.Mifepristone and Dinoprostone gel are comparable in fetomaternal outcome. Thus, mifepristone can be a safe alternative to dinoprostone gel in induction of labour, especially when prostaglandins are contraindicated. Therefore future trials will be needed comparing mifepristone with the routine cervical ripening agents currently in use for inducing labour. There is little information on effects on the baby.

References

[1]. Arulkumaran S. Induction of labour. In: Arjun G,Penna L.The Management of Labour. 3rd ed:University Press,2011.p 368
[2]. S Petrou, SE Taher, G Abangma, O Eddama, P Bennett. Cost- effectiveness analysis of prostaglandin E2 gel for the induction of labour at term. BJOG 2011; 118: 726-734.
[3]. G. K. Pandis, A.T. Papageorghiou, C. M. Otigbah, R. J. Howard and K. H.Nicolaides. Randomized study of vaginal misoprostol (PGE1) and dinoprostone gel (PGE2) for induction of labor at term. 2001; 629-635.
[4]. FrydmanR,Lelaidier C, Baton-Saint-Mleux C, Fernandez H, Vial M,Bourget P. Labor induction in women at term with mifepristone (RU 486): a double-blind, randomized, placebo-controlled study. Obstet Gynecol. 1992 Dec; 80(6):972-5.
[5]. Clark K., Ji, H., Feltovich, H., Janowski, J., Carroll, C., Chien, E.K., Am J ObstetGynecol 2006, 194, 1391-1398.
[6]. Sailatha R et al Mifepristone: an alternate to dinoprostone in induction of labour. Int J ReprodContraceptObstetGynecol 2017; 6:1880-4.
[7]. GaikwadVidya, Mittal Bilsi, MangalPuri. Comparative Analysis of Safety,Efficacy and FetomaternalOutcome ofInduction of Labour with Mifepristone versus IntracervicalDinoprostone Gel.RJPBCS.2014; 5(2):611.
[8]. Fassett MJ, Wing DA. Uterine activity after oral mifepristone administration in human pregnancies beyond 41 weeks' gestation. GynecolObstet Invest. 2008; 65(2):112-5.
[9]. Induction of labour with mifepristone-a randomized, double-blind study versus placebo) Stenlund PM, et al Induction of labour with Mifepristone, - A randomized, double-blind study versus placebo, Volume 78, 1999 ActaObstetriciaetGynecologicaScandinavica.
[10]. DharaniHapangama and James P Neilson, The Cochrane database of systematic reviews Europe PMC Funders, 2009.
[11]. Sailatha R et al Mifepristone: an alternate to dinoprostone in induction of labour. Int J ReprodContraceptObstetGynecol 2017; 6:1880-4.

[12]. FathimaShanitha, Nayak S.R, RaoBharathi, Praveena Gandhi, ShameemV.P.A. Mifepristone in the induction of labour at term.Int J Pharm Biomed Res 2013, 4(3), 164-166.
[13]. Yellikar K, Deshpande S, Deshpande R, Lone D. Safety and efficacy of oral mifepristone in preinduction cervical ripening and induction of labor in prolonged pregnancy. J ObstetGynecol India. 2015; 65(4):221-5.
[14]. AthawaleRutuja , AcharyaNeema, Samal S, Hariharan C .Effect of mifepristone in cervical ripening for induction of labour.International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2013 Mar; 2(1):35-38.

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