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COMPARATIVE STUDY OF MISOPROSTOL SUBLINGUALLY AND DINOPROSTONE GEL INTRACERVICALLY FOR INDUCTION OF LABOUR

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Abstract

BACKGROUND: The incidence of induction varies widely from 5-30%. For majority of women, labour starts spontaneously and results in vaginal delivery at or near term. Sometimes because of medical or obstetric complications of pregnancy, cervical ripening and induction of labour is often required. Induction of labour is indicated when the benefits to either the mother or fetus outweigh those of continuing the pregnancy.

OBJECTIVE: This study was design to compare efficacy of induction of labour with intracervical dinoprostone gel and sublingual misoprostol with respect to induction delivery interval and maternal and fetal outcome of both groups.

Material and Methods: In this study ,a total of 180 pregnant women were recruited and randomized in two groups .GroupA received 25-50µg misoprostol sublingually repeated every 4 hours for maximum of 4-6 doses(maximum of 200 µg) or till patient went into active labour or adequate uterine contraction was achieved.Group B- received cerviprime gel 0.5 mg PGE2intra-cervically just below internal Os,it was repeated till a maximum of 3 doses every 6 hours or till induction achieved.

Results:In both group Postdatism is most common indication. Dinoprostone group required more augmentation of labor (24.5% vs. 13.3%) .The mean induction to delivery interval was shorter in misoprostol group (7.46±2.26 hrs) as compared to dinoprostone group (11.31±2.61) which was statistically significant. In misoprostol group, most common foetal complication was meconium stained liquor which was observed in 14 (15.6%) while in dinoprostone group it was reported in 11 (11.2%) mothers for which LSCS was done.

Conclusion:Sublingual misoprostol significantly reduces the induction to-delivery interval and has fewer induction failures, more successful, stable at room temperature and lower-cost agent for induction of labor than intracervical dinoprostone gel.

Key words: Induction ;Dinoprostone;Misoprostol; Postdated

INTRODUCTION

Induction implies stimulation of contractions before the spontaneous onset of labor, with or without ruptured membranes.The incidence of induction varies widely from 5-30%.The goal of Obstetrics is a pregnancy that results in a healthy infant and a healthy mother. For majority of women, labour starts spontaneously and results in vaginal delivery at or near term. Sometimes because of medical or obstetric complications of pregnancy, cervical ripening and induction of labour is often required. Induction of labour is indicated when the benefits to either the mother or fetus outweigh those of continuing the pregnancy.[1]

Common indications for labour induction include preeclampsia, premature rupture of membranes, chorioamnionitis, intrauterine growth retardation, isoimmunization, maternal medical problems, fetal demise, postdated pregnancy and oligohydramnios. The chief contraindications to labour induction are placenta previa, transverse lie, prolapsed umbilical cord, active genital herpes infection, and pelvic structural deformities, cephalopelvic disproportion. The success of induction depends to a large extent on the consistency, compliance and configuration of the cervix.[2] The unripe cervix thus remains a well-recognized impedent to the successful induction of labour.[3]

An ideal inducing agent is one which achieves labour in the shortest possible time, with a low incidence of failure to achieve vaginal delivery, with no increase in perinatal morbidity compared to spontaneous labour. Pharmacologic agents available for cervical ripening and labour induction include prostaglandins, misoprostol, mifepristone and relaxin. Local application of Prostaglandin E_2 (PGE_2 or Dinoprostone) has been in use for cervical ripening since late 1960s.[4,5]Prostaglandins have dual action of cervical ripening and uterine contraction inducing effect. Prostaglandin E2 (cerviprime gel), a registered inducing agent in many countries is expensive and needs to be refrigerated due to its sensitivity to temperature changes. It is instilled intracervically or placed high in the posterior fornix of the vagina and may need to be re-instilled after 6 h if required.It causes direct softening of the cervix by a number of different mechanisms.[4,5] Another alternative is misoprostol which is used in various dosages. It is stable at room temperature, comparatively cheaper and can be given via several routes (oral, vaginal, sublingual, buccal and rectal).[6]Uterine tachysystole and accompanying foetal distress is reported following administration of PGE_2 in 1 to 5 percent of women .[7]Misoprostol is proposed for induction in WHO model list of essential medicines for labour induction at term to be used in low dose (25-50 microgram).[8]

MATERIAL AND METHODS

The study was a hospital based prospective randomized controlled study extending over a period from October 2018 to August 2019in Obstetrics &Gynaecology department of Dr.Sushila Tiwari Memorial Government Hospital, Haldwani, Uttarakhand, India.

The study population comprised of pregnant women admitted for induction of labour in our labor room at Obstetrics &Gynaecology department of Dr. Sushila Tiwari Memorial Government Hospital, Haldwani, Uttarakhand, India.

Indications for induction in our study were, mild pre-eclampsia, Severe pre-eclampsia, postdated pregnancy, mild polyhydramnios, mild oligohydramnios, gestational diabetes mellitus, chronic hypertension and Rh negativepregnancy.
Inclusion criteria were singleton fetus with cephalic presentation, >= 37 weeks of gestation, reactive fetal heart pattern, unfavorable cervix Bishop score ≤ 4 and no contraindication to vaginal delivery.

Exclusion criteria includes previous LSCS or any uterine surgery, mal presentation, grand Multiparity, abnormal foetal heart rate pattern, contraindication to prostaglandins and pregnancy <37 weeks.

A total of 180 patients were included in the study after obtaining written informed consent. They were divided into two groups:

Group A - Patients who received 25-50µg misoprostol sublingually for induction of labour. It was given sublingually and repeated every 4 hours for maximum of 4-6 doses(maximum of 200 µg) or till patient went into active labour or adequate uterine contraction was achieved.

Group B- Patients who received cerviprime gel 0.5 mg PGE2 in 2.5 ml syringe inserted intra-cervically just below internal OS for induction of labour. It was repeated till a maximum of 3 doses every 6 hours or till induction achieved.
A partograph was strictly maintained in all patients induced.

The subjects selected for the study were evaluated initially by modified Bishop's score and CTGtest for fetal well-being. Patients with a modified bishops score ≤4 and a reactive NST were induced.After drug insertion, patients were monitored for signs of labour, maternal vital signs, fetal heart rate and progress of labour. The fetal heart rate was monitored by either intermittent auscultation or continuous fetal heart rate monitoring. Progress of Labor was observed and noted by per abdominal and vaginal examination.

The data collection included indication for induction, booked/ unbooked case, maternal age, parity, gestational age on entry into the study,modified Bishop's Score at time induction, induction – delivery interval,oxytocin augmentation, type of delivery, Apgar score of the baby,maternal and neonatal complications etc.
The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analyzed and statistically evaluated using SPSS-PC-17 version.

RESULTS

A total of 180 pregnant women admitted for induction of labour.They were randomly divided into two groups. Group A received 50µg misoprostol sublingually while group B received cerviprime gel 0.5 mg PGE2 in 2.5 ml syringe inserted intra-cervically. The observations and results of the study are presentedas below.

Table 1: Modified Bishop score at 0 hours in study subjects

Bishop score at 0 hours	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
2	14	15.6	14	15.6	28	0.15
3	75	83.3	70	77.8	145	
4	1	1.1	6	6.7	7	

In present study, at start of induction mean Bishop score was 2.86±0.38 in Dinoprostone gel group while it was 2.91±0.46 in Misoprostol group. No significant difference was observed between both group. Most of the women were having bishop's score of 2-3 in both the groups

Table 2:Indication of induction in study subjects

Indication of induction	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total
	No.	%	No.	%	
Post Dated	40	44.4	43	47.8	83
Rh-ve	19	21.1	20	22.2	39
Mild PE	11	12.2	15	16.7	26
Severe PE	3	3.3	0	0.0	3
GDM	6	6.7	3	3.3	9
Polyhydramnios	2	2.2	2	2.2	4
Post Dated + Mild Preeclampsia	1	1.1	0	0.0	1
Oligohydramnios	6	6.7	5	5.5	11
Chronic Hypertension	2	2.2	2	2.2	4

40 (44.4%) pregnant women in Dinoprostone group and 43 (47.8%) in Misoprostol group were induced for Postdatism. 19 (21.1%) of the women were induced for Rh-ve in the Dinoprostone group as compared to 20 (22.2%) in the Misoprostol group. 14 (15.6%) in the Dinoprostone group and 15 (16.7%) in the Misoprostol group were induced at term for Preeclampsia/severe preeclampsia. Other causes for induction were Oligohydramnios, Polyhydramnios and GDM.

Table 3: Maternal complications in study subjects

Maternal complications	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
Hyper stimulation	0	0.0	2	2.2	2	0.49
Intrapartum pyrexia	1	1.1	9	10.0	10	<0.01
Diarrhoea	4	4.4	0	0.0	4	0.12
Vomiting	8	8.9	0	0.0	8	<0.01

Most common maternal complication observed were intrapartum pyrexia (1 case in dinoprostone gel group and 9 cases in misoprostol group) and vomiting (8 case in dinoprostone gel group and 0 cases in misoprostol group). 2 cases of hyperstimulation were also seen in misoprostol group while diarrhoea was observed in 4 cases in dinoprostone group. Apart from that we have not seen any other complication in mothers

Table 4: Need of augmentation in study subjects

Need of augmentation	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
Yes	22	24.5	12	13.3	34	0.05
No	68	75.5	78	86.7	146	

Dinoprostone group required more augmentation of labor (24.5% vs. 13.3%) compared to Misoprostol group although difference was statistically not significant.

Table 5: Induction to delivery interval in study subjects

Induction to delivery interval	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
<6 hours	1	1.1	16	17.8	17	<0.01
6-12 hours	49	54.4	66	73.3	115	
>12 hours	40	44.4	8	8.9	48	

In dinoprostone group 50 (55.6%) out of 90 women and 82 (91.1%) women in misoprostol group delivered within 12 hrs of induction.

Figure 1: Induction to delivery interval in study subjects

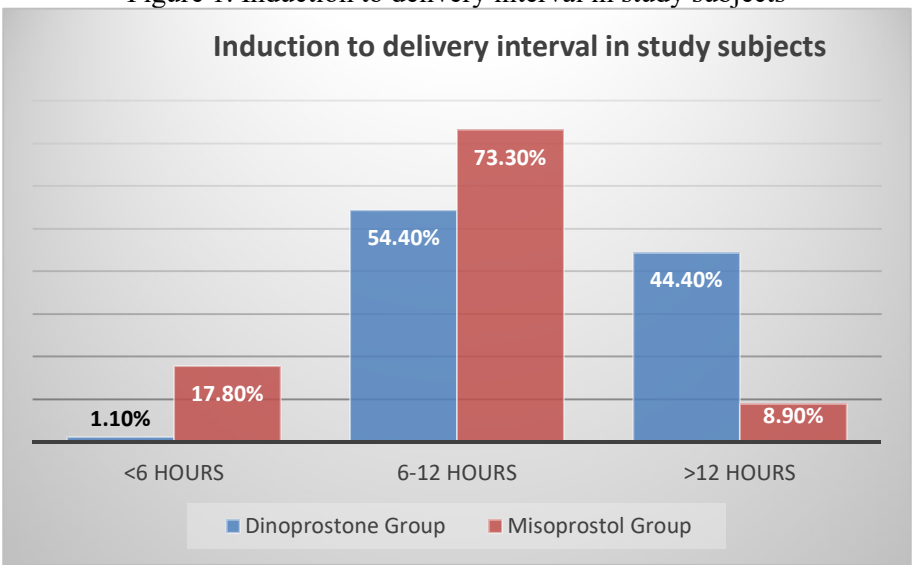

Table 6: Induction to delivery interval comparison between both group

	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		P value
	Mean	SD	Mean	SD	
Induction to delivery time (hours)	12.24	3.80	9.01	4.93	<0.01

The mean induction to delivery interval in our study was shorter in Misoprostol group (9.01±4.93 hrs) as compared to Dinoprostone group (12.24±3.80 hrs) which was statistically significant.

Table 7: Success of induction in study subjects

Success of induction	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
Success	85	94.4	84	93.3	169	0.98
Failed	5	5.6	6	6.7	11	

In present study, out of 90 subjects in each group, induction was failed in 5 (5.6%) subjects in dinoprostone group while in misoprostol group induction failed in 6 (6.7%) subjects.

Table 8: Mode of delivery in study subjects

Mode of delivery	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
LSCS	19	21.1	26	28.9	45	0.23
Vaginal delivery	71	78.9	64	71.1	135	

As far as mode of delivery was concerned it has been seen that 78.9% and 71.1% of the subject delivered vaginally in Dinoprostone and Misoprostol group respectively whereas LSCS was conducted in 21.1% and 28.9% in Dinoprostone and Misoprostol group respectively.

Figure 2: Mode of delivery in study subjects

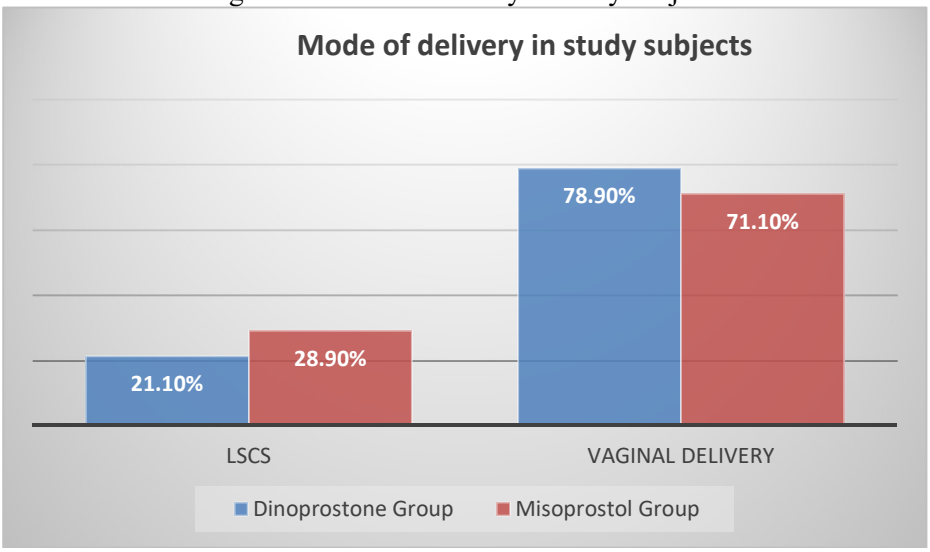

Table 9: Foetal complications in study subjects

Fetal complications	Dinoprostone Group (N=90)		Misoprostol Group (N=90)		Total	P value
	No.	%	No.	%		
Fetal distress	11	11.2	6	6.7	17	
MSL	3	3.3	14	15.6	17	<0.01

In misoprostol group, most common foetal complication was meconium stained liquor which was observed in 14 (15.6%) study subjects while in dinoprostone group foetal distress was most common complication which was reported in 11 (11.2%) mothers.

DISCUSSION

A total of 180 were randomly divided to receive either dinoprostone gel vaginally or misoprostol sublingually. The findings of the study are as follows:
Most of the study subjects were between the age group of 19-22 years in both group. (48.9% in dinoprostone group v/s 58.9% in misoprostol group). Mean age in dinoprostone group was 23.57±3.27 years while mean age in misoprostol group was 22.70±3.25 years.

Most of the women were primigravida constituting 61.1% and 60.0% in the two groups, respectively while rest were muiltigravida

Mean gestational age in PGE2 gel group was 39.36±1.43 weeks while mean age in misoprostol group was 39.34±1.21 weeks. The greatest numbers of patients were having gestational age between 38 to 39 weeks and 40-42 weeks.

In present study, at start of induction mean Bishop score was 2.86±0.38 in dinoprostone gel group while it was 2.91±0.46 in misoprostol group. Veena B et al [6] found maximum number of women in the study group had a Bishop's score of 3–4

Out of 90 subjects in each group, 34 (37.8%) pregnant women in both the group were induced for postdatism.Veena B et al[6] and Yadav S et al[9] also reported same. Other studies also reported postdatismas most common indication for induction. [10,14].21.1% of the women were induced for Rh-ve in the dinoprostone group as compared to 18.9% in the misoprostol group. 15 (16.6%) in the dinoprostone group and 14 (15.6%) in the misoprostol group were induced at term for preeclampsia/severe preeclampsia. PROM was cause of induction in 17.8% women in misoprostol group while it was responsible for induction in 6 (6.7%) women in dinoprostone group.,

Induction failed in 5 (5.6%) subjects in dinoprostone group while in misoprostol group induction failed in 6 (6.7%) subjects. Munzar Z et al[10] also reported failed induction in 4% and 6% cases in misoprostol and dinoprostone group respectively.

Most common maternal complication observed were intrapartum pyrexia (1 case in dinoprostone gel group and 9 cases in misoprostol group) and vomiting (8 case in dinoprostone gel group and 0 cases in misoprostol group). 2 cases of hyperstimulation were also seen in misoprostol group while diarrhoea was observed in 4 cases in dinoprostone group. Apart from that we have not seen any other complication in mothers.

Dinoprostone group required more augmentation of labor (24.5% vs. 13.3%) compared to misoprostol group although difference was statistically not significant.Yadav S et al[9],found same.

In dinoprostone group 54 (62.2%) out of 90 women and 95.5% women in misoprostol group delivered within 12 hrs of induction.The mean induction to delivery interval in our study was shorter in misoprostol group (7.46±2.26 hrs) as compared to dinoprostone group (11.31±2.61) which was statistically significant.Similar observation has been found by Veena B et al[6] ,Jha N et al[12],Patil KP et al[11] ,by Yadav S et al[9].So all the study supported finding of our study that misoprostol reduced induction to delivery interval.

As far as mode of delivery was concerned it has been seen that 78.9% and 71.1% of the subject delivered vaginally in whereas LSCS was conducted in 21.1% and 28.9% in dinoprostone and misoprostol group respectively.similar to few other existing evidences (28 vs 24 %)[13]. Similarly, Parmar et al[13] also have found significant higher caesarean rate in PGE1 group when administered vaginally.Finding of our study was contradicted by Veena B et al[6] .

In misoprostol group, most common foetal complication was meconium stained liquor which was observed in 14 (15.6%) study subjects while in dinoprostone group foetal distress was most common complication which was reported in 11 (11.2%) mothers.Similar to our study, Fetal Distress was more common in group PGE2 (16.0%) as compared to 6.0% in group PGE1 in study by Yadav S et al[9].

Mean Apgar scores were comparable in both groups – 8.36±0.77 at 1 minute and 8.90± 0.82 at 5 minutes in the dinoprostone group and 8.32± 0.83 at 1 minute and 9.0± 1.17 at 5 minutes in the misoprostol group.

Out of 90 subjects in both group low birth weight was seen in 22.2% subjects in dinoprostone group and 34.4% subjects in misoprostol group.

NICU admission rate was 13.3% in dinoprostone group while in misoprostol group 16 (17.8%) baby admitted to NICU. No significant difference was observed between both groups (p>0.05).

Conclusion:

Sublingual misoprostol significantly reduces the induction to-delivery interval and has fewer induction failures So, by the present study, it was concluded that sublingual misoprostol is a more successful, stable at room temperature and lower-cost agent for induction of labor than intracervical dinoprostone gel. Sublingual misoprostol can also be preferred option where repeated internal examinations has to be avoided like PROM.Because of short induction to delivery interval in the study group misoprostol can be especially useful in pre-eclampsia and eclampsia patients.In our study vaginal delivery is slightly higher after using dinoprostone gel.Still Multicentre trial with larger sample size are needed to see effectiveness and to compare side effects.

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