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Original Research Article

Comparative Study of 25 µg Vaginal Misoprostol V/S Cerviprime Gel for Induction of Labour at Term at Obstetrics and Gynaecology Department of DMCH, Laheriasarai, Bihar

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Abstract:

Background: This comparative study was conducted to compare the effectiveness of 25 µg of intravaginal misoprostol with intracervical cerviprime gel in terms of efficacy of drug, foeto-maternal outcome, side effects and complications of drugs.

Methods: 100 primigravida at term; who were admitted for induction of labour were included in this study. They were randomly selected to receive either intravaginal misoprostol or intracervical cerviprime gel. 50 women received intravaginal 25 µg Misoprostol (Group A) every 6 hours for maximum of 5 doses and 50 women received 0.5 mg (2.5 ml) of intracervical cerviprime gel (Group B) till maximum of 3 doses. Comparison was done in terms of time taken for induction to delivery, mean time taken for onset of labour, APGAR score at 1 and 5 minutes and the neonatal outcome in either of the groups.

Results: The mean time taken for onset of labour was less in the misoprostol group than in the cerviprime group (6.5hours v/s 8 hours, P = 0.49). Similarly duration from induction to delivery was less (20.08 ± 8.24 hours v/s 23.19 ± 9.59 hours, P >0.05) for misoprostol than cerviprime gel. Need for Oxytocin augmentation was less (16%) in misoprostol group as compared to cerviprime group (46%), P = 0.001. Cesarean section rate was slightly higher in misoprostol group (8% v/s 6%). Maternal complications were minimal in either group & the neonatal outcome was good in both the groups. The induction cost was much less in the misoprostol group.

Conclusion: Compared to cerviprime gel; misoprostol is safe, efficacious, cheap, well tolerated drug by mother andfetus. It was found to be a better inducing agent, has short induction to delivery interval thus short duration of labour with similar maternal and fetal safety profile.

Keywords: Misoprostol, Cerviprime Gel, Induction of Labour.

Introduction

Induction of labour is an intervention that artificially initiates uterine contractions leading to progressive dilatation and effacement of cervix and expulsion of fetus prior to spontaneous onset of labour. [1] In some 5-25% of pregnancies, there comes a time when the fetus and/or mother would be better off if delivery was conducted. [2] Prostaglandin analogue has been emerged for use in labour induction. Prostaglandins alter the extracellular ground substance of the cervix, ripen the cervix and also increase the activity of collagenase in the cervix. They also allow for an increase in intracellular calcium levels, causing contraction of myometrial muscle. [3,4] The FDA revised its labelling for misoprostol in April 2002 from "contraindicated in pregnancy" to "contraindicated in pregnancy for the treatment and prevention of NSAID induced ulcers". [5] Currently, two prostaglandin analogs PGE1 (Misoprostol) and PGE2 (Cerviprime gel) are available for the purpose of cervical ripening. Misoprostol (15-deoxy-16-hydroxy-16 methyl-PGE1) was the first synthetic prostaglandin analogue to be made available for the treatment of peptic ulcer. Impressed by its stimulant actions on the uterus, Sanchez Ramos in 1993 used it for the management of several obstetric conditions. Misoprostol is available as 25, 50, 100, 200 microgram tablets. Cerviprime (PGE2) is a synthetic preparation of naturally occurring prostaglandin E2. PGE 2 gel is available in 2.5 ml syringe for an intracervical application of 0.5 mg of cerviprime. [6] The American College of Obstetrics & Gynecology recommends the use of 25

microgram of misoprostol for labour induction, but their guidelines were developed in the absence of large well designed clinical studies. 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). This clinical study was conducted to compare the efficacy and safety of intravaginal 25 microgram misoprostol with that of cerviprime gel containing 0.5 mg PGE2 in cervical ripening and labour induction at term.

Material and Methods

This comparative study was conducted in the department of obstetrics & gynecology, Darbhanga Medical College & Hospital, Laheriasarai, Bihar over a period of January 2018 to December 2018. 100 women admitted for induction of labour in our hospital were randomly selected for study.

Inclusion Criteria

All primigravida of ≥37 completed weeks of gestation that were not in labour with Bishop Score<6 included in study. They have been induced for either maternal or obstetric indication.

Exclusion Criteria

Multiple pregnancies, abnormal presentation, previous caesarean section, cardiopulmonary disease, unexplained vaginal bleeding during pregnancy, intrauterine death, allergy to prostaglandin. A written informed consent was obtained from all the participants in the study after explaining the consequences. Patient population was divided in two groups:

Group A (study group): Patients who received 25 µg misoprostol per vaginally for induction of labour. It is inserted in posterior fornix and repeated every 6 hours for maximum of 5 doses or till patient went into active labour or adequate uterine contraction was achieved i.e. 3 per 10 minutes or fetal distress developed whichever occur earlier.

Group B (control group): Patients who received cerviprime gel 0.5 mg PGE2 in 2.5 ml syringe inserted intracervically just below internal os for induction of labour. It is repeated till a maximum of 3 doses every 6 hours or till induction is achieved.

50 women received 25 µg intravaginal misoprostol and another 50 women received 0.5 mg of intracervical cerviprime gel. Labour was managed according to labour ward protocol. Progress of labour was observed and noted by per abdominal and vaginal examination. Uterine contractions in terms of frequency and duration per 10 minutes noted. Adequate contractions were defined as 3 per 10 minute each lasting for 45 seconds. Tachysystole, hypertonus and hyper stimulation were noted. The patient was considered in the active phase when there was cervical dilatation of at least 3-4 cm. Women in labour were cared for, according to current obstetric practices. When they entered active phase, depending on the pattern of uterine contractility, syntocinon was used for augmentation. If women did not reach active phase within 24 hours of induction, caesarean section was done for failed induction. No augmentation was done when uterine contractions reached a frequency of 3 in 10 minutes. The primary outcome measures were induction to onset of labour, induction to delivery interval, maternal and fetal complications. Success of induction was defined as entry into active phase within 24 hours of the initial administration of the drug. Other measures studied were; need for syntocinon augmentation, mode of delivery, need for caesarean section, and side effects. Neonatal outcome was measured according to the Apgar score. The results were represented as mean & standard deviation. Student t test & Chi square tests were applied to know the statistical significance. Qualitative variables were expressed as percentages.

Results

Patient population was divided in two groups; group A (study group): 50 Patients who received 25 µg Misoprostol per vaginally and group B (control group): 50 Patients who received cerviprime gel 0.5 mg PGE2 intracervically. Most of the patients in both groups were between 20-30 years. Mean age was statistically not significant in both groups (23.32 ± 2.91years vs. 23.68 ± 3.11 years). There was no significant difference of bishop score in both groups. The indications of induction were similar in either group as mentioned in Table 3. Majority of patients were induced due to post-dated pregnancy. Other most common indications were pregnancy induced hypertension, intrauterine growth restriction. Comparatively higher no of dosages are required in misoprostol group than in cerviprime group. But as compared to cerviprime gel (215 Rs.) misoprostol (5 Rs. per tablet) is cost effective. On the contrary misoprostol does not require refrigeration and there is less need for syntocinon augmentation.

The mean time taken for onset of labour was significantly less (P <0.05) in the misoprostol group (6.5 hours v/s 8 hours). Thus Misoprostol leads to early labour and thus early delivery as compared to the cerviprime. It is evident that 17.3% patient in misoprostol group delivered within 12 hours, while 14.8% in cerviprime group. In misoprostol group the time taken for induction to delivery (20.08 ± 8.24 vs. 23.19 ± 9.59) was slightly less which is statistically not significant (P >0.05). Mean duration of labour was not statistically significant (P >0.05) in both groups (14.04 ± 7.62 vs. 14.90 ± 5.95). Syntocinon augmentation was required in 16% of patients in

misoprostol group whereas 46% of cases required augmentation in cerviprime group. It indicates that oxytocin requirement was significantly less in misoprost induced cases (P <0.001). 92% of patients in misoprost group and 94% in cerviprime group delivered normally. There were more (8%) cesarean deliveries in group A than in group B (6%) but the difference was statistically not significant (P = 0.695). Caesarean section was done for fetal distress in both groups. 4 (8%) patients in group A and 3 (6%) patients in group B underwent caesarean section due to fetal distress. Nonprogress of labour or failed induction was not observed. 97% patient in group A and 98% in group B delivered smoothly without experiencing any significant side effect. Only two out of 50 (4%) in group A and 1 (2%) in group B had hyper stimulation, which is not statically significant.

Only 1 women is group A had perineal laceration and 2 degree tear and 1 women in group B had cervical tear.

No significant difference was observed d in mean birth weight of neonate in both groups. Mean APGAR score at 1 minute and 5 minute was also found to be similar in both groups.

Table 1: Distribution according baseline data

	Group A (Mean±SD)	**Group A (Mean±SD)**	**P value**
Age group (years)	23.32±2.91	23.68±3.11	>0.05 (NS)
Booked	92%	100%	>0.05 (NS)
Unbooked	8%	0%	
Status of membrane			
Present	70%	76%	>0.05 (NS)
Absent	30%	24%	

Table 2: Distribution according to pre-induction Bishop score

Bishop Score	**Group A**		**Group B**	
	No.	**%**	**No.**	**%**
GDM	2	4	3	6
IUGR	2	4	4	8
Oligohydramnios	4	8	4	8
PIH	14	28	13	26
Postdatism	20	40	18	36

Table 3: Distribution according to doses

No. of doses	**Group A**		**Group B**	
1	7	14	25	50
2	15	30	13	26
3	9	18	12	24
>3	19	38	0	0

Table 4: Distribution according to induction to onset of labour

Onset of labour (hour)	**Group A**		**Group B**	
1-6	25	50	19	38
7-12	25	50	24	48
13-18	0	0	3	6
19-24	0	0	4	8
>24	0	0	0	0
Total	50	100	50	100
Median (range)	6.5 (1-11)		8 (1-20)	

Chi value 7.84; p = 0.049 (Significant)

Table 5: Distribution according to induction delivery intervals

Interval (hours)	**Group A**		**Group B**	
0-6	1	2.1	1	2.10
7-12	7	15.22	6	12.70
13-24	26	56.22	22	46.80
>24	12	26.00	18	38.30
Total	46	92	17	94
Mean±SD	20.08±8.24 hours		23.19±9.59 hours	

"t" value = 1.74; p>0.05 (Not Significant)

Table 6: Distribution according to mean duration of labour

Duration of labour (hour)	Group A		Group B	
0-6	5	10.87	3	6.38
7-12	21	46.65	14	29.79
13-18	10	21.74	15	31.91
19-24	7	15.22	13	27.66
25-30	1	2.17	1	2.13
31-36	1	2.17	1	2.13
37-42	1	2.17	0	0
Total	46	92	47	94
Mean±SD	14.04±7.62 hours		14.90±5.95 hours	

"t" value = 0.94; p>0.05 (Not Significant)

Table 7: Distribution according to augmentation by syntocinon

	Group A		Group B	
Syntocinon required	8	16	23	46
Not required	42	84	27	54
Total	50	100	50	100

Table 8: Distribution according to mode of delivery

Mode of delivery	Group A		Group B	
Normal	46	92	47	94
Forceps	-	-	-	-
LSCS	4	8	3	6
Total	50	100	50	100

Chi value 0.15; P = 0.69 (Not significant)

Table 9: Distribution according to indication for caesarean section

Indication	Group A		Group B	
Foetal distress	4	8	3	6
Failure of induction	0	0	0	0
Total	50	8	3	6

Table 10: Common maternal events and complications

Associated events	Group A		Group B	
Perineal lacerations	1	2	0	0
Vomiting	1	2	2	4
Nausea	4	8	6	12
Arrested labour	0	0	0	0
Pyrexia	1	2	0	0
PPH	1	2	1	2
Prolonged labour	0	0	0	0
Precipitate labour	0	0	0	0
Uterine hyper stimulation	2	4	1	2
Cervical tear	0	0	1	2
Perinal tear	1	2	0	0

Table 11: Neonatal Outcome

	Group A	Group B
Average birth weight (kg)	2.50 ±0.42	2.74 ± .36
Mean apgar at 1 min	7.9± 0.2	7.5 ± 0.2
Mean apgar at 5 min	8.5±0.2	8.5 ± 0.2

Discussion

The introduction of Prostaglandins to clinical practice, particularly their local use for cervical ripening, has decreased major difficulties of labour induction. Induction to delivery interval has been decreased dramatically by introduction of prostaglandins.

Similarly it also decreased associated complication of amnionitis and fetal infection. It is a very cost effective drug for cervical ripening and labour

induction. Labour induction is required when mother and or fetus is at jeopardy.

In our study postdatism was most common indication for induction, (40% and 36% in group A and group B respectively) followed by PIH (28% in group A and 26% in group B).Greagsons et al. in their study showed that 95% patients in misoprostol group and 94% in cervigel group were induced for postdatism. Similarly C. N. Sheela et al. demonstrated that postdatism (36% & 32% respectively) and PIH (22% & 26% respectively) were most common indications in both groups.

Misoprostol has been found to be more effective for earlier onset of labour. The mean time taken for onset of labour was less in misoprost group as compared to cerviprime group (6.5 hours vs. 8 hours). Also takes lesser time from induction to delivery. The mean induction to delivery interval was less in the misoprost group (20.08 ± 8.24 hours vs. 23.19 ± 9.59 hours). In the study of Murthy Bhaskar Krishnamurthy in 2006, induction delivery interval was shorter in the misoprostol group. Other reported studies also had parallel observation. Thus misoprostol reduces the mean duration of labour which reduces the duration of suffering of a patient in labour and also provides fast delivery which is required in cases of premature rupture of membranes, eclampsia and fetal distress. Syntocinon augmentation was required in 16% of patients in misoprostol group whereas 46% of cases required augmentation in cerviprime group. It indicates that oxytocin requirement was significantly less in misoprost induced cases (P <0.001).

The misoprostol had decreased rate of Cesarean section (6%) compared to cerviprime (22%). 92% of patients in misoprost group and 94% in cerviprime group delivered vaginally. Although a little bit higher cesarean deliveries were done in group A (8%) than in group B (6%), but the difference was statistically not significant (P = 0.695).

This was consistent with the study of Sahu Latika et al. (8% vs. 20%) and also with the study of Patil Kamal et al. and Murthy Bhaskar et al.

Most common indication for caesarean section was fetal distress. 4 (8%) patients in group A and 3 (6%) patients in group B undergone caesarean section due to fetal distress. Nonprogress of labour or failed induction was not observed. The meconium stained liquor was seen more in the study group.

Maternal side effects were minimal in both the groups. 97% patient in group A and 98% in group B delivered smoothly without experiencing any significant side effect. In misoprost group, 16% patients had fever with chills, 8% had nausea and 2% had vomiting. Only two out of 50 (4%) in group A and 1(2%) in group B had hyper stimulation, which is not statically significant. only 1 women is group A had perineal laceration and 2 degree tear and 1 women in group B had cervical tear.

Hypertonus was defined as one contraction with a duration of >2 minutes, tachysystole as >6 contractions in 10 minutes for two consecutive 10 minute periods. Uterine hyper stimulation is when either of these condition (hypertonus or tachysystole) leads to a non-reassuring fetal heart rate pattern. Because of the frequency of tachysystole with vaginal administration of misoprostol, some researchers are studying oral and sublingual/buccal routes to determine if effectiveness can be maintained while decreasing the incidence of tachysystole. In 2000, G. D. Scarle& company notified physicians that misoprostol is not approved for labour induction or abortion. Despite this American college of obstetricians & gynecologists (2000) quickly reaffirmed its recommendation for use of the drug because of proven safety & efficacy.

No significant difference was observed in mean birth weight of neonate in both groups. Mean APGAR score at 1 minute and 5 minute was also found to be similar in both groups. Sahu Latika et al. also had 12% newborns with APGAR <7 at one minute in the cerviprime group which is consistent with our study. The mean overall induction cost in misoprostol group was much less in contrast to cerviprime gel group. As misoprostol does not need refrigeration, its affordability as well as its availability in the peripheral areas is more than the cerviprime gel which requires refrigeration.

Conclusion

Our study results revealed that, misoprostol is better inducing agent as compared to the cerviprime gel because it has short induction to delivery intervals and thus short duration of labour and advantage of rapid labour as required in cases of pre-eclampsia and eclampsia. The need of oxytocin augmentation was less with the misoprostol and it results in more vaginal deliveries compared to cerviprime.

Thus misoprostol reduces the Cesarean section rate and also has less chances of failure of induction. Although hyper stimulation and meconium stained liquor was more in misoprostol group in few patients and did not have any effect on the neonatal outcome. Misoprostol also does not need cold chain storage and is cheaper. Thus misoprostol can be considered as safe, efficacious, cheap and mother and fetus friendly drug for the induction of labour.

This study was designed to assess efficacy of specifically developed 25 μg misoprostol vaginal

tablet for labour induction. Findings confirm that it is as effective as cerviprime gel for cervical ripening and labour induction. It was found to have similar maternal and fetal safety profile. Use of misoprostol was found to be cost effective than cerviprime gel. This drug was well tolerated. Therefore its use is recommended for cervical ripening and labour induction in developing countries.

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