10.5005/jp-journals-10006-1196

CONTEMPORARY STUDY

Comparison of Oral and Vaginal Administration of Low-dose Misoprostol for Labor Induction

Mamta Mahajan, Kumud Bala Gupta, Renu Sharma, Ragweshwar Jyoti

ABSTRACT

Objective: Comparison of oral and vaginal administration of low-dose misoprostol for induction of labor at term.

Materials and methods: Two hundred pregnant women after 37 weeks of gestation with an indication for induction were given 25 µg of misoprostol orally (study group) or vaginally (control group), every 3 hours to a maximum of 8 doses. The induction to delivery interval, requirement of oxytocin, dose of misoprostol used, maternal and neonatal outcome were analyzed statistically.

Results: The median induction to delivery interval was significantly shorter in those induced with vaginal misoprostol (p = 0.06). The median induction to delivery interval was 21.35 ± 7.44 hours in study group and 14.64 ± 5.49 hours in control group. Eighty-two percent women in study group and 84% women in control group had vaginal delivery. Cesarean section rate was lower in control group, 16% *vs* 18% in study group, but the difference was not statistically significant (p = 0.790). Oxytocin augmentation was needed for 80% cases in the study group and 54% cases in control group, which was statistically significant (p = 0.006). The incidence of abnormal FHR was more in control group as compared to study group (30 *vs* 14%). Hyperstimulation syndrome was observed in 4% cases in control group and 2% cases in study group. Neonatal outcome was found to be similar in both groups.

Conclusion: Vaginal misoprostol achieved higher success rate within a short induction interval but was associated with increase in abnormal FHR pattern and abnormal uterine activity as compared to the oral route. Oral route had comparable efficacy, was safe and well-tolerated route of misoprostol administration for induction of labor at term.

Keywords: Misoprostol, Prostaglandin, Induction of labor.

How to cite this article: Mahajan M, Gupta KB, Sharma R, Jyoti R. Comparison of Oral and Vaginal Administration of Low-dose Misoprostol for Labor Induction. J South Asian Feder Obst Gynae 2012;4(3):137-140.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

When delivery is necessary and ripening has not had time to occur, or has failed to be initiated, this natural process has to be accelerated. Number of methods used to ripen the cervix. These may be natural, surgical, mechanical and pharmacological. Two different approaches to labor induction are used, often in combination: one relies upon pharmacological agents to modify cervical form with or without stimulating uterine contractions, and the other uses mechanical stimulations to provoke cervical effacement, dilatation and ultimately uterine contractions.

During the past 15 years the introduction of misoprostol, 15-deoxy-16hydroxyl-16-methyl analog of prostaglandin E1, has been the major focus of attention for labor induction. Misoprostol is stable at room temperature and is effective if taken orally. It has no bronchoconstrictive action and slight broncodilatory action and is inexpensive and readily accessible. It is also cheaper than the alternative prostaglandin.

Multiple trials have proved that misoprostol is an effective agent for cervical ripening and labor induction.[1] It has been successfully used for induction even in patients with term prelabor rupture of membranes.[2] However, investigations are still going on regarding the optimal dose, dosing regimen and route of administration. Recently, few studies have demonstrated efficacy of oral route comparable with vaginal route.[3-5]

MATERIALS AND METHODS

Objective

Comparison of oral and vaginal administration of low dose misoprostol for labor induction. The present study was conducted in the Department of Obstetrics and Gynecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla. The inclusion criteria were singleton pregnancy with vertex presentation, confirmed gestational age 37 to 42 weeks, parity ≤ 3, intact membranes and Bishop score ≤ 5. The exclusion criteria were antepartum hemorrhage (placenta previa), fetal distress, cephalopelvic disproportion, previous uterine surgery, women with history of glaucoma, bronchial asthma, epilepsy, known allergy to PGE_1, all contraindications to vaginal delivery, heart disease, renal/hepatic failure and clinically suspected chorioamnionitis. After consent, 200 women with an indication for induction of labor were divided equally into study group (oral misoprostol) and control group (vaginal misoprostol). They received 25 µg of misoprostol orally or vaginally every 3 hours, maximum of 8 doses. The appropriate dose of misoprostol was obtained by cutting a standard 100 µg tablet into 4 equal parts with a scalpel blade.

Fetal heart rate was monitored before administration of the drug and for 30 minutes after administration of misoprostol. Uterine tachysystole, hypertonus and hyperstimulation syndrome were ruled out in these 30 minutes. If present, next dose of misoprostol was withheld. Before administration of next dose of misoprostol, per abdomen examination and Bishop's score assessment was done. The subsequent dose of the drug was withheld if; active labor was established, i.e. greater than 3 contractions in 10 minutes, cervix was favorable (Bishop's score ≥ 6) or spontaneous ruptures of membranes.

In case, the progress was found to be slow on the partogram as a result of inadequate contractions, artificial rupture of membranes was performed and oxytocin infusions in incremental doses were given. Oxytocin was not administered

less than 4 hours after last dose of misoprostol. The labor was managed partographically.

If at the end of 8 doses of misoprostol, the Bishop's score ≤ 5 and there were no uterine contractions, the inductions were considered failed. Dose of misoprostol used, need for augmentation of labor, mode of delivery, total duration of labor, duration of different stages of labor, duration of rupture of membrane and approximate blood loss were monitored and recorded. In case of operative delivery, indications were recorded. After delivery, condition of the baby, Apgar score at 1 minute and 5 minutes, birth weight and any congenital malformation, if present, was noted. Complications like birth asphyxia, meconium, aspiration and resuscitation, if required, was recorded. The neonates admitted to NICU were those who required PPV or incubation and further monitoring. All the observations were subjected to statistical analysis.

RESULTS

The distribution of maternal and gestational age, preinduction Bishop score and indication for induction of labor were similar in both the groups (Table 1). The study group required more doses of misoprostol. The mean dose of misoprostol used was 4.62 ± 1.56 in the study group and 3.60 ± 1.08 in control group. The difference between the two groups was statistically significant (p = 0.031), presented in Table 2.

The number of cases requiring oxytocin for augmentation of labor (Table 2) in study group was more as compared to those in control group (80 *vs* 54 cases). The difference was statistically significant (p = 0.06).

The number of cases delivered within 24 hours of induction were 70.7 cases in study group and 95.3 cases in control group (Table 2). The mean induction to delivery interval was 21.35 ± 7.44 hours in study group and 14.64 ± 5.49 hours in control group. The induction delivery interval was 7 hours shorter in those induced with vaginal misoprostol. The difference between the two groups was statistically significant (p = 0.006).

Eighty-two cases in the study group had vaginal delivery of which 4 cases had instrumental delivery, while 84 cases in control group had vaginal delivery of which 10 cases had instrumental delivery (Table 3). In control group rate of operative vaginal delivery was more, but the difference was not statistically significant (p = 0.068). The cesarian section rate in the two groups was similar, 18 cases in study group and 16 cases in the control group. However, the indication for cesarian section was different in the two groups. In the control group nonreassuring fetal heart rate with meconium stained liquor was the only indication for cesarian section (16 cases). Whereas, in the study group nonreassuring FHR was seen in 12 cases, failure of induction in 2 cases and non progress of labor was an indication for cesarian section in 4 cases.

The incidence of hyperstimulation was higher in control group as compared to the study group (4 *vs* 2 cases, p = 0.568). There was a higher rate of tachysystole in control group (2 cases). Two cases in oral misoprostol group had hypertonus (Table 4). None of the cases with excessive uterine activity received a tocolytic for uterine relaxation. Presence of intrapartum meconium stained liquor was found in 12 cases in study group and 26 cases in the control group. The incidence of meconium stained liquor was higher in vaginal misoprostol group, hence, more intensive intrapartum monitoring is required in patient receiving vaginal misoprostol.

It was observed that cases had only minor gastrointestinal side-effects in form of nausea and vomiting. None of the patients required antiemetics. None of the cases had fever or diarrhea. There was no case of rupture uterus. Neonatal outcome in both the groups was similar (Table 5).

DISCUSSION

Prostaglandins are agents of choice to ripen cervix before induction of labor. PGE2 is expensive, not available in many developing countries and requires refrigeration. Misoprostol on the other hand is cheap, readily available and stable at room temperature. There is increasing evidence that misoprostol administration either oral, vaginal or sublingual route is an effective method of labor induction. An oral inducing agent that is safe, effective, inexpensive and well tolerated by patients will be attractive to patient and health-care providers. The probable benefits include avoidance of intravenous line in some parurients, less need for vaginal examination and greater freedom of upright positioning.

This study shows women induced with vaginal misoprostol though required less dosing and faster induction to delivery interval (14.64 ± 5.49 *vs* 21.35 ± 7.44 hours) with less need for oxytocin augmentation when compared with similar group of women induced with oral misoprostol. Similar observations were made in other studies comparing oral and vaginal

Table 1: Maternal demographic data. Values are given as median ± SD

	Oral misoprostol (n = 100)	*Vaginal misoprostol (n = 100)*	*p-value*
Mean maternal age (years)	26.6 ± 4.59	26.0 ± 3.74	0.312 (NS)
Nulliparous	68	64	0.684 (NS)
Mean gestational age (weeks)	38.72 ± 0.96	38.88 ± 1.14	0.284 (NS)
Mean preinduction Bishop score	3.04 ± 0.96	3.52 ± 0.88	0.828 (NS)
Indications for induction of labor			
Hypertensive disorders	44	38	
Post date	30	36	
IUGR	24	20	
Decrease fetal movements	2	6	

NS: Not statistically significant (p ≥ 0.05)

Table 2: Primary induction outcome

	Study group (oral misoprostol) n = 100	*Control group (vaginal misoprostol) n = 100*	*p-value*
Mean dose of misoprostol	4.62 ± 1.56	3.60 ± 1.08	0.031
Oxytocin augmentation	80	54	0.006
Induction to delivery interval in hours	21.35 ± 7.44	14.64 ± 5.49	0.006
Induction to delivery interval ≤24 hours	58	80	

Table 3: Mode of delivery and indications of operative delivery

Mode of delivery	*Oral misoprostol (n = 100)*	*Vaginal misoprostol (n = 100)*	*p-value*
Spontaneous vaginal delivery	80	74	0.476
Forceps delivery	2	10	0.092
Cesarean section	18	16	0.790
Indication for cesarean section			
MSL and nonreassuring FHR	12*	16*	0.070
Nonprogress of labor	4	–	0.151
Failure of induction	2	–	0.317
Total	18	16	
Indication for forceps delivery			
MSL and nonreassuring FHR		10*	0.068
Fetal bradycardia	2*	4*	0.068
Total	2	14	
Total incidence of abnormal FHR	14*	30*	

Table 4: Intrapartum complications

	Study group (n = 100)	*Control group (n = 100)*	*p-value*
Hyperstimulation	2	4	0.918
Tachysystole	—	2	0.44
Hypertonus	2	—	0.174
Meconium stained liquor	14	26	0.835

Table 5: Neonatal outcome

	Study group (n = 100)	*Control group (n = 100)*	*p-value*
Mean Apgar score at 1 minute (mean ± SD)	8.15 ± 1.26	8.08 ± 1.14	0.488 (NS)
Mean Apgar score at 5 minute (mean ± SD)	8.36 ± 0.98	8.43 ± 0.49	0.488 (NS)
Neonatal resuscitation	8 cases	8 cases	0.223 (NS)
NICU admission	4 cases	4 cases	0.782 (NS)
Neonatal hyperbilirubinemia	8 cases	4 cases	0.384 (NS)

NS: Nonsignificant

misoprostol.[3-5] The incidence of abnormal fetal heart rate leading to operative vaginal delivery was more in cases induced with vaginal misoprostol (30%) as compared to those induced with oral misoprostol (14%). Also, there was a trend toward more frequent tachysystole and hyperstimulation in cases induced with vaginal misoprostol.

Toppazada et al[4] compared vaginal and oral misoprostol from induction of labor in a small randomized trial using 100 µg of misoprostol. When no response was noted 3 hours after the first 100 µg dose, 200 µg was administered every 3 hours until a maximum dose of 1000 µg was reached. The authors concluded that vaginal misoprostol resulted in a shorter time to delivery ($p < 0.005$), but more abnormal FHR patterns and uterine hyperstimulation occurred ($p \leq 0.05$).

Bennette et al[5] in their study randomized 206 cases to receive 50 µg of misoprostol either orally or vaginally every 4 hours as needed to induce labor. They observed that there is a shorter interval from induction to vaginal birth with vaginal misoprostol ($p = 0.004$), however, more frequent occurrence of FHR graph abnormalities and more frequent tachysystole ($p < 0.01$) and hyperstimulation ($p < 0.04$).

CONCLUSION

The result of present study suggests that vaginal misoprostol is associated with higher success rate within a short induction interval but there is increase in abnormal FHR pattern and abnormal uterine activity, which is a potential disadvantage. Oral route with a comparable efficacy and safety may be a better alternative for labor induction, especially where intense cardiotocographic monitoring is not possible as is required with vaginal misoprostol. Further trials are needed

to improve the success with oral misoprostol and to know optimal dose and dosing interval without increasing abnormal FHR pattern.

REFERENCES

1. Bartusevicius A, Barcaite E, Nadisauskiene R. Oral, vaginal and sublingual misoprostol for induction of labor. International Journal of Gynecology and Obstetrics 2005;91:2-9.
2. Crane JMG, Delaney MD, Hutchens BN. Oral misoprostol for premature rupture of membranes at term. Am J Obstet Gynecol 2003;189(3):1-6.
3. Kwon SJ, Davies AL, Mackenzie VP. A comparison of oral and vaginal misoprostol for induction of labor at term: A randomized trial. Br J Obstetr Gynaecol 2001;108:23-26.
4. Toppozada MK, Anwar MYM, Hassan HA, El-Gazaerly WS. Oral or vaginal misoprostol for induction of labor. Int J Gyn Obs 1997;56:135-39.
5. Bennett KA, Butt K, Crane JMG, Hutchens D, Young DC. A masked randomized comparison of oral and vaginal administration of misoprostol for labor induction. Obstet and Gynecol 1998;92(4):481-86.

ABOUT THE AUTHORS

Mamta Mahajan (Corresponding Author)

Senior Resident, Department of Obstetrics and Gynecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla-171002, Himachal Pradesh, India, Phone: 09418032990 e-mail: drmamtamahajan@gmail.com

Kumud Bala Gupta

Professor and Head, Department of Obstetrics and Gynecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India

Renu Sharma

Professor, Department of Obstetrics and Gynecology, Kamla Nehru State Hospital for Mother and Child, Indira Gandhi Medical College Shimla, Himachal Pradesh, India

Ragweshwar Jyoti

Gynecologist, DDU Zonal Hospital, Shimla, Himachal Pradesh, India