International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

Comparative Study of Misoprostol Sublingually and Dinoprostone Gel Intracervically for Cervical Ripening and Induction of Labor

Dr. Payal H.Panchal[1], Dr. Margi H. Sheth[2], Dr. Sushma R. Shah[3], Dr. Ami V. Mehta[4]

[1]MD, Assistant Professor, Department of Obstetrics and Gynaecology, Smt NHL Municipal Medical College and VS General Hospital, Ahmedabad, India

[2]MBBS 3rd year resident, Department of Obstetrics and Gynaecology, Smt NHL Municipal Medical College and VS General Hospital, Ahmedabad, India

[3]MD, DGO, Professor, Department of Obstetrics and Gynaecology, Smt NHL Municipal Medical College and VS General Hospital, Ahmedabad, India

[4]MD, DGO, Fetal Medicine Fellow, Associate Professor; Department of Obstetrics and Gynaecology, Smt NHL Municipal Medical College and VS General Hospital, Ahmedabad, India

Abstract: ***Background*: Both Prostaglandin E1 and E2 analogues are being used for cervical ripening. The aim of study was to compare the efficacy and safety profile of sublingual misoprostol (PGE1) and intracervical dinoprostone (PGE2) for cervical ripening and induction of labor. *Methods*: Two hundred nulliparous women with single live fetus and with gestational age of more than 37 weeks admitted for induction of labor were recruited for the study. Patients were randomized to receive either 25µg of misoprostol sublingually or dinoprostone gel (0.5mg) intracervically. *Results*: There was shorter induction to delivery time intervals, less requirement of oxytocin augmentation, higher vaginal delivery rate (81% vs 76%) and lower caesarean section rate (19% vs 24%) in misoprostol group than dinoprostone gel group. Incidence of tachysystole was higher in misoprostol group than dinoprostone gel group. Maternal and neonatal complications were similar in both the groups. *Conclusions*: Use of misoprostol in lower dose is a safe and cost-effective method for cervical ripening and induction of labor.***

Keywords: Dinoprostone, Labor Induction, Misoprostol, Prostaglandin

1. Introduction

Induction of labor at term with an intention of achieving a vaginal delivery is a common accepted obstetric intervention when continuation of pregnancy is deleterious to mother or fetus or both. It is an intervention that artificially stimulates uterine contractions leading to progressive dilatation and effacement of cervix and expulsion of fetus prior to onset of spontaneous labor.[1]

Many studies have shown the advantages of using prostaglandins in cervical priming and labor induction in terms of reduced induction-delivery interval and lower operative rate compared to oxytocin alone. 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.[2,3] Currently, two prostaglandin analogues, PGE1 (misoprostol) and PGE2 (dinoprostone gel) are available for 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. It is inexpensive, can be stored at room temperature and has few systemic side effects.[5,6] In 2011, WHO issued guidelines on induction of labour, which included the use of oral and vaginal misoprostol for induction of labour[7]. Trials with doses ranging from 25 to 100 micrograms indicate that vaginal administration of the lowest of these doses at interval of 3–6 hours might be optimal[8]. Nowadays misoprostol has received increased attention as a cervical ripening agent. It can be administered by various routes like oral, vaginal, sublingual, buccal and rectal routes. There has been interest in the sublingual route for labour induction, on the assumption that avoidance of the first pass hepatic circulation would yield bioavailability similar to that achieved with the vaginal route. An additional possible advantage is that avoidance of direct cervical effects might reduce the risk of uterine hyperstimulation.[9]

Dinoprostone has been the agent of choice for preinduction cervical ripening for several decades. Although safe and effective, it is expensive and requires refrigeration for storage.

This study was undertaken to compare the efficacy and safety of sublingual misoprostol 25 µgm with intracervical dinoprostone gel 0.5 mg for induction of labour at term.

2. Materials and Method

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology, Smt NHL Municipal Medical College and VS General Hospital, Ahmedabad between August 2018 and July2019.

The study was conducted on total 200 nulliparous females in the age group of 20-30 years with gestational age more than

Licensed Under Creative Commons Attribution CC BY

37 weeks. They were alternatively assigned to receive either intracervical dinoprostone gel or sublingual misoprostol with 100 pregnant women in each group. Gestational age was confirmed with previous scan reports. Vital signs were checked. Abdominal examination was done to confirm the gestational age, presentation, liquor volume and foetal heart rate. Sonography was done to confirm the presentation, estimated foetal weight and amniotic fluid index. Vaginal examination was done to ascertain the bishop's score and NST was done to confirm the foetal well-being.

Inclusion criteria

- Nullipara
- Singleton term pregnancies.(>37 weeks of gestational age)
- Live fetus –Cephalic presentation.
- Reassuring fetal heart rate tracing.
- Preinduction Bishop's score of less than 5.

Exclusion criteria

- multipara
- Previous uterine scars.
- Estimated fetal weight on scan greater than 3.75kg
- Amniotic fluid Index less than 5 cm.
- Foetal malformations.
- Any contraindication to vaginal delivery like placenta previa, abruptio placenta or unexplained vaginal bleeding.
- Significant foetal or maternal comorbidities like severe pre-eclampsia or early onset IUGR
- History of bronchial asthma, glaucoma, serious cardiovascular disorders, renal diseases or allergy to misoprostol

Administration of Drug

- Dinoprostone Group: An intracervical application of Dinoprostone gel 0.5mg was done. This was repeated every 6 hours until (a) 3 or more uterine contractions lasting for 40 seconds at 10 minutes interval was established or (b) maximum of 3 doses was given or (c) cervical dilatation more than or equal to 4 cms was reached. Bishops score was assessed at each induction with PGE2 gel.
- Misoprostol Group: 25mcg misoprostol was administered sublingually. The dose was repeated every 4 hours .The criteria to discontinue further doses were when (a) more than 3 uterine contractions lasting for 40 seconds at 10 minutes interval was established or (b) maximum of 5 doses given or (c) cervical dilatation more than or equal to 4 cms was reached. A vaginal examination was repeated after the third dose or when adequate uterine contractions were established. Fetal heart rate and uterine activity were monitored during induction with each dose.
- Spontaneous rupture of membranes was not an indication to stop further doses.
- Oxytocin drip if required was started 6 hrs after the last dose of induction for both the drugs. ARM was done prior to oxytocin augmentation to note the amount and colour of liquor.

Failed induction was defined as a) if the woman did not get into active labour 6 hours after administration of the last dose of the drug and b) Caesarean section or an alternative method of induction was decided as per the discretion of the consultant

All the patients were monitored closely throughout the course of labour. Progress of labour was charted on a partograph in active labour. Intermittent auscultation or continuous cardiotocography was used as the case indicated.

Uterine tachysystole was defined as more than five contractions per 10 minutes, uterine hypertonus as when one contraction lasted more than 2 minutes and hyperstimulation syndrome as the presence of non-reassuring FHR tracing combined with either tachysystole or hypertonus. Non-reassuring FHR patterns were defined as persistent or recurring episodes of severe variable decelerations, late decelerations, prolonged fetal bradycardia or a combination of decreased beat-to-beat variability and a decelerative pattern.[10]

3. Result

In present study, 200 cases were included. 100 cases were induced with misoprostol 25µgm sublingually and 100 cases with intra cervical dinoprostone gel. The desired outcomes were compared and results were analyzed.

Misoprostol had higher success rate (81% vs 76%) and lower caesarean section rate (19% vs 24%) and also required less augmentation with oxytocin for labour. 78% patients delivered in the first 24 hrs in misoprostol group compared to 52% patients in dinoprostone group.

	Misoprostol	Dinoprostone
Vaginal delivery	81	76
Caesarean delivery	19	24
Need for augmentation	34%	67%
Delivery in 1st 24 hours	78%	52%

The mean induction to active phase time and Mean induction to delivery time was also less in the misoprostol group than dinoprostone group. (11.8 hrs vs 11.97 hrs and 14.5 hrs vs 20 hrs respectively)

	Misoprostol	Dinoprostone
Mean induction to active phase time	11.8 hrs	14.5 hrs
Mean induction to delivery time	11.97 hrs	20 hrs

Maximum numbers of women in the study group had a Bishop's score of 3-4. Postinduction Bishop's score was 8.59 in Misoprostol group as compared to 6.76 in Dinoprostone group.

Mean Bishop's score	Misoprostol	Dinoprostone
Preinduction	3.32	3.45
Postinduction	8.59	6.76

Only 3 patients in misoprostol group had failure of induction whereas in dinoprostone group 14 patients had failure of induction. The main indication of Cesarean section in dinoprostone group was failure of induction as mentioned in below Table. In the misoprostol group, Cesarean section was done mainly for meconium stained liquor which was also the

Licensed Under Creative Commons Attribution CC BY

second major indication for Cesarean section in the dinoprostone group.

Indication for caesarean section	Misoprostol	Dinoprostone
Induction failure	16%	58%
Meconium stained liquor	47%	25%
Fetal distress	37%	17%

The neonatal APGAR scores at 1 and 5 minute were found similar in subjects treated either with sublingual Misoprostol or dinoprostone gel. The incidence of NICU admission was also similar in both the groups.

	Misoprostol	Dinoprostone
1 minute APGAR <=7	9	8
5 minute APGAR <=7	2	2
NICU Admission	10	8

The incidence of side effects like vomiting, diarrhea, hyperthermia was similar in both the groups. Incidence of tachysystole was more in subjects treated with sublingual misoprostol than in subjects treated with dinoprostone gel.

	Misoprostol	Dinoprostone
Tachysystole	2	0
Hyperstimulation	1	0
Vomiting	4	3
Diarrhea	3	3
hyperthermia	1	1

Cost of one dose of dinoprostone gel was Rs 240 and of misoprostol was Rs 4 and 60 paisa. Mean number of doses required for induction of labor with misoprostol and dinoprostone were 2.7 and 2.2 respectively. So Mean cost of induction with Dinoprostone was Rs.528 /- and with Misoprostol was Rs.12/-.

4. Discussion

The ideal agent for cervical ripening and induction of labor should be effective, non-invasive, economical, rapid in action and safe to both mother and fetus. None of the methods or agents currently available fulfill all these criteria, but prostaglandins are one of the most effective means of achieving cervical ripening and induction of labor providing, good clinical efficacy and patient satisfaction. FIGO has given his recommendation for the use of intravaginal Misoprostol.

(25µg 4 hourly for maximum six dosages) for induction of labor at term.[11] Therefore Misoprostol can be such an agent with the advantages of cost and convenience, despite of the fact that it is not FDA-labeled for this purpose.

Praveen et al done comparative studies of sublingual (S/L), oral and vaginal misoprostol for cervical ripening and reported that administration of misoprostol by the sublingual route is better than the oral and vaginal routes for cervical ripening.[12] Therefore in this study we compare sublingual misoprostol with intracervical dinoprostone gel in cervical ripening and induction of labor.

Patients receiving sublingual administration of misoprostol have shorter induction to active phase, induction to delivery time intervals and also require less oxytocin for augmentation than the patients in which intra cervical dinoprostone gel was administered. Similar to present study Wing et al, McKenna et al, Liu et al, and Jha et al reported shorter induction to delivery time interval in Misoprostol group than in Dinoprostone group.[13-16] However Zhang et al did not find significant difference in induction to delivery time interval in two groups.[17]

Similar to present study Zhang et al reported higher rate of tachysystole in women receiving misoprostol than in those receiving PGE2 gel.[12] APGAR score at 1 minute and at 5 minute as well as neonatal complications was similar in both the groups. Liu et al, Langen egger et al and Patil et al also reported the same.[15, 18, 19]

5. Conclusion

Misoprostol is demonstrated to be a viable alternative technique of labor induction since it is efficacious, easily administered, not expensive, stable at room temperature, needs no refrigeration with a longer shelf-life than dinoprostone gel. It allows the better patient acceptability although uterine hyper stimulation and meconium staining is the main concern with misoprostol use, close maternal-foetal monitorization and timely intervention measures would prevent devastating adverse effects during labor induction and increase tolerability of the drug by both the mother and foetus. So, by the present study, it was concluded that sublingual misoprostol is a more successful, lower-cost agent for induction of labor than intracervical dinoprostone gel.

References

[1] Houghton Mifflin Company. Induction of labor. In: American Heritage Dictionary, eds. The American Heritage Dictionary, 4th ed. Boston, MA. Houghton Mifflin Harcourt; 2006:1074.
[2] Witter FR. Prostaglandin E2 preparations for pre-induction cervical ripening. Clin Obstet Gynecol. 2000; 43:469-74.
[3] Arias F. Pharmacology of oxytocin and prostaglandins. Clin Obstet Gynecol. 2000; 43:455-68.
[4] American College of Obstetricians and Gynecologist. New U.S. food and drug administration labeling on cytotec (misoprostol) use and pregnancy. In: ACOG, eds. Committee Opinion. Washington, DC: American College of Obstetricians and Gynecolgists; 1999:283.
[5] Li XM, Wan J, Xu CF, Zhang Y, Fang L, Shi ZJ, Li K. Misoprostol in labor induction in term pregnancy: a meta-analysis. Chin Med J (Engl). 2004; 117:449-52.
[6] Schroder AK, Taulhert S, Diedrich K. induction of labor at term with misoprostol: an effective, safe and inexpensive alternative. Zenrealbl Gynecol. 2004;126:54-8.
[7] WHO recommendations for induction of labour. Geneva: World Health Organization, 2011.
[8] ACOG. Induction of Labour. Washington, DC, USA: The American College of Obstetricians and Gynecologists, ACOG Practice Bulletin Number 10. 1999.
[9] Shetty A, Mackie L, Danielian P, Rice P, Templeton A. Sublingual compared with oral misoprostol in term

Licensed Under Creative Commons Attribution CC BY

labour induction: a randomised controlled trial. *BJOG: an international journal of obstetrics and gynaecology* 2002; **109**:645–50.
[10] American College of Obstetricians and Gynecologists: Fetal heart rate patterns: monitoring, interpretation, and management. ACOG Practice Bulletin no.207 Washington, DC: American College of Obstetricians and Gynecologists; 1995.
[11] Weeks A, Faúndes A. Misoprostol in obstetrics and gynecology. Int J Gynecol Obstet. 2007;99(2):S156-9.
[12] Parveen S, Khateeb ZA, Mufti SM, Shah MA, Tandon VR, Hakak S et al. Comparison of sublingual, vaginal, and oral misoprostol in cervical ripening for first trimester abortion. Indian J Pharmacol. 2011;43(2):172-5.
[13] Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cervical ripening and labor induction. Am J Obstet Gynecol. 1995;172(6):1811-6.
[14] McKenna DS, Ester JB, Proffitt M, Waddell KR. Misoprostol outpatient cervical ripening without subsequent induction of labor: A randomized trial. Obstet Gynecol. 2004;104(3):579-84.
[15] Liu A, Lv J, Hu Y, Lang J, Ma L, Chen W. Efficacy and safety of intravaginal misoprostol versus intracervical dinoprostone for labor induction at term: a systematic review and meta-analysis. J Obstet Gynaecol Res. 2014;40(4):897-906.
[16] Jha N, Sagili H, Jayalakshmi D, Lakshminarayanan S. Comparison of efficacy and safety of sublingual misoprostol with intracervical dinoprostone gel for cervical ripening in prelabor rupture of membranes after 34 weeks of gestation. Arch Gynecol Obstet. 2015;291(1):39-44.
[17] Zhang Y, Wang J, Yu Y, Xie C, Xiao M, Ren L. Misoprostol versus prostaglandin E2 gel for labor induction in premature rupture of membranes after 34 weeks of pregnancy. Int J Gynecol Obstet. 2015;130(3):214-8.
[18] Langenegger EJ, Odendaal HJ, Grove D. Oral misoprostol versus intracervical dinoprostone for induction of labor. Int J Gynecol Obstet 2005;88:242-8.
[19] Patil KP, Swamy MK, Rao RK. Oral misoprostol vs intra-cervical dinoprostone for cervical ripening and labor induction. J Obstet Gynecol India. 2005;55(2):128-131.

Licensed Under Creative Commons Attribution CC BY