THE JOURNAL OF OBSTETRICS AND GYNECOLOGY OF INDIA

The Journal of Obstetrics and Gynecology of India (July–August 2014) 64(4):270–273
DOI 10.1007/s13224-014-0521-8

ORIGINAL ARTICLE

Labor Induction with 50 µg Vaginal Misoprostol: Can We Reduce Induction-Delivery Intervals Safely?

Sareen Sweta · Chawla Indu · Singh Pushpa

Received: 13 March 2013 / Accepted: 8 February 2014 / Published online: 12 April 2014

Abstract

Objective To compare the efficacy and safety profile of two methods of labor induction i.e., intracervical dinoprostone gel (0.5 mg 8 h) and misoprostol (50 µg 4 h) for induction of labor in women with a poor Bishop's score.

Design Observational study.

Study Period January 1st, 2009 to December 31st, 2010.

Population A total of 329 women with unfavorable cervices induced at or near term.

Methods Two cervical ripening agent study arms were used: dinoprostone gel (193 women) and misoprostol (137 women).

Main Outcome Measures Induction to delivery interval, cesarean section, incidence of meconium stained liquor, FHR pattern, incidence of uterine hyperstimulation, and neonatal outcomes.

Results The induction to delivery interval was significantly shorter in the misoprostol group as compared to the dinoprostone group ($p < 0.001$). There was no difference in cesarean section rates between the two groups (dinoprostone gel 43 %; misoprostol 33 %; $p = 0.144$). The incidence of non-reassuring fetal heart rate pattern, meconium stained liquor, and uterine hyperstimulation were equivalent in both the groups ($p = 0.529$; 0.733; and 0.321, respectively). The neonatal outcomes in both the groups were comparable in terms of Apgar scores at birth ($p = 0.160$) and NICU admissions ($p = 0.951$).

Conclusions Labor induction in women with unfavorable cervices results in high caesarean section rates. However, the use of misoprostol significantly reduces the induction to delivery interval, without adversely affecting the caesarean section rates and neonatal outcomes. Hence it may become a cost-effective alternative to dinoprostone gel in resource-poor settings like India.

Keywords Labor induction · Misoprostol · Dinoprostone · Induction-delivery interval

Introduction

Induction of labor is a common intervention in obstetrics required in up to 30 % of pregnancies [1]. In recent years, synthetic prostaglandins (PGs) have emerged as useful labor induction agents. Dinoprostone gel, a PGE_2 analog, has been approved by US FDA for this purpose. Misoprostol, a PGE_1 analog, has been under trial for this indication [2–15]. The present study compares the use of vaginal misoprostol (50 µg at 4 h intervals) with intracervical dinoprostone gel (0.5 mg 8 h) for induction of labor.

Sareen S. (✉), Senior Resident · Chawla I., Associate Professor · Singh P., Professor & Head of Department
Department of Obstetrics & Gynecology, Dr. RML Hospital & PGIMER, New Delhi 110001, India
e-mail: drswetanayyar@gmail.com

Sareen S., Senior Resident
3/18, 2nd Floor, Old Rajender Nagar, New Delhi 110060, India

Methods

The present retrospective study was conducted at the Department of Obstetrics and Gynecology, Dr. RML Hospital and PGIMER, New Delhi. All women who were subjected to induction of labor between January 2009 and December 2010 were reviewed in the study. Pregnant women over 36 weeks gestation, with a singleton fetus in cephalic presentation and a modified Bishop score of 0–4 who underwent induction of labor were included. Exclusion criteria were contraindications for the administration of prostaglandins and/or for vaginal delivery, previous uterine surgery, low-lying placenta, any active infection of the lower vaginal tract, or an abnormal pre-induction fetal heart rate (FHR) tracing.

The women were induced using either intracervical dinoprostone gel (0.5 mg) or vaginal 50 μg misoprostol tablet after written, informed consent. Those in the dinoprostone group received a maximum of three doses, once every 8 h. The women in the misoprostol group received a maximum of three 50 μg doses in the posterior fornix once every 4 h. All the women underwent cardiotocography (CTG) 30 min prior to and 45 min after administration of each dose of the medication. Thereafter, fetal monitoring was done by a combination of intermittent auscultation and CTG. FHR traces were considered non-reassuring if there was persistent reduced baseline variability, late decelerations, and/or complicated variable decelerations.

In women with onset of labor after three doses of induction agents, amniotomy was performed after cervical dilatation of 3 cm. Oxytocin augmentation was commenced if there were inadequate contractions 1 h after membrane rupture. The oxytocin infusion was titrated to maintain regular moderate to strong contractions. The WHO partogram was plotted in active labor. In women with no response even after three doses of induction agents, amniotomy was performed if the cervical findings were conducive. Oxytocin infusion was started and titrated as stated earlier. A failed induction of labor was defined as follows: inability to rupture the membranes even after three doses of prostaglandin ripening agents; or cases where amniotomy could be performed but there was failure to progress to the active phase despite 6 h of oxytocin infusion after amniotomy. Abnormal uterine contractions were defined as tachysystole of five or more contractions in a 10-min period for at least two consecutive periods and hypertonus (uterine contraction with a duration of >2 min). Hyperstimulation of the uterus was defined as either tachysystole or hypertonus with changes in FHR patterns.

The primary outcome measure was induction-to-delivery interval. Secondary outcomes were the incidence of operative delivery (including instrumental vaginal delivery), indications for operative delivery, uterine hyperstimulation, staining of the amniotic fluid with meconium, requirement for augmentation with oxytocin, and occurrence of postpartum bleeding. The neonatal outcomes recorded were the Apgar score at 1 and 5 min after birth and admission to the neonatal intensive care unit (NICU).

Results

During the period reviewed, 351 pregnant women underwent induction of labor for various indications. Of these, 329 women met the inclusion criteria, of which 192 were induced using dinoprostone gel and 137 using 50 μg misoprostol.

Complete data were obtained for these women and analyzed using the software SPSS. Results were calculated by applying Fisher's exact test, χ^2-test, t test, and calculating the p value using an alpha level of 0.05 for Type I errors.

Both the groups had similar baseline demographic characteristics with respect to age ($p = 0.901$), parity ($p = 0.729$), and gestational age ($p = 0.401$). Indications for induction of labor were comparable between the two groups. There was no statistically significant difference between the two groups with respect to pre-induction Bishop's score ($p = 0.872$) (Table 1).

Out of the 329 women included in the study, 201 delivered vaginally (spontaneous or instrumental) and 128 required cesarean sections. The mean induction-delivery interval with misoprostol was 18.3 h as compared to 25.1 h with dinoprostone gel.

As can be seen from Table 2, of the 137 women induced using misoprostol, 92 delivered vaginally, all within 24 h of receiving the first dose. Of the 192 women induced using dinoprostone gel, 109 delivered vaginally, with only 39 (35.8 %) women delivering within 24 h of the first dose ($p < 0.001$). Considering the time frame from the first dose of induction agent, 90 (97.8 %) women had labor onset within 6 h in the misoprostol group as compared to 9 (8.3 %) in the dinoprostone group (p value < 0.001). The duration of latent phase was less than 6 h in 56 (60.9 %) women in the misoprostol group as compared to 37 (33.9 %) in the dinoprostone group (p value < 0.001). Active phase was shortened to less than 6 h in 72 (78.3 %) women in the misoprostol group and 65 (59.6 %) in the dinoprostone group (p value $= 0.005$). Fifty seven (41.6 %) women in the misoprostol group had labor onset and progression after two doses, whereas 121 (63.0 %) women in the dinoprostone arm required three doses for labor onset (p value < 0.001). Oxytocin augmentation was required in 100 (73 %) women in the misoprostol group as

Table 1 Demographic and obstetric characteristics

	Dinoprostone	Misoprostol	*p* value
Age (years)			0.901
18–20	35 (18.23)	27 (19.71)	
21–30	132 (68.75)	94 (68.61)	
>30	25 (13.02)	16 (11.68)	
Parity			0.729
0	150 (78.13)	110 (80.29)	
1	22 (11.46)	12 (8.76)	
2	20 (10.42)	15 (10.95)	
Gestational age (weeks)			0.401
36–40	106 (55.21)	82 (59.85)	
Post-dates	86 (44.79)	55 (40.15)	
Indication for induction			
Post-dates	70 (36.46)	49 (35.77)	
PIH	45 (23.44)	35 (25.55)	
GDM	28 (14.58)	20 (14.60)	
Low BPS	24 (12.50)	15 (10.95)	
IUGR	17 (8.85)	13 (9.49)	
Oligoamnios	01 (0.52)	02 (1.46)	
Others	07 (3.65)	03 (2.19)	
Modified Bishop score			0.872
1–2	109 (56.77)	79 (57.66)	
3–4	83 (43.23)	58 (42.34)	

Table 2 Delivery outcomes

	Dinoprostone	Misoprostol	*p* value
Induction-delivery interval (h)			<0.001
<24 h	67 (34.9)	110 (80.29)	
>24 h	125 (65.1)	27 (19.71)	
Vaginal delivery within 24 h	39 (35.78)	92 (100.00)	<0.001
Vaginal delivery within 12 h	1 (0.92)	13 (14.13)	<0.001
Time to onset of labor <6 h	9 (8.26)	90 (97.83)	<0.001
Duration of latent phase <6 h	37 (33.94)	56 (60.87)	<0.001
Duration of active phase <6 h	65 (59.63)	72 (78.26)	0.005
Requirement of repeat dose			<0.001
Nil	10 (5.21)	48 (35.04)	
One	61 (31.77)	57 (41.61)	
Two	121 (63.02)	32 (23.36)	
Requirement of oxytocin augmentation	167 (86.98)	100 (72.99)	0.001
Mode of delivery			0.144
Vaginal delivery	106 (55.21)	90 (65.69)	
Cesarean section	83 (43.23)	45 (32.85)	
Instrumental vaginal delivery	3 (1.56)	2 (1.46)	
Indication for cesarean section			0.722
Failed induction	39 (46.99)	18 (40.0)	
Non-reassuring FHR	33 (39.76)	21 (46.67)	
Non-progress of labor	11 (13.25)	6 (13.33)	

compared to 167 (87 %) in the dinoprostone group (p value = 0.001).

Cesarean sections were required in 45 (32.8 %) subjects in misoprostol group and in 83 (43.2 %) in the dinoprostone group (p value = 0.144). The main indication for cesarean section in the misoprostol group was fetal distress, and this occurred more often than in the dinoprostone group (n = 21, 46.7 % vs n = 33, 39.8 %, respectively). Cesarean sections were performed more often for failed induction in the dinoprostone group than in the misoprostol group (n = 39, 47 % vs n = 18, 40 %, respectively). The incidence of (Table 3) uterine hyperstimulation was similar in both the groups (about 2 %). The incidence minor side effects like shivering, fever, diarrhea, vomiting, etc., were similar in the two groups (p value = 0.733). None of our subjects suffered uterine rupture or placental abruption.

Considering the neonatal outcomes in this study, there were more cases of meconium staining of (Table 4) amniotic fluid in the misoprostol arm (n = 13, 6.8 %) as compared to dinoprostone arm (n = 8, 5.8 %) (p value = 0.733). The incidence of low Apgar score at 1 min was 5.8 % (n = 8) in the misoprostol group as compared to 6.8 % (n = 13) in the dinoprostone group (p value = 0.160). Low Apgar score at 5 min was seen in 2 (1.5 %) neonates in the misoprostol group as compared to 9 (4.7 %) in the dinoprostone group (p value = 0.195). The rate of NICU admission was 22.6 % (n = 31) in the misoprostol group as compared to 22.9 % (n = 44) in the dinoprostone group (p value = 0.951).

Discussion

The present study concluded that misoprostol was more efficacious than dinoprostone gel for labor induction. This finding is in agreement with the conclusions of a recent meta-analysis conducted by Sanchez-Ramos et al. [16] comprising of 44 RCTs.

In the past, concerns have been raised over the increased incidence of operative delivery with the use of misoprostol [1]. In the present study, the rate of cesarean sections was similar in the two groups, but the indications for cesarean sections were different. In the dinoprostone arm, more cesarean sections were performed for failed induction of labor, while in the misoprostol arm, more sections were done for non-reassuring FHR. However, these FHR abnormalities did not transpire into adverse neonatal outcomes like low Apgar scores or increased rate of NICU admissions. Earlier studies have also shown increased incidence of fetal heart rate abnormalities after misoprostol application [8, 10] but no increase in adverse neonatal outcomes [2–9, 11–15].

Table 3 Adverse maternal outcomes

	Dinoprostone	Misoprostol	*p* value
Minor side effects	13 (6.77)	8 (5.84)	0.733
Hyperstimulation	3 (1.56)	4 (2.92)	0.400
Abruptio placentae	Nil	Nil	
Uterine rupture	Nil	Nil	
PPH			0.892
Atonic	7 (3.65)	6 (4.38)	
Traumatic	1 (0.52)	1 (0.73)	

Table 4 Neonatal outcomes

	Dinoprostone	Misoprostol	*p* value
Birth weight (kg)			0.845
<2.0	13 (6.77)	10 (7.30)	
2.0–2.5	17 (8.85)	9 (6.57)	
2.5–3.0	97 (50.52)	74 (54.01)	
>3.0	65 (33.85)	44 (32.12)	
Meconium stained liquor	8 (5.84)	13 (6.77)	0.733
Apgar <7 at 1 min	13 (6.77)	8 (5.84)	0.160
Apgar <7 at 5 min	9 (4.69)	2 (1.46)	0.195
NICU admission	44 (22.92)	31 (22.63)	0.951

As regards the dosage regimen, American College of Obstetricians and Gynecologists committee opinion stated that 25 μg misoprostol should be used for cervical ripening and labor induction [17]. This opinion was based on the greater incidence of tachysystole noted with larger doses of misoprostol. In a review article, Sanchez-Ramos [18] stated the following regarding vaginal misoprostol doses of 25 or 50 μg. Patients who received the 25 μg dose had a lower incidence of tachysystole and hyperstimulation; however, they also had a longer interval to vaginal delivery, and a lower proportion of these patients delivered vaginally within 12–24 h. No differences were noted in the cesarean delivery rate, cesareans performed for fetal heart rate abnormalities, operative delivery rates, or NICU admissions.

To conclude, misoprostol in a dosage regimen of 50 μg 4 h offers a distinct advantage over intracervical dinoprostone gel (0.5 mg) in being significantly more effective in inducing labor and in shortening the induction process, while maintaining a similar safety profile for the mother and the fetus. In a low-resource setting, misoprostol is a good alternative as it is relatively inexpensive, simpler to administer, and does not require refrigeration for storage.

References

1. ACOG (1999) Induction of labour. ACOG practice bulletin number 10. Washington, DC, USA: The American College of Obstetricians and Gynecologists.
2. Wing DA, Jones MM, Rahall A, et al. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. Am J Obstet Gynecol. 1995;172:1804–10.
3. Wing DA, Rahall A, Jones MM, et al. Misoprostol: an effective agent for cervical ripening and labor induction. Am J Obstet Gynecol. 1995;172:1811–6.
4. Chuck FJ, Huffaker BJ. Labor induction with intravaginal misoprostol versus intracervical prostaglandin E2 gel (prepidil gel): randomized comparison. Am J Obstet Gynecol. 1995;173:1137–42.
5. Varaklis K, Gumina R, Stubblefield PG. Randomized controlled trial of vaginal misoprostol and intracervical prostaglandin E2 gel for induction of labor at term. Obstet Gynecol. 1995;86:541–4.
6. Mundle WR, Young DC. Vaginal misoprostol for induction of labor: a randomized controlled trial. Obstet Gynecol. 1996;88:521–5.
7. Gottschall DS, Borgida AF, Mihalek JJ, et al. A randomised clinical trial comparing misoprostol with prostaglandin E2 gel for preinduction cervical ripening. Am J Obstet Gynecol. 1997;177:1067–70.
8. Buser D, Mora G, Arias F. A randomised comparison between misoprostol and dinoprostone for cervical ripening and labor induction in patients with unfavorable cervices. Obstet Gynecol. 1997;89:581–5.
9. Sanchez-Ramos L, Peterson DE, Delke I, et al. Induction with prostaglandin E1 misoprostol compared with dinoprostone vaginal insert: a randomised trial. Obstet Gynecol. 1998;91:401–5.
10. Kolderup L, McLean L, Grullon K, et al. Misoprostol is more efficacious for labor induction than prostaglandin E2, but is it associated with more risk? Am J Obstet Gynecol. 1999;180:1543–5150.
11. Danielian P, Porter B, Ferri N, et al. Misoprostol for induction of labor at term: a more effective agent than dinoprostone vaginal gel. Br J Obstet Gynaecol. 1999;106:793–7.
12. Nunes F, Rodrigues R, Meirinho M. Randomized comparison between intravaginal misoprostol and dinoprostone for cervical ripening and induction of labor. Am J Obstet Gynecol. 1999;181:626–9.
13. Fletcher H, Mitchell S, Frederick J, et al. Intravaginal misoprostol versus dinoprostone as cervical ripening and labor-inducing agents. Obstet Gynecol. 1994;83:244–7.
14. Surbek DV, Boesiger H, Hoesli I, et al. A double-blind comparison of the safety and efficacy of intravaginal misoprostol and prostaglandin E2 to induce labor. Am J Obstet Gynecol. 1997;177:1018–23.
15. Wing DA, Ortiz-Omphroy G, Paul RH. A comparison of intermittent vaginal administration of misoprostol with continuous dinoprostone for cervical ripening and labor induction. Am J Obstet Gynecol. 1997;177:612–8.
16. Sanchez-Ramos L, Kaunitz AM, Wears RL, et al. Misoprostol for cervical ripening and labor induction: a metaanalysis. Obstet Gynecol. 1997;89:633–42.
17. American College of Obstetricians and Gynecologists (1999) Induction of labor with misoprostol. ACOG committee opinion no. 228. Washington, DC 7: American College of Obstetricians and Gynecologists.
18. Sanchez-Ramos L. Induction of labor. Obstet Gynecol Clin N Am. 2005;32:181–200.