Original Article

Comparative evaluation of 25 µg and 50 µg of intravaginal misoprostol for induction of labor

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Abstract

Objectives: To compare the efficacy and safety of 25 µg vs 50 µg of intravaginal misoprostol for induction of labor
Methods: One hundred forty eight pregnant females requiring induction were randomly assigned to receive either 25 µg (80 cases-group A) or 50 µg (68 cases – group B) of intravaginal misoprostol every 4 hours till adequate contractions were achieved or maximum dose of the drug up to 200 µg was used. **Results:** The onset of contraction was earlier in group B (3.40 ± 1.88) as compared to group A (4.56 ± 2.25); 81.2% of the cases in group A and 83.8% of the cases in group B delivered vaginally. Induction to delivery interval was shorter in group B (43.9%) cases; while 29% cases in group A delivered within 12 hours. Mean dose for successful induction in group A was high compared to group B. Requirement for oxytocin infusion was higher in group A (25% vs 16.2%) ($p=0.189$). Abnormal contractility pattern was seen in 14.7% cases in group B as compared to 6.25% cases in group A ($p=0.765$). GIT side effects were common in group B (38.2%) as compared to group A (28.75%) ($p=0.22$). Rupture uterus did not occur in any group. In group B 34.7% neonates had apgar score <7 at 1 min. and required NICU admission as compared to only 14.9% in group A. **Conclusion:** 50 µg dose though more efficacious than 25 µg dose, appears to be less safe both for mother and baby due to the high incidence of tachysystole, hyperstimulation and intrauterine passage of meconium.

Key words: misoprostol, induction, labor, intravaginal

Introduction

Misoprostol (PGE_1) is a new promising agent for labor induction. Initially it was launched for treatment of NSAID induced gastric ulcer but it was found that it had excellent cervical ripening and uterotonic

properties. Though not US FDA approved, it is being increasingly used in pregnant females for elective medical abortions, cervical ripening before surgical abortion, evacuation of uterus in cases of fetal death and induction of labor. However, FDA recognizes that in certain circumstances off label uses of approved products are appropriate, rational, and accepted medical practice¹.

Advantages of misoprostol over other inducing agents include stability at room temperature, easy administrability and low cost. Various studies have shown that it can be administered by a variety of routes

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and in different doses. However its ideal dose, route and frequency of administration are still under investigation. This study was planned to compare the efficacy and safety of 25 µg versus 50 µg intravaginal misoprostol for labor induction.

Material and Methods

The study was carried out on pregnant females (37 weeks or more) requiring induction of labor for any medical or obstetrical indication. The study duration was one year and it was approved by the Ethical Committee of the hospital.

Women with singleton pregnancy at =37 weeks gestation with reactive nonstress test were included after informed consent. Pregnant females with favorable cervix (Bishop score ≥ 6), any contraindication to vaginal birth, previous uterine surgery and ruptured membranes were excluded from the study. The study included 148 pregnant females out of which 80 cases received 25 µg (Group A, V_{25}) and 68 cases received 50 µg (Group B, V_{50}) of intravaginal misoprostol. The tablet was placed in the posterior vaginal fornix without any lubricant. The drug was repeated every 4 hours till regular adequate uterine contractions were achieved or maximum up to 200 µg of dose of the drug was used up. Females with inadequate contractions or no uterine contractions despite 200 µg dose were augmented using oxytocin.

The data was analyzed using Chi-square test and student 't' test.

Observations

Table 1 shows sociodemographic profile of the females included in the study. There was no significant difference in case distribution according to sociodemographic profile. Various indications for induction were post-dated pregnancy 36(24.3%), IUGR/Oligohydramnios 27(18.24%), hypertension 25(16.89%), intrauterine death 18(12.16%), congenital anomalies 12(8.108%) and miscellaneous 30(20.27%). The mean Bishop score in Group A was 3.0 ± 1.23 while in Group B it was 3.0 ± 1.52 ; 64 cases (43.2%) had Bishop score < 3 while 84 cases (56.75%) had Bishop score ≥ 3 . The mean interval of onset of contraction in Group A (V_{25}) was 4.56 ± 2.25 hours while in Group B (V_{50}) it was 3.40 ± 1.88 and the difference was statistically significant ($t=3.367$, $p<0.001$). Females receiving 25 µg required oxytocin augmentation more

frequently than did those receiving 50 µg (25% vs. 16.2%, $p=0.189$).

Table 2 shows induction to delivery interval. The induction to delivery interval was shorter in group B as compared to that in group A (43.9%) (V_{50}) and 29.1% (V_{25}) delivered in less than 12 hours ($p<0.001$). There was no difference between the groups with respect to mode of delivery. Approximately 81.2% in group A and 83.8% in group B delivered vaginally. Mean dose required in Group A was 105.7 µg while in Group B it was 147.8 µg ($p<0.001$).

Various indications for LSCS were irregular fetal heart rate, meconium, non-progress of labor and failed induction. Common indication for LSCS in group B was fetal distress (9/11 cases (V_{50}), 6/15 (V_{25}); $p=0.032$) while in group A it was failed induction [40% (V_{25}) vs 9.09% (V_{50}); $p=0.079$].

Abnormal contractility pattern was seen in 14.7% cases of Group B (V_{50}) as compared to 6.25% cesarean in group A (V_{25}) ($p=0.765$) (Table 3).

Various misoprostol related side effects, especially gastrointestinal side effects (nausea, vomiting, diarrhea, fever, headache) were common with higher dose (V_{50}) as compared to low dose group (V_{25}) (38.2% vs. 28.75%; $p=0.22$). Fatal complication of rupture uterus and postpartum hemorrhage did not occur in any of the patients.

Table 4 shows fetal outcome in two groups. Newborns with low apgar score (< 7) and those requiring neonatal admission were more in Group B as compared to Group A (34.7% vs. 14.9%, $p=0.01$; 35.6% vs. 16.4%, $p=0.005$ respectively).

Table 1. Demographic analysis of cases in different groups.

S.No.	Parameters	Group A	Group B
1.	Mean age (years)	26.24 $\pm$ 4.84	25.22 $\pm$ 4.98
2.	Parity		
	Primi	46 (57.5%)	41 (60.29%)
	Multi	34 (42.5%)	27 (29.71%)
3.	Mean height (cm)	150.3 $\pm$ 8.53	151.4 $\pm$ 6.57
4.	Mean weight (kg)	53.5 $\pm$ 9.54	56.4 $\pm$ 15.59

Table 2. Induction to delivery interval in vaginally delivered cases.

S.No.	Induction to delivery interval (hrs)	Group A (n=65)	Group B (V50) (n=57)
1.	<12	29.1%	43.9%
2.	12-24	35%	33.3%
3.	24-36	16.92%	14.04%
4.	>36	18.46%	8.77%

Table 3. Abnormal contractility pattern in different groups.

S.No.	Indications	Group A (V25) (n=80)	Group B (V50) (n=68)
1.	Tachysystole	3 (3.75%)	4 (5.9%)
2.	Hypertonus	1 (1.25%)	3 (4.4%)
3.	Hyperstimulation	1 (1.25%)	3 (4.4%)
	Total	5 (6.25%)	10 (14.7%)

Table 4. Fetal outcome analysis in different groups (excluding IUD and congenital anomaly cases).

S.No.	Outcome	Group A (V25) (n=69)	Group B (V50) (n=49)
1.	Apgar <7 at 1 min	10(14.9%)	17(34.7%)
	>7	59(85.5%)	32(65.3%)
2.	Resuscitation	30(44.8%)	27(55.1%)
3.	Admission	11(16.4%)	19(35.6%)
	NIIU	9	15
	NICU	2	4
4.	Meconium	7(10.4%)	6(12.2%)
5.	Phototherapy	5(7.5%)	4(8.2%)

Discussion

Misoprostol the PGE₁ and analogue appears to be safe and effective but the optimal dose needs to be determined so that successful vaginal deliveries can be accomplished with less number of side effects to mother and fetus in a short span of time.

In our study induction delivery interval was shorter in

Group B (V₅₀) as compared to Group A. Lisa et al² in their study on 399 pregnant females also reported shorter induction delivery interval in females who received 50 µg of misoprostol (826 min vs 970 min, p>0.02). Fewer cases in Group B (V₅₀) required oxytocin augmentation in our study. A Cochrane review by Hofmeyr³ also revealed that lower doses were associated with more need for oxytocin augmentation.

In the present study no difference was noted in the cesarean or other operative delivery rates among the cases in the two different groups, showing that both high and low dose were equally effective in inducing labor. However the cases with failed induction were more common in low dose group as compared to those in high dose group. This finding was consistent with the study of Meydanli et al⁴. Their study also reported that the proportion of women delivering vaginally with one dose of vaginal misoprostol was significantly greater in 50 µg group (0/49 vs 41/47; p<0.001).

In a comparative study reported by Hans et al⁵ the rate of cesarean section due to fetal distress was higher with the higher dose (28.6 vs 10.3%, p<0.05). This was comparable to our study [40% (V₂₅) vs 81.8% (V₅₀)].

We observed that the incidence of abnormal contractility pattern (tachysystole, hyperstimulation) was higher in 50 µg group (14.7% vs. 6.25%). Sanchez-Ramos et al⁶, in their meta-analysis of five randomized controlled trials also made similar observations. In contrast to this Farah et al² in their study reported that the incidence of hyperstimulation was similar between the two groups but the incidence of tachysystole was higher in the 50 µg group (32.8% vs. 15.6%; p>0.0001).

Minor side effects were common with higher dose but catastrophic complication of rupture uterus did not occur in any case in our study. However, there are studies that have reported serious complications with the use of misoprostol. A systematic review by Wagner⁷ of 16 medicolegal cases agreed with these findings. He reported hyperstimulation in all the 16 cases, with uterine rupture in 7 cases and hypoxic encephalopathy in 14 cases. Thomas et al⁸ reported rupture uterus in a primigravida patient after the use of 100 µg of misoprostol (25 µg given 4 hourly).

Neonatal outcome was also adversely affected in females who received higher dose. Babies with low apgar score, requiring resuscitation and NICU admission were significantly higher in 50 µg group. This

was in concurrence with the observations made by Has et al⁵. Contrary to this Sanchez-Ramos et al⁶ in their meta-analysis of five randomized clinical trials reported comparable neonatal outcomes with the two doses.

Conclusion

Misoprostol is a highly effective agent for labor induction. Complications remain a matter of concern. These can be minimized by judicious selection of dosages. 50 µg dose though more efficacious than 25 µg dose appears to be less safe both for mother and baby due to high incidence of tachysystole, hyperstimulation and meconium.

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