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Clinical Investigation

Comparative study of 25µg versus 50µg of intravaginal misoprostol for induction of labor

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Abstract

Background: To determine and compare the efficacy and safety of 25 µg and 50µg of intravaginal misoprostol for induction of labor at term and to study the maternal and fetal outcome in both groups. ***Methods:*** This prospective study was conducted in R.L.Jalappa Hospital and Research Centre, Kolar. Total of 200 cases meeting inclusion criteria were divided in to Group A and Group B who were induced with 25µg and 50µg of misoprostol intravaginally respectively and dose was repeated every sixth hourly interval till the patient gets adequate uterine contractions or cervical dilatation of ≥ 3cms or a maximum of 6 doses. PGE2 or oxytocin was used for delivery if required. Total dose of induction, induction delivery interval, mode of delivery, maternal and fetal outcome were recorded. The collected data was analyzed using student's' test and chi-square test. ***Results:*** Mean number of doses required and mean induction delivery interval was significantly less in 50µg group when compared to 25µg group (1.76±0.77 vs. 2.13±1.01, p=0.013) and (12.98±4.71 vs. 16.07±6.71 hours, p=0.001) respectively. Oxytocin augmentation was required less frequently in 50µg group B as compared to 25µg group A (35.2% vs. 70.1%, p <0.001**). Meconium stained liquor and fetal heart rate abnormalities were more among 50µg group compared to 25µg group (p=0.022* and p= 0.021*respectively). Maternal adverse effects were more common among 50µg group (11% vs 30%, p=0.001). Babies with low Apgar score, requiring resuscitation and NICU care were significantly higher in 50µg group. ***Conclusion:*** The intravaginal misoprostol used for induction of labor as 50 µg is more efficacious than 25µg of intravaginal misoprostol but it appears to be less safe both for the mother and the fetus.

Key words: Induction of labor, Meconium, Misoprostol.

Introduction

Misoprostol is PGE1 [1] was initially approved by US FDA's for prevention of peptic ulcer disease. Later on due its excellent cervical ripening and uterotonic properties, it is being increasingly used in pregnant women for induction of labor [2]. Various studies have shown that misoprostol can be administered by a variety of routes and in different doses. However its ideal dose, route of administration are still under investigation. Minor maternal side effects include diarrhea, nausea, vomiting, abdominal pain, chills, shivering and hyperthermia which are dose dependent. Uterine hyper stimulation and meconium stained amniotic fluid are also reported with higher dosage. This comparison was studied with the objective to whether by reducing the dosage the side effects can be reduced.

Materials and Methods

A prospective study was carried out in the department of Obstetrics and Gynecology, Sri Devaraj Urs Medical College, Kolar from January 2011 to August 2012. Approval of institutional ethical committee was obtained prior to commencement of study. Women with singleton pregnancy ≥ 37weeks gestation with vertex presentation; intact membrane and reactive CTG were included after informed consent. Those with favorable cervix (modified bishop score ≥ 6), previous cesarean section or any other uterine surgery, gravida ≥ 5, any contraindication for vaginal delivery, any contraindication to the use of prostaglandins i.e. women with history of asthma, glaucoma, cardiac disease or any hypersensitivity to the use of prostaglandins. Total number of 200 cases

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meeting inclusion criteria were divided into Group A (25µg) and Group B (50µg). A complete history including maternal age, parity, gestational age and indication for induction of labor were noted. Abdominal examination was done to know the presentation, uterine tone and the fetal heart rate. Per vaginal examination was done to know the modified Bishop score and to rule out cephalopelvic disproportion. Cardiotocograph (CTG) and Obstetric scan were done to all the patients to ascertain the fetal well being. An informed written consent was taken prior to induction. Following exclusion of uterine contractions or a non-reassuring CTG and confirmation of Modified Bishop score ≤ 5, patients received intravaginal misoprostol either 25µg (Group A) or 50µg (Group B), allotted alternatively till the patient gets adequate uterine contractions (3 contractions in 10 minutes) or cervical dilatation of ≥ 3cms or a maximum of 6 doses are administered. If they do not respond to the above protocol (after receiving 6 doses of misoprostol), they were considered as failed induction and further PGE2 or oxytocin was used for delivery if required. The progress of labor was monitored by partogram in active stage of labor. Labor was augmented with oxytocin if required. Total dose of induction, induction delivery interval, mode of delivery, oxytocin requirement, maternal side effects and fetal outcome like meconium stained liquor, FHR abnormalities, Apgar score, neonatal resuscitation and NICU admission were recorded. All the results were analysed by using Student 't' test and chi-square test.

Results

The mean maternal age, parity, gestational age and pre-induction modified Bishop Score of both groups were well matched. The most common indication for induction of labor in both the groups was post-dated pregnancy and pre-eclampsia/eclampsia (Figure 1).

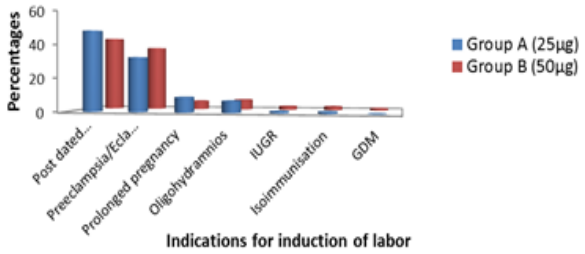

Fig:1 – Showing indications for induction of labor

Total 29 (40.8%) cases of group B and 25 cases (28.7%) of group A delivered with only single dose of misoprostol (p=0.110) which is statistically significant. The mean number of doses in group A (25µg) was 2.13±1.01 whereas group B (50µg) was 1.76±0.77 with p value of 0.013*. It was observed that in group B total 28 cases (39.4%) as compared to 24 cases (27.6%) in group A went into active stage of labor within 6 hours of induction. The mean induction to active stage interval was significantly less in Group B (8.32 hrs) as compared to Group A (10.78 hrs) with P value of 0.004**

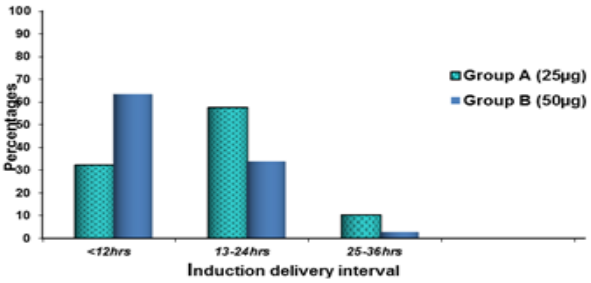

Fig:2 – Showing induction delivery interval

In the above figure 2, 45 (63.4%) cases delivered within 12 hours of induction in group B when compared to only 28 cases (32.2%) in group A, p= 0.022. Mean induction delivery interval is significantly less in Group B (12.98±4.71) when compared to Group A (16.07±6.71) with P=0.001**. In group A, 61(70.1%) cases required oxytocin augmentation whereas only 25(35.2%) cases required oxytocin augmentation in group B with P<0.001**.

Mode of delivery	Group A (25µg) (n=100)		Group B (50µg) (n=100)	
	No	%	No	%
Spontaneous vaginal delivery	84	84.0	65	65.0
Operative vaginal delivery	3	3.0	6	6.0
Cesarean section	13	13.0	29	29.0
Inference	LSCS is significantly more associated with Group B (29.0%) when compared to Group A			

Table :1 – Representing mode of delivery

The above table 1 shows the mode of delivery among the two groups. Among group A (25µg) 87% delivered vaginally whereas in group B (50µg) 71% delivered vaginally. The cesarean section rate was high among group B (29%) when compared to group A (13%) with p<0.001**. It was observed that 7 cases (53.84%) in group A underwent cesarean section for fetal distress as compared to 21 cases (72.4%) among group B, but this was not statistically significant with p=0.238. Maternal adverse effects (Figure 3) were significantly more in Group B (30.0%) when compared to Group A (11.0%) with P=0.001**. Minor adverse effects (nausea, vomiting, diarrhea and fever) were significantly more among 50µg group when compared to 25µg. Abnormal uterine contractions were also more commonly seen among 50µg group

than with 25µg group. Postpartum hemorrhage was similar among both the groups i.e. 2% and 3% among group A and B respectively.

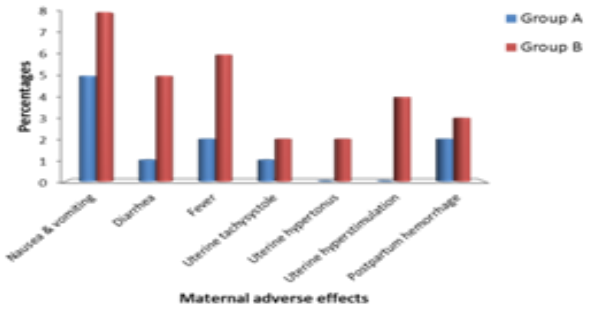

Fig:3 – Represents maternal adverse effects

Fetal outcome	Group A (25µg) (n=100)		Group B (50µg) (n=100)		P value
	No	%	No	%	
FHR abnormalities	16	16.0	31	31.0	0.021*
Meconium Stained Liquor	18	18.0	32	32.0	0.022*
1 minute Apgar score <7	6	6.0	20	20.0	0.003**
Neonatal resuscitation	18	18.0	32	32.0	0.022*
NICU admission required	5	5.0	15	15.0	0.018*

Table :2 – Representing fetal outcome

With regards to the fetal outcome (Table 2) it was observed that fetal outcome in group A is better compared to group B. The fetal heart rate abnormalities were significantly high in group B. Meconium stained liquor was 18% in group A (25µg) and 32% in group B (50µg). 1 minute Apgar score <7 was 20% in group B as compared to only 6% in group A. which was statistically significant with p=0.003**. NICU admission was 15% in group B when compared to 5% in group A which was statistically significant with p=0.018*.

Discussion

Misoprostol the PGE1 analogue appears to be safe and effective however its optimal dose needs to be determined so that successful vaginal deliveries can be accomplished without affecting the maternal and fetal outcome. In the present study, mean number of doses are significantly less in 50 µg group when compared to 25µg group (1.76±0.77 vs. 2.13±1.01, p=0.013). Even Meydanli et al in their study found that the mean number of misoprostol doses was significantly lower in the 50µg group as compared to 25 µg group. (1.1±0.3 vs. 2.8±0.7, p<0.001) [3]. In this study, 40.8% in group B (50µg) delivered vaginally only with single dose when compared to only 28.7% in group A (25µg) with p value of 0.110 which was statistically not significant. Farah et al in his study states that 38% of patients in 50µg group were delivered vaginally after one dose versus 25% of patients in the 25µg group (p < 0.007).[4]El-Sherbiny et al and Meydanli et al also support this finding [3, 5].

In the present study, the mean induction to active stage interval was significantly less among group B (8.32 hrs) when compared to group A (10.78 hrs) with p=0.004**.The mean induction delivery interval was significantly less (12.98±4.71 hours) in 50µg group when compared to (16.07±6.71 hours) 25µg group with p= 0.001. This result was comparable to a study reported by Elhassan et al in 2005, the mean induction delivery interval was significantly longer in the 25µg vs 50µg group (21.9±4.3h vs 9.6±2.2h, p=0.04)[6]Farah et al and Gupta et al in their study also reported similar findings [4,7].

Farah et al in their study found no difference among 2 groups with regard to delivery within 12 hours of induction (75.5% vs 72.9%) [4]. But in the present study , 63.4% of patients group B and 32.2% among group A delivered within 12 hours of induction with p=0.022 which is statistically significant. Similarly Meydanli et al in their study also found that women in 50µg group were more likely to deliver vaginally within 12 hours of labor induction as compared to 25µg group (37/47 vs. 22/49, p=0.001) [3].The oxytocin augmentation required was also less in group B when compared to group A (35.2% vs. 70.1%, p<0.001**). A Cochrane review by Hofmeyer also revealed that lower doses were associated with more need for oxytocin augmentation [8]. In the present study, 87% delivered vaginally in group A and 71% delivered vaginally among group B. Cesarean section rate was high in group B (29%) as compared to 13% among group A. This was statistically significant with p value of < 0.001. The most common indication for cesarean section among 50µg group was fetal distress most probably contractions induced by higher dose may be stronger sometime. Meydanli et al in their study also said that there was no significant difference in the rate of cesarean section in the two treatment groups [3].

Although in our study, meconium stained liquor was significantly higher in 50µg group. But study by Elhassan mentioned that there was no significant difference between two groups in meconium stained amniotic fluid [6]. Maternal adverse effects were more common in 50µg group (30%) when compared to 25µg group (11%), p=0.001, but catastrophic side effects like uterine rupture did not occur in any of the cases in our study. This was comparable to the study by Gupta et al [7]. Although abnormal uterine contractions were more common with higher dose, maternal complications like postpartum hemorrhage were

comparable in both the groups. However, El-Sherbiny et al in their study reported that tachysystole was significantly more common with 50µg. Atonic PPH was also found to be more common with 50µg group (9.78% vs. 2.15%, p<0.05) [5]. Neonatal outcome was also adversely affected in females who received higher doses. Babies with low Apgar score, requiring resuscitation and NICU care were significantly higher in 50µg group, which is in concurrence with the observation made by Hans et al and Gupta et al [7, 9] Contrary to this, Sanchez-Ramos et al in their metaanalysis of five randomized clinical trials reported comparable neonatal outcomes with the two doses [10].

Conclusion

The intravaginal misoprostol used for induction of labor as 50 µg is more efficacious than 25µg of intravaginal misoprostol but it appears to be less safe both for the mother and the fetus.

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