Original Research Article

Indian Journal of Obstetrics and Gynecology
Volume 6 Number 3, May - June 2018
DOI: http://dx.doi.org/10.21088/ijog.2321.1636.6318.12

Comparative Evaluation of 25 Microgram and 50 Microgram Intravaginal Misoprostol for Induction of Labour

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Abstract

Background: Misoprostol is being in use as an agent for preinduction cervical ripening. But still the ideal dosage, route of administration of this agent is not exactly known. *Aim:* To evaluate the efficacy and safety of 25 mcg and 50 mcg intravaginal misoprostol for labor induction. *Materials and Methods:* We carried our study on 120 low-risk singleton pregnancies reported to the antenatal ward of Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India. The sample was categorized in to two groups, group A women were given 25 mcg (n = 60) and group B women received 50 mcg (n = 60) of intravaginal misoprostol. The dosage was repeated every four hours (limiting maximum number of doses to 3 doses). Induction vaginal delivery interval was the main outcome measure. *Results:* Most of the patients of both groups were 20 to 25 years. We found primigravidae cases in Group A and B to be 75 and 55% respectively. The percentage of cases of term pregnancies was 53.33% and 40% cases in group A and B respectively. Oxytocin augmentation was need in 41.66% cases (Group A) and 33.33% cases (Group B). After six hours, Modified Bishop's score was 7-10 in 70% (Group A) and 71.67% (Group B) cases. Vaginal deliveries were more in Group A (66.66%) than Group B (50%). Cesarean section rate was more in group B (36.66%) when compared with group A (16.67%). *Conclusion:* 25 mcg misoprostol is safe and successful for labor induction.

Keywords: Cervical Ripening; Labor Induction; Prostaglandin; Vaginal Misoprostol.

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Received on 09.03.2018,
Accepted on 02.04.2018

Introduction

Indications for term labor inductions are post term pregnancy, preeclampsia, intrauterine fetal growth restriction, oligohydramnios and abnormal antepartum fetal surveillance results [1,2].

It is reported that more than 15% of gravid women require assist in cervical ripening and labor induction. There is an extensive interest for an effectual and safe method of assistance. The greatest obstacle to labor induction is the immature cervix. Because oxytocin only affects uterine contractions and not cervical ripening, prostaglandin agents are the first choice for labor inductions because they apply a local effect on the cervix, causing effacement and dilatation and stimulate myometrial contraction, increasing the probability of success [3-4].

Misoprostol is an artificial prostaglandin E1 analogue, has been used as an agent for preinduction cervical ripening. It has several potential advantages: stable at room temperature, is relatively inexpensive, and can be administered by several routes (oral, vaginal, sublingual, and buccal). Hence it is used for labor induction, mainly in settings where prostaglandin E2 is not available, storage facility not available and or due to economic reasons [1-3].

Ideal dosage, frequency and route of administration of misoprostol is still under

research. Many authors advocated a dosage range of 25 μg to 100 ìg, inserted intravaginally into the posterior fornix. The most frequent vaginal dose used was 50 μg, once or every four to six hourly intervals. But 25 μg at six hourly intervals intravaginally has been related with the least side effects. Although vaginal application of misoprostol has been validated as a reasonable means of induction, there is patient resistance to repeated digital examination necessary for placement of the agent. Another complication being risk of ascending infection due to frequent vaginal examinations [3,4].

Successful induction depends chiefly on the state of the cervix at the beginning of induction and the parity. Bishop's score is used to evaluate the state of cervix. Unfavourable cervix makes labor induction to be prolonged, tiresome and may result in failed induction. There have been few trials assessing the efficacy and tolerability of vaginal misoprostol [5,6]. We carried out this study to evaluate the effectiveness and safety of 25 and 50 mcg intravaginal misoprostol for labor induction.

Materials and Methods

We carried this study in the department of obstetrics and gynaecology at Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, Telangana, India. 120 cases of low-risk singleton pregnancies who attended antenatal ward were selected by simple random sampling technique. A comprehensive history was taken and a meticulous general physical and obstetrical examination was made after obtaining informed consent from all the subjects.

Inclusion Criteria

1. Age of 18-30 years
2. Singleton pregnancy
3. Above 37 weeks of gestation,
4. Vertex presentation,
5. Unfavorable cervix (Bishop score <4) and
6. Patients not in labor,
7. Intact membranes.

Exclusion Criteria

1. Patients who underwent previous uterine surgery, with nonvertex presentation and abnormal fetal heart rate pattern,
2. Allergic to prostaglandins,
3. Patients with bronchial asthma and multiple pregnancies.

Methodology

Initially patients were evaluated by modified Bishop's score and Non Stress Test for fetal well being. The sample was equally divided in to 2 groups randomly

Group A (n=60): Received 25 mcg intravaginal misoprostol and

Group B (n=60): Received 50 mcg intravaginal misoprostol.

In both the groups, after moistening the misoprostol tablet with distilled water, it was placed in the posterior fornix. After four hours a second dose was repeated based on the uterine contractions and cervical changes. The parameters observed were signs of labor, maternal vital signs, fetal heart rate and progress of labor. We maintained a partogram of all patients.

Oxytocin was given at a dose of 5 units in primigravida and 2.5 units in multipara for intensification of labor in case of arrest of dilatation or lack of adequate uterine contractions after 6 hours of last dose

We collected details about maternal age, gestational age, parity, indication for induction, modified Bishop's score at the time of induction and six hours later, induction to delivery interval, oxytocin augmentation, mode of delivery, APGAR score of the baby, maternal and fetal complications. The observations attained were subjected to statistical analysis by means of student t-test and a p-value <0.05 was taken as significant. The statistical analysis of the data was performed using statistical software (Statistical Package for the Social Sciences, SPSS Inc., Chicago, USA).

Results and Observations

After analysing the results, we arrived at the following observations.

Age: Most of the cases from both groups were in the age group 20 to 25 years, i.e. 58 and 44% respectively.

Primigravidae and Term pregnancies: We found primigravidae cases in both the groups as 75 and 55% respectively. The percentage of cases of term pregnancies was 53.33% and 40% cases in group A and B respectively.

Need for Oxytocin: Oxytocin augmentation was need in 41.66% cases in Group A and 33.33% cases in Group B.

Modified Bishop's score: It was 7-10 in 70% (Group A) and 71.67% (Group B) cases after 6 hours.

Mode of Delivery: Vaginal deliveries were more with 25 mcg (66.66%) when compared to 50 mcg (50%). Cesarean section rate was more in group B (36.66%) when compared with group A (16.67%) (Table 1).

Mean Induction Delivery Interval: It was 13.45 hours with 25 mcg and 9.30 hours with 50 mcg, p-value < 0.001 statistically significant. Majority of cases in group B delivered vaginally within 12 hours with single dose (Table 2).

Indications for Caesarean Section: We found 10 cases with failed induction in group A, with an incidence of 13.33%, out of which 6 cases were due to failure to progress and 4 due to fetal distress. Whereas in group B, the total number of failed induction were 22, with an incidence of 36.66%, majority in this group were due to fetal distress (15), five cases with maternal distress and two cases due to failure to progress (Table 3 and Graph 1).

Adverse Effects: When the side effects of misoprostol were recorded, we found that there was 26% and 14% incidence in group B and A respectively. hyperstimulation and tachysystole were found only in group B. The disparity among

Table 1: Variables distribution in the study group

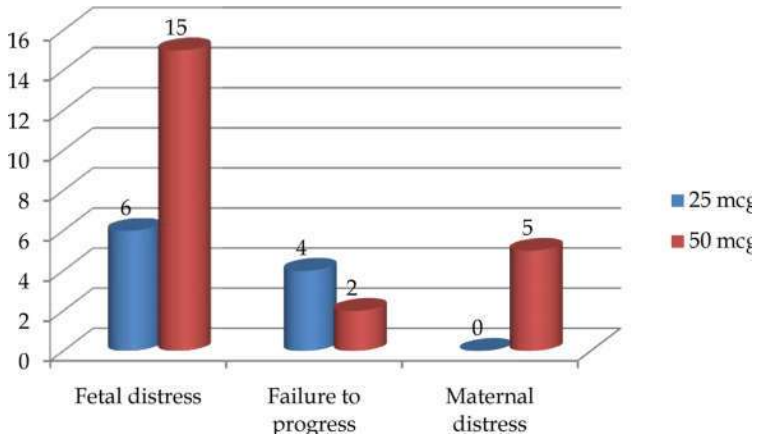
Variable		Group A		Group B	
		Number	Percentage	Number	Percentage
Age	less than 20 years	20	33.33%	22	36.66%
	21-25 years	34	56.67%	27	45%
	26-30 years	6	10%	11	18.33%
Obstetric score	G2A1	-	-	3	5%
	G2P1	15	25%	17	28.33%
	G3P1	-	-	4	6.67%
	G3P2	-	-	3	5%
	P	45	75%	33	55%
Gestational age (weeks)	37-40	38	63.34%	31	51.66%
	40-42	22	36.66%	29	48.34%
Indication for induction	Term	32	53.33%	24	40%
	Post-Term	4	6.66%	7	11.64%
	Post EDD	20	33.33%	20	33.33%
	Intrauterine death	4	6.66%	9	15%
Bishop's score before induction	1	13	21.66%	11	18.33%
	2	18	30%	42	70%
	3	13	21.66%	4	6.67%
	4	16	26,67%	3	5%
No. of doses required	1	39	65%	48	80%
	2	21	35%	12	20%
Oxytocin Augmentation	Yes	25	41.66%	20	33.33%
	No	35	58.34%	40	66.64%
Modified Bishop's score after 6 hours	1-3	2	3.33%	4	6.66%
	4-6	16	26.64%	13	21.67%
	7-10	42	70%	43	71.67%
Mode of delivery	Vaginal	40	66.66%	30	50%
	Caesarean section	10	16.67%	22	36.66%
	Vaginal instrumental	10	16.67%	8	13.33%

Table 2: Induction delivery interval

No. of hours	25 mcg				50 mcg			
	Single dose	%	Double dose	%	Single dose	%	Double dose	%
<12	13	33.33%	3	7.69%	22	36.66%	3	5%
12-24	18	46.15%	4	10.25%	7	11.66%	6	10%
>24	-	-	1	2.56%	-	-	-	-

Table 3: Indications for caesarean section

Indication	25 mcg		50 mcg	
	Number	Percentage	Number	Percentage
Fetal distress	6	10%	15	25%
Failure to progress	4	6.66%	2	3.33%
Maternal distress	-	-	5	8.33%



Graph 1: Caesarean section indications

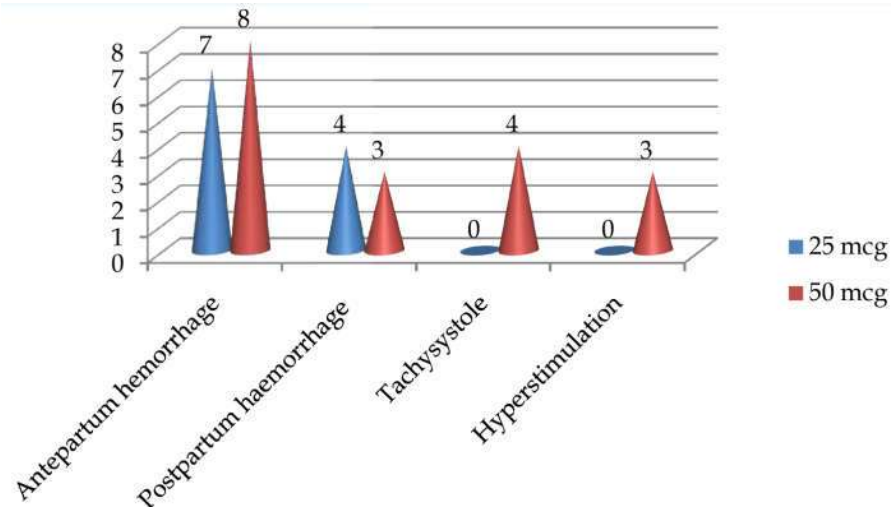
the groups was statistically significant (p<0.04) (Table 4 and Graph 2).

Apgar Scores: One case in group A had scores of 3 at one minute and group B had six cases (Table 5).

Fetal Complications: In group A fetal distress and NICU admissions were 6% each, whereas in group B was 26% and 12% (Table 6).

Table 4: Effects on mother

Effects on mother	25 mcg	50 mcg	Total
Antepartum hemorrhage	7	8	15 (20%)
Postpartum haemorrhage	4	3	7 (5.83%)
Tachysystole	-	4	4 (3.33%)
Hyperstimulation	-	3	3 (2.5%%)
Total	11 (18.33%)	18 (30%)	29 (24.16%)



Graph 2: Effects on mother

Color of liquor: We found the incidence of meconium stained liquor to be both thick and thin in 23.33% and 38.33% in 25 mcg and 50 mcg groups respectively (Table 7).

Discussion

Many studies have reported the efficacy and safety of misoprostol for cervical ripening and labor induction. When compared with PGE2, misoprostol was found to be more effectual regarding shorter induction-to-delivery interval and less requirement of oxytocin [7,8]. But few studies reported side effects such as abnormal uterine contractions, meconium-stained amniotic fluid, and babies born with umbilical cord arterial pH < 7.16 after use of misoprostol. Hence, American College of Obstetricians and Gynecologists recommend 25-mcg misoprostol to be inserted into the posterior vaginal fornix and to be repeated every 3 to 6 hours as required [4-6,9,10].

Misoprostol can be used by different routes like oral and vaginal and in different doses ranging from 25 to 200 mcg, however many authors used 25 or 50 mcg. We compared the safety and efficacy of 25 and 50 mcg intravaginal misoprostol.

In our study, we found that in the majority of the cases, age ranged between 20 to 25 years, alike to Fletcher et al and Louis Sanchez Ramos [11,12].

We also found that primigravida cases were 75% and 55% in 25 mcg and 50 mcg groups respectively. Our findings are similar to Bharathi et al (2013) [1].

Bishop score is considered as a significant parameter in assessing the progress in delivery process. We found that Bishop's score was better in group B (71.67%) than group A (70%) after 6 hours, indicating 50 mcg misoprostol is effictual in cervical ripening. Our findings are in accordance with Bharathi et al. and Bugalho et al [1,13,14].

We found that a single dose was required for induction of labor in 39 (65%) and 48 (80%) cases in groups A and B respectively, similar to Bharathi et al. (2013), who found 32 cases (64%) and 41 cases (82%) in 25 mcg and 50 mcg groups respectively. We also found that the percentage of women who delivered vaginally with a single dose of misoprostol vaginally was considerably more in 50 mcg group [1]. 25 (41.66%) patients in group A and 20 (33.33%) in group B needed oxytocin after 6 hours of last dose of misoprostol. The difference among both the groups was statistically insignificant, similar to El-Sherbiny et al. and Sanchez Ramos et al [12,15].

When the rate of vaginal deliveries was evaluated, it was 66.66% and 50% in 25 mcg and 50 mcg groups, the difference being statistically significant (P<0.05). Whereas the rate of caesarean section was greater in 50 mcg group [22cases (36.66%)] in comparison with 25 mcg group [10 vases (16.67%)]. Our findings were similar to Wing et al and Meydanli et al [4,16].

Table 5: Effects on fetus

Apgar Score	25 mcg		50 mcg	
	1 minute	5 minutes	1 minute	5 minutes
5	1 (1.96%)	-	6 (13.33%)	-
6-8	50 (98.04%)	8 (15.69%)	39 (86.67%)	7 (15.55%)
9-10	-	43 (84.31%)	-	38 (84.45%)
Total	51	51	45	45

Table 6: Fetal complications

Complication	25 mcg	50 mcg	Total	Z value	P value
Fetal distress	4	8	12	1.048	>0.247 (NS)
NICU admission	4	8	12	1.048	>0.247 (NS)

NS=Not significant

Table 7: Color of liquor

Color of Liquor	25 mcg	50 mcg	Total
Clear	46	37	83
Thick meconium	6	16	22
Thin meconium	8	7	15
Total	60	60	120

Regarding the mean induction delivery interval, it was 13.45 hours with 25 mcg and 9.30 hours with 50 mcg, p-value being < 0.001 (statistically significant). 13 (32%) cases in group A delivered vaginally within 12 hours of induction, 20 (47%) cases within 24 hours and one case delivered after 24 hours. In group B, 19 cases (61%) delivered within 12 hours and 16 (20%) cases within 24 hours. This was in accordance with studies Wing et al and El-Sherbiny et al. [4,16].

Zieman et al. found that plasma concentration of misoprostol rose slowly, reached maximum levels within a time period of 60 to 120 minutes. It is probable to anticipate misoprostol to attain a threshold concentration for initiating uterine activity when applied intravaginally.

Concerning to the potential direct effects on the cervix, 50 mcg dose is likely to be more potent than 25 mcg dose. Hence it is not surprising to detect more women to be delivered vaginally within 12 hours of induction in the 50 mcg group in comparison to 25 mcg group, as in our study [17].

However Aspden in their study observed that there was a decline in plasma misoprostol concentration to an average of 61% of the peak level at 240 minutes after vaginal administration. Thus, repeated doses of 25 mcg misoprostol at 4 hours interval may comprise a cumulative plasma misoprostol concentration during a longer interval than the 50 mcg dose, and may initiate uterine activity by attainment of threshold level at a later stage. Considerably more women delivered vaginally within 12 to 24 hours of induction in group A can be clarified on this basis [18].

Maternal adverse outcomes are important factors to be considered. We noticed fewer side effects in group A. There was no significant difference between mean birth weight and Apgar scores in both groups. Fetal distress and NICU admission was less with 25 mcg group suggesting that 25 mcg of misoprotol is safe and associated with less neonatal complications when compared to 50 mcg, similar to studies of Meydanli et al [4].

Strengths of the Study

Ours is a prospective randomised controlled trial in which all the data of recruited participants could be analysed and both study groups received comparable care.

Limitations of the Study

1. Small sample size
2. The trial was not masked and the outcome assessors were not blinded. Hence the possibility of inadvertent bias cannot be excluded.

Conclusion

Intravaginal misoprostol has advantage of rebeing cost effective, temperature stability when evaluated with other routes of prostaglandin preparations. In our study the vaginal delivery rates was greater in 25 mcg group when compared with 50 mcg group and the former dosage was found to be safer, even though 50 mcg dosage lead to faster delivery with less augmentation. Keeping in mind of the existing data and our findings, we conclude that 25 mcg of intravaginal misoprostol four hours apart appears to be safe and effective for labor induction.

References

1. Bharathi A, Kumar KA, Ganga AP. A Comparative Study of 25 mcg vs 50 mcg of vaginal Misoprostol for Induction of Labor. J South Asian Feder Obst Gynae 2013;5(3):111-15.
2. Cheng et al. Titrated Oral Compared With Vaginal Misoprostol for Labor Induction. Obstet Gynecol 2008;111:119–25.
3. Girija et al. Comparison of two dosing regimens of vaginal misoprostol for labor induction: a randomised controlled trial. J Turkish-German Gynecol Assoc 2009;10:220-5.
4. Meydanli et al. Labor induction post-term with 25 micrograms vs. 50 micrograms of intravaginal misoprostol. International Journal of Gynecology and Obstetrics 2003;81:249–55.
5. Kubli FW, Hone EH, Khazin AF, Takemura H. Observations on heart rate and pH in human fetus during labor. Am J Obstet Gynecol 1969;104: 1190–1206.
6. American College of Obstetricians and Gynecologists. Umbilical artery blood acid-base analysis. ACOG Technical Bulletin No. 216. Washington: ACOG, 1995.
7. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labor induction: a meta-analysis. Obstet Gynaecol 1997;89:633–42.
8. Sanchez-Ramos L, Kaunitz AM, Del Valle GO, Delke I, Schroeder PA, Briones DK. Labor

induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: a randomized trial. Obstet Gynaecol 1993;81:332–6.

9. 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 Gynaecol 1998; 92:481–6.
10. Kolderup L, McLean L, Grullon K, Safford RN, Kilpatrick SJ. Misoprostol is more efficacious for labor induction than prostaglandin E2, but is it associated with more risk? Am J Obstet Gynaecol 1999;180:1543–7.
11. Fletcher HM, et al. Intravaginal misoprostol as cervical ripening agent. Br J Obstet Gynecol 1993;100:641-44.
12. Sanchez-Ramos L, et al. Labor induction with 25 mcg vs 50 mcg intravaginal misoprostol: a systematic review. Int J Obstet Gynecol 2006;113:1366-76.
13. Bugalho A, Bique C, et al. Induction of labor with intravaginal misoprostol in intrauterine fetal death. Am J Obstet Gynecol 1994;171(2):538-41.
14. Bugalho A, et al. Comparative study of vaginal misoprostol and intravenous oxytocin for induction of labor. Obstet Gynecol 1995;39: 252-56.
15. El-Sherbiny MT, et al. Labor induction with 25 mcg vs 50 mcg vaginal misoprostol. Intl J Obstet Gynecol 2001;72:25-30.
16. Wing DA. Labor induction with misoprostol. Am J Obst Gyencol l999;181(2):339-45.
17. Zeiman M, Fong SK, et al. Absorption kinetics of misoprostol with oral or vaginal administration. Obst and Gynae 1997;90:88.
18. Aspden RM. The theory of fiber freinforced composition materials applied to the mechanical properties of the cervix during pregnancy. J Theol Biol 1988;130:213-21.