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Original Research Article

Comparative Assessment of the Efficacy and Safety of Two Different Doses of Intravaginal Misoprostol for Induction of Labor

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Abstract

Aim: The aim of the present study was to compare the efficacy and safety of 25 mcg intravaginal misoprostol vs 50 mcg misoprostol for induction of labor.

Methods: This study was conducted in the Department of Obstetrics and Gynecology at Patna Medical College and Hospital, Patna, Bihar, India. This study group consisted of 200 cases of low-risk singleton pregnancies attending the antenatal clinic of Patna Medical College and Hospital, Patna, Bihar, India, or admitted to the antenatal ward.

Results: Maximum cases from both groups were in the age group 20 to 25 years. Most cases are booked cases in both groups accounting for 82 and 79% in both groups respectively. Most cases in 25 mcg group were term pregnancies (65%) and in 50 mcg group postdated pregnancies (54%).Oxytocin augmentation need in both groups was similar. Vaginal deliveries are more with 25 mcg (74%) when compared to 50 mcg (51%). Cesarean section rate is more with 50 mcg (39%). In the present study, it was seen that the induction delivery interval with 50 mcg misoprostol was less than 12 hours in 62 cases (62%) and, in 25 mcg, it was in 33 cases (33%). Most cases in 50 mcg group delivered vaginally within 12 hrs with single dose. Majority of failed induction were due to failure to progress. In 50 mcg group the total number of failed induction were 39 out of 100 patients giving an incidence of 39%. Majority of failed induction were due to fetal distress. There was 26% incidence of side-effects in 50 mcg misoprostol group and 14% of incidence in 25 mcg group. Tachysystole and hyperstimulation were found only in 50 mcg group.

Conclusion: Local application of misoprostol tablet in the posterior fornix is more convenient and easier procedure. Misoprostol offers benefits of reduced cost, temperature stability when compared to other prostaglandin preparation. Change in Bishop's score is good with both the groups, 50 mcg is proved to be a better cervical ripening agent statistically. Induction delivery interval is significantly less with 50 mcg group (9.45 hrs) in comparison to 25 mcg group (14.5 hours).

Keywords: Labor induction, Misoprostol, Cervical ripening

Introduction

Induction of labor is usually performed when the risks of continuing pregnancy are higher than the benefits of delivery. [1-3] Undoubtedly, uterine cervical tissue ripening or its softening has a close relationship with success rate of delivery. There are several effective methods for cervix ripening including mechanical with osmotic dilators [4] or balloon catheters [5], and biochemical with prostaglandins [6], antiprogestins [7], or nitric oxide donors. [8] Among many proper methods for cervical ripening, there is still no agreement on which method is the best for labor induction of cases with unripe cervix.

Misoprostol is a prostaglandin E1 methyl ester and is used orally for the prevention or treatment of peptic ulcer. [9] Oral misoprostol with a rapid absorption is de-esterified to active misoprostol acid in the liver rapidly. Misoprostol acid has a half-life of between 20 and 40 minutes and is excreted in the urine. Misoprostol stimulates myometrial contractions in a pregnant uterus by selectively binding to EP2/EP3 prostanoid receptors. [10] In

1992, misoprostol was first reported for the termination of a pregnancy with a live fetus. [11]

Misoprostol is inexpensive and effective and can be stored at room temperature. In contrast to other prostaglandins, misoprostol has no significant effect on the lungs or vessels and can be safely used in patients with asthma. The Food and Drug Administration (FDA) has not approved misoprostol for labor induction or cervical ripening yet, but this medication has been used successfully in several clinical trials. The ideal dose and routes of the administration of misoprostol for the induction of labor at full term are still a matter of controversy. The National Institute for Health and Clinical Excellence (NICE) released a clinical guideline in 2008 and restricted the use of misoprostol only to clinical trials and termination of pregnancies with a dead fetus. [12] However, the American College of Obstetricians and Gynecologists (ACOG) supported its usage in 2009 for women who did not have a previous Cesarean delivery or a major uterine surgery. [13]

The aim of the present study was to compare the efficacy and safety of 25 mcg intravaginal misoprostol vs 50 mcg misoprostol for induction of labor.

Materials and Methods

This study was conducted in the Department of Obstetrics and Gynecology at Patna Medical College and Hospital, Patna, Bihar, India for one year. This study group consisted of 200 cases of low-risk singleton pregnancies attending the antenatal clinic of Patna Medical College and Hospital, Patna, Bihar, India, or admitted to the antenatal ward.

The distribution of cases was matched with respect to their age and parity in all the cases, a detailed history was obtained and a thorough general physical and obstetrical examination was done.

Indications for induction—Term pregnancy, post expected date of delivery pregnancy (postdatism), Post-term pregnancy, intrauterine death.

Patients with age 18 to 35 years, singleton pregnancy, over 37 weeks of gestation, vertex presentation, unfavorable cervix (bishop score <4) and patients not in labor, reactive fetal heart rate pattern, intact membranes, no contraindications to vaginal delivery are included.

Patients with previous uterine surgery, nonvertex presentation, abnormal fetal heart rate pattern, known allergy to prostaglandins, patients with bronchial asthma and glaucoma, multiple pregnancies, grand multipara are excluded.

After taking informed consent, patients were evaluated initially by modified bishop's score and NST for fetal well being. Fifty cases were selected at random to receive 25 mcg of misoprostol intravaginally and the other 50 cases, in a random selection received 50 mcg of misoprostol intravaginally. Misoprostol was placed in the posterior fornix after moistening the tablet with distil water. Second dose was repeated after 4 hours depending on the uterine contractions and cervical changes. After the drug insertion, patients were monitored for signs of labor, maternal vital signs, fetal heart rate and progress of labor. A partogram was maintained for all patients. Oxytocin was started depending on the modified bishop's score and in the absence of adequate uterine contractions after 6 hours of last dose, or for augmentation of labor in case of arrest of dilatation. Oxytocin was started at a dose of 5 units in case of primigravida and 2.5 units in case of multipara dose titrated every 30 minutes based on uterine contractions.

Failed as been defined by Duff et al (1984) as failure to enter the active phase of labor after 12 hours of regular uterine contractions.11 Tachysystole-more than six uterine contractions per 10 minutes without fetal heart rate changes, for 2 cosecutive 10-minute periods. Hyperstimulation-tachysystole resulting in nonreassuring FHR changes. Hypertonus-one contraction lasting for more than 2 minutes.

The data collected included maternal age, parity, booked or unbooked case, gestational age, indication for induction, modified bishop's score at the time of induction and 6 hours later, induction to delivery interval, oxytocin augmentation, mode of delivery, APGAR score of the baby, maternal and fetal complications.

The results obtained were subjected to statistical analysis by student t-test and p-value <0.05 was considered significant.

Results

Table 1: Distribution of variables across the study group

	Parameters	25 mcg	Percentage (%)	50 mcg	Percentage (%)
Age (years)	≤ 20	35	34	40	40
	21-25	57	57	42	42
	26-30	8	8	18	18
Booked/unbooked	Booked	82	82	79	79
	Unbooked	18	18	21	21
Obstetric score	G2A1	-	-	7	7
	G2P1	25	25	27	27
	G3P1	-	-	6	6
	G3P2	-	-	4	4
	P	75	75	56	56
Gestational age (weeks)	>37-40 wks	65	65	54	54
	>40-42 wks	35	35	46	46
Indication for induction	Term	55	55	42	42
	Post-term	5	5	10	10
	Post EDD	35	35	30	30
	Intrauterine death	5	5	18	18
Bishop's score before induction	1	23	23	19	19
	2	29	29	68	68
	3	21	21	7	7
	4	24	24	6	6
Number of doses required	1	66	66	84	84
	2	34	34	16	16
Oxytocin augmentation	Yes	43	43	34	34
	No	57	57	66	66
Modified bishop's scoreafter 6 hours	1-3	2	2	4	4
	4-6 7-10	28 70	28 70	20 76	20 76
Mode of delivery	Vaginal	74	74	51	51
	cesarian section	14	14	39	39
	Vaginal instrumental	12	12	10	10

Maximum cases from both groups were in the age group 20 to 25 years. Most cases are booked cases in both groups accounting for 82 and 79% in both groups respectively. Most cases in 25 mcg group were term pregnancies (65%) and in 50 mcg group postdated pregnancies (54%).Oxytocin augmentation need in both groups was similar. Vaginal deliveries are more with 25 mcg (74%) when compared to 50 mcg (51%). Cesarean section rate is more with 50 mcg (39%).

Table 2: Induction delivery interval

No. of hours	Single dose	25 mcg Percentage	Double dose	Percentage	Single dose	50 mcg Percentage	Double dose	Percentage
<12	33	33	6	6	62	62	6	6
12-24	46	46	15	15	18	18	10	10
>24	-	-	3	3	-	-	-	-

In the present study, it was seen that the induction delivery interval with 50 mcg misoprostol was less than 12 hours in 62 cases (62%) and, in 25 mcg, it was in 33 cases (33%). In the present study, mean induction delivery interval was 14.5 hours with 25 mcg and 9.45 hours with 50 mcg, p-value < 0.001 statistically being significant. Most cases in 50 mcg group delivered vaginally within 12 hrs with single dose.

Table 3: Indication for cesarean section

Indication	25 mcg		50 mcg	
	No.	Percentage	No.	Percentage
Fetal distress	**5**	**5**	**25**	**25**
Failure to progress	**9**	**9**	**3**	**3**
Maternal distress			**11**	**11**

Majority of failed induction were due to failure to progress. In 50 mcg group the total number of failed induction were 39 out of 100 patients giving an incidence of 39%. Majority of failed induction were due to fetal distress.

Table 4: Effects on mother

Effects onmother	25 mcg	50 mcg	Total	p-value
Antepartum hemorrhage	6	10	16	>0.36
TPPH	4	4	8	>0.7
Tachysystole		6	6	<0.043
Hyperstimulation		4	4	>0.077
8V	2	2	4	>0.5
F	2		2	>0.245
Total	14	26	40	

There was 26% incidence of side-effects in 50 mcg misoprostol group and 14% of incidence in 25 mcg group. Tachysystole and hyperstimulation were found only in 50 mcg group.

Table 5: Fetal complications

	25 mcg	50 mcg	Total	p-value
Fetal distress	5	20	25	>0.252
NICU admission	6	12	18	>0.265

In 25 mcg group fetal distress was 5% when compared to 50 mcg group which was 26%. NICU admissions were 6% in 25 mcg group, 12% in 50 mcg group.

Table 6: Color of liquor

Liquor	25 mcg	50 mcg	Total
Clear	78	62	140
Thick meconium	10	28	38
Thin meconium	12	10	22

In 25 mcg group incidence of meconium stained liquor was 22% (both thick and thin). In 50 mcg group incidence of meconium stained liquor was 38% (both thick and thin).

Discussion

The spontaneous onset of labor is a robust and effective mechanism and should be given to operate on its own. We should only induce labor when we are sure that we can do better. Sir Alec Turnbull (1976) [14,15] Induction of labor is defined as an intervention intended to artificially initiate uterine contractions resulting in the progressive effacement and dilatation of the cervix.12 Induction of labor is one of the most commonly performed obstetric intervention. Induction rate varies greatly between different countries from 4 to 40%. [14,16] Maximum cases from both groups were in the age group 20 to 25 years and similar to studies of fletcher et al and Louis Sanchez Ramos. [17,18] Most cases belonged to postdatism group. [19]

Most cases are booked cases in both groups accounting for 82 and 79% in both groups respectively. Most cases in 25 mcg group were term pregnancies (65%) and in 50 mcg group postdated pregnancies (54%).Oxytocin augmentation need in both groups was similar. Vaginal deliveries are more with 25 mcg (74%) when compared to 50 mcg (51%). Cesarean section rate is more with 50 mcg (39%). This indicates that 50 mcg misoprostol is efficient in the process of cervical ripening, similar with studies of Bugalho et al. [19,20] In the present study, it was seen that the induction delivery interval with 50 mcg misoprostol was less than 12 hours in 62 cases (62%) and, in 25 mcg, it was in 33 cases (33%). Most cases in 50 mcg group delivered vaginally within 12 hrs with single dose. Majority of failed induction were due to failure to progress. In 50 mcg group the total number of failed induction

were 39 out of 100 patients giving an incidence of 39%. Majority of failed induction were due to fetal distress. The difference in both the groups is not statistically significant which is similar to study conducted by Sherbiny et al [21], Sanchez Ramos et al.[18]

There was 26% incidence of side-effects in 50 mcg misoprostol group and 14% of incidence in 25 mcg group. Tachysystole and hyperstimulation were found only in 50 mcg group. In 25 mcg group fetal distress was 5% when compared to 50 mcg group which was 26%. NICU admissions were 6% in 25 mcg group, 12% in 50 mcg group. In 25 mcg group incidence of meconium stained liquor was 22% (both thick and thin). In 50 mcg group incidence of meconium stained liquor was 38% (both thick and thin). Significantly more women in 50 mcg group delivered vaginally within 12 hours of induction, where as there were significantly more women in the 25 mcg group who delivered within 12 to 24 hours. Zieman et al [22] reported that plasma concentration of misoprostol in women receiving misoprostol rose gradually, reached maximum levels within 60 to 120 minutes. It is plausible to expect misoprostol to reach a threshold concentration for initiating uterine activity when misoprostol is applied intravaginally. The potential direct effects of misoprostol on the uterine cervix in initiating physiological events must be taken into account. It is probable for the 50 mcg dose. Regarding to the potential direct effects on the cervix, the 50 mcg dose is expected to be more potent than the 25 mcg dose. In this background, it is not extraordinary to observe more women to be delivered vaginally within 12 hours of induction in the 50 mcg group when compared with 25 mcg group.

Conclusion

Local application of misoprostol tablet in the posterior fornix is more convenient and easier procedure. Misoprostol offers benefits of reduced cost, temperature stability when compared to other prostaglandin preparation. Change in Bishop's score is good with both the groups, 50 mcg is proved to be a better cervical ripening agent statistically. Induction delivery interval is significantly less with 50 mcg group (9.45 hrs) in comparison to 25 mcg group (14.5 hours). A single dose of 50 mcg misoprostol is effective in culminating vaginal delivery within 12 hours. Rate of vaginal delivery is more with 25 mcg group in comparison to 50 mcg group. A 25 mcg dose was safer than 50 mcg dose when given every 4 hours, although the 50 mcg regimen resulted in faster delivery with less augmentation.

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