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ORIGINAL ARTICLE

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Oral misoprostol vs intra-cervical dinoprostone for cervical ripening and labour induction

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OBJECTIVE(S) : To compare efficacy, safety and tolerance of oral misoprostol with intracervical dinoprostone for cervical ripening and labor induction.

METHOD(S) : One hundred and ninety women with single live fetus, term gestation, cephalic presentation and reactive fetal heart pattern admitted for induction of labor were included in the study. They were randomized to receive either a single dose of 200 μg of oral misoprostol (study group) or 0.5 mg of intracervical dinoprostone for a maximum 3 doses at 8 hourly intervals (control group).

RESULTS : Induction-delivery interval was significantly shorter in the study group (11.68 hours vs 14.83 hours; P<0.01). Failure of induction was higher in the control group (14.83 vs 1.05%). Cesarean section rate in the study group was comparable with that in the control group (17.89% vs 20%). In the study group most of the cesarean sections were done for fetal distress (35.2%). Neonatal outcome was comparable in the two groups. Incidence of abnormal uterine activity was significantly higher in the study group.

CONCLUSION(S) : Single dose of 200 □g oral misoprostol was more effective for cervical ripening and labor induction than 0.5 mg of intracervical dinoprostone given 8 hourly.

Key words : labor induction, cervical ripening, oral misoprostol, intracervical dinoprostone

Introduction

Labor induction near term is required in 10-20% of women. Medications that will ripen the cervix in a short period of time play an important role in modern obstetrics. The process which generally used to take days is now compressed into a day. To date no medication or technic has been proved to be ideal for the induction of labor in a woman with an unripe cervix. The methods commonly available for the purpose of induction are artificial rupture of membranes (ARM) or use of drugs like oxytocin, dinoprostone gel and misoprostol.

Induction of labor with oxytocin is unlikely to lead to a vaginal delivery in a reasonable period of time especially in an unripe cervix. Dinoprostone gel (PGE_2) requires an intracervical application, needs refrigeration and is expensive. Oral misoprostol (PGE_1) has better user acceptability, does not require cold chain for storage and is cost effective. In our study a reasonable oral dose of misoprostol was used and compared with our standard hospital protocol of intracervical dinoprostone (PGE_2).

Material and Methods

Women admitted for induction of labor with Bishop's score $\leq$ 6 from September 2001 to August 2002 were included in the study after approval from the local ethical committee. Literature study revealed that to show a difference with a two- tailed alpha level of 0.05 and power (1-β) of 80% a sample size of 190 was required. The inclusion criteria were women with single live fetus, cephalic presentation, term pregnancy with reactive fetal heart rate (FHR) and previous one lower segment cesarean section (LSCS). Those with cephalic presentation, multiple gestation, ruptured

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membranes, preterm pregnancy, nonreactive FHR, placenta previa and grand multiparity were excluded from the study. After taking informed consent, the women were randomized to receive misoprostol or dinoprostone gel. Assignments were concealed by sequentially numbered opaque envelopes prepared by a medical student not involved in the study. Women in the study group received single dose of oral misoprostol (200 □g tablet) and women in the control group received 0.5 mg of intracervical dinoprostone 8 hourly for a maximum of 3 doses.

Active phase was defined as complete cervical effacement and dilatation of at least 3 cm. Women in labor were cared for according to current obstetric practices. When they entered active phase, depending on the pattern of uterine contractility oxytocin was initiated. If women did not reach active phase within 24 hours of induction (initiation), cesarean section was done for failed induction. No augmentation was done when uterine contractions reached a frequency of 3 in 10 minutes. Continuous electronic FHR monitoring and cardiotocography were used after half an hour of induction.

The primary outcome measure was the interval from start of induction to active phase. Success of induction was defined as entry into active phase within 24 hours of the initial administration of the drug. Other measures studied were need for oxytocin augmentation, interval from active phase to delivery, mode of delivery, need for cesarean section, and side-effects like fever, gastrointestinal symptoms, hyperstimulation and neonatal outcome.

The results were represented as mean and standard deviation and modified t test was applied to know the statistical significance. Qualitative variables were expressed as percentages.

Results

The baseline data of the study population included maternal age, gravidity, previous cesarean section and gestational age. They were comparable in the two groups. The mean gestational age was identical i.e. 37 to 42 weeks. The median preinduction score did not differ between the two groups. (Table 1)

Indications for induction were similar (Table 2). 52.63% of the women were induced for postdatism in the study group as compared to 50.52% in the control group. 31.57% in the study group and 29.47% in the control group were induced at term for preeclamptia/pregnancy induced hypertension. One in each group was induced for postdated pregnancy with one previous LSCS. The other indications for induction were intrauterine growth restriction, and reduced fetal movements with reactive non-stress test.

Table 1. Baseline data.

		Study Group PGE_1 n=95	Control Group PGE_2 n=95
Mean age (years)		23.38	23.36
Gravidity	1	46 (48.42%)	47 (49.47%)
	2	31 (32.63%)	27 (28.42%)
	3	18 (18.94%)	21(22.10%)
Gestational age (weeks)			
37-40		45 47.36%	47 (49.47%)
40.1 – 41		50 52.63%	48 (50.52%)

98.95% in the study group and 89.47% in the control group reached active phase of labor. One in the study group and 11 in the control group failed to achieve active phase. The woman of failed induction in the study group was successfully induced with dinoprostone. One woman of failed induction in the control group was successfully induced with misoprostol. Rest of the women with failed induction in the control group underwent LSCS for failed induction.

82.10% (78/95) in the study group had vaginal delivery of which 11.5 (9/78) had instrumental delivery while 80% (76/95) in the control group had vaginal delivery of which 7.9% (6/76) had instrumental delivery.

Induction to active phase interval was shorter in the study group than in the control group and the difference was statistically significant (5.78 $\pm$ 2.34 hours vs 6.78 $\pm$ 4.51 hours; P = 0.017, modified t = 2.436). (Table 2)

Table 2. Indications for induction.

Indications	Study Group (n=95)	Control Group (n=95)
Postdatism	50 (52.63%)	48 (50.52%)
Preeclampsia/pregnancy induced hypertention	30 (31.57%)	28 (29.47%)
Eclampsia	2 (2.10%)	3 (3.15%)
Intrauterine growth restriction	11 (11.57%)	11 (11.57%)
Full term pregnancy with previous LSCS	1 (1.05%)	1 (1.05%)
Decreased fetal movements	4 (4.21%)	4 (4.21%)

Mean active phase to delivery interval was 6.68 $\pm$ 2.90 hours in the study group and 7.78 $\pm$ 4.03 hours in the control group. This difference was not statistically significant (P = 0.081) (Table 3).

Table 3. Results.

Interval (hours)	Study Group	Control Group	Modified t	P
Induction to active phase (hours)	5.78 ± 2.34 (n= 94)	6.78 ± 4.51 (n=85)	2.436	0.017
Active phase to delivery (hours)	6.68 ± 2.90 (n= 77)	7.78 ± 4.03 (n= 76)	1.763	0.081
Induction to delivery (hours)	11.68 ± 4.49 (n= 77)	14.83 ± 7.08 (n= 76)	2.985	0.004

P < 0.05 Significant

The induction to delivery interval ranged from 11 – 26 hours in the study group and 14 – 45 hours in the control group. The mean induction to delivery interval in the study group was 11.68 ± 4.49 hours and in the control group 14.83 ± 7.08 hours. Applying the modified t test of significance, this difference was statistically significant (P = 0.004) (Table – 3).

The cesarean section rates in the two groups were similar viz.,17.89 or 17/95, in the study group vs 20% or 19/95 in the control group. However, the indications for cesarean section in the two groups were different. Most of the cesarean sections in the study group were done either for fetal distress as evidenced by cardiotocogram (5.2%; 6/17) or for meconium stained liquor (23.9%;4/17). Another 29.41%(5/17) required cesarean section for hypertonic contractions not responding to pharmacologic drugs and 11.71% (2/17) for failure to progress. The majority of cesarean sections in the control group were done for failed induction 52.6% (10/19), while 21% (4/19) were done for fetal distress as evidenced by cardiotocogram and 26.3% (5/19) for meconium stained liquor.

The mean Apgar scores were comparable in the two groups – 6.6 at 1 minute and 8.9 at 5 minutes in the control group and 6.9 at 1 minute and 8.8 at 5 minutes in the study group.

The incidence of abnormal uterine activity in the study group was 13.68% (13/95) – 4.21% (4/95) had hypertonus, 4.21% (4/95) had tachysystole and 5.26% (5/95) had hyperstimulation. The other side effects in the study group were shivering in five and hyperthermia in two. The side effects in the control group were negligible. There was no abnormal uterine activity, two had diarrhea and two had vomiting. No incidence of disruption of scar in cases of previous uterine incision were seen in any woman.

Discussion

We found better results with 200 μg of oral misoprostol than with dinoprostone gel. Induction to active phase and induction to delivery intervals were statistically significantly shorter in the misoprostol group. Misoprostol was also associated with less need for oxytocin augmentation and for cesarean section for failed induction. Moreover misoprostol was cost effective. Ngai et al [1] compared 200 μg of oral misoprostol with placebo before intravenous oxytocin infusion for cervical ripening in women with premature rupture of membranes at term. They found that dose effective for improving Bishop score, reducing incidence of oxytocin infusion for labor induction and decreasing leaking-to-delivery interval. Besides it did not increase maternal side effects or perinatal morbidity. Adair et al [2] in a randomized double masked trial of 178 women found similar efficacy between 200 μg of oral misoprostol and 50 μg of vaginal misoprostol but the oral route was associated with high incidence (44.1%) of hyperstimulation syndrome. This could be explained by the fact that they used a repetitive dose of 200 μg of oral misoprostol. To decrease this high rate, Windrim et al [3] used low dose of misoprostol viz., 50 μg but this was less effective than dinoprostone [3]. Only one study that compared oral with vaginal misoprostol recommended the oral route [4]. Another study by Bartha et al [5] compared 200 μg of oral misoprostol with intracervical dinoprostone in a randomized trial of 190 women. They found a significant decrease in induction to active phase to rupture of membranes to delivery intervals in the misoprostol group. Cesarean rate for failed induction was lower in the misoprostol group. There were no significant differences in the rates of tachysystole (20% vs 30%), hypertonus (20% vs 15%), and hyperstimulation (6% vs 2%). Perinatal outcome was comparable. Dallenbach et al [6] found no difference in terms of effectiveness and safety between low dose oral misoprostol (20 μg every 2 hourly, increased to 40 μg) and vaginal dinoprostone. This regimen avoids excess uterine contractility noted in previous studies. In our study, oral misoprostol was well tolerated at 200 μg dose. We employed continuous cardiotocography monitoring after half an hour as most women complained of pain in abdomen following half an hour of drug administration. Tachycardia was noted in almost all fetuses after half an hour of misoprostol intake. Women with tachysystole could be managed with 250 μg terbutaline subcutaneously. In women with previous uterine scar, no untoward effect was seen. Misoprostol can be used with strict vigilance. However, there is a need for further study in this regard and half the dose may be tried for women with uterine scar.

Labor was successfully induced in 98.95% in the study group and 89.47% in control group. The mean induction to active

phase interval and induction to delivery interval were significantly shorter in the study group (P = 0.017; P = 0.004 respectively). But there was no difference in the rate of progress of labor in the two groups once active phase was reached. Because of short induction to delivery interval in the study group misoprostol is especially useful in pre-eclampsia and eclampsia patients. More cesarean sections were done in the study group for fetal distress and for abnormal uterine action. As this is a matter of concern, reducing the dose of misoprostol to half may reduce cesarean section rate. Intracervical dinoprostone gel had minor side effects like nausea and vomiting, while oral misoprostol administration was associated with side effects like shivering, itching and hyperthermia, and more dreaded complications like hyperstimulation and hypertonus. The neonatal outcome was comparable in both the groups. Lastly, oral misoprostol does not need cold chain storage and is cheaper.

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