Original Article

Misoprostol versus Dinoprostone for induction of labor at term: a randomized controlled trial

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Objective: To compare the safety and efficacy of 25 microgram of sublingual misoprostol with 2 mg of vaginal dinoprostone for induction of labor at term.

Methodology: This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology of Cantonment General Hospital, Rawalpindi, Pakistan. All pregnant women aged 20-40, at 37-41 weeks with a live singleton fetus who required induction of labor were eligible for the study. 106 patients were randomized into 2 groups; one group received 25 microgram misoprostol sublingual 4 hourly up to a maximum of four doses and other group received 2mg dinoprostone gel vaginally 6 hourly up to a maximum of 2 doses. Both groups were compared for induction to delivery interval and number of doses, which were the primary outcome measures.

Results: A larger number of women in the misoprostol group delivered within 24 hours although this difference did not reach clinical significance (p value 0.301). Lesser number of doses of dinoprostone were required and a larger number of women in the dinoprostone group delivered with a single dose (29 vs 16). This was a clinically significant difference (p=0.04). However, larger number of women in the dinoprostone group required augmentation with syntocinon (p=0.03).

Conclusion: A 25 microgram of sublingual misoprostol has been found to be a safe and effective alternate to 2 mg of vaginal dinoprostone for induction of labor at term. The difference between the two groups did not reach clinical significance (p<0.103). (Rawal Med J 2014;39: 307-310).

Key words: Sublingual misoprostol, dinoprostone, induction of labour. Induction to delivery interval, term pregnancy.

INTRODUCTION

Induction of labor is one of the commonest obstetric interventions.[1] Unpublished data from WHO global survey on maternal and perinatal health showed an overall induction rate of 9.6%. Lowest rates were reported from Africa.[2] Induction of labor in the presence of an unripe cervix is associated with higher rates of failure, especially when oxytocin is used alone. This may result in prolonged labors and high cesarean section rates with markedly increased maternal and perinatal morbidity.[3]

Interventions used for induction of labor include mechanical methods, amniotomy and pharmacologic agents (oxytocin, prostaglandins). Prostaglandin E2 has been in use since 1968 and has been the agent of choice for past several decades.[4] There are, however, issues of cost and storage which are particularly relevant to our circumstances.[5] Misoprostol is an E1 analogue, originally used for treatment of gastric ulcer, has now been approved by many international bodies for induction of labor. Although the doses for various gestational ages have been defined by FIGO, the minimum effective dose and the most suitable route at term is still debated. Aim of our study was to determine the optimal dose of misoprostol in terms of safety and efficacy.

METHODOLOGY

This randomized controlled trial was conducted in the Department of Obstetrics and Gynecology, Cantonment General Hospital, Rawalpindi, Pakistan from January 1, 2013 to December 31, 2013. It was Approval of Ethical committee of the hospital and Informed consent was taken from women to participate in randomization process. All pregnant women aged 20-40, at 37-41 weeks of gestation with a live singleton fetus, who required induction of labor were eligible for the study. Grandmultiparas, women with nonreassuring fetal status, any contraindication to vaginal birth and

those with previous uterine surgery were excluded from the study.

Patients were randomization by opening sequentially numbered folded forms with already stamped intervention. Group 1 received 25 microgram misoprostol sublingual 4 hourly up to a maximum of four doses. Group 2 received 2mg dinoprostone gel vaginally 6 hourly up to a maximum of 2 doses. The dose was halved in those who were >Para 3. Cardiotocography was repeated after administration of each dose of inducing agent. Partogram was maintained for every patient in active phase.

Subsequent dose of inducing agent was withheld if cervix was suitable for amniotomy (ARM) or if the patient was in active labor or if there was evidence of fetal distress or hyper stimulation. Induction was considered to have failed if active phase of labor failed to establish following administration of above described doses and cesarean section was performed. Both groups were compared for induction to delivery interval and number of doses, which were the primary outcome measures. Secondary outcome measures included tachysystole, hypertonus, hyperstimulation syndrom, rate of failed induction, requirement for augmentation, maternal side effects, fetal distress, meconium staining of amniotic fluid and need for admission in neonatal intensive care unit. Successful induction was defined as achievement of vaginal delivery (spontaneous or instrumental). Failed induction was defined as failure of onset of regular progressive uterine contractions with cervical effacement and dilatation up to 3 cm.

Data were analyzed using SPSS v. 17. Frequencies and percentages were calculated for categorical variables. A comparison of means was done for demographic characteristics and bishop score at the time of admission using student t test. Chi square test was used to compare outcome variables between the two groups.

RESULTS

The two groups were comparable in terms of age, gravidity, parity, gestational age, Bishop score at the time of induction and indication of induction of labor (Table 1). There was a small difference in the birth weights of infants in the two groups but this was not possible to predict antenatally. Induction of labor was successful in 71.6% patients in misoprostol group and in 77.3 % in dinoprostone group (p=0.970). The two groups did not differ regarding mode of delivery or indications for emergency lower segment cesarean section.

Table 1. Demographic features of two groups.

Variable	Misoprostol n=53	Dinoprostone n=53	P value
Age	25.53 ± 3.974	26.55 ± 3.462	0.162
Gravidity	2.11± 1.340	2.28 ± 1.561	0.549
Parity	.92 ± 1.174	1.15 ± 1.433	0.376
Gestational age	39.23 ± 1.281	39.43 ± 1.201	0.391
Bishop score at the time of induction	2.57 ± 1.065	1.98 ± 1.152	0.008
Birth weight of the baby	3.023 ± .3593	3.211 ± .2679	0.003
Indication for induction of labor: Postdates pregnancy. Premature rupture of membranes. Poor biophysical profile. Abnormalities of liquor volume Miscellaneous	 n=15 n=13 n=7 n=16 n=2	 n=19 n=13 n=5 n=11 n=5	0.555

Induction to delivery interval was the primary outcome variable. The difference between the two groups did not reach clinical significance (p=0.103). A larger number of women in the misoprostol group delivered within 24 hours although this difference did not reach clinical significance (p=0.301). The other primary outcome was required number of doses. Less number of doses of dinoprostone were required and a larger of women in the dinoprostone group delivered with a single dose (29 vs 16) (p=0.04). However, larger number of women in the dinoprostone group required augmentation with syntocinon (p=0.03) (Table 2).

Table 2. Primary outcome measures.

	Misoprostol n=53	Dinoprostone n=53	P value
Induction to delivery interval (hours)	12.053 + 3.2462	14.054 + 4.8588	0.103
Number of doses required 1 dose (n= 57) 2 doses (n= 43) 3 doses (n= 6)	1.72 + .662 n= 21 n=26 n=6	1.32 + .471 n=36 n=17 n=0	0.003

More women in the dinoprostone group experienced fetal distress (11 vs 9), while in the misoprostol group more women had meconium stained amniotic fluid (6 vs 1). Both of these did not reach clinical significance (p values 0.5 and 0.056, respectively).

Table 3. Secondary outcome measures.

	Misoprostol n=53	Dinoprostone n=53	P value
Success rate	71.6%	77.3%	0.970
Delivery with single dose	30.1%	54.7%	0.04
Delivery within 24 hours	71.6%	66.0%	0.340
Mode of delivery Spontaneous vaginal delivery Instrumental delivery Emergency lower segment cesarean section	 62.2% 9.4% 18.8%	 67.9% 7.5% 20.7%	 0.342 0.51 0.500
Indications of cesarean section Fetal distress Failed induction Failed progress of labor	 9.4% 3.7% 5.6%	 5.6% 3.7% 11.3%	 0.358 0.691 0.244
Requirement for augmentation	0.09%	26.4%	0.03
Hyperstimulation syndrome	0%	0%	
Tachysystole	0%	0%	
Maternal side effects	0%	0%	
Apgar score less than 7	0%	0%	
Fetal distress	16.9%	18.8%	0.5
Meconium staining of amniotic fluid	11.3%	1%	0.056
Admission in neonatal intensive care unit	1%	0	0.5

None of the fetus had an APGAR score less than 7 at 5 minutes or admission to neonatal intensive care unit. There was no stillbirth in either group or no case of hyperstimulation or tachysystole. None of the women experienced maternal side effects.

DISCUSSION

Induction of labor at term with misoprostol has been a subject of active research in the recent decades. Various doses ranging from 100 ug to 25 ug have been described.[6-8] The most effective route is also unknown. In our study, we used 25 ug through sublingual route. It has various advantages including ease of administration for the patient as well as prescribing doctor. It reduces the number of vaginal examinations, which is particularly relevant in case of ruptured membranes. It also avoids the first pass effect. In our study, we compared this dose with dinoprostone, which has a well established safety and efficacy with standard doses.

Various parameters have been used to describe a successful induction. These include admission to delivery interval,[6] induction to delivery interval and interval from induction to the onset of labour.[5].We used induction to delivery interval because it described the time when the intervention was actually instituted and eliminated the interobserver error in diagnosis of onset of active first stage of labor. Concurrent use of oxytocin[9] and sequentially increasing regimens[10] have also been described. We used the above described regimen as it conformed more to the pharmacokinetics of sublingual route.

The success rates in our study were similar to those in studies by others.[11,12] Mean induction to delivery intervals in our study was also similar. The pattern of labor, however, needs special attention. In the misoprostol group, fewer patients went into labor with single dose but once in labor, a significantly lesser number of women required augmentation. On the other hand, in the dinoprostone group although more patients went in to labor with single dose, more required augmentation with oxytocin. Thus, misoprostol resulted in a pattern of labor, which simulates physiology of normal labor more closely. Importantly, number of women delivering in 24 hours was not significantly different among the two groups despite a higher number of doses used in misoprostol group.

No maternal side effects, tachysystole, hypertonus contrations or hyperstimulation were noted. The rates of fetal distress and meconium stained liquor were similar to the other studies.[11,12] With misoprostol, more patients delivered within 12 hours when higher doses are used. This is at the cost of more hyperstimulation,[8,13] fetal distress,[14,15] meconium stained liquor,[15] instrumental delivery[16] and admission to neonatal intensive care unit.[14]

CONCLUSION

Misoprostol, at a dose of 25 ug sublingual 4 hourly was found to be a safe and effective alternative to 2 mg vaginal dinoprostone for induction of labor at term. However, more studies are needed to be

conducted with large number of ladies to establish safety and efficacy of 25 micrograms of misoprostol administered sublingually.

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Conception and design: Nighat Shaheen, Safia Khalil
Collection and assembly of data: Safia Khalil, Nighat Shaheen
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Critical revision of the article for important intellectual content: Nighat Shaheen
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