COMPRASION OF INTRAVAGINAL ISOPROSTROL AND DINOPROSTONE FOR INDUCTION OF LABOUR

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ABSTRACT
Objective: *To assess the efficacy and safety of intravaginal misoprostol for induction of labour at term, in comparison with Dinoprostone on define parameters.*
Study Design: *It was a prospective randomized comparative study.*
Setting & Duration: *This study was conducted in Labour Room of Liaquat National Hospital Karachi from June 2003 To December 2003.*
Methodology: *It was a blind randomized comparative study and women meeting the criteria, with indication for induction of labour were randomized to receive either Dinoprostone or Misoprostol intravaginally. Misoprostol was used in 50 microgram dose 6 hourly to a maximum of three doses. A total of 70 patients were included in the study out of which 35 were induced with Misoprostol and 35 were induced with Dinoprostone. The inclusion criteria were Primigravida between 32 and 42 completed weeks of gestation, Single fetus with cephalic presentation, medical and obstetrical indication for induction of labour, pre induction normal CTG and un favourable cervix (BISHOP score less then 5). The exclusion criteria were revious uterine surgery, absolute CPD, malpresentation, active genital herpes, grand multipara, unsatisfactory CTG, severe intrauterine growth retardation, vaginal bleeding in second half of pregnancy.*
Results: *The result showed that Misoprostol group has significant reduction in induction to delivery interval compared to Dinoprostone group; 9 hours versus 13 hours. In addition 63% women in Misoprostol group delivered after single dose compared to 31% in Dinoprostone group. Mode of delivery was vaginal in72% and 74% of misprostol and dinoprostone group respectively and abdominally in 28% Misoprostol group and 26% in Dinoprostone group. The neonatal outcome in both the groups was same.*

KEYWORDS: *Misoprostol, Dinoprostone, Prostaglandins, Cervical Ripening*

INTRODUCTION

Induction of labour refers to initiation of uterine contraction before the spontaneous onset of labour by medical/surgical means leading to cervical dilatation and effacement and delivery of baby.

An estimated 15% of pregnant women undergo labour augmentation and another 15% require aid in labour augmentation and labour induction.[1] Induction of labour at term is a common obstetrical intervention and cervical ripening in these cases is considered to be of importance. Many obstetrical and medical condition require induction of labour eg: Pre-eclampsia, Gestational diabetes , Post dates etc.

Labour induction in presences of unfavourable cervix is often prolonged, tedious and may lead to induction failure. A protracted induction may also incur other antepartum complications such as chorioamnionitis, uterine hypertonus or water intoxication when oxytocics are used. Commonly used methods are intravenous oxytocins, intracervical or intravaginal prostaglandin E2 or both.

Systemic review and meta analysis have shown that there are advantages in using vaginal prostaglandins as compared to oxytocins alone in the presences of unripe

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cervix with regard to shorter induction to delivery interval and lower operative delivery rate.[2] Literature supports the use of two intravaginal prostaglandin preparations for the induction of labour and cervical ripening which are Misoprostol (PGE1) Dinoprostone (PGE2).

Among these two forms only Dinoprostone is FDA approved for cervical ripening. More recent attention has been focused on the use of PGE1 analogues such as misoprostol (cytotec) for cervical ripening.[3-5] Although such preparations are FDA approved only for the treatment of peptic ulcer disease and not received approval for use during pregnancy, they have been used for induction of labour.

The purpose of the study was to assess the efficacy and safety of intravaginal misoprostol for induction of labor at term, in comparison with those of dinoprostone by:

1) Comparison of induction to delivery interval between misoprostol and dinoprostone group and need for repetition.
2) Comparing number of patients requiring oxytocin for augmentation of labour in both groups.
3) Comparing mode of delivery in two groups.
4) Comparing neonatal outcome with regard to APGAR score, meconium staining of amniotic fluid and neonatal admission to neonatal ICU.

METHODOLOGY

It was a prospective randomized trial carried out in the **o**bstetrics ward of Liaquat National Hospital Karachi. It is a tertiary care hospital and in addition to booked cases it takes unbooked and referred cases from periphery and other clinics. Total number of deliveries per year is approximately 2000-2500. It was conducted for a period of 6 months from June 2003 to December 2003. Total deliveries per month are approximately 200, and number of patients in whom medical induction is indicated is 8%-10% per month. A total of 70 patients were included in the study out of which 35 were induced with misoprostol and 35 with dinoprostone.

INCLUSION CRITERIA:
Primigravida between 32 and 42 completed weeks of gestation. Single fetus with cephalic presentation, medical and obstetrical indication for induction of labour, pre-induction normal CTG and unfavourable cervix (Bishop score less then 5).

EXCLUSION CRITERIA:
Previous uterine surgery, absolute CPD, malpresentation, Active genital Herpes, grand multipara, unsatisfactory CTG, severe IUGR, vaginal bleeding in second half of pregnancy.

Seventy pregnant were selected using inclusion and exclusion criteria after their informed consent. They were admitted through OPD or emergency. Booked or unbooked and referred patient with indication for induction of labour were included in the trial. The detailed histories of women were taken on admission. Gestational age was confirmed by last menstrual period and early ultrasound, if available. Information about booked patients was also taken from their antenatal record card. a thorough general and physical examination was done. Obstetrical examination was also conducted and assessment of fundal height, lie of fetus, presenting part and its engagement, fetal heart sound and CTG was done. Pelvic examination for Bishop score and adequacy of pelvis was assessed.

Women were randomly assigned to be induced either with Misoprostol or Prostaglandin E1 using alternate numbers. Misoprostol is available in 200 microgram. The dose of misoprostol which was used for induction of labour was 50 microgram, that is one quarter of 200 microgram tablet after pre induction assessment and CTG. 50 microgram tab was placed in the post fornix by doing pervaginal examination. Post induction CTG was performed 2 hours after cytotec insertion. Next vaginal examination was done after 6 hours and if bishop was still poor, misoprostol was repeated to a maximum of 3 doses.

Other group was induced with Dinoprostone 3mg, after pre induction assessment and CTG, table Dinoprostone was inserted in the posterior fornix digitally. Post induction CTG done after 2 hours meanwhile careful monitoring of fetal heart and uterine contraction was done. Patient was reassessed after 6 hours by doing bishop scoring and if required doses were repeated to maximum of 3 doses at six hours interval.

During the course of induction fetal heart and uterine contractions were monitored. Strict watch for uterine hyperstimulation and tachysystole was kept. When patient develop uterine contraction with increasing strength and frequency, she was evaluated again by doing pervaginal examination. Her findings of dilation of os, length and position of cervix, station of presenting part and status of membranes were noted. If Bishop score was found favourable i.e. above 8 then artificial rupture of membrane was done. Partogram of every patient was maintained. Performa for induction were filled which carried information like her name, age, parity, booked unbooked, referred, indication for induction, Bishop score after 6 hours, number of doses used for induction, induction to delivery interval, whether augmentation of labour was done or not, mode of delivery and neonatal outcome and side effects of drug like

uterine hyperstimulation and tachysystole. The main outcome measures were:

Obstetrical Criteria: Induction to delivery interval, number of doses required Oxytocin requirement in labour, mode of delivery.

Fetal Criteria: Presence of meconium in amniotic fluid, fetal distress (abnormal CTG)

Neonatal Criteria: Apgar score at one and five minutes, meconium aspiration, transfer to neonatal intensive care unit.

Maternal Safety: Uterine hyperstimulation, tachysystole

RESULTS

A total of 70 patients at term,gestation varying between 37-42 weeks were recruited in the study in whom induction of labour was indicated. Out of 70 patients half i.e. 35 patients were induced with misoprostol and the other half i.e.35 patients were induced with dinoprostone. The age of the patients ranged between 21yrs to 32 yrs. and gestational age varied between 37-42 weeks in both the groups the patients were matched for age, parity, gestation and Bishop score (Table I).

The indication for induction were same in both the groups, post date being most common (Table II). The mean induction to delivery interval in those who delivered vaginally was significantly shorter in misoprostol group i.e. 9 hours vs 13 hours, mean difference of 4 hours, p-value <.005 (Table III).

In addition more women in misoprostal group delivered by single dose 63% vs 31%, more women delivered within 12 hours of induction 77% vs 31%. More women delivered after first dose of misoprostal 63% vs 31% The route of delivery differed slightly between the two groups.

Vaginal delivery occurred in 72% in misoprostol group and 74% in dinoprostone group, out of these 5 had vaccum vaginal delivery in misoprostol group. 10(28%) patient in misoprostol group had caesarian section, whereas 9(26%) in dinoprostone group had caesarian. The indications for caesarian section in dinoprostone group were failed induction, non progress of labour, fetal distress and prolong second stage of labour. During labor there was no significant difference between two groups regarding the presence of meconium in amniotic fluid.

Neonatal outcome regarding the birth weight of babies, apgar score at 1 and 5 minutes and admission to neonatal unit were similar between two groups. Total number of neonates admitted in neonatal unit were 5, three from misoprostol group and two from dinprostone group. In misoprostol group indication of admission were, 1 due to meconium aspiration, 1 due to hypoglycemia, (infant of diabetic mother) and 1 due to congenital malformation (cleft lip and palate). In dinoprostone group both neonates were admitted due to meconium aspiration.

DISCUSSION

Prostaglandin preparations are generally used for induction of labour at term. This trial is the first study in Liaquat National hospital to assess the efficacy and safety of vaginal Misoprostol (PGE 1 analogue) in comparison with vaginal Dinoprostone (PGE2 analogue). Our results showed that when misoprostol was used there was reduction in induction to delivery interval of 7 hours, which has been found in other studies as well.[6-8]

Induction to delivery interval is of major importance when labour is induced. Most of the time labour is induced to expedite delivery with hope of better outcome. With advances in methods of induction and inducing agents, there is considerable reduction in induction to delivery interval. Misoprostol, an effective agent for induction of labour, has shorter induction to delivery interval compared to Dinoprostone group.In a study by Danielian[9] the induction to delivery time was reduced by 8 hours. Papanikolaou[10] stated that

Table I. Maternal demographic details and values are given as mean (range)

Group	Misoprostol Group (n=35)	Dinoprostone Group (n=35)
Age (Years)	23(16-30)	24(16-32)
Parity	Primigravida uptil	Primigravida
Uptil	3rd Gravida	3rd Gravida
Gestation (Weeks)	41 (37-42)	41 (38-42)
Bishop Score (at Initial examination)	4 (2-5)	4 (3-5)

Indication	Misoprostol Group (n=35)	Dinoprostone Group (n=35)
Prolong Pregnancy	15 (42.8%)	15 (42.8%)
Rupture of membranes at term	14 (11.4%)	7 (20%)
Diabetes	2 (5.7%)	3 (8.5%)
Pregnancy induced hypertension	9 (25.7%)	6 (17.17%)
Intrautering growth retardation	2	3
Decreased fetal movement	2	1
Miscellaneous	1	--

Table II. Indication for Induction of Labour

induction to delivery interval was significantly reduced in women who were induced with Misoprostol. Kadanali[11] found a difference of 6 hours in induction to delivery interval as compared to Dinoprostone. From all these studies it can be concluded that Misoprostol effectively induces labour with shorter induction to delivery interval as compared to Dinoprostone. The 50 microgram dose regimen was selected with regard to other published trials, showing high effectiveness and less side effects. It may be possible that efficacy can be retained and side effects reduced even further with dose of 25 microgram.

Trials using lower doses of vaginal Misoprostol have shown it to be effective as compared with Prostaglandin E2 in a study by Farah[12], that compared 25 microgram with 50 microgram dose vaginally every 3 hours, the main induction to delivery interval was shorter in 50 microgram but incidence of tachysystole was less in 25 microgram. Wing[13] found that there was no increase in meconium in amniotic fluid in labour when 25microgram dose was used compared to 50 microgram dose which they had seen in there earlier studies. Wing[14] found that 25 microgram dose given at 6 hours interval had more failed induction, longer induction delivery interval and more frequently required oxytocin augmentation. From all these studies it is suggested that there is no standard dose and dosage interval for vaginally administered Misoprostol.

In our trial with 50 microgram dose of misoprostol, there was a shorter induction delivery interval, less need for oxytocin and no difference in uterine tachysystole and fetal distress as compared to vaginal dinoprostone. These findings are similar to the trial conducted by Danelian.[9] The incidence of meconium staining of amniotic fluid in both groups is insignificant. Wing[13] suggested that the meconium staining of amniotic fluid is possibly due to hyperstimulation or a direct effect of absorbed misoprostol metabolites on fetal gastrointestinal tract.

An important advantage of misoprostol is its cost effectiveness. This drug is significantly less expensive as compared to other prostaglandin preparations. Misoprostol can be stored at room temperature, whereas dinoprostone needs to be stored in refrigerator. Being an inexpensive drug, stable at room temperature, less number of doses required and less need for oxytocin requirement, its highly cost effective, all these factors are important consideration in a developing country like ours.

CONCLUSION

From this study we inferred that a dose of 50 microgram of misoprostol given at an interval of 6 hours is safe in carefully selected cases and it reduces the induction to delivery interval significantly, there is less need of

Table III. Comparison of outcome in labour values are given as no. (%) mean (range)

Outcome	Misoprostol Group	Dinoprostone Group	P-value
Induction - delivery interval (hours)	9 (6-14)	13 (9-21)	0.005
No. delivered after single dose	22 (63%)	11 (31%)	0.016
No. delivered after 2nd dose	9 (25%)	15 (40%)	--
No. delivered after 3rd dose	4 (11%)	9 (29%)	--

oxytocin and successful outcome with majority delivering vaginally and having a favourable neonatal outcome compared to dinoprostone.

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