

DINOPROSTONE AND MISOPROSTOL FOR INDUCTION OF LABOUR AT TERM PREGNANCY

Bushra Iftikhar, Shehla M Baqai*

Combined Military Hospital Nowshera/National University of Medical Sciences (NUMS) Pakistan, *Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

ABSTRACT

Objective: Objective of this study is to compare the safety and the efficacy of Prostaglandin E1 (Misoprostol) with Prostaglandin E2 (Dinoprostone).

Study Design: Quasi experimental

Place and Duration of Study: Department of Obstetrics and Gynecology, PNS SHIFA, Karachi from 22nd March 2006 to 22nd September 2006.

Material and Methods: Sixty patients in whom labour induction was indicated were included in the study. They were divided into group A and group B containing 30 patients each. Group A received 50microg of Misoprostol with maximum of 4 doses while group B received Prostaglandin E2 maximum of 2doses. They were primi or second gravida having singleton pregnancy with vertex presentation and Bishop Score less than 4.

Results: The results showed that misoprostol group has significant reduction in time for induction and duration of labor as compared to dinoprostone. In misoprostol group more women delivered after single dose compared to dinoprostone. More women in misoprostol group delivered vaginally than abdominally with fewer women require oxytocin augmentation. Neonatal outcome in terms of apgar score and admission in neonatal intensive care unit was similar in two groups. Further and randomized control trials with large sample size are required to assess the safety of drug.

Conclusion: Misoprostol with proper monitoring and supervision is an effective agent for induction of labour at term. Its cost effectiveness and easy shelf storage proves it to be a better option, especially in a tropical developing country like ours.

Keywords: Cervical ripening, Dinoprostone, Misoprostol.

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INTRODUCTION

Induction of labor is indicated when the benefits to either the mother or the fetus outweigh the benefits of continuing the pregnancy¹. Ripening of the cervix greatly facilitates labor and increases the likelihood of vaginal delivery. If the cervix is unfavorable and the induction is necessary then ripening with prostaglandins is required².

In the past 20 years prostaglandins have been used in a variety of formulations for labor induction and cervical ripening. Prostaglandins were used intravenously in late 1960s but the route of administration was associated with

significant side effects³.

Systemic review and data analysis have shown that there were advantages in using vaginal prostaglandin as compared to oxytocin alone in the presence of unripe cervix with regards to shorter induction to delivery interval and lower operative delivery later on^{4,5}. Literature supports the use of two intra-vaginal prostaglandin preparation for induction labor which includes dinoprostone (prostaglandin E2) and misoprostol (prostaglandin E1)⁶. Among these two forms dinoprostone is FDA approved, whereas misoprostol has not yet been approved by FDA for induction of labor at term with a viable fetus⁷. Misoprostol which is prostaglandin E1 analogue which was initially introduced for treatment of gastric ulcer in patients taking NSAID's because of its prostaglandin it is also

Correspondence: Dr Bushra Iftikhar, Classified Gynaecologist, CMH Nowshera Pakistan (Email: bushra.iftikhar@yahoo.com)
Received: 29 Jan 2015; revised received: 17 Mar 2015; accepted: 27 Mar 2015

very useful for cervical ripening and induction of labour. It proved to be a useful agent for termination of pregnancy in first, second and third trimester⁸. Misoprostol can be given orally, sublingually, vaginally or rectally. Route of administration may be chosen in accordance to

the neonatal outcomes are same for both induction regimes¹¹. From a clinical and perinatal perspective misoprostol is an acceptable choice for induction of labor. Misoprostol is a cost effective and easily storable at room temperature drug as compared to prostaglandin E2 which is

Table-I: Duration of Labour.

	Drug used	N	Mean	S.D
Duration of labour	Misoprostol	30	5.5667	1.0063
	Dinoprostol	30	9.4667	1.7167

p -value<0.05(significant).

Table-II: Number of doses.

Group	No. of patients responded with		Total no of Patients	Response with Dose 1st (%)	Response with Dose 2nd (%)	Frequency (No. of doses)
	First Dose	Second Dose				
A (Misoprostol)	27	3	30	90.00	10	33
B (Dinoprostal)	25	5	30	83.33		35

Table-III: Showing summary statistics.

Variable		Drug Used		Total
		Misoprostol	Dinoprostal	
Augmentation by oxytocin	Yes	7	26	33
	No	23	4	27
Total		30	30	60

p -value<0.05 (Significant)

Mode of delivery	Vaginal	24	21	45
	Cesarean	6	9	15
Total		30	30	60

p -value>0.05 (Insignificant)

Complication	Fetal Distress	2	2	4
	Uterine Hypertention	2	0	2
	Nil	26	28	54
Total		30	30	60

p -value>0.05 (Insignificant)

the preference of the patient. Vaginal route has shown to be more effective than oral. Although diarrhea, fever with shivering occur after taking more than 400 micrograms. Other reported adverse effects are uterine hyperstimulation, rupture or perforation, amniotic fluid embolism, severe vaginal bleeding, retained placenta, shock, fetal bradycardia, and fetal death. Now there is a considerable interest for its use in labor induction for a term pregnancy with a viable fetus^{9,10}. According to the study misoprostol is significantly more effective for labor induction than oxytocin and prostaglandin E2 maternal and

more expensive and requires cold storage. Many studies have been carried out in past few years to establish best dose, administration route and interval between doses for cervical ripening and labour induction. Since the misoprostol shows significant effectiveness for induction of labor however there is still a need to better establish its safety.

MATERIAL AND METHODS

Study was carried out in the department of Obstetrics and Gynaecology at PNS SHIFA, Karachi. Sixty (30 each group) were selected through non-probability purposive sampling in

the period of six months Primi and Second Gravida at term with vertex presentation, singleton pregnancy and Bishop Score less than 4.

A detailed history was elicited followed by examination which included the pelvic examination and assessment of Bishop score. Then informed consent were taken from the patients. Misoprostol and Dinoprostone were be used for induction of labour on alternate basis amongst patients.

The trial was conducted over two groups of patients for labour induction. Group A comprising of 30 patients received 50 micro grams of Misoprostol 4 hourly for a maximum of four doses. Group B comprised of 30 patients and received Prostin E2 vaginal tablet (3mg) maximum of two doses. Misoprostol was discontinued with cervical dilatation of 2.5 cm or regular uterine contraction and for dinoprostone second dose was repeated after six hours to achieve regular uterine contraction. Augmentation of labor was done by amniotomy and syntocinon infusion. Fetal well being was confirmed by cardiotocograph prior to every

till the onset of regular painful uterine contractions), duration of labour (time from regular uterine contractions till delivery), mode of delivery, complications including uterine hyperstimulation (more than 5 contractions in 10 mins or contraction lasting more than 2mins) fetal distress by CTG and fetal heart rate monitoring and in the end fetal outcome in terms of APGAR score at 0, 5 and 10mins and admission in NICU.

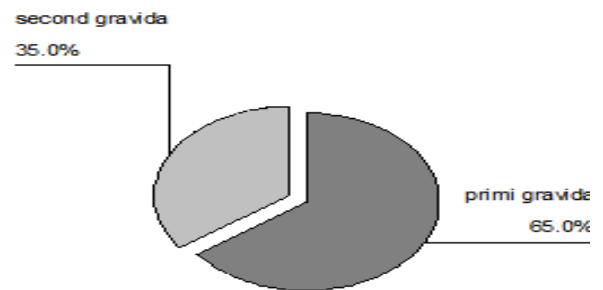


Figure-1: Distribution of patient according to parity.

Data Analysis

Data were analyzed by using SPSS version-10. Relevant descriptive statistics was used for data presentation. Frequency and

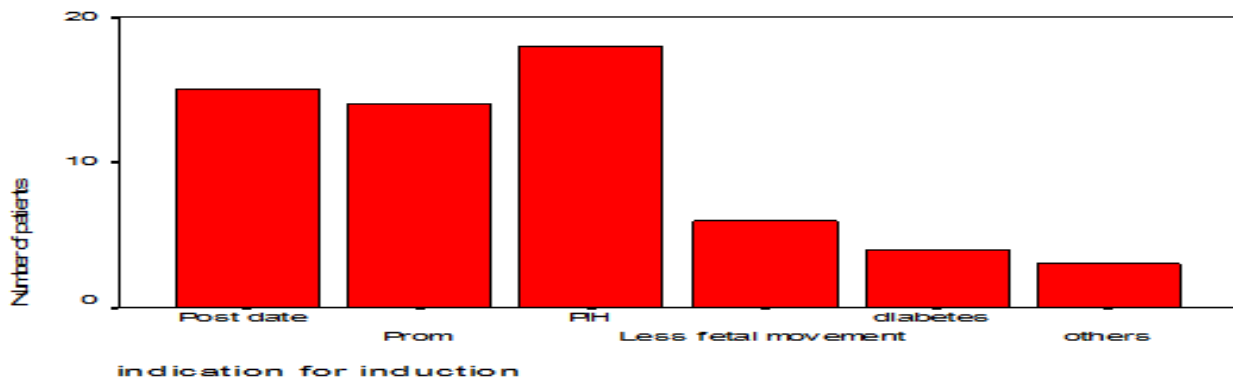


Figure-2: Number of patients according to indication for induction.

dose. Labour was managed by normal labour ward protocols. Patients were monitored for onset of labour, uterine activity, fetal heart rate monitoring by intermittent auscultation and CTGs.

Data were collected through a proforma. The variable in this study are time for induction (time recorded when 1st dose of tablet placed vaginally

percentages were computed to present qualitative variables including indication for induction, need for augmentation, mode of delivery, maternal and fetal complications. Chi-square test was applied to compare these variables between these two groups and to test the hypothesis^{3-5,&7}.

Quantitative data including age, induction time, duration of labor and fetal APGAR score

were presented by Mean \pm Standard Deviation. Student's t-test was applied to compare these variables and to test hypothesis^{1,2,6}. Statistical significance was taken at $p < 0.05$.

RESULTS

The patients included in the study were 17-35 years of age. The highest numbers of patients were between 20 & 30 years and the mean was 25 years. All patients in this study were between 37-41 weeks gestation. The greatest numbers of patients were having gestational age between 39 & 40 weeks. The patients included in our study were primi and second gravida. Most of the patients were primi gravidas (39 out of 60) while 21 out of 60 were second gravidas.

The leading causes of induction of labour in this study were pregnancy induced hypertension, pre-labour rupture of membranes and post date pregnancy.

Time for induction includes the time recorded with first dose of the tablet placed till the onset of regular uterine contractions. The time was less in the Misoprostol group i.e. 2.5 hrs as compared to the Dinoprostone.

The result of our study revealed that the duration of labour was less in the Misoprostol group (5.5 hours) as compared to the Dinoprostone (9.4 hours).

Results of the study showed that number of doses required are more in the Dinoprostone group than in Misoprostol (table-II).

In this study the use of oxytocin for augmentation of labour were required in only 7 cases where induction was done by Misoprostol and in Dinoprostone group 26 out of 30 patients required augmentation by oxytocics (table-III).

The mode of delivery was vaginal in 80% of the patients induced with Misoprostol, while 70% of the patients in Dinoprostone group delivered vaginally. Indication of caesarean section was failed progress in 6 out of 8 patients having caesarean section from Dinoprostone. In the Misoprostol group two cases of uterine

hyper-stimulation were recorded leading to caesarean section (table-III).

In this study two cases of hyperstimulation were reported from Misoprostol group while no case of uterine hyperstimulation recorded in Dinoprostone group (table-III).

Neonatal outcome was recorded in terms of

Group wise number of doses

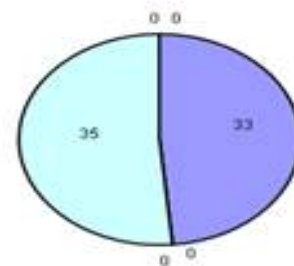


Figure-3: Group wise number of doses.

apgar score at birth, 5 mins and 10 mins. Neonatal outcome was also judged by the neonatal admission rate in neonatal intensive care unit. The study revealed that there is not much difference in the apgar score of the fetuses and admission in NICU comparing the two drugs.

DISCUSSION

Induction of labour is one of the most commonly performed obstetrical procedures. The rate of labour induction is approximately 20%, having risen to 40% in some places for various reasons.

During the last 15 years the concept of cervical ripening or priming has gained momentum and involves treatment to render the cervix more favorable followed by a formal induction method. Cervical ripening is an important pre-requisite of labor induction. Cervical ripening agents that have been proposed include vaginal prostaglandins E₂, Pessaries, Gels, Extra amniotic catheters, Hydroscopic dilators and locally applied hormones.

Prostaglandin E₂ has been the most commonly used agent for cervical ripening in the last two decades. Its efficacy requires cold storage

and it can only be used vaginally. Prostaglandin E2 vaginal tablet cost upto Rs. 700.00 and a repeat insertion will further increase the cost.

Misoprostol, a methyl ester of prostaglandin

8hrs of induction with less need for oxytocin augmentation. This is in accordance with previous trials

A meta analysis reported that Misoprostol

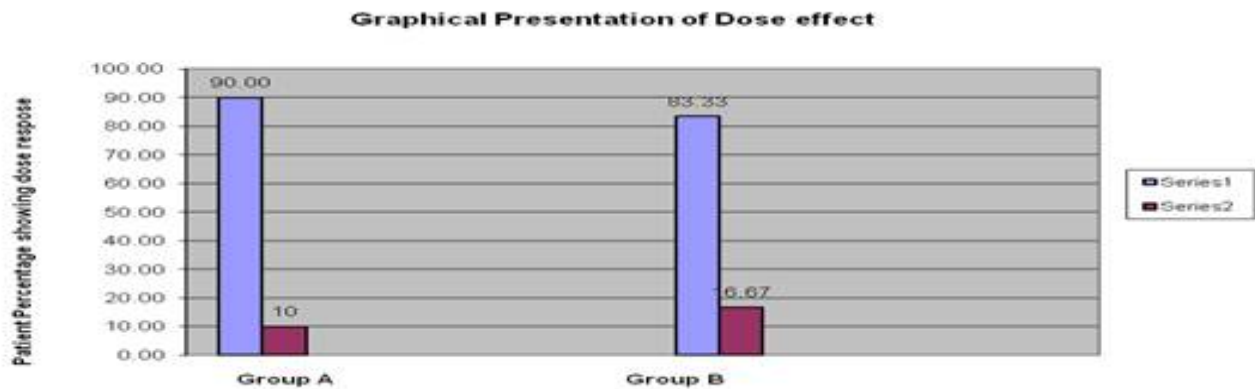


Figure-4: Graphical presentation of doses effect.

E1 is now being increasingly used for labor induction at term and pregnancy termination because of its greater efficacy as compared to prostaglandin E2^{12,13}. A tablet of 200 microg of Misoprostol (cytotec) cost approximately Rs. 35.00. It can be broken to provide 50microg aliquots. That means a single dose of cytotec will cost less than Rs. 10.00. It is easily stored at room temperature and rapidly absorbed both orally and vaginally. Several reports confirmed that Misoprostol is a highly effective agent for cervical ripening and labor induction¹⁴.

Misoprostol is associated with complications like uterine hyperstimulation, meconium stained liquor and uterine rupture¹⁵. In our study two cases of uterine hyperstimulation have been reported and it is consistent with the study reported by Chuk FJ, Huffaker BJ¹⁶. Therefore the area of concern is safety of its use. In several trials Misoprostol was associated with uterine contraction abnormalities¹⁷. Incidence of uterine tachysystole and hyperstimulation is reported to be higher than Prostaglandin E2 vaginal tablet¹⁸.

Our results showed that Misoprostol in a dose of 50 microg compared to Prostaglandin E2 vaginal tablets resulted in a shorter induction time and also shorter induction to delivery interval. Most women were delivered less than

improved cervical ripening better than Prostaglandin E2 vaginal insert and is more effective for labour induction¹⁹. Oxytocin augmentation was also required less often with Misoprostol than with Prostaglandin E2 (relative risk of 0.65)^{20,21}.

It is postulated by Hofmeyr²² that Prostaglandin used for labour induction crossed the placenta and stimulate the fetal bowel smooth muscles and cause meconium passage in utero. Despite increasing incidence of non reassuring fetal heart rate trace in Misoprostol group the overall caesarean section rate was reduced to 20% compared with 30% in Prostaglandin E2 group. Danielian et al. found a caesarean section rate of 11% in patients induced with Misoprostol compared to 14% in Prostin group²³.

Regarding the appropriate dose of Misoprostol for labour inductions several trials have been made using 25 microg, 50 microg, and 100 microg²⁴. It is suggested that there is no benefit of higher dose of Misoprostol but increased incidence of meconium stained liquor, fetal distress, tachysystole and uterine rupture. In a study by Farah et al²⁵. that compared 25 microg with 50 microg Misoprostol every 3 hrs showed a shorter induction to delivery interval with higher doses but with more fetal acidosis and caesarean

section for fetal distress. In our trial we found that 50 microg Misoprostol 4 hrly compared to Prostaglandin E2 vaginal 6hrly (2 doses) had no marked difference in fetal outcomes.

Regarding the safety concerns about Misoprostol, although precipitate labour, post partum haemorrhage, cervical and vaginal tears were seen more frequently and few cases of uterine rupture have been reported. Our results suggest that all these risks can be minimized by use of small dosages, proper monitoring and careful selection of the patients.

CONCLUSION

The efficacy of Misoprostol as a ripening agent was greater than that of Dinoprostone. It is economical and more easily stored than Prostaglandin E2 vaginal tablet. It is strongly recommended that Misoprostol may be used for induction of labour at term as an alternative to Prostaglandin E2 vaginal tablet, however because of the risk uterine hyperstimulation careful patient selection and monitoring is required. It is also recommended that further studies with larger sample size to be carried out to establish safety of the Misoprostol.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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