

A Randomized Controlled Clinical Trial to Compare The Effect of Intracervical Prostaglandin E2 (Dinoprostone) Gel and Intravaginal Prostaglandin E2 (Dinoprostone) Pessary on Ripening of Cervix and Induction of Labour

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Abstract

Objective: The aim of study was to compare the effect of intracervical prostaglandin E2 (dinoprostone) gel and intravaginal prostaglandin E2 (dinoprostone) pessary on ripening of cervix and induction of labor along with their effect on fetal heart rate and caesarian delivery rate.

Study Design: A randomized controlled clinical trial conducted in the Department of Obstetrics and Gynaecology, Hussain Memorial Hospital, Multan Road Lahore.

Methodology: One hundred and forty two patients who needed induction of labour and fulfilling the inclusion criteria were assigned randomly to one of two groups. Group A, was induced intravaginally with prostaglandin E2 pessary 3 mg (n=71). Group B, was induced intravaginally with prostaglandin E2 gel 0.5 mg (n=71). On the basis of bishop scores, the pessary or gel was reapplied at six hours interval for a maximum of two doses. Labour was augmented with oxytocin in selected cases who failed to undergo labour.

Results: Average age of the patients was 28.5 years (19-38 years). Maximum number of patients who were included in both groups was primigravidas. Most common indication for induction of labour was pregnancy induced hypertension/preeclampsia and postdates pregnancy. There was greater change in Bishop score with prostaglandin E2 gel (Group B) but no significant difference in induction delivery interval (P value=0.513) and oxytocin required for augmentation in both groups. 80.28% patients delivered in <24 hours in both groups. The caesarian delivery rate in the two groups was 33.80% and 42.25% respectively. Most common indications for caesarian section were fetal distress and failure of induction. Mean apgar score at 5 minute was 7.03 ± 1.42 in group A and 7.00 ± 2.27 in group B that was not significant (P value=0.929) statistically. Fetal bradycardia, nausea, vomiting, and diarrhea were more in group A as compared to group B. While two patients in group B had uterine hyper stimulation.

Conclusion: Prostaglandin E2 endocervical gel is more effective in achieving cervical ripening however induction to delivery interval, oxytocin requirement and apgar score are similar with these two agents. The overall cost of dinoprostone gel is more. So there is no extra advantage of using gel over pessary.

Key Words: Prostaglandin E2, Induction of labor, Cervical ripening.

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Introduction

Induction of labor is the stimulation of uterus with the aim of starting labour before natural onset of labour itself, to ensure delivery of fetus at an appropriate time when the baby is thought to be safe outside uterus than inside. Labour is induced in more than 13% of deliveries in united states.^{1,2} Induction of labour is indicated when the benefits of delivery to either the mother or fetus outweigh the benefits of continuing pregnancy³. There are various indications for induction of labour in the maternal or fetal interest.^{4,5} Most common are; Post date pregnancy >41 weeks, post term pregnancy, prelabour rupture of membranes at term, potential fetal compromise, oligohydramnios, IUGR, non-reactive NST(non-stress test), fetal rhesus iso-immunization, pregnancy induced hypertension/preeclampsia, diabetes associated with macrosomia, fetal demise and maternal request before 41 weeks etc.

To induce labour successfully a good cervical status and favorable obstetrical conditions are necessary. If these conditions are not present, cervical ripening must take place before induction of labour⁶. The cervix is metabolically active during ripening and passive during active labour. A ripe cervix indicates readiness for labour and predicts successful induction of labour. Clinician evaluate cervical readiness for labour using the Bishop score.⁷ The state of cervix (dilatation, effacement, and consistency) are the most important factors which influence the choice of method for induction of labour. Various methods used in clinical practice are sweeping of membranes, amniotomy, oxytocin administration, mechanical methods (catheters, balloons etc), prostaglandins (PGF₂alpha, PGE₂, PGE₁) and antiprogesterins (mifepristone).

The commonest method of induction in current use is with prostaglandins. Prostaglandins can be used intravenously, orally or vaginally but the first three routes often produce severe side effects and are best avoided in labour.¹ For local administration, prostaglandin E₂ pessaries and gels are available. These are absorbed in the circulation through the vaginal and cervical epithelium returning within blood supply to the uterus¹. Benefits of using gel preparations (Dinoprostone cervical gel 0.5 mg) are that plasma level of prostaglandin are higher with these preparations and they increase the volume of blood flow to the cervix similar to that observed in early stages of spontaneous labour.

Side effects of prostaglandins may be nausea, vomiting, uterine hyperstimulation, fetal bradycardia and failed induction.

Methodology

This study was conducted in the department of Obstetrics and Gynaecology, Hussain Memorial Hospital, Multan Road Lahore from September 2013 to February 2014. Patients in whom induction of labour was indicated and fulfilling the inclusion criteria were assigned randomly to receive either Dinoprostone pessary (3mg) intravaginally (group A control group) or Dinoprostone gel (0.5 mg) intracervically (group B) The approval from hospital ethical committee was taken before start of the study.

Systematic random sampling technique was used to select the patient for the study. The sample size was calculated using the hospital prevalence of the term patients presented in Obstetric emergency department/labour room of Hussain Memorial Hospital, Multan Road Lahore. The sample size was calculated to be 142 patients. These patients are divided with random allocation into two groups. Each group had 71 patients.

Data Collection Method: Study Proforma was designed according to the objectives of the study. Proforma was filled by the 2nd researcher who does not know about the pharmacological agent used in the particular patient. Written informed consent was taken from all the patients who were included in the study before the start of data collection.

Inclusion Criteria:

Low parity (≤ 3 previous term deliveries)

Bishop score ≤ 4

Exclusion Criteria:

Previous uterine scar

Patients with ruptured membranes

Data Analysis: Student's T – test was used to compare the two means. Regression analysis was used to assess the relationship between the affect and the outcome. The data was analysed with the help of SPSS (version 20). P value was calculated at 95% Confidence interval. Mean \pm SD was calculated for bishop score and induction to delivery interval. Caesarian rate was calculated as percentage.

Results

Table I reveals about indications of induction in both groups. Highest number of patients 31(43.6%) in group A were induced for P.I.H / Pre eclampsia and in group B highest number of patient 32 (45.07) were induced for postdates.

Table I (Indications for Induction of Labour)

Indications	Dinoproston pessary (3 mg) (group A)	Dinoproston gel (0.5 mg) (group B)
P.I.H/Pre eclampsia	31 (43.66%)	22 (30.99%)
Post date gestation	27 (38.03%)	32 (45.07%)
Decreased fetal movements	10 (14.08%)	06 (8.45%)
Placental abruption	01 (1.41%)	02 (2.82%)
Congenital anomalies	01 (1.41%)	03 (4.23%)
IUGR	-	02 (2.82%)
IUD	01 (1.41%)	04 (5.62%)
Total	71 (100%)	71 (100%)

20 patients (28.17%) in group A had a maximum duration of induction delivery interval of 6-10 hours and 20 patients (28.17%) in group B had a duration of 11-15 hours. The comparison showed that there was no significant difference between two groups ($P>0.05$) (Table II). 80.28% patients delivered in less than 24 hours in both groups.

Table II: (Induction Delivery Interval)

Duration (hours)	Dinoproston pessary(3mg) (Group A)	Dinoproston gel(0.5 mg) (Group B)
No. of patients		
<5	04 (5.63%)	-
6-10	20 (28.17%)	16 (22.54%)
11-15	17 (23.94%)	20 (28.17%)
16-20	09 (12.68%)	10 (14.08%)
21-25	07 (9.86%)	11 (15.49%)
26-30	05 (7.04%)	04 (5.63%)
>35	09 (12.68%)	10 (14.09%)
TOTAL	71 (100%)	71 (100%)
MEAN±SD	16.39±9.62	17.39±8.53

Table III shows comparison of the mode of delivery in two groups. In group A patients delivered by normal vaginal delivery were 41(57.75%) and in group B, 37(52.11%). 4 patients (5.63%) delivered by outlet forceps delivery in group A and 2 patients (2.82%) in group B. 2 patients (2.82%) delivered by ventoux extraction in group A and 2 patients (2.82%) in group B. 24 patients (33.80%) delivered by caesarian section in group A and 30 patients (42.25%) in group B.

Table III: Mode of Delivery

Mode of delivery	Dinoproston pessary(3mg) group A	Dinoproston gel (0.5 mg) Group B
No. of patients		
Normal vaginal delivery	41 (57.75%)	37 (52.11%)
Outlet forceps delivery	4 (5.63%)	2 (2.82%)
Ventouse extraction	2 (2.82%)	2 (2.82%)
Caesarian section	24 (33.80%)	30 (42.25%)
Total	71 (100%)	71 (100%)

Table IV shows the occurrence of fetal bradycardia after induction in both groups. In group A fetal bradycardia was present in 16 patients (22.5%) and in group B it was seen in 10 patients (14.1%).

Table IV: Fetal Bradycardia

Fetal Bradycardia	Dinoprostone Pessary(3mg) Group A	Dinoproston Gel (0.5 mg) Group B
No. of patients		
Yes	16 (22.5%)	10 (14.1%)
No	55 (77.5%)	61 (85.9%)
Total	71 (100%)	71 (100%)

Table V reveals the data about indications for caesarian section. There were 12 patients with indication of fetal distress in group A and 8 patients in group B. 8 patients had LSCS due to failure of induction in group A and 13 in group B. 4 patients who fail to progress were in group A and 7 patients in group B. There was no patient of uterine hyperstimulation in group A and 2 patients in group B.

Table V: Indications for Caesarian Section

Indication	Dinoproston prssary(3mg)	Dinoproston gel (0.5 mg)
	Group A	
	No. of patients	
Fetal distress	12	8
Failure of induction	8	13
Failure of progress of labour	4	7
Uterine hyperstimulation	0	2

Discussion

The success of induction depends on ripening of cervix and if the cervix is unripe, amniotomy and oxytocin titration will result in high levels of fetal and maternal complications. The secret of success of induction of labour lies in ripening as closely as the process of spontaneous parturition. Prostaglandin E2 (dinoproston) has a dual action of ripening and promoting uterine contractility. The aim of the study was to compare the effect of dinoproston intravaginal pessary 3 mg group A and dinoproston intracervical gel 0.5 mg group B on ripening of cervix, induction of labour, fetal heart rate and caesarean delivery rate.

71 patients were randomly assigned to each group. Most common indications for induction of labour were pregnancy induced hypertension/pre-eclampsia and postdates pregnancy in both groups. These results are comparable with the study conducted by Wieland D, Friedman F, Jr in Jacobi Medical Centre, Bronx, USA Aug 1999 in which no significant difference was noted between two groups in indications for induction of labour⁸. Also same results were observed in the study conducted by Joscha Reinhard, Roberta Rosler, Juping Yuan, Biomed Research Intl volume 2014, Article ID 682919.¹⁶ Comparable results were seen In study conducted by Saima Qamar, Adeela Bashir, Faiza lbrar.¹³

The analysis of mean duration of labour (induction delivery interval) shows that there is no significant difference between the two groups (P=0.513). 80.28% patients delivered in less than 24 hours in both groups. These results are comparable to a randomized trial conducted by Ottinger W S, Menard MK, Brost BC at the Medical University of South Charleston, USA. Aug 1998 which showed that there was no statistically

significant difference in percentage delivered in < 24 hours¹⁰. Similar results were also obtained by Wieland D, Friedman F, Jr at Jacobi Medical Center, Bronx , USA Aug 1999 in a randomized trial⁸. Comparable results were seen in study conducted by Fazia Raza Saeeda Majeed.¹¹

In this study 33.80% patients delivered by caesarian section in group A while 42.25% patients in group B which means that caesarian delivery rate was higher among patients induced with dinoprostone gel. Most common indications for caesarian section was fetal distress in group A and failure of induction in group B. these results are not comparable to a meta analysis done by Hughes EG, Kelly AJ, Kavanagh J at Mc Master University Medical Center, Ontario, Canada, May 2001, in which caesarian section rate was similar in both groups.⁹ Also no rise in caesarian section rate was seen in study conducted by Marconi AM, Bozzeti P, Morabito A in 2008¹². The most probable reason may be that my study includes only 142 patients as compared to this meta analysis. A large multicenter trial would be required to determine actual differences.

In this study, fetal bradycardia is more in group A (22.5%) as compared to group B (14.1%). Other side effects like nausea, vomiting, and diarrhea are also more common in group A as compared to group B. These results are comparable with the results obtained by Wieland D, Friedman F in a randomized trial done at Jacobi Medical Center, USA Aug 1999.⁸ Comparable results were also seen in study conducted by Kho EM, Sadler L, Macowan L in 2008.¹⁴

In this study, 2 patients developed hyperstimulation of uterus with the use of PGE2 gel but this side effect was not seen with PGE2 pessary. The results are comparable to the study conducted by H Akram,Z Khanum,T Rana¹⁵.

Conclusion

It is concluded from above discussion that although dinoprostone intracervical gel is more effective in achieving cervical ripening, however, induction to delivery interval and percentages delivered in <24 hours is similar with these two dinoprostone agents. So there is no extra advantage to induce patients with dinoprostone gel rather than pessary. The overall cost is also more with dinoproston gel as compared to pessary. However, a multicenter trial would be required to determine actual differences in efficacy, safety, and cost of these two agents.

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