



A COMPARATIVE STUDY BETWEEN DINOPROSTONE GEL AND SUSTAINED RELEASE DINOPROSTONE PESSARY FOR INDUCTION OF LABOUR

Obstetrics & Gynaecology

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ABSTRACT

Introduction: Induction of labour is a method of prematurely or artificially stimulating the onset of labour prior to onset of spontaneous labour. Different preparations of prostaglandins are available differing in their effectiveness, side effects and price. Most commonly used agent for induction among prostaglandins is the shorter acting PGE2 gel. Recently the longer acting sustained release PGE2 vaginal pessary has become available in India. **Aims & Objectives:** To compare PGE2 gel and Sustained release Dinoprostone pessary for induction of labour. **Materials & Methods:** A total of 80 antenatal cases were included in this study (40 in each group). Group I given PGE2 gel for maximum 3 doses at 6 hours interval and group II given one dose of PGE2 vaginal pessary. Patients were examined for cervical ripening, uterine contractions, foetal heart monitoring, augmentation, labour duration, mode of delivery and complications. **Results:** The induction to delivery time in gel group was 23.58±9.17 hours and 20.38±8.56 hours in pessary group which was statistically significant ($p=0.038$). There was no difference in the mode of delivery between two groups. **Conclusions:** There was no significant difference in efficacy and complications. The significant difference noted was decreased induction to delivery time and reduced need for augmentation of labour in pessary than PGE2 gel.

KEYWORDS

Induction, PGE2 gel, PGE2 vaginal pessary.

INTRODUCTION

Induction of labour is a method of prematurely or artificially stimulating the onset of labour prior to onset of spontaneous labour. It consists of preinduction cervical ripening and acceleration of uterine contractions. Labour is often induced due to various fetal-maternal conditions using different methods and drug formulations¹. The World Health Organization Global Survey on Maternal and Perinatal Health conducted in 24 countries, showed that 9.6% of the deliveries in developed countries were induced. In developing countries up to 25% of all term deliveries at term now involve induction of labour².

Three criteria must be satisfied for induction to be successful. First the mother should have adequate uterine contractions and progressive dilatation of cervix. Secondly there should be minimum risk to mother and baby. Thirdly induction should end in vaginal delivery.

When labour is induced using any pharmacological method, less than two-third of patients deliver vaginally without any further intervention, about 15% require Assisted Vaginal delivery and 22% undergo emergency Caesarean section¹.

In Obstetric practice, induction of labour is indicated when risk of continuing pregnancy exceeds the risk of induction of labour artificially for both mother and foetus. Common indications for induction of labour include Postdated pregnancy, Hypertensive disorders in pregnancy, premature rupture of membranes, Uncontrolled Gestational Diabetes Mellitus (GDM), Fetal growth restriction (FGR), Intrahepatic Cholestasis of pregnancy (IHCP) and some fetal conditions like isoimmunization, oligohydramnios or non-reassuring fetal status.

Commonly used agents for induction of labour are pharmacological (prostaglandin E2, prostaglandin E1, oxytocin) surgical (artificial rupture of membranes, sweeping of membranes), mechanical (intracervical foley's catheter, laminaria tents, hygroscopic dilators) and even some non-pharmacological methods (nipple stimulation, enema, acupuncture, castor oil)^{3,4}. These methods can be used alone or in combination. Prostaglandins remain preferred method for cervical ripening and labour induction for long times.

Prostaglandins play a crucial role in cervical ripening by increasing inflammatory mediators in cervix and inducing cervix remodelling by acting on collagen in cervix and causing degradation of collagen by peptidases and proteases, which in turn increases the glycoaminoglycans and water content of cellular matrix, thus, making the collagen fibres loose and separated. It is used when Bishop's score is < six.⁵

Different preparations of prostaglandin are available differing in their effectiveness, side effects, and price^{5,6}. But the most commonly used agent for induction of labour among PGE2 is PGE2 gel. However, recently the longer acting PGE2 vaginal pessary has become available in India.

PGE2 gel is available as 0.5 mg of Dinoprostone in 2.5 ml syringe. It is placed intra-cervically. Dose is repeated every 6 hours for a maximum of 3 doses.

PGE2 vaginal Pessary (Propess) has controlled release hydrophilic matrix containing 10 mg of Dinoprostone. It is a thin, flat, rectangular polymeric wafer within a white mesh polyester sac with long tail. It releases drug at a rate of 0.3 mg/hour for 24 hrs.

The advantage of longer acting pessary is single application, easy administration, easy removal when required need for fewer vaginal examinations, thus reducing the risk of ascending infections and reducing maternal anxiety related to induction of labour^{7,8}.

AIM-

Aim of the study was to compare the effectiveness of PGE2 gel versus PGE2 vaginal pessary in induction of labour.

METHODS

Study design

The study design was of randomised controlled study.

Place of study

The study carried out at Department of Obstetrics and Gynaecology, LLRM Medical College, Meerut. The study conducted from March 2022 to November 2022.

Inclusion criteria

Inclusion criteria included-term patient, singleton pregnancy, cephalic presentation, clinically adequate pelvis, Bishop's score of 6 or <6, intact fetal membranes, reactive fetal heart rate pattern.

Exclusion criteria

Patients with - previous Caesarean delivery, H/O antepartum haemorrhage, hypersensitivity to PGE2, H/O upper segment scar, previous traumatic delivery, suspected cephalopelvic disproportion, cervical carcinoma, genital infection. Fetal-Malpresentation, cord prolapse, non-reassuring fetal heart pattern, Rh negative pregnancy, placenta previa, vasa previa, unexplained vaginal bleedings were excluded from the study.

Sample size

Sample size included-80 with 40 in each group.

Procedure

Those women who fulfil the inclusion criteria were subjected to study. Consent was taken from participants in the study. Women were randomly allocated in two groups. Group A was given PGE2 gel and group B was given vaginal pessary.

After per vaginal examination, Bishop scoring was done. Group I was given PGE2 gel which was repeated for maximum of 3 doses at 6 hours interval. Patients were examined for cervical ripening, uterine contractions, fetal heart rate monitoring, Augmentation, labour duration, type of delivery and complications were noted for both groups.

Group II was given one dose of PGE2 vaginal pessary taken out from the freezer, and inserted horizontally in the posterior fornix. It acts for a period of 24 hours. Patient was kept in recumbent position for 30 minutes after insertion. Patient was examined for uterine contractions, fetal heart rate, induction delivery interval, mode of delivery, any adverse reaction.

Pessary was removed after 24 hours of insertion or if patient entered into active labour, spontaneous rupture of membranes, uterine hyperstimulation, uterine tachysystole or fetal distress.

Statistical analysis

The data generated was analyzed using SPSS version 20. Continuous variables were represented as 'mean (SD)' and categorical variables were represented as 'frequency (percentage)'. Chi square test or Fisher's exact test used to assess differences in categorical data. Student unpaired T test used for differences in means of two independent data. There were cross tabulations and correlations to explore relationship. The p value of <0.05 considered significant at a confidence interval of 95%.

RESULTS

Induction of labour is a common obstetric intervention. Failed induction results in caesarean section. Judicious use, selection of patients, timing of induction and method of induction plays a crucial role for successful induction.

In my study, maximum participants in the age group of 20-35 years in both groups. In PGE2 gel group, mean age was 26.8 ± 4.4 years while in PGE2 pessary group, mean age was 26.5 ± 4.4 years with a p value (0.38). Term pregnancy and Post dated pregnancy were also nearly similar in both groups with a p-value (0.32). In Gel group, 65% of females were Primigravida followed by 27.5% G2 & 7.5% G3, while In Pessary group, 57.5% were Primigravida followed by 37.5% G2 & 5% G3, making these two groups comparable in terms of parity with a p value (0.68).

Mean Bishop's score in gel was 3.5 ± 0.74 while it was 3.45 ± 1.04 in Pessary group, making it non-significant with a p-value of 0.36.

Table 1: Baseline characteristics of patients in PGE2 gel and PGE2 vaginal pessary groups.

Characteristics	PGE2 gel	PGE2 vaginal pessary	P value
Age (years)			
20-35 years	38	38	0.38
>35 years	2	2	
Mean age	26.8 years	26.5 years	
Gestational age(weeks)			
37-40	32	30	0.32
>40	8	10	
G1	65%	57.5%	0.68
G2	27.5%	37.5%	
G3	7.5%	5%	
Modified Bishop's Score (Mean)	3.52	3.45	0.36

In Gel group, the most common indication for induction in my study was IHCP in term pregnancy followed by Postdated pregnancy. The other common indications for induction were gestational hypertension

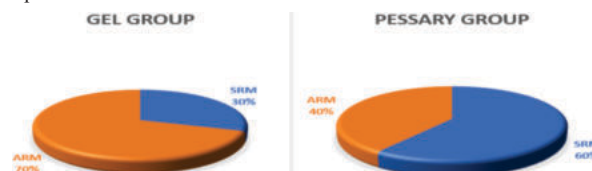
and oligohydramnios. While In Pessary group, the most common indication was Postdated pregnancy followed by IHCP. Other common indications were Reduced fetal movements and FGR.

Table 3: Maternal and fetal outcome following induction of labour.

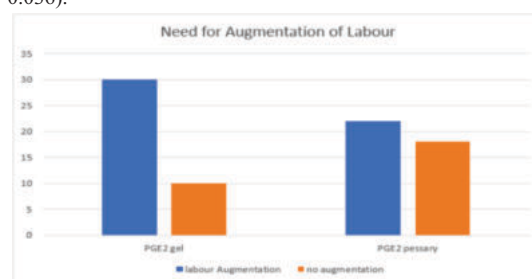
VARIABLES	PGE2 GEL	PGE2 PESSARY	P VALUE
Rupture of membranes			
Spontaneous	12(30%)	24(60%)	0.0016
Artificial	28(70%)	16(40%)	
Labour Augmentation	30(75%)	22(55%)	0.036
Induction to Delivery time (hours)	23.58 $\pm$ 9.17 hours	20.38 $\pm$ 8.56 hours	0.038
Vaginal Delivery	29	28	0.41
Instrumental Delivery	0	1	
LSCS	11	11	
Maternal Complications	0	01	
NICU Admissions	03	02	

INDICATIONS	PGE2 GEL	PGE2 PESSARY
IHCP	17	9
POSTDATED PREGNANCY	8	10
FGR	1	5
REDUCED FETAL MOVEMENTS	0	6
GDM	2	4
GESTATIONAL HTN	7	3
OLIGOHYDRAMNIOS	4	2
PRE- ECLAMPSIA	1	1
TOTAL	40	40

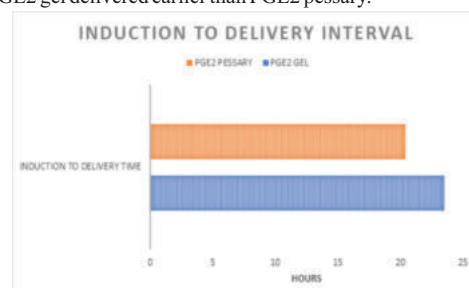
After induction of labour in both groups, there was Spontaneous rupture of Membranes in 30% females of Gel group while SRM was seen in nearly 60% females in Pessary group, making it significant with a p-value of 0.0016.



The need for augmentation of labour was less for Pessary than PGE2 gel group, 75% females in gel group required Augmentation with Oxytocin, in contrast to pessary group where only 55% females required Augmentation with Oxytocin (statistically significant p=0.036).



Mean induction to delivery interval in Gel group was 23.58 ± 9.17 hours, whereas in Pessary group was 20.38 ± 8.56 hours, which is statistically significant with a p-value of 0.038. Thus, patient induced with PGE2 gel delivered earlier than PGE2 pessary.



There was no difference in the mode of delivery between two groups.

Vaginal delivery was 72.5% in gel group and 70% in pessary group. LSCS due to failed induction -27.5% in both gel group and pessary group. 2 cases of PPH were found in proppess group than PGE2gel. There was not much difference in the Apgar score between the two groups. Fetal complications were less in my study.

DISCUSSION

The induction of labour has continued to increase over past few decades⁸. In developed countries, number of deliveries following induction is as high as one in four deliveries. According to the global survey conducted by world health organisation (WHO) in 3,00,000 antenatal mothers over 24 countries, about 9.6% were delivered by induction of labour. The result of the survey showed lower rates of induction in African countries compared with Asian and South American countries¹⁰.

Proper selection of patients and timing of induction are most important for successful induction and avoiding complications as induction of labour causes more strain than spontaneous labour to mother and foetus. There are various risk for induction like caesarean delivery, postpartum haemorrhage and chorioamnionitis.

The PGE2 is a naturally occurring prostaglandin and is widely used in Obstetrics, in gel or pessary form for induction of labour. Dinoprostone is the only prostaglandin agent approved by FDA for labour induction in nulliparous or parous women with singleton post-term pregnancies. CDSO(Central drugs standard control organization) approved Dinoprostone gel in 1990 and Dinoprostone pessary in 2001 in India⁴.

In my study, there was no significant difference in rate of vaginal delivery and failure of induction. Induction to Delivery time was found to be less in pessary group as compared to gel. Need for Augmentation was also found to be less in pessary group. No difference was found for maternal complications like PPH or fetal outcome in these two groups.

Various published literatures have shown a mixed view over both preparations, some studies shows no clear advantage of one preparation over other in terms of rate of vaginal delivery and Shorter IDI. These results can be because of variable regimens, indications for Induction of labour and Bishop's score of the subjects in study. In a study done in London, UK in 2011, Gel preparation had shorter IDI than pessary and more failure of induction with pessary than gel group, this result is complete in contrast with our study¹¹. In a Cochrane review in 2014, there was no significant difference in these two groups¹².

There are 2 meta-analyses on the efficacy of Dinoprostone vaginal pessary for labor induction. Sanchez-Ramos et al¹³ conducted a review on four clinical trials and concluded that the vaginal pessary was "less effective than other prostaglandins for cervical ripening and labour induction," whereas Hassan et al¹⁴ concluded that vaginal insert is equally effective as other prostaglandin routes of administration in terms of delivery by 24 hours, rate of uterine hyperstimulation with fetal heart rate changes and caesarean delivery rate. Indian studies also find no advantage in IDI and vaginal delivery rate¹⁵. However, few studies demonstrated more vaginal delivery with vaginal pessary^{16,17}. In a randomized controlled trial, Trigalia, it was found that the pessary achieved a significantly higher rate of spontaneous vaginal delivery¹⁶. More hyperstimulation has been seen with PGE2 insert than PGE2 gel¹⁸. In a study done in Jaipur, vaginal pessary showed a Shorter IDI¹⁹. Another study carried out in ESI Hospital, New Delhi, India found shorter IDI with PGE2 gel than pessary²⁰. This heterogeneity of results can be explained partly by different parity and Bishop score in the study population.

In our study, no added advantage of PGE2 pessary over PGE2 gel was found in terms of rate of vaginal delivery or less hyperstimulation. There is definitely an advantage of Shorter IDI in pessary group with a benefit of single application and removal of pessary if hyperstimulation occurs and no need of oxytocin infusion, as 45% of our patients in PGE2 pessary group delivered with pessary alone.

The rate of postpartum haemorrhage was equal in both groups. Hyperstimulation was not an indication for LSCS in any patient. The fetal complications noted in my study were asymptomatic hypoglycaemia and meconium aspiration syndrome. There was no significant difference in fetal complications between two groups.

Cost factor in developing countries like our country India, needs consideration. At present in India, the market price of PGE2 pessary stands at 2,450, while it stands 250 per PGE2 gel. Oxytocin ampoule cost is 14 for five units; so, there is no financial benefit of reduced oxytocin needed with PG pessary. In our study, we did not find any benefit of using the expensive PGE2 pessary preparation over gel preparation. The major limitation of our study was the small sample size for comparison of both preparations of PGE2. Future studies with larger sample size are needed to justify use of one PGE2 preparation over other.

CONCLUSION

Both formulations of PGE2 (gel and pessary) showed similar outcomes for rate of vaginal delivery, and failure rate. There was less induction to delivery interval and lesser need for oxytocin augmentation in pessary group. The PGE2 pessary has the advantage of single application and its ability to remove by thread in case of hyperstimulation. But it is expensive compared to intracervical PGE2 gel. For a developing country like India, because of its high-cost and less benefits over other preparations, it can not be used as a induction agent of choice.

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