"A COMPARATIVE STUDY OF OUTCOME OF INDUCTION OFLABOUR BY DINOPROSTONE GEL AND DINOPROSTONE RELEASE PESSARY"

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INTRODUCTION

Induction of labour is a common procedure worldwide with overall rates in many countries now exceeding 20% of all births.[1,2] Induction of labour is indicated when the risk of continuing pregnancy, for the mother or the fetus, exceeds the risk associated with induced labour and delivery.[3] Preeclampsia
≥37 weeks, significant but stable antepartum hemorrhage, chorioamnionitis, suspected fetal compromise and prelabour rupture of membranes at term are the high priority indications for induction of labour at term.

The goal of induction of labor is to achieve a successful vaginal delivery.[3] induction of labor has two important components: cervical ripening and stimulation of uterine contractions, to achieve dilatation of the cervix and delivery of the fetus. The purpose of induction is to achieve vaginal delivery and to avoid operative delivery by Caesarean-section.

It is well recognized that the success of induction of labor, which ultimately aims at achieving vaginal delivery, depends to a great extent on the favorability of the cervix or its readiness to go into labour. Agents used for cervical ripening may lead in the establishment of contractions to women with an unfavorable cervix. Many different methods have been used, but prostaglandins remain a preferred method for cervical ripening and labour induction.[1,4,5]

Dinoprostone is a Prostaglandin (PGE 2) which acts on the collagen structural network of the cervix and makes it favourable thus increasing the chances of a successful of a vaginal delivery. Dinoprostone is the preferred form of prostaglandin and has been shown to increase the rate of vaginal delivery within 24 h and is generally given when the cervix has a Bishop's score of ≤six.[6]

Dinoprostone vaginal pessary is presented as a thin, flat semi- transparent polymeric vaginal delivery system which is rectangular in shape with rounded corners contained within a knitted polyester retrieval system containing 10 mg of dinoprostone which is dispersed throughout it's matrix. Dinoprostone is expensive and heat labile. An intense cold chain is to be maintained to achieve the desirable effects. Owing to hot climate, storage problems significantly reduce its efficacy. Exclusive vaginal route also limits the use in PROM as the risk of sepsis increases.[8-9]

Local application of cerviprime gel is used for cervical ripening. It is usually available as 0.5 mg gel and can be used both intra-vaginally and intra- cervically. Intra-cervical PG-E2 gel not only ripens the cervix but also induces labour and reduces the risk of failed induction. About 40% of women do not need further induction. [10]

The current study was conducted to compare Effectiveness and Safety of Two Forms of Dinoprostone (Gel and Pessary) For Induction of Labour at a tertiary healthcare institute.

MATERIAL AND METHODS: It was a Hospital based Randomized controlled trial conducted in pregnant women admitted for delivery in Obstetrics and Gynaecology department of Krishna Hospital, Karad over a duration of 19 months.

Inclusion criteria: Subjects with Singleton pregnancy irrespective of parity, Cephalic

presentation, Bishop's score ≤6, Gestational age of 37 - 42 weeks, No previous caesarean section, and Intact membranes were included in the current study.

Exclusion criteria: Subjects with Multiple pregnancy, preterm, Previousuterine surgery, Fetal malpresentation, Contraindication to vaginal delivery, Hypersensitivity to the dinoprostone, Contraindications to dinoprostone, and Patients not willing for normal trial were excluded from the current study.

Sample size estimation: According to the study carried out by Dr. Anita kumari proportion of instrumental deliveries performed in cases used Dinoprostone gel was 31.8% and in cases used Dinoprostone vaginal pessarywas 10.5% [6].Thus, minimum 54 women dinoprostone gel was applied and in minimum 54 women pessary was used.

Method: Patients satisfying inclusion and exclusion criteria were randomly allocated into two groups,

- Group(A)for Dinoprostone gel.
- Group(B) for Dinoprostone pessary.

Women illegible to enroll in the study were explained the purpose of the study.Written informed consent was taken from those willing to participate in the studydetailed history of the patient and bishop score was determined.The clinical history, examination findings, investigation findings were recorded with the help of standard, semi-structured, pre-validated case record proforma.

Out of the total cases, patients who fulfilled the inclusion criteria were randomized into Group (A) and Group (B).A gel containing 0.5mg of PGE2 was used for ripening of cervix. Preinduction Non Stress Test was done. With all the aseptic precautions gel was instilled intracervically. Half hour later post-induction Non Stress Test was done.

Half hourly contractions and FHS was evaluated. Reassessment was done 6 hours later, to know the improvement in the Bishop's Score. If the Bishop score is still <6, reinstillationwas required. If cervical ripening did not occur after two instillation it was termed as failed induction.

Dinoprostone controlled release vaginal pessary was placed in theposterior fornix of the vagina. Each pessary contains 10 mg Dinoprostone releasing 0.3mg per hourly. The pessary was removed after 24 hours or if active labour ensued. Active labour was considered if there were at least 4 contractions during a 10 minute period, cervical effacement and >3cm dilated.Failure of Induction was defined as failure to achieve active labour after 24 hours from the beginning of induction

Outcome indicators:

The primary outcomes of the study were: Failure of induction & Successful induction

The secondary outcomes of the study were: Duration of induction to active phase, Duration of induction to delivery interval, Modes of delivery: Vaginal delivery, operative vaginal delivery, Caesarian section, Neonatal outcome: 5 Min APGAR SCORE, NICU Admission

Statistical analysis: The data was entered with the help of Microsoft Excel software. The data was analysed with the help of SPSS version 22 software. The data was represented in the form of tables and charts for frequency analysis. Mean, Mode, Median and standard deviation was calculated forquantitative variables to assess its central tendency and deviation. Chi-square test was used to study association between nominal or categorical variables (qualitative data). Students T-test was used to study association between quantitative variables. P-value less than 0.05 was considered to be statistically significant.

RESULTS

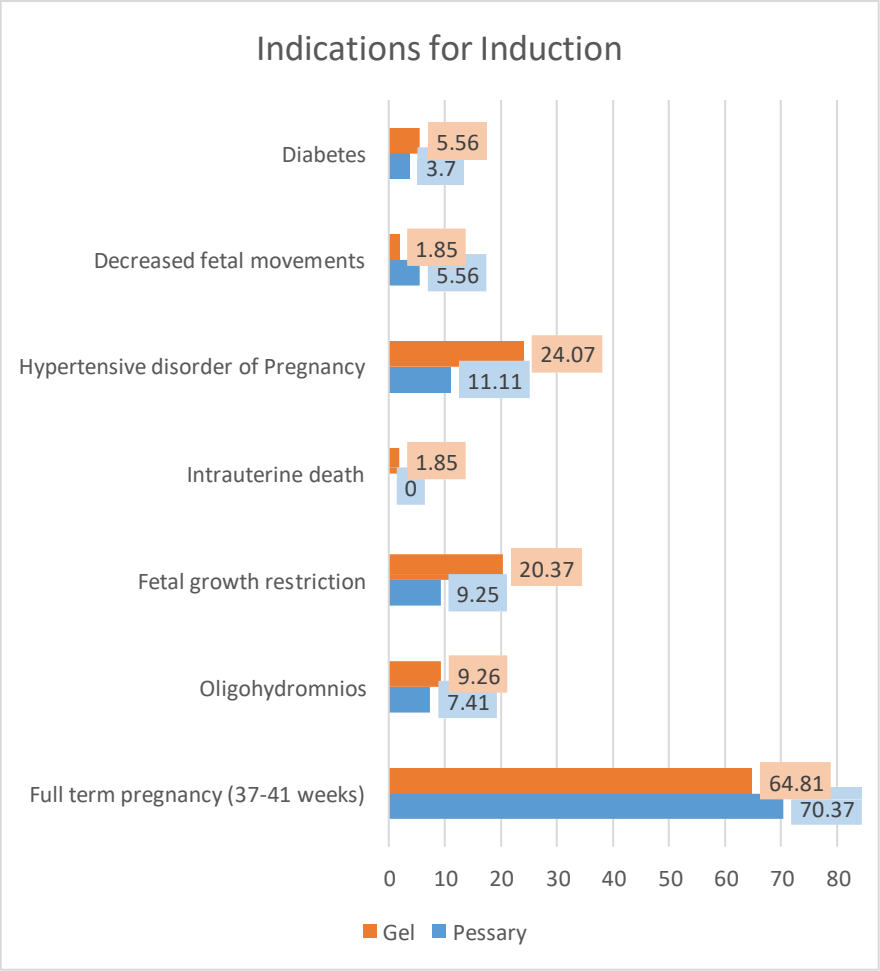
Baseline demographic characteristics: In the current study we observed that the mean age was 26.24 years in Pessary group and 28.59 years ijn Gel group. 78% subjects in Pessary group and 73% in Gel were primigravida, whereas 22% and 27% in either groups were multigravida. Mean gestational age at induction was 37-41 weeks. Mean BMI in first group was 23.2 ± 2.7 (20.2–26.1), whereas in second group was 21.2 ± 3.1 (19.8–24.6)(Table 1). Hence the baseline characteristics among the study subjects were comparable in both the study groups. (Table 1)

Table 1: Baseline demographic characteristics

Baseline demographic characteristics	Pessary group	Gel group	P-value
Maternal age (mean)	26.24 years	28.59 years	0.3
Primigravida	42 (78%)	39 (73%)	0.504
Multigravida	12 (22%)	15 (27%)	
Gestational age at induction, (median)	37–41 weeks	37–41 weeks	0.07
Body mass index (kg/m2) (median)	23.2 ± 2.7 (20.2–26.1)	21.2 ± 3.1 (19.8–24.6)	0.09

Indications for induction: In this study we assessed clinical baseline characteristics of the study subjects. Full term pregnancy was noted among 70.37% and 64.81% study subjects in either study groups. Oligohydromnios was noted among 7.41% and 9.26% study subjects in either groups. Fetal growth restriction was noted among 9.25% in Pessary group and 20.37% in Gel group. 3.7% and 5.56% subjects in either groups were diabetics.Hypertensive disorder of Pregnancy was noted among 11.11% and24.07% subjects in either respective groups. (Figure 1)

Figure 1: Indications for induction of labour



Bishops score: In the current study we assessed the Bishops score among the study subjects. We observed that in Pessary group, 79.63% subjects had Bishops scoremore than 6. Whereas among 20.37% Bisops score was less than 6.In Gel group, at the end of 6 hrs, 83.33% subjects had score less than 6, while 16.66% had score more than 6. At the end of 12 hrs, out of 45 subjects with unfavourable cervix, 53.33% had score more than 6 (favourable).However at the end of 18 hrs, 9 study subjects (16.66%) had Bishops score less than 6 (failure to induction). In this study total 39 study subjects delivered throught vaginal delivery, and rest of the study subjects underwent caesarian section delivery.

Delivery outcomes in pessary and gel groups: In the current study we assessed the delivery outcomes among the study subjects. We observed significantly greater incidence of spontaneous delivery in pessary group (75%) as compared to gel group (57%). Incidence of Operative vaginal delivery was greater in Gel group (15%). (Table 2)

Primary outcomes: In this study we assessed the primary outcomes among the study subjects. We observed that failure to induction was reported more among Gel group (16.66%), as compared to Pessary group (3.7%). The observations were found to be statistically significant. Pessary usage showed significantly lesser incidence of failure of induction as compared to gel administration.(Table 2)

Table 2: Outcomes

Outcomes		Pessary group	Gel group	P - value
Delivery outcome	**Vaginal delivery**	41 (75)	31 (57)	0.04
	Operative vaginal delivery	2 (3)	8 (15)	0.04
	Cesarean section	11 (22)	15 (28)	0.36
Primary outcome	**Failure of induction**	2 (3.7%)	9 (16.66%)	0.025
	Successful Induction of labour	52 (96.29%)	45 (83.33%)	
Secondary outcome	**Induction to active phase, (median)**	12 h (8–31 h)	13 h (8–27 h)	0.45
	Induction to delivery time, (median)	15 h (11–31 h)	18 h (12–33 h)	0.38
	Cesarean section for fetal distress	8 (14)	10 (18)	0.6
	Birth weight, mean ± SD	2.5 kg to 3 kg	2.3 kg to 3.2 kg	0.2
	Hyperstimulation	6	10	0.33

Secondary outcomes: Detailed observations of secondary outcomes is mentioned in following table. Induction to active phase and Induction to delivery time was comparatively higher in Gel group as compared to Pessary group. However the observations were not statistically significant. Hyperstimulation was noted more in Gel group (10 subjects) as compared to 6subjects in Pessary group. (Table 2)

Mode of delivery: In this study we assessed Primary outcome in nulliparous women. We observed that significantly greater proportion of Vaginal delivery in Pessary group (73%) as compared to Gel group (52%) was observed in primigravida women (p-value: 0.03).

In this study we assessed Primary outcome in primigravida and multigravida women. We observed that significantly greater proportion of vaginal delivery in primigravida women (p-value: 0.03) as compared to multigravida women who showed in-significant difference between the observations (p-value: 0.41). (Table 3)

Table 3: Mode of delivery & neonatal outcomes

Mode of delivery & neonatal outcomes		Pessary group	Gel group	P - value
Mode of delivery in Primigravida	**Nulliparous**	42	39	0.4
	Vaginal delivery	31 (73)	20 (52)	0.03
	Operative vaginal delivery	2 (4)	5 (13)	0.2
	Cesarean section	9 (23)	13 (33)	0.23
Mode of delivery in Multigravida	**Parous**	12	15	0.3
	Vaginal delivery	9 (75%)	9 (60%)	0.41
	Operative vaginal delivery	1 (1%)	3 (22%)	0.39
	Cesarean section	3 (31%)	3 (28%)	0.75
Neonatal outcomes	**espiratorydistress**	**3 (5.55%)**	**5 (9.55%)**	**0.44**
	NICU admission	**5 (9.55%)**	**11 (20.37)**	**0.104**

Neonatal outcomes: In the present study we assessed the neonatal outcomes among the study subejcts. We observed that respiratory distress was reported more in gel group (9.55%) as compared to 5.55% neonates in pessary group. In the current study NICU admission was needed among 9.55% subjects in Pessary group which is comparatively lesser as compared to 20.37% study subjects in Gel group. However the differeces between the observations were not found to be statistically significant.(Table 3)

DISCUSSION: Induction of labor is a widely used obstetricalpractice for different indications, the most frequentbeing prolonged pregnancy. The success of inductionis strictly dependent on the cervical status eitherassessed by Bishop score or by sonographic measurement of cervical length [5–7]. Various studies compared these two methods of cervical assessment,failing to consistently show an advantage of any ofthe two compared to the other in the prediction ofvaginal delivery, while confirming that parity remainsan independent predictive factor [8–11].

Prostaglandins have a central role inthe physiological events of cervical ripening andparturition, and have been widely used for induction oflabor[12]. These can be administered orally, vaginally,intracervically, endovenously and by extra-amnioticor intra-amniotic routes. Dinoprostone is one of thesynthetic prostaglandins most commonly used toachieve cervical ripening and labor induction, andcan be administered as tablets, suppositories, gel(vaginal and intracervical) or as a controlled-releaseintravaginal pessary. The controlled- release pessaryhas some potential advantages: a single application isrequired; the insert is easily administered and can beremoved as soon as labor starts or at the first sign ofuterine hyperstimulation. Studies comparing thedinoprostone vaginal insert to other prostaglandinformulations have shown variable results, probablyinfluenced by drug administration regimens, indications for induction and cervical conditions of thewomen[13,14].

In the current study we observed that the mean age was 26.24 years in Pessary group and 28.59 years ijn Gel group. 78% subjects in Pessary group and 73% in Gel were primigravida, whereas 22% and 27% in either groups were multigravida. Mean gestational age at induction was 37-41 weeks. Mean BMI in first group was 23.2 ± 2.7 (20.2–26.1), whereas in second group was
21.2 ± 3.1 (19.8–24.6). Hence the baseline characteristics among the study subjects were comparable in both the study groups.

Mamatha C et al[15] in their study included 100 antenatal patients undergoing labour induction with dinoprostone vaginal pessary, among whom 67 % were nulliparous women and 33 % were multiparous women. About 46 %of patients were under the age group of 25 to 28 years with the most common medical disorder complicating pregnancy which is gestational diabetes.

In the current study we assessed the Bishops score among the study subjects. We observed that in Pessary group, 79.63% subjects had Bishops scoremore than 6. Whereas among 20.37% Bisops score was less than 6.In Gel group, at the end of 6 hrs, 83.33% subjects had score less than 6, while 16.66% had score more than 6. At the end of 12 hrs, out of 45 subjects with unfavourable cervix, 53.33% had score more than 6 (favourable). However at the end of 18 hrs, 9 study subjects (16.66%) had Bishops score less than 6 (failure to induction). In this study total 39 study subjects delivered throught vaginal delivery, and rest of the study subjects underwent caesarian section delivery.

In this study we assessed clinical baseline characteristics of the study subjects. Full term pregnancy was noted among 70.37% and 64.81% study subjects in either study groups. Oligohydromnios was noted among 7.41% and 9.26% study subjects in either groups. Fetal growth restriction was noted among 1.85% subjects in each group. 3.7% and 5.56% subjects in either groups were diabetics.Hypertensive disorder of Pregnancy was noted among 11.11% and 24.07% subjects in either respective groups.

Tempe A et al[16] in their study observed that postdatism was the most common indication for IOL in both the groups (50.9% in Group A and 66% in Group B). Other indications of IOL In Group A were: Gestational Diabetes Mellitus (15.1%), decreased fetal movements (13.2%), Fetal growth restriction (7.5%) Intrahepatic Cholestasis Of Pregnancy (7.5%), Gestational Hypertension (3.8%), and oligohydramnios (1.9%), while in Group B were: decreased fetal Movements (9.4%), gestational hypertension (9.4%), Fetal Growth Restriction (7.5%), Oligohydramnios (3.8%), Gestational Diabetes Mellitus (1.9%) and intrahepatic Cholestasis of pregnancy (1.9%).

In the current study we assessed the delivery outcomes among the study subjects. We observed significantly greater incidence of spontaneousdelivery in pessary group (75%) as compared to gel group (57%). Incidence of Operative vaginal delivery was greater in Gel group (15%). Induction to labour duration was comparatively larger in gel group as compared to Pessary group,however the observations were not statisticallty singnificant. **Ee Min Kho et al[17]**ion their study observed that induction to vaginal birth interval was longer among nullipara receiving the pessary compared to those receiving intravaginal gel (21.5 vs 17.8 h, P=0.004). **Tempe A et al[16] i**n their study observed that overall Group B (Pessary) had a shorter time from induction to delivery (12.53 ± 6.565 hours vs. 19.72 ± 11.185 hours; $P < 0.001$). In Group B, more number of patients delivered within 12 hours from induction (50.9%) compared to Group A (30.2%). And none of these patients had precipitatelabor, that is, delivery in <3 hours. Only one patient in Group A was delivered after 48 hours of induction while rest all of the patients were delivered within 48 hours in both the groups.

Our results are in concordance with previous studies which showed that induction to delivery interval was significantly shorter with PGE2 vaginal pessary in comparison to dinoprostone cervical gel. Of note, other authors demonstrated contradicting results. Some concluded that the vaginal insert was less effective than other prostaglandins for cervical ripening in terms of longer time interval from induction to vaginal delivery and in terms of achieving vaginal delivery within 12 hours, whereas others, demonstrated that slow-release PGE2 vaginal insert was as equally effective as other prostaglandins in terms of delivery by 24 hours. Reasons for these contrasting conclusions could be the heterogeneity in terms of inclusion criteria, preinduction Bishop score, primary outcome measures, and varying protocols of induction.

Mamatha C et al[15] in their study observed that about 60.3% of primigravida entered active phase within 12 hours with a mean induction to active phase time interval of 12 hours 03 minutes and 95.2 % of primigravida delivered < 24 hours with a mean induction to delivery time interval of 17 hours 36 minutes. 4 % of primigravida had failed induction. About 84.8 % of multigravida entered active phase within 12 hours with mean induction to active phase time interval of 08 hours 57 minutes and 100% of multigravida delivered < 24 hours with a mean induction to delivery time interval of 12hours 19 minutes.

Chaudhary P et al in their study observed that the induction to delivery interval was calculated for both the groups. In Misoprostol group 36 patients had delivery with in 12 hours that is 72% while in Dinoprostone pessary group 39 patients had delivery within 12 hours that is 78%. Delivery with in 24 hours was achieved in 14 patients (28%) in misoprostol group while 11 Patients (22%) in Dinoprostone pessary group.[18]

In this study we assessed the primary outcomes among the study subjects. We observed that failure to induction was reported more among Gel group (16.66%), as compared to Pessary group (3.7%). The observations were found to be statistically significant. Pessary usage showed significantly lesser incidence of failure of induction as compared to gel administration.

In this study we assessed Primary outcome in primigravida women. We observed that significantly greater proportion of Spontaneous vaginal delivery in Pessary group (73%) as compared to Gel group (52%) was observed in nulliparous women (p-value: 0.03) as compared to multigravida women who showed in-significant difference between the observations (p-value: 0.41).

Maria Teresa Triglia et al in their study observed that the rate of spontaneous vaginal

delivery was significantly higher in the pessary group (72%) than in the gel group (54%), paralleled by a lower rate of operative vaginal deliveries (3 vs. 15%). The difference in cesarean section rate (25 vs. 31%) did not reach statistical significance.[19] **Tempe A et al[16] i**n their study observed that Group B (pessary) had more vaginal deliveries as compared to Group A (gel) (83% vs. 67.9%) but this difference was not found to be statistically significant (P = 0.088). There were only two out of 53 patients (3.8%) in each group who had instrumental delivery.

Mamatha C et al[15] in their study observed that out of 100 patients, 80 % of patients delivered by spontaneous vaginal delivery with episiotomy, 5 % of patients delivered by assisted vaginal delivery with episiotomy and 15 % of patients delivered by Caesarean section. Almost 97 % of multiparous women delivered vaginally. **Chaudhary P et al** in their study observed that in Misoprostol group 62% had vaginal delivery and 16% required vacuum delivery totalling to 78% by vaginal route while 22% required caesarean section as a route of delivery. In Dinoprostone pessary group 58% had vaginal delivery and 18% required vacuum delivery totalling to 76% by vaginal route while 24% required caesarean section as a route of delivery. [18]

Detailed observations of secondary outcomes is mentioned in following table. Induction to active phase, and Induction to delivery time, was comparatively higher in Gel group as compared to Pessary group. However the observations were not statistically significant. Hyperstimulation was noted more in Gel group (10 subjects) as compared to 6 subjects in Pessary group.

Ee Min Kho et al ion their study observed that there was a trend to more uterine hyperstimulation among women induced with the pessary compared with those induced with intravaginal gel (22 (4.5%) vs 11 (2.4%) relative risk (RR) 1.9 (0.9-3.9)). Hyperstimulation associated with an abnormalfetal heart pattern (14 (2.9%) vs 2 (0.4%), RR 6.5 (1.5-28.9)) or treated with
tocolytics (9 (1.8%) vs 1 (0.2%), RR 8.4 (1.1-66)) was more common inwomen who received the pessary.[17]

The study by **Facchinetti et al.** compared cervical application of gel with vaginal insert for preinduction cervical maturation in 144 nulliparous women with a Bishop score < 4 who required induction of labor at term. All patients enrolled were nulliparous, the gel was administered cervically and the vaginal pessary was removed 12 hours after the beginning of treatment. The use of the vaginal pessary was associated with a lower rate of cesarean section, shorter hospital stay and better outcome in terms of rate of delivery within 12 and 24 hours, failure of induction, changes in cervical ripening and clinical complication rate[20].

Strobelt and colleagues randomized 107 patients with a Bishop score
£ 4 to either a 12-hour dinoprostone pessary or 0.5-mg dinoprostone cervical gel. Vaginal pessary patients ad a shorter induction-todelivery time, with a mean difference of 5 hours and 46 minutes between the groups. Even though patients who received the vaginal pessary showed a trend for an increased incidence of abnormal fetal heart rate and hyperkinetic labor, the incidence of cesarean section, cesareans for fetal distress and an umbilical artery pH < 7.1 was comparable between the two groups[21].Similar to our study **MT Triglia et al** also observed that the spontaneous vaginal delivery rate was higher in the pessary group (72%) than in vaginal gel group (54%), with a significant difference (p = 0.03)[19]

In the present study we assessed the fetal outcomes among the study subejcts. We observed that respiratory distress was reported more in gel group (9.55%) as compared to 5.55% neonates in pessary group. In the current study NICU admission was needed among 9.55% subjects in Pessary group and 20.37% study subjects in Gel group.

CONCLUSIONS: Pessary usage showed significantly lesser incidence of failure of induction as compared to gel administration. Induction to active phase and Induction to delivery time was comparatively higher in Gel group as compared to Pessary group. However the observations were notstatistically significant. Hyperstimulation was noted more in Gel group as compared to

Pessary group. In this study we observed that significantly greater proportion of vaginal delivery in primigravida women as compared to multigravida women who showed in-significant difference between the observations

In the present study we assessed the neonatal outcomes among the study subejcts. We observed that respiratory distress was reported more in gel group as compared to pessary group. In the current study NICU admission was needed comparatively lesser among Pessary group as compared to Gel group.

The present study suggests that Dinoprostone vaginal pessary is highlyeffective and more superior in theinduction of labour at term in properly selected cases.

CONFLICT OF INTEREST: None to declare

SOURCES OF FUNDING: None

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