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Feto-maternal outcome using two different dinoprostone vaginal preparations: A randomized clinical trial of gel & controlled release vaginal insert

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ABSTRACT:

Background: Induction of labour by using different prostaglandin preparations is generally preferred to avoid complications of prolonged pregnancy. Dinoprostone vaginal gel or insert are commonly used for this purpose. The present study compares the different indications of induction of labour, feto-maternal outcome and cost effectiveness analysis between the two groups.

Materials & methods: This prospective randomized comparative study was carried out in 200 pregnant mothers (100 mothers receiving dinoprostone vaginal gel and 100 mothers receiving dinoprostone vaginal insert) undergone labour induction with unfavorable Bishop score. Then the different indications of induction of labour, feto-maternal outcome and cost effectiveness analysis between the two groups were compared. Statistical analysis was done by IBM SPSS Ver.25 statistical software.

Results: The most common indication for induction was Post dated pregnancy (32% in gel & 41% in insert group) followed by premature rupture of membrane (21% vs 18%) and hypertensive disorders in pregnancy (20% vs 15%) among the studied groups. The rate of caesarean section was 41% in gel group & 25% in Insert group. No cases or episodes of uterine hyperstimulation was seen in either groups. Average duration of hospital stay following delivery was less those who received vaginal insert compared to gel, which was statistically significant ($p < 0.001$). Regarding fetal and neonatal outcome, statistically significant difference was found in incidence of meconium stained liquor (22% vs 17%, $p < 0.011$), APGAR score at 1 and 5 minutes ($p< 0.001$) between the two groups. But no statistically significant difference was found between the two groups regarding neonatal birth weight, fetal deceleration, delayed crying after birth or NICU admission rate.

Conclusion: Dinoprostone vaginal insert for cervical ripening demonstrate a high degree of efficacy and safety for both mother and fetus in terms of decrease chance of caesarean section, shorter hospital stay after delivery, lesser incidence of meconium stained liquor & less incidence of fetal distress. Also patient acceptability is better as single application is sufficient to achieve cervical ripening in majority of patients.

Keywords: Dinoprostone, gel, insert, feto-maternal outcome.

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Introduction:

Induction of labour is initiation of labour before it's spontaneous onset, for safe delivery of feto-maternal unit. In developed countries around 20 % of cases induction is used in pregnant women.[1] It is one of the most abused procedure nowadays in Obstetrics. Therefore one should causious about the indications of induction so as to reduce the rising trend of caesarean section rate above WHO recommended level. Nowadays Post dated pregnancies & hypertensive disorders in pregnancy accounts for 80% of all induction cases.[2]

Labour should be induced in appropriate point of time during which maternal and perinatal benefits are optimum if the pregnancy is interrupted than continued.[3] Elective induction of labour in hypertensive disorders of pregnancy & Post dated cases result in better feto-maternal outcome comparable to expectant management of these cases.[4,5]

Nowadays for induction of labour the availability of oxytocin and newer induction techniques using dinoprostone are more effective and predictable. Dinoprostone is commonly used nowadays for cervical ripening & induction of labour, which can be administered via various routes and preparations like gel, insert etc.

There are some potential advantages of controlled release vaginal insert compared to gel such as single application, easy administration & can be removed as soon as labour starts, uterine hyperstimulation appears and or abnormal fetal heart rate changes occur during the ripening process.[6]

Despite the frequency of induction around 20 %, the best preparation to proceed for induction in patient with an unfavorable cervix is still not out of controversies. Previous studies comparing PGE 2 vaginal insert to other prostaglandin preparations showed variable results in terms of inclusion criteria, indications of induction, pre induction Bishops score, different caesarean section rate for failed induction, different primary feto-maternal outcome measures & various drug administration regimens.[7] Some studies Showed better fetal outcomes with dinoprostone vaginal insert.[8] On the contrary to other study did not report any difference in the maternal and fetal outcomes between the two groups.[9]

There is absence of standard outcome measures in comparative studies investigating various agents used in induction of labour. National Institute for Clinical Excellence (NICE) has recommended further research in to different prostaglandin preparations used for induction of labour, with further emphasis on feto-maternal outcome measures & cost effectiveness analysis. Thus this randomized controlled trial was conducted to confirm or refute these finding.

Material & Methods:

This prospective randomized comparative study was conducted in the department of Obstetrics and Gynecology, VIMS & RKMSP, Kolkata. The study was carried out in 200 pregnant women undergone labour induction with unfavorable Bishops score for fetal and maternal indications for

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the duration of one year, among which 100 pregnant mother using controlled release dinoprostone vaginal insert and 100 pregnant mother using dinoprostone vaginal gel for induction. The study was conducted after approval of institutional ethics committee. Then the pregnancy outcome (maternal, fetal and neonatal) between controlled release dinoprostone vaginal insert and dinoprostone vaginal gel were compared.

Inclusion criteria: 18 to 35 years old singleton primi-gravida mothers with cephalic presentation between 37 to 42 weeks gestational age with Bishops score less than equal to 5 were included in our study.

Exclusion criteria: Pregnant women with previous uterine surgery like caesarean section, myomectomy, metroplasty etc, known case of bronchial asthma, glaucoma, suspected CPD, fetal malpresentation, placenta praevia, rupture of membranes, known hypersensitivity to PGE2 or other conditions contraindicating vaginal delivery were excluded from the study.

Statistical analysis was done using IBM SPSS Ver.25 statistical software. Continuous variables were compared with unpaired t- test, categorical variables with Chi- square test. Statistical significance was defined at p – value less than 0.05 with all 2- sided tests.

Result: This prospective randomized comparative study was conducted in 200 pregnant women undergone labour induction with unfavorable Bishop score for fetal neonatal and maternal indications for duration of one year, among which 100 pregnant mother using controlled release dinoprostone vaginal gel and 100 pregnant mother using dinoprostone vaginal insert for induction.

Table 1: Shows the demographic characteristics of the studied women. Statistically significant differences was found in respect to maternal age but no significant difference was there in respect to gestational weeks.

VARIABLES	DINOPROSTONE VAGINAL GEL GROUP(n=100)	DINOPROSTONE VAGINAL PESSARY GROUP(n=100)	P value
MATERNAL AGE(YEARS)	26.3+/- 3.4	25.3 +/- 3.5	0.04
GESTATIONAL WEEK	38.4 +/- 0.6	38.6 +/- 0.9	0.06
MEDICAL CO-MORBIDITIES	50(50%)	75(75%)	
SURGICAL CO-MORBIDITIES	3(3%)	1(1%)	0.13

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Table 2: Compares different indications for induction of labour. Post dated pregnancy was the most common indication in both the group (32% in gel vs 41% in Insert) followed by PROM (21% in gel vs 18% in insert) & hypertensive disorders in pregnancy (20% in gel vs 15% in Insert).

INDICATIONS OF INDUCTION OF LABOUR:

INDICATIONS	DINOPROSTONE VAGINAL GEL GROUP(n=100)	DINOPROSTONE VAGINAL PESSARY(n=100)
POSTDATED PREGNANCY	32(32%)	41(41%)
PREMATURE RUPTURE OF MEMBRANE(PROM)	21(21%)	18(18%)
HYPERTENSIVE DISORDERS IN PREGNANCY	20(20%)	15 (15%)
GESTATIONAL DIABETES MELLITUS	9(9%)	11(11%)
FETAL GROWTH RESTRICTION	7(7%)	6 (6%)
OLIGOHYDRAMNIOS	6 (6%)	6 (6%)
OBSTETRIC CHOLESTASIS	5 (5%)	3(3%)

TABLE 3: Compares the different maternal outcome between the two groups. No single case of uterine hyperstimulation encountered in any of the studied group. There was significant difference regarding rate of caesarean section between the two groups (41% in gel vs 25% in Insert). Dinoprostone vaginal insert was associated with shorter hospital stay Compared to gel group (p value < 0.001).

MATERNAL OUTCOME:

VARIABLES	DINOPROSTONE VAGINAL GEL GROUP(n=100)	DINOPROSTONE VAGINAL PESSARY(=100)	P value
UTERINE HYPERSTIMULATION	0	0	
RETAINED PLACENTA	3(3%)	2(2%)	
RUPTURED UTERUS	0	0	
ATONIC PPH	7(7%)	4(4%)	
COAGULOPATHY	0	0	
COMPLETE	3(3%)	1(1%)	

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PERINEAL TEAR			
CERVICAL TEAR	3(3%)	1(1%)	
PERINEAL HEMATOMA	1(1%)	3(3%)	
CAESAREAN SECTION	41(41%)	25 (25%)	
HOSPITAL STAY AFTER DELIVERY	3. +/ 1.8	2.7+/ 1.2	<0.001

Table 4: Compares the different fetal and neonatal outcome between the two groups. No statistically significant difference was observed between the studied groups regarding neonatal birth weight, fetal heart rate deceleration, delayed crying after birth or NICU admission rate. But statistically significant difference was found in the incidence of meconium stained liquor, APGAR score at 1 and 5 minutes.

FETAL AND NEONATAL OUTCOME:

NEONATAL BIRTH WEIGHT (GRAMS)	2092.5 +/- 280.7	2844.3+/-336	0.19
FETAL TACHYCARDIA/DECELERATION	6(6%)	3(3%)	0.31
MECONIUM STAINED AMNIOTIC FLUID	22(22%)	17(17%)	0.011
DELAYED CRY AFTER BIRTH	12(12%)	9(9%)	0.48
APGAR SCORE AT 1 MINUTE	4.4 +/- 0.6	5.6+/-1	<0.001
APGAR SCORE AT 5 MINUTES	8.4+/-1.1	9.2+/-1.1	<0.001
NICU ADMISSION	7(7%)	7(7%)	1

Discussion:

Induction of labour is widely used in Obstetrics practice for various indications; the most frequent one is prolonged pregnancy. The success of induction is mainly depends on status of the cervix which is either assessed by Bishop score or by ultrasonographic measurement of the length of the cervix, as study conducted by Strobel E et al, Tan PC et al &Roman H et al. We decided to use the modified Bishop score as it does not need any machinery assistance, hence making our observation more practical. When the cervix is unripe, amniotomy and oxytocin titration will result in high level of fetal and maternal complications. Dinoprostone (PGE2) has a dual action of ripening as well as promoting uterine contractility.

Most of the previous studies done were randomized control trial (RCT) type similar to the present study. RCTs are now typically considered as the "gold standard "to evaluate the efficacy of a therapy or intervention intended to improve outcome. This prospective, randomized comparative study was conducted on 200 singleton pregnancies with Bishop score<5 & with no

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contraindications to vaginal delivery, which were randomly assigned into two groups (100 in insert & 100 in gel).

The aim of this study was to evaluate the various indications of induction & cesarean section as well as to compare the pregnancy outcome (maternal, fetal and neonatal) between controlled release dinoprostone vaginal insert and dinoprostone vaginal gel.

In this present study the mean age of mothers in gel group was 26.3+/-3.4 years, while that in pessary group was 25.3+/-3.5 years (p 0.04). The mean gestational age was 38.4+/-0.6 weeks in the gel group while it was 38.6+/-0.9 weeks in the pessary group (p 0.06). Similar study was done by Kalkat RK et al and Abdelaziz A et al, whose reported result were similar to the present research.[10,11]

In this present study the most common indications for induction was Post dated pregnancy followed by premature rupture of membrane & hypertensive disorders in pregnancy. Heimstad R et al observed that occasionally women are best delivered before the spontaneous onset of labour like post dated pregnancy & hypertensive disorders during pregnancy, which account for 80% of all induction.[2]

We did not encounter any case of uterine hyperstimulation in the two groups. Triglia MT et al studied a randomized control trial of 24 hours vaginal dinoprostone pessary compared to dinoprostone gel for labour induction at term with Bishop score<=4 & found that both the methods of labour induction were safe, without any cases or episodes of uterine hyperstimulation.[12]

Current study suggests that there was significant difference regarding outcome of caesarean section when dinoprostone gel was compared with dinoprostone insert with the values of 41% & 25% respectively. This study also showed that the average duration of hospital stay after delivery was 3.5+/-1.8 days for the gel group and 2.7+/-1.2 for pessary group. Similarly in a meta-analysis done by Zeng X et al Showed that dinoprostone vaginal insert was associated with shorter hospital stay as well as decrease rate of caesarean section when compared to dinoprostone gel.[13] In a systematic review and meta-analysis conducted by Fabio Facchinetti et al also found that dinoprostone vaginal insert was associated with decrease of caesarean section rate in nulliparous women by 24% compared to the other ways of administration.[14]

In our study 22% of mothers in gel group & 17% mothers in pessary group had thick meconium stained liquor (p 0.011). Mean APGAR score at 1 minute was 4.4+/-0.6 in gel group compared to 5.6+/-1 in pessary group (p <0.001). Mean APGAR score at 5 minutes was 8.4+/-1.1 in gel group compared to 9.2+/-1.1 in pessary group (p <0.001). In a randomized control trial of 24 hours vaginal dinoprostone pessary compared to gel for labour induction at term with Bishop score <=4 and found that both the methods for induction appeared to be safe, with no cases of 5 minutes APGAR score were < 7.[12]

Current study also noted that there was no significant difference between the two groups related to neonatal birth weight (p 0.19), fetal tachycardia or deceleration (p 0.31), delayed crying after birth (p 0.48) or NICU admission as study done by others.[15]

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Conclusion:

Dinoprostone vaginal insert for cervical ripening demonstrate a high degree of efficacy and safety for both mother and fetus, in terms of decrease chance of caesarean section, shorter hospital stay after delivery, lesser incidence of meconium stained liquor, less incidence of fetal heart rate deceleration.

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Conflict of interest: None declared.

Ethical approval: The study was approved by the Institutional Ethics Committee.

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