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Fetomaternal Outcomes Following Single versus Double Application of Intracervical Dinoprostone (PGE2) Gel for Induction of Labour in Term Pregnancy: A Prospective Comparative Study

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Abstract

Induction of labour with intracervical dinoprostone (prostaglandin E2) gel is a well-established method for cervical ripening in women with an unfavourable cervix. This prospective comparative interventional study was conducted to compare fetomaternal outcomes following single versus double intracervical application of dinoprostone E2 gel (0.5 mg) in 200 term pregnant women with Bishop score ≤4 at the Department of Obstetrics and Gynaecology, SMS Medical College and Attached Hospitals, Jaipur, Rajasthan, India, from March 2023 to January 2024. Patients were randomly allocated to Group A (single dose, n=100) and Group B (repeat dose at 6 hours if Bishop score remained less than 4, n=100). Both groups were comparable at baseline. Time to onset of labour was found to be significantly shorter in Group A (277±63 versus 693±117 minutes; p<0.001), while duration of active labour was shorter in Group B (390±77 versus 468±87 minutes; p<0.001). Oxytocin augmentation was required significantly less often in Group B (27% versus 47%; p=0.005). The lower segment caesarean section rate was significantly higher in Group B (23% versus 13%; p<0.05). APGAR scores at 1 minute (7.67 versus 7.34; p=0.010) and 5 minutes (7.60 versus 7.25; p=0.023) were significantly better in Group A. Neonatal intensive care unit admission rates were significantly higher in Group B (23% versus 10%; p=0.013). Single-dose intracervical dinoprostone E2 gel is associated with better neonatal outcomes and lower caesarean delivery rates. Although double application achieves faster cervical ripening and shorter active labour, it carries higher risk of caesarean delivery rates and poorer neonatal outcomes. Double application should therefore be reserved for carefully selected cases with strict and continuous fetomaternal surveillance.

Keywords: Dinoprostone; Prostaglandin E2 gel; Induction of labour; Cervical ripening; Bishop score; Lower segment caesarean section; Neonatal outcomes

Introduction

Labour induction remains one of the most frequently performed obstetric interventions worldwide — carried out when the risks of continuing the pregnancy outweigh the benefits of allowing it to progress naturally.[1] Its success depends largely on how ripe the cervix is at the time of induction. The Bishop scoring system, introduced in 1964, remains the most practical and widely used bedside tool for this assessment. [2] When the score is ≤4, the cervix is considered unripe, and attempting induction without prior cervical preparation significantly raises the risk of failed induction and emergency caesarean delivery.[3]

Prostaglandin E2 (PGE2), available commercially as intracervical dinoprostone gel (0.5 mg in a prefilled 3 g syringe), is the only prostaglandin formally approved by the United States Food and Drug Administration (FDA) for cervical ripening and labour induction.[3,4] The mechanism of action is well characterised: PGE2 acts on G-protein-coupled EP receptors in the cervical stroma, triggering collagenase activity, disorganisation of collagen fibrils, leukocyte infiltration, and a local pro-inflammatory cytokine response that collectively produce cervical softening, effacement, and dilatation.[5] The approved regimen permits dosing every 6 hours, up to a maximum of 1.5 mg within any 24-hour period.[3]

In routine clinical practice, however, a single application does not always bring about adequate cervical change. Whether administering a second dose in this situation improves overall outcomes — or simply increases exposure and risk — is a question that deserves careful study. Published comparisons between single and double-dose regimens often focus on cervical response or time-to-delivery intervals, and data specifically addressing fetomaternal outcomes from tertiary-care centres in India remain limited.[6,8,10] This study was therefore designed to prospectively compare the two dosing strategies across a comprehensive and clinically relevant set of maternal and neonatal outcome measures.

Aim & Objectives

Aim: To compare fetomaternal outcomes following single versus double intracervical application of dinoprostone E2 gel in term pregnancies requiring induction.

Objectives

- To assess changes in Modified Bishop score after single versus double application.
- To compare mode of delivery (vaginal versus caesarean section) between the two groups.
- To document and compare maternal and foetal complications in each group.

Materials and Methods

Study Design and Setting: This was a prospective, comparative, interventional study conducted over 11 months (March 2023 to January 2024) at the Department of Obstetrics and Gynaecology, SMS Medical College and Attached Hospitals, Jaipur — a tertiary-care teaching hospital. The study received approval from the Institutional Ethics Committee (IEC), the Clinical Trial Screening Committee, and the Rajasthan University of Health Sciences (RUHS).

Sample Size

Based on vaginal delivery rate differences reported by Khajotia et al.[6] — 50% vs. 30% between dosing groups — a sample size of 100 women per group was calculated to achieve 80% statistical power at a 95% confidence interval (CI), giving a total of 200 participants.

Eligibility Criteria

Women were eligible for inclusion if they had a singleton viable term pregnancy (≥37 weeks) with cephalic presentation, intact membranes, an unscarred uterus (no prior lower segment caesarean section [LSCS] or myomectomy), a Modified Bishop score (MBS) ≤4, and were willing to provide written informed consent.

Women were excluded if they had active genital tract infection, asthma, or glaucoma (prostaglandin contraindications); prior uterine surgery or difficult instrumental delivery; malpresentation; suspected cephalopelvic disproportion (CPD); placenta praevia; a known allergy to prostaglandins; or had already received any alternative method of labour induction.

Randomisation and Intervention

Participants were allocated to one of two groups by simple randomisation using a coin-flip method. All gel applications were performed under aseptic conditions with direct speculum visualisation, with the gel instilled into the endocervical canal just below the internal os. Women remained supine for 30 minutes following the procedure. Foetal heart rate (FHR) and maternal vital signs were recorded every 15 minutes. A per-vaginal (PV) examination was scheduled at 6 hours, or earlier if uterine contractions began or membranes ruptured.

Group A (Single Application, n=100): Received a single intracervical dose of dinoprostone PGE2 0.5 mg. Oxytocin augmentation was initiated only if required, and no sooner than 6 hours after gel application.

Group B (Repeat Application, n=100): Received the same initial dose; if the Bishop score had not reached ≥4 at the 6-hour review, a second 0.5 mg dinoprostone gel was administered under identical conditions. Oxytocin was withheld for at least 6 hours after the last dose.

Modified Bishop Score

Cervical assessment was performed using the Modified Bishop Score (MBS), which incorporates five parameters: cervical dilatation (cm), cervical length (cm), consistency, position, and foetal station — each scored 0–3. A total score of ≤4 was considered unfavourable and was the entry criterion for all participants. Table 1 summarises the scoring components.

Table 1: Modified Bishop Score components used for cervical assessment. Inclusion criterion: MBS ≤4 (unfavourable cervix)

Parameter	Score 0	Score 1	Score 2	Score 3
Dilatation (cm)	Closed	1–2	3–4	5+
Cervical Length (cm)	>4	3–4	1–2	0
Consistency	Firm	Medium	Soft	—
Position	Posterior	Midline	Anterior	—
Foetal Station	−3	−2	−1, 0	+1, +2

Statistical Analysis

Data were recorded in Microsoft Excel and analysed using SPSS version 23 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean ± standard deviation (SD) and compared using an independent samples t-test. Categorical variables are expressed as frequencies and percentages; between-group comparisons were made using the Chi-square (χ^2) test or Fisher's exact test as appropriate. A p-value of ≤0.05 was taken as the threshold for statistical significance at 95% CI.

Results and Discussion

Baseline Demographic Profile

The two groups were well-matched across all demographic and obstetric baseline parameters (Table 2).

Most women were aged 22–25 years (47%), lived in rural areas (70.5%), and were primigravid (62%). Hindu women comprised 75.5% of the total cohort, and the proportion of booked versus unbooked cases was comparable between groups. None of the baseline comparisons reached statistical significance, supporting the adequacy of the randomisation process.

Table 2: Baseline demographic and obstetric profile of study participants. NS = Not significant (p>0.05)

Variable	Group A – Single (n=100)	Group B – Repeat (n=100)	Total (n=200)	P value
Age 18–21 yr	23 (23%)	20 (20%)	43 (21.5%)	
Age 22–25 yr	48 (48%)	46 (46%)	94 (47%)	
Age 26–29 yr	21 (21%)	23 (23%)	44 (22%)	0.636 (NS)
Age ≥30 yr	8 (8%)	11 (11%)	19 (9.5%)	
Hindu religion	76 (76%)	75 (75%)	151 (75.5%)	0.999 (NS)
Rural residence	72 (72%)	69 (69%)	141 (70.5%)	0.756 (NS)
Booked status	70 (70%)	76 (76%)	146 (73%)	0.426 (NS)
Primigravida	64 (64%)	60 (60%)	124 (62%)	0.662 (NS)
History of abortion	16 (16%)	11 (11%)	27 (13.5%)	0.408 (NS)

Indications for Induction of Labour

Post-datism was the most frequent reason for induction across both groups, accounting for 61.55% of all cases. Hypertensive disorders of pregnancy (HDP) ranked second (27.55%), followed by premature rupture of membranes (PROM, 8%), pre-eclampsia (3.55%), prior history of abortions (3%), intrauterine growth restriction (IUGR, 2.55%), and oligohydramnios (1.55%). The distribution of indications was statistically comparable between the two groups (Table 3), ensuring that the type of indication did not confound the primary outcome measures.

Table 3: Indications for induction of labour. HDP = Hypertensive disorders of pregnancy; PROM = Premature rupture of membranes; IUGR = Intrauterine growth restriction.

Indication	Group A n (%)	Group B n (%)	P value
Post-datism	60 (60%)	63 (63%)	0.702 (NS)
HDP	27 (27%)	28 (28%)	0.999 (NS)
PROM	4 (4%)	12 (12%)	0.068 (NS)
Pre-eclampsia	4 (4%)	3 (3%)	1.001 (NS)
History of abortions	3 (3%)	3 (3%)	0.241 (NS)
IUGR	5 (5%)	0 (0%)	0.070 (NS)
Oligohydramnios	3 (3%)	0 (0%)	0.248 (NS)

Bishop Score Response

At the time of induction, mean Bishop scores were comparable between Group A (1.34±1.13) and Group B (1.17±0.83; p=0.228, not significant). After the first gel application in Group B, scores rose significantly to 2.25±0.68 — a statistically meaningful change compared to both pre-induction values (p<0.01; Table 4). This confirms that a single dose produces genuine cervical change, even when it falls short of triggering active labour. This pattern mirrors the stepwise progression

described by Mainprize et al.,[7] who documented a significant rise in Bishop score after each sequential intracervical PGE2 application, and aligns with Parate et al.,[8] who reported a mean post–two-dose Bishop score of 6.84.

Table 4: Comparison of mean Modified Bishop Score between groups at different time points. S = Significant; NS = Not significant

Time Point	Group	Mean Bishop Score ± SD	P value
At induction	Group A (P1)	1.34 ± 1.134	P1 vs P2: 0.228 (NS)
At induction	Group B (P2)	1.17 ± 0.829	
After 1st gel (Group B)	Group B (P3)	2.25 ± 0.68	P1 vs P3: <0.01 (S) P2 vs P3: <0.01 (S)

Labour Induction Parameters

Time from the first gel application to labour onset was considerably longer in Group B (693±117 vs. 277±63 minutes; p<0.001) — an expected consequence of the mandatory 6-hour waiting period and second instillation built into that protocol. Once active labour was established, however, it progressed more efficiently in Group B, with a significantly shorter active phase duration (390±77 vs. 468±87 minutes; p<0.001), suggesting that more complete cervical preparation promotes coordinated uterine contractility. Group B also required oxytocin augmentation significantly less often (27% vs. 47%; p=0.005; Table 5). Khajotia et al.[6] noted a similar reduction in induction-to-delivery time with double application, and Parate et al.[8] found that 94% of women in their double-dose group progressed to spontaneous labour without oxytocin.

Table 5: Comparison of labour induction parameters between the two groups. S = Significant (p≤0.05).

Parameter	Group A – Single	Group B – Repeat	P value
Time to labour onset (min), Mean±SD	277 ± 63	693 ± 117	<0.001 (S)
Duration of active labour (min), Mean±SD	468 ± 87	390 ± 77	<0.001 (S)
Oxytocin augmentation required, n (%)	47 (47%)	27 (27%)	0.005 (S)

Mode of Delivery

Vaginal delivery rates were higher in Group A (84% vs. 76%), though this difference did not reach statistical significance (p=0.223). However, the LSCS rate was significantly higher in Group B (23% vs. 13%; p<0.05; Table 6). Karadag et al.[9] similarly documented a vaginal delivery rate of only 30.2% in their repeat-dose group, attributing the excess caesareans largely to foetal distress and failed induction. By contrast, Khajotia et al.[6] and Mashkaria et al.[10] found no significant difference in LSCS rates between dosing strategies — likely explained by differences in institutional caesarean section thresholds, patient mix, and definitions of induction failure.

Table 6: Mode of delivery by study group. S = Significant; NS = Not significant.

Mode of Delivery	Group A n (%)	Group B n (%)	P value
Vaginal Delivery	84 (84%)	76 (76%)	0.223 (NS)
Lower Segment Caesarean Section (LSCS)	13 (13%)	23 (23%)	<0.05 (S)
Instrumental Delivery	3 (3%)	1 (1%)	0.621 (NS)

Indications for Caesarean Section

Foetal distress or meconium-stained liquor was the leading indication for caesarean in both groups (46.2% in Group A, 36% in Group B). Placental abruption ranked second in Group A (38.4%). In Group B, additional indications included hypertonic uterine contractions (16%), failed induction (12%), and non-progression of labour (8%) — patterns directly attributable to the higher cumulative prostaglandin load in that group (Table 7).

Table 7: Indications for caesarean section by group (expressed as percentage of LSCS cases in each group).

Indication for LSCS	Group A (n=13)	Group B (n=25)
Foetal distress / Meconium-stained liquor	46.2%	36%
Placental abruption	38.4%	28%
Uterine hyperstimulation	15.4%	—
Failed induction	—	12%
Hypertonic uterine contractions	—	16%
Non-progression of labour	—	8%

Maternal Complications

The overall complication rate was noticeably higher in Group B (54% vs. 36%). Gastrointestinal (GI) symptoms — nausea, vomiting, and diarrhoea — were more common (16% vs. 12%), as were uterine hyperstimulation (8% vs. 4%), antepartum haemorrhage (APH, 8% vs. 5%), and meconium-stained liquor (14% vs. 10%; Table 8). These differences reflect the dose-dependent adverse effect profile of prostaglandins, consistent with the findings of Khajotia et al.[6] While GI side effects were generally managed conservatively, hyperstimulation and APH are complications that demand prompt clinical attention.

Table 8: Maternal complications by study group

Complication	Group A n (%)	Group B n (%)
No complication	64 (64%)	46 (46%)
GI symptoms (nausea/vomiting/diarrhoea)	12 (12%)	16 (16%)
Meconium-stained liquor	10 (10%)	14 (14%)
Post-partum haemorrhage (PPH)	7 (7%)	5 (5%)
Antepartum haemorrhage (APH)	5 (5%)	8 (8%)
Uterine hyperstimulation	4 (4%)	8 (8%)

Neonatal Outcomes

Neonates born to Group A mothers had significantly better APGAR scores at 1 minute (7.67±0.74 vs. 7.34±1.02; p=0.010) and at 5 minutes (7.60±0.93 vs. 7.25±1.21; p=0.023). Neonatal intensive care unit (NICU) admission was more than twice as common in Group B (23% vs. 10%; p=0.013; Table 9). Rates of birth asphyxia (13% vs. 7%) and meconium aspiration syndrome (MAS, 10% vs. 7%) were also higher in Group B, though neither reached individual significance. Karadag et al.[9] reported a strikingly similar NICU admission disparity in their repeat-dose group (13.6% vs. 4.4%; p=0.006). Taken together, these findings make a compelling case that when a repeat dose of dinoprostone is given, it must be accompanied by continuous foetal

surveillance and a low threshold for intervention at the first sign of compromise.

Table 9: Neonatal outcomes. S = Significant; NS = Not significant.

Neonatal Parameter	Group A Mean±SD / n(%)	Group B Mean±SD / n(%)	P value
APGAR at 1 minute	7.67 ± 0.74	7.34 ± 1.02	0.010 (S)
APGAR at 5 minutes	7.60 ± 0.93	7.25 ± 1.21	0.023 (S)
No foetal complication	86 (86%)	77 (77%)	0.123 (NS)
Birth asphyxia	7 (7%)	13 (13%)	0.142 (NS)
Meconium aspiration syndrome	7 (7%)	10 (10%)	0.467 (NS)
NICU admission	10 (10%)	23 (23%)	0.013 (S)

Limitations

- Single-centre tertiary-care study; findings may not generalise to community hospitals or lower-resource settings.
- Coin-flip randomisation, while pragmatic, is less robust than computer-generated concealed allocation.
- Non-blinded design; however, the primary outcomes (APGAR scores, NICU admissions, LSCS rate) are objective and less susceptible to observer bias.
- Confounding variables such as parity, specific indication for induction, and foetal weight were not fully explored in multivariate modelling.
- Long-term neonatal neurodevelopmental follow-up was beyond the scope of this study and warrants future investigation.

Conclusion

Intracervical dinoprostone remains a practical and generally safe approach to labour induction in women with an unripe cervix. This study shows that a single 0.5 mg application is preferable from both a neonatal safety and operative-delivery standpoint. Repeating the dose does achieve faster cervical ripening and a shorter active labour phase, with reduced need for oxytocin — but these benefits come at the cost of a higher caesarean section rate and meaningfully worse neonatal outcomes, most notably greater NICU admissions and lower APGAR scores. A second application should not be routine practice; it should be reserved for carefully selected women, administered only when clinically justified, and paired with continuous cardiotocographic (CTG) monitoring and a low threshold for operative intervention. Well-designed multicentre randomised controlled trials with larger sample sizes are needed to establish clearer, evidence-based dosing guidelines.

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