e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(10); 276-281

Original Research Article

Effect of Vaginal PH on Efficacy of Dinoprostone Gel for Labour Induction: A Cross-Sectional Study in Eastern India

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Received: 25-07-2024 / Revised: 23-08-2024 / Accepted: 26-09-2024

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Conflict of interest: Nil

Abstract:

Objectives: To evaluate whether vaginal pH alters the efficacy of dinoprostone gel for induction of labor, to find out whether vaginal pH affects cervical ripening and Bishop's score prior to induction, and to evaluate whether parity or age affects vaginal pH.

Materials and Methods: This prospective study was conducted at a tertiary care center in Kolkata for a period of 18 months, and included 200 women undergoing induction with dinoprostone gel. Participants were categorized based on vaginal pH: Group A (pH ≤4.5) and Group B (pH >4.5). The primary outcomes that were assessed included changes in Bishop's score, time to active labour, and mode of delivery.

Results: The majority of participants were aged 21-25 years, with a significant association found between higher vaginal pH and gravidity (P=0.002). Group B demonstrated greater mean changes in Bishop's score after 12 hours (5.70 vs. 4.19), a lower need for repeat gel (57.34% vs. 78%), and a shorter induction-to-active labour duration (13.97 vs. 17.98 hours) compared to Group A. Furthermore, caesarean section rates were notably lower in Group B (24.26% vs. 51.5%).

Conclusion: The study concludes that parity affects vaginal pH, which in turn significantly impacts labour induction outcomes with dinoprostone gel. Higher vaginal pH correlates with improved induction success, prompting further research to explore this relationship in a larger, randomized context. These findings indicate that higher vaginal pH positively influences the efficacy of dinoprostone gel in labour induction. The results align with some of the previous studies highlighting the role of vaginal pH in drug release and absorption, suggesting that measuring vaginal pH could enhance patient selection and improve induction outcomes.

Keywords: Efficacy, pH, Dinoprostone, Cerviprime Gel, Labour Induction.

Introduction

Induction of labour is a medical intervention aimed at artificially initiating uterine contractions to facilitate cervical dilation, effacement, and ultimately the birth of the baby. This is relevant for pregnancies at or beyond fetal viability [1], with 10-33% of pregnancies requiring induction [2]. Over the last 15 years, the prevalence of labour induction has nearly doubled [2]. Successful induction is defined as achieving a vaginal delivery within 24 to 48 hours post-induction, heavily influenced by cervical condition. An unfavorable cervix can lead to failed induction, necessitating operative vaginal delivery or caesarean section [3]. Indications for labour induction include post-term pregnancy, rupture of membranes without labour, preeclampsia/eclampsia, and maternal medical conditions like chronic hypertension, diabetes, and chronic renal disease. Prior to induction, it is crucial to confirm fetal lung maturity, gestational age, and fetal position. Methods of induction are classified into pharmacological and non-pharmacological approaches. Non-pharmacological methods include surgical and mechanical techniques, as well as natural methods. Pharmacological options include oxytocin and prostaglandins (such

as Misoprostol E1 and Dinoprostone E2). Notably, the use of prostaglandins has been shown to enhance rates of successful vaginal deliveries while reducing caesarean sections and improving maternal satisfaction. Prostaglandins are essential for stimulating uterine contractions and facilitating cervical ripening. Specifically, the E and F series of prostaglandins are pivotal during labour and postpartum. Prostaglandin E series, in particular, is more effective in cervical ripening due to the constant presence of their receptors in myometrial tissue, unlike oxytocin which requires receptor induction later in pregnancy. Current clinical use involves synthetic prostaglandins, with natural forms like PGE2 and PGF2α retaining their molecular structure.

Vaginal pH, typically between 3.8 and 4.8, can influence drug ionization and absorption, thereby affecting clinical outcomes [4,7]. Studies indicate that vaginal pH may impact the efficacy of controlled-release PGE2 vaginal inserts and gels, particularly in cervical priming or labour induction [5,6,9,10]. Additionally, variations in vaginal pH have been linked to preterm delivery, suggesting a broader role in cervical ripening.

The objectives of this study are to evaluate whether vaginal pH alters the efficacy of dinoprostone gel for induction of labor, to find out whether vaginal pH affects cervical ripening and Bishop's score prior to induction, and to evaluate whether parity or age affects vaginal pH. Understanding these interactions could enhance patient selection for PGE2 induction and reduce instances of failed induction, ultimately improving maternal and fetal outcomes.

Materials and Methods

This is an institutional based prospective study conducted in the dept. of Gynaecology and Obstetrics at a tertiary care centre in Kolkata for a period of 18 months. Study population were women undergoing induction of labour with dinoprostone gel for medical/obstetric indication. Sample size is 200 (minimum calculated was 99.4 pq/l^2) and sample design was purposive.

Inclusion criteria of the study: an unfavourable cervix with a Bishop's score of < 5, singleton pregnancy with vertex presentation and no contraindication to vaginal delivery, reassuring fetal heart rate.

Exclusion criteria of the study: known hypersensitivity to prostaglandins, placenta previa, suspected chorioamnionitis, parity of >3, previous caesarean delivery or a history of uterine surgery, previous attempted induction of labour, cephalopelvic disproportion.

The following parameters were evaluated for each selected case: demographic details, previous obstetric history, details of the current pregnancy, Bishop's score, mode of delivery and neonatal outcomes. The study tools used in this study were: a pre-designed, pre-tested proforma for data collection, hospital records such as Operation Theatre (OT) notes and labour room records.

Before other examinations were performed, each participant underwent a speculum examination and vaginal pH value was assessed. Patients were divided into two groups, Group A & Group B, on the basis of their vaginal pH. Group A included patients with vaginal pH ≤4.5 and Group B included those with vaginal pH >4.5. A vaginal examination was then performed to determine the Bishop's score. After ruling out all contraindications Dinoprostone gel was applied endocervically. Following application, the patient was instructed to remain recumbent for at least 30 minutes. The patient was then continuously monitored.

After 6 hours, depending on Bishop's Score and uterine contractions, either PGE2 gel was repeated (maximum 3 doses) or labour was augmented as per labour room protocol. The time taken to enter into active phase of labour was assessed. The differences between the groups with respect to age, parity, pre-induction Bishop's Score, need for a second induction, time to enter into active phase of labour and the final mode of delivery were compared and analysed. Birth weight, Apgar score and any neonatal complications, if present, were noted. Baseline and outcome data were compiled in Microsoft Excel spreadsheet (office 2021). Numeric values were expressed as mean ± SEM and ordinal values were expressed as number (percentage). Chi-square tests, student's t test, were used to calculate the "p" value. A "p" value of <0.05 was considered to be statistically significant. Data was interpreted using Statistical Package for Social Sciences software (version 22). Ethical approval was obtained from institutional ethics committee (Reference No.-MC/Kol/IEC/Nonspon/730/12). Informed written consent was obtained from each patient/guardian.

Results and Analysis

Induction efficacy was assessed by the need for a repeat Dinoprostone gel. In Group A, 50 patients (78%) required a second gel, whereas in Group B, 78 patients (57.34%) needed a second gel (Table 1). A significant association was noted between vaginal pH and the need for a second gel, with lesser requirements in the higher pH group (57.34%).

Regarding the time taken from induction to active labour, Group A had a mean duration of 17.98 hours (SEM: 0.53) compared to 13.97 hours (SEM: 0.29) in Group B (Table 2). A significant association was found between vaginal pH and the induction-to-active labour duration, with shorter times recorded in the higher vaginal pH group. Caesarean section rates varied significantly between groups; in Group A, 51.5% (33 patients) underwent a Caesarean section, compared to only 24.26% (33 patients) in Group B,

while the remaining had vaginal delivery (Figure 3). A significant correlation existed between Caesarean section rates and vaginal pH, indicating lower rates of Caesarean Section in the higher pH group.

The initial Bishop's scores indicated that 34% of patients had a score of 3, and 34% had a score of 4; 27% had a score of 2, and 5% had a score of 1 (Figure 1).

Group A's mean initial Bishop score was 2.81 (SEM: 0.10), while Group B's mean was 3.04 (SEM: 0.79). There was no significant association between vaginal pH and the initial Bishop score. The Mean Bishop Score Change for Group A was 4.19 (SEM: 0.25) and for Group B, it was 5.70 (SEM: 0.16) (Figure 2). A significant correlation was observed between vaginal pH and the change in Bishop's score after 12 hours, with a greater score change in the higher vaginal pH group. The study population was predominantly comprised of patients aged 21-25 years, accounting for 66% of the sample. The mean age for Group A was 23.67 years (SEM: 0.32), while Group B had a mean age of 23.72 years (SEM: 0.21) (Table 2). No statistically significant association was found between maternal age and the two groups. 67.5% of patients were multigravida, while 32.5% were primigravida (Table 2). A significant association was identified between vaginal pH and gravidity, with higher parity subjects exhibiting a higher vaginal pH (>4.5) (P=0.002).

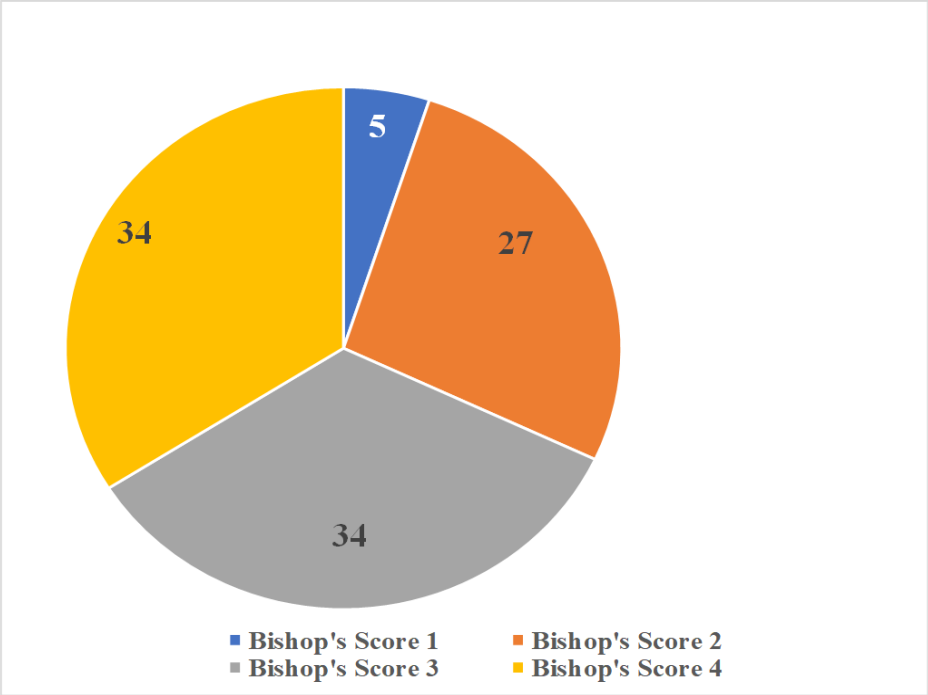

Figure 1: Pie chart distribution of initial Bishop's Score (in %)

Table 1: Comparison between two groups for Second Dinoprostone gel repeat for induction (p=0.004)

	Group A	Group B
Yes (2nd gel given)	50 (78%)	78 (57.34%)
No (2nd gel not given)	14 (22%)	58 (42.66%)

Table 2: Comparison between two groups with respect to Induction to active labour duration (hours), age (years) and gravidity

	Group A	Group B	p value
Induction to active labor mean ± SEM (hours)	17.98 ± 0.53	13.97 ± 0.29	0.0001
Age mean ± SEM (years)	23.67 ± 0.32	23.72 ± 0.21	0.897
Gravidity mean ± SEM	1.64 ± 0.087	2.07 ± 0.065	0.002

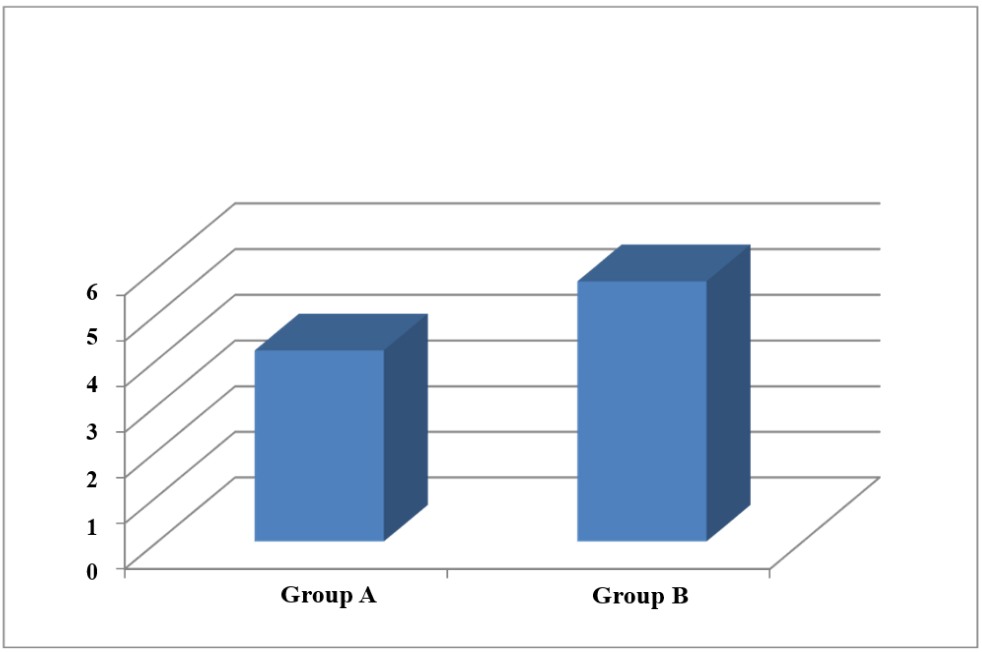

Figure 2: Bar Diagram showing Mean Bishop's Score Change (after 12 hours) (p=0.001)

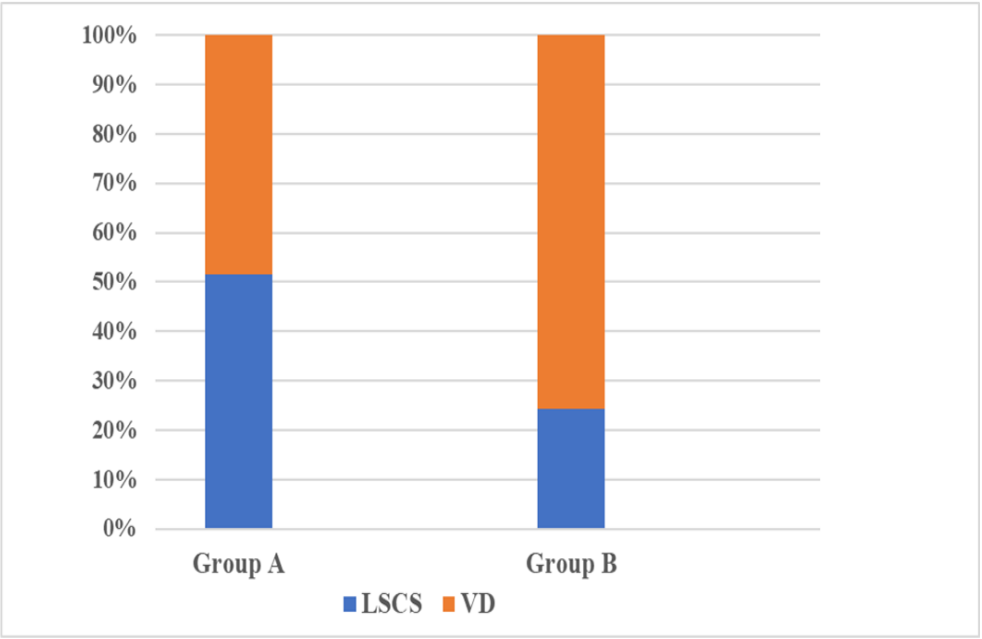

Figure 3: Bar diagram comparison between two groups for Mode of Delivery (p=0.0001)

Discussion

This study investigates the effect of vaginal pH on labour induction using Dinoprostone gel and the subsequent labour outcomes, and the primary indication for induction was postdatism, followed by oligohydramnios and gestational hypertension. A significant difference was noted with respect to gravidity, with a higher mean gravidity in the group with elevated vaginal pH (Group B).

The higher vaginal pH group (pH > 4.5) (Group B) demonstrated a greater mean change in Bishop's score after 12 hours, reduced need for a second Dinoprostone gel, shorter time to enter active labour, and higher rates of vaginal delivery as compared to the lower vaginal pH group (pH < 4.5) (Group A).

Johnson et al. examined the in vitro release of PGE2 from various commercially available preparations, reporting a higher release of prostaglandins at elevated pH levels [5].

In response to that, AVG Taylor noted that the acidic environment encountered at term delays PGE2 release, and a significant increase in pH might explain the occasional cases of uterine hyperstimulation associated with this preparation [12]. MacDonald and Weir [7] later detailed the role of pH in the dissolution of PGE2 in vitro, finding

that higher PGE2 release occurred from hydrogel pessaries at pH levels between 6.5 and 7.5. At pH 7.5, PGE2 is predominantly ionized (pKa 4.9), potentially diminishing its absorption.

Lyrenas et al. (2001) demonstrated that the PGE2 release rate in women with premature rupture of membranes (PROM) was non-linear; rather, it depended on vaginal pH, with faster release rates at higher pH levels [10]. Conflicting results were presented in Ramsey et al.'s studies conducted in 2002 and 2003. The 2002 study, which utilized PGE2 gel, found a significant association between higher vaginal pH and shorter times to enter active phase, achieve full dilation, and delivery [8]. Conversely, the 2003 study using a PGE2 vaginal insert found no significant associations [9].

Basirat et al. (2007) reported that while the average duration of the latent phase did not differ significantly between low and high pH groups, the active phase duration was significantly shorter in the high pH group ($p=0.019$) [11]. Additionally, no differences were observed in caesarean section rates between women with low or high vaginal pH [11]. Onen et al. (2008) found that in the high vaginal pH group, the change in Bishop score over 12 hours following the first Dinoprostone vaginal insert was statistically higher than in the low pH group (5.5 ± 3.4 versus 3.9 ± 3.3, $p<0.05$) [13].

However, no significant differences were noted in time to active labour or time to complete delivery between the two groups [13]. Poomalar GK et al (2021) reported that there was no significant effect of change in vaginal pH on effectiveness of intracervical PGE2, nor was there was any significant association between vaginal pH and time from induction to active labour as well as time from induction to delivery [14]. Similarly, there was no significant association between mode of delivery and oxytocin usage with vaginal pH in labour.

Overall, while some studies suggest a relationship between vaginal pH and the efficacy of Dinoprostone, the findings across the literature are not entirely consistent, implying the need further research. Additional randomized studies are needed to compare the effectiveness of vaginally administered PG inserts and intracervical PGE2 gels in labour induction, specifically examining their impact on vaginal and cervical pH.

Conclusion

In conclusion, this study suggests that parity influences vaginal pH, which significantly impacts induction of labour by using Dinoprostone gel. Higher vaginal pH is associated with a better response to a single induction, a greater mean change in Bishop's score after 12 hours, reduced need for a second Dinoprostone gel, shorter time to enter active labour, and higher rates of vaginal delivery. Thus, measuring vaginal pH prior to induction may serve as a valuable tool for predicting labour outcomes in patients undergoing induction with PGE2 gel.

Acknowledgements: Special thanks to Professor Dr. Partha Mukherjee (Head of the department) and Professor Dr. Bandana Biswas.

References

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Munson ML. Births: final data for 2002. Natl Vital Stat Rep. 2003 Dec 17; 52(10):1-113. PMID: 14717305.
2. Mazhar SB, Jabeen K. Outcome of mechanical mode of induction in failed primary labor induction. J Coll Physicians Surg Pak. 2005 Oct; 15(10):616-9. PMID: 19810299.
3. Rayburn WF, Zhang J. Rising rates of labor induction: present concerns and future strategies. Obstet Gynecol. 2002 Jul; 100(1):164-7. doi: 10.1016/s0029-7844(02)02047-1. PMID: 12100818.
4. Johnson TA, Greer IA, Kelly RW, Calder AA. The effect of pH on release of PGE2 from vaginal and endocervical preparations for induction of labour: an in-vitro study. Br J Obstet Gynaecol. 1992 Nov; 99(11):877-80. doi: 10.1111/j.1471-0528.1992.tb14433.x. PMID: 1450134.
5. Hauth JC, Macpherson C, Carey JC, Klebanoff MA, Hillier SL, Ernest JM, Leveno KJ, Wapner R, Varner M, Trout W, Moawad A, Sibai B. Early pregnancy threshold vaginal pH and Gram stain scores predictive of subsequent preterm birth in asymptomatic women. Am J Obstet Gynecol. 2003 Mar; 188(3):831-5. doi: 10.1067/mob.2003.184. PMID: 12634666.
6. Gleeson RP, Elder AM, Turner MJ, Rutherford AJ, Elder MG. Vaginal pH in pregnancy in women delivered at and before term. Br J Obstet Gynaecol. 1989 Feb; 96(2):183-7. doi: 10.1111/j.1471-0528.1989.tb01659.x. PMID: 2930742.
7. MacDonald IA, Weir RF. The effect of pH on release of PGE2 from vaginal and endocervical preparations for induction of labour. Br J Obstet Gynaecol. 1993; 100(11): 1066-8.
8. Ramsey PS, Ogburn PL Jr, Harris DY, Heise RH, Ramin KD. Effect of vaginal pH on efficacy of the dinoprostone gel for cervical ripening/labor induction. Am J Obstet Gynecol. 2002 Oct; 187(4):843-6. doi: 10.1067/mob.2002.126987. PMID: 12388961.
9. Ramsey PS, Ogburn PL Jr, Harris DY, Heise RH, DiMarco CS, Ramin KD. Effect of vaginal pH on efficacy of the controlled-release dinoprostone vaginal insert for cervical ripening/labor induction. J Matern Fetal Neonatal Med. 2003 Apr; 13(4):250-3. doi: 10.1080/jmf.13.4.250.253. PMID: 12854926.

10. Lyrenäs S, Clason I, Ulmsten U. In vivo controlled release of PGE2 from a vaginal insert (0.8 mm, 10 mg) during induction of labour. BJOG. 2001 Feb; 108(2):169-78. doi: 10.1111/j.1471-0528.2001.00039.x. PMID: 11236117.
11. Basirat Z, Barat SH, Ghanbarpour A, GolsorkhtabarAmiri M. Does vaginal pH affect the efficacy of dinoprostone in cervical ripening/labor duration? Clin Exp Obstet Gynecol. 2012; 39(4):522-5.
12. Taylor AVG, MacKenzi IZ. The effect of pH on release of PGE2 from vaginal and endocervical preparations for induction of labour. BJOG. 1993 May; 100(5):500–01. doi: 10.1111/j.1471-0528.1993.tb15286.x.
13. Önen F et al. The Role of Vaginal pH on Efficacy of Controlled-Release Dinoprostone Vaginal Insert for Cervical Ripening/Labor Induction: A Prospective Double-Blind Study. J Turkish-German Gynecol Assoc. 2008; 9(4): 206-10.
14. Poomalar GK, Fathima Shantini N, Ezhil R. Effect of vaginal pH on efficacy of dinoprostone gel for labour induction: a cross-sectional study. J Obstet Gynaecol. 2022 Feb; 42(2):228-231. doi: 10.1080/01443615.2021. 1904225. Epub 2021 May 21. PMID: 340205.