RESEARCH

Effect of vaginal pH in cervical ripening with dinoprostone gel

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ABSTRACT

Objective: The purpose of this study was to evaluate whether vaginal pH has an effect on the efficacy of the Dinoprostone gel for cervical ripening. **Methodology**: Hundred ten women who had indication for labor induction with Bishop's score ≤5 were enrolled in this prospective observational study. After initial vaginal pH and Bishop Score assessment all women received dinoprostone gel intracervically for cervical ripening with repeated dosing twelve hours later or oxytocin / misoprost induction were initiated depending on cervical status. Clinical outcomes were evaluated. Statistical analysis was done using SPSS 16.0. **Results**: Average initial vaginal pH was 5.305±0.931 (range 3.5-7.5). No significant differences were noted between those patients with vaginal pH≤4.5 (group 1) compared with those with high pH> 4.5 (group II) with respect to maternal age, gestational age and gravidity. Difference in mean initial Bishop Score was slightly significant being 0.0493. Bishop score change over 12 hours (2.57 vs 5.71), time to active labor (21.45 vs. 11.99 hours), induction delivery interval (28.48 vs. 16.67 hours), and mode of delivery (vaginal vs. CS) were highly significant between the two groups. **Conclusion:** Vaginal pH has significant effect on cervical ripening and delivery outcome.

Keywords: Dinoprostone gel, vaginal pH, cervical ripening.
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Induction is indicated when there is risk either to the mother or the baby of continuing the pregnancy. In modern times 10-33% of obstetric cases require induction of labor. The success of induction depends largely on the condition of the cervix. An unripe cervix fails to dilate well in response to myometrial contraction. The mainstay of induction of labor with an unfavorable cervix is the use of exogenous prostaglandins. Prostaglandins induce enzymatic changes that promote collagen breakdown, facilitate the rearrangement of collagen fibers and alter the cervical extracellular matrix, which result in cervical softening and effacement [1].

Prostaglandin E_2 is available in different formulations for local administration. Although

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safety and efficacy of different forms were compared in many studies, few studies have studied factors that affect the relative clinical efficacy of these vaginally administered prostaglandin preparations. In general vagina maintains a pH between 3.8-4.8, which is influenced by frequency of coitus, presence of cervical mucus and the amount of vaginal transudate. The lactic acid produced from glycogen by lactobacillus present in vagina plays an important role in maintaining acidic pH environment [2].

A variety of factors can alter the normal vaginal pH. Several factors such as lower genital tract infection; bacterial vaginosis, rupture of membrane, douching etc can alter the vaginal pH. The acidity of the vagina may alter the release of the drug and this could result in variable clinical response. Prostaglandins are organic acids that have diminished solubility in aqueous solution with a low pH [3].

The aim of this study is to investigate if vaginal pH has any effect on the efficacy of Dinoprostone gel for cervical ripening in patients with unfavorable cervix.

Materials and methods

This is a prospective observational study of pregnant women who had indication for labor induction with Bishop's score ≤5 in the Department of Obstetrics & Gynaecology, Gauhati Medical College and Hospital, Guwahati for One year- 1st June 2013 to 31st May 2014. Hundred ten cases were purposively taken.

Written and informed consent was obtained from all the patients after the study was approved by the Institutional Ethic Committee of Gauhati Medical College & Hospital.

Inclusion criteria were (1) An unfavorable cervical Bishop score of ≤ 5, (2) Singleton pregnancy with vertex presentation and no contraindication to vaginal delivery. (3) Assuring fetal heart rate.

Exclusion criteria included (1) Known hypersensitivity to prostaglandins (2) Placenta praevia (3) Suspected chorioamnionitis (4) Parity of >3 (5) A previous cesarean delivery or a history of uterine surgery (6) Previous attempted induction of labor for this pregnancy (7) cephalopelvic disproportion.

Before other examinations were performed, each participant underwent a speculum examination and vaginal pH value was assessed by using pH indicator paper (both broad & narrow spectrum).The indicator paper was placed on the lateral vaginal wall between the two valves of Cusco's speculum until it became wet. Color change of the strip was immediately compared with the manufacturer's colorimetric scale and the finding was recorded. Patients were divided into two groups as Group I & Group II on basis of their vaginal pH. Group I included patients with vaginal pH ≤4.5 and Group II included 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 is instructed to remain recumbent for at least 30 minutes. The patient is then continuously monitored.

After the initial 12 hours of cervical ripening, a repeat Bishop's score was assigned. Some patients received repeat Dinoprostone who had minimal change of Bishop Score. Women who had some change but were not in an adequate labor received Oxytocin or Misoprostol depending on the Bishop's score. Misoprostol was used in cases with lower Bishop's score change and Oxytocin in patients with higher Bishop's score change for augmentation. Standardized intrapartum treatment guidelines were used for all the patients.

Baseline and outcome data were compiled in Microsoft excel. Numeric values were expressed as mean ± SD 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. The SPSS 16.0 statistical package was used for statistical analysis.

Primary outcome measure was changes in Bishop Score's over initial 12 hours. Secondary outcome measures were requirement of augmentation, time to active labor, induction to delivery interval, neonatal and maternal complications.

Results

A total of 110 women with unfavourable cervix were enrolled. There were 35 cases in group I and 75 cases in group II.

Baseline characteristics were shown in table I. There was no statistically significant association between the two groups with respect to maternal age, gravidity and gestational age but difference in mean initial bishop's score was slightly significant being 0.0493.

Table I. Baseline characteristics

Characteristics	Group I	Group II	*P* value
Age(years)	24.4±3.47	23.13±3.95	0.107
Gestational age (days)	279.97±17.19	280±13.68	0.993
Gravidity (no)	1.46±0.741	1.45±0.664	0.979
Initial Bishop score	1.74±1.597	2.33±1.379	0.0493
Vaginal pH	4.17±0.29	5.83±0.58	

Comparison between primary and secondary outcomes is shown in Table II. In group II bishop score change over 12 hour , time to active labor, induction delivery interval were significantly different between the two groups. Out of 110 cases, 53 (48%) required augmentation either with Oxytocin or Misoprostol, 23 (21%) belonged to group I and 30 (27%) to group II. Out of the 57 (52%) cases who did not require augmentation 12(7%) were of group I and rest 45(41%) belonged to group II.

The table III shows comparison of mode of delivery between the two groups. Group two had higher rate of vaginal delivery.

There were 14 neonatal complications all together shown in table IV. 2 cases one from each group had Apgar score ≤7 at 5 minutes of birth, 1 case died in NICU (B. Wt=900 gm) which belonged to Group I and 11 cases had neonatal hyper-bilirubinemia of which 3 cases were in Group I and 8 cases in Group II. On applying Fisher exact test got an insignificant *p* value of 1.000.

Table II. Comparison of labor outcomes

Outcomes	Group I	Group II	*p* value
Bishop score change (over 12 hr)	2.57±1.8	5.71±1.4	0.000*
Augmentation not required (%)	7	41	0.0209**
Time to active labor (hrs)	21.45±8.81	11.99±7.65	0.000*
Induction delivery interval (hrs)	28.48±7.92	16.67±9.350	0.002*
			**student's t test, ** chi-square test.*

There were 5 cases of post-partum maternal complications shown in table V. In Group I there was a case of wound infection & 1 case of puerperal pyrexia who had cold. In Group II there was a case of atonic PPH and 2 cases of puerperal pyrexia. Among the puerperal pyrexia cases of Group II one had UTI and the other one had breast engorgement. There was no maternal death.

Table IV: Showing distribution of fetal complication in the two groups.

Neonatal Complications	Group I(%)	Group II(%)	Total
5min Apgar score < 7	1(20%)	1(11.2%)	2(14.2%)
Death in NICU	1(20%)	0	1(7.1%)
Neonatal Hyper-bilirubinemia	3(60%)	8(88.8%)	11(78.7%)
Total	5(100%)	9(100%)	14(100%)
			*P value =1.000 *fisher's exact test*

Discussion

In this study the effect of vaginal pH in cervical ripening with Dinoprostone gel and labor outcome have been investigated.

A statistically significant change was found in bishop Score over 12 hour, time to active labor, induction delivery interval and mode of delivery in the present study. It suggests that pH may have effect in both ripening of cervix and priming of the uterus. In contrast to previous studies there was slightly significant difference in the initial bishop score between the two groups which may be because of the variability of gestational age among the cases in this study, the previous studies were on postdated

Table III. Mode of delivery

Mode of delivery	Group I (%)	Group II (%)	Total	
Vaginal Delivery	7(20%)	54(72%)	61(55.45%)	x2 =26.24 *p*=0.000* df=3
LSCS	28(80%)	21(28%)	49(44.55%)	
Total	35(100%)	75(100%)	110(100%)	

Table V: Showing distribution of maternal complications in the two groups.

Maternal Complications	Group I	Group II	Total
PPH	0	1(33.3%)	1(20%)
Puerperal pyrexia	1(50%)	2(66.7%)	3(60%)
Wound Infection	1(50%)	0	1(20%)
Total	2(100%)	3(100%)	5(100%)

pregnancies only.

Johnson et al studied in vitro release of PGE_2 from many commercially available preparations and reported higher release of prostaglandin in higher pH [4].

AVG Taylor in response to Johnson et al pointed out that the acidic environment encountered at term delays PGE_2 release and a significant increase in pH could explain the occasional case of uterine hyperstimulation associated with this preparation [5].

Mac Donald and Weir later described the role of pH in relation to PGE_2 dissolution in vitro, reporting higher PGE_2 release from hydrogel PGE_2 pessary with increased pH of 6.5 to 7.5. PGE_2 is predominantly ionized at pH 7.5 (pka 4.9, pka is logarithmic form of equilibrium constant) which may have diminished the potential for absorption [6].

Lyrenas et al (2001) have shown that the PGE_2 release rate in women with PROM was not linear. The PGE_2 release rate was dependent on vaginal pH, with a faster release rate at higher vaginal pH [7].

Ramsey PS et al (2002) showed that vaginal pH was not significantly associated with bishop score change over initial 12 hours but had significantly shorter time to active labor and vaginal delivery in women with high vaginal pH>4.5 [8].

Basirat Z et al (2007) in their study found that the average duration of latent phase between individuals with low and high pH was not significantly different, but the duration of active phase in patients with high pH was lower than low pH which was significant (p=0.019). In the study the cesarean section rate in women with low or high vaginal pH showed no difference [9].

Onen et al (2008) in their study found that in the high vaginal pH group, bishop's score change over 12 hour after commencement of the first Dinoprostone vaginal insert was statistically higher than those in the low vaginal pH group (5.5±3.4 versus 3.9±3.3, $p<0.05$). But there was no significant difference in time to active labor and time to complete delivery between the high and low pH groups [10].

It is seen that the authors found some relation between vaginal pH and efficacy of Dinoprostone though the results are not similar. This may be because only two groups had been made for comparison.

Conclusion

The result of this study shows that vaginal pH may have influence on the functions of Dinoprostone gel. It was seen that in higher vaginal pH there is better change of bishop's score and shorter induction delivery interval. So the higher vaginal pH may lead to improved clinical efficacy of Dinoprostone gel. A well designed pharmacological study with bigger study population is needed to evaluate the role of vaginal pH in absorption and overall efficacy of Dinoprostone gel which in future could increase the efficacy and reduce unwanted outcomes.

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