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Effect of vaginal pH on efficacy of dinoprostone gel for labour induction

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Abstract

Background: Induction of labour is defined as an intervention designed to artificially initiate uterine contractions leading to progressive dilatation and effacement of the cervix. Prostaglandin (PGE₂) is a well-established agent that has a primary action in softening the cervix. They are organic acids that have diminished solubility in aqueous solution with a low pH. In general vagina maintains a pH between 3.8-4.8. A variety of factors may alter there lease of the drug and this could result in variable clinical response.

Objective: The purpose of this study was to evaluate whether vaginal pH has an effect on the efficacy of the PGE_2 dinoprostone gel for labour induction.

Methodology: 150 women with indication for labor induction with Bishop's score ≤ 6 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 4.75±0.89. No significant differences were noted between those patients

with vaginal pH \leq 4.5 (group 1) compared with those with high pH> 4.5 (group II) with respect to maternal age . Subjects with higher parity were associated with higher vaginal pH parity (55.5% primigravida in group Ivs 53.2% primigravida in group II). Higher vaginal pH was associated with a higher Bishop score prior to induction(4.94 in group IIvs 3.12 in group II), responded to single induction, and had a higher number of vaginal deliveries than those with lower vaginal pH(41.45 % in group I vs 70.6% in group II.) There was no significant association found in vaginal pH and the time taken to enter into active phase of labour.

Conclusion : Vaginal pH has significant effect on cervical ripening and labour events by PGE_2 gel induction.

Keywords - Induction, Vaginal pH, PGE₂, Labour

Introduction

Induction of labour is defined as an intervention designed to artificially initiate uterine contractions leading to progressive dilatation and effacement of the cervix and birth of the baby. About 20% of pregnant women will have labour induced for a variety of reasons. There are various medical and surgical methods of Induction/Cervical ripening. Overall, induction of labour using prostaglandins seem to improve the rate of

Page]

successful vaginal delivery, lower the rate of caesarean section, lower epidural usage and to be associated with improved maternal satisfaction.^[1,11]

Cervical ripening is the process that culminates in the softening and distensibility of the cervix, which facilitates labour and delivery. The cervix contains relatively few smooth muscle cells and derives its rigidity from collagen bundles surrounded by proteoglycans. In pregnancy nearing term, there are various factors that induce certain changes in the cervix leading to cervical ripening. There are agents that can artificially induce these changes if it has not occurred. It is difficult to separate methods of cervical ripening and labour induction.^[2]

Prostaglandin (PGE₂) is a well-established agent that has a primary action in softening the cervix. Compounds such as IL-8 act synergistically with PGE₂ in attracting neutrophils.^[3] The human uterine cervix can produce nitric oxide (NO),a free radical with an ultra-short half-life. Nitric oxide in the human uterine cervix acts as an endogenous ripening factor with an unknown mechanism of action. Nitric oxide and PGE₂ are the two pathways that, cross activating each other, trigger the cascade of events responsible for cervical ripening.^[4]

M. Norman et al studied the metabolism of cervical connective tissue in cervical biopsies from non-pregnant and pregnant cases. The concentration of proteoglycans in the pregnant cervix was found to be approximately onehalf of that in the non-pregnant cervix indicating that the turnover of proteoglycans in pregnant cervical tissue was significantly increased. After prostaglandin inductionit found decrease was that the in sulfatedGAGS(glycosaminoglycans) could decrease electrostaticinteractions that would weaken interfibrillar interactionsthat would be consistent with a decline in of cervicalresistance. The involvement matrix metalloproteinases(MMP) i.e. MMP-2 and MMP-9 in the

ripening.3,4 To summarize, the complex interactions of variouscytokines bring about profound changes in theproteoglycans in the cervix which eventually leads tocervical ripening. 14 Recently, vaginal pH has been investigated as a potential factor influencing the efficacy of prostaglandins forcervical ripening and labour induction but the results havebeen conflicting. Studies have been conducted on the effects of vaginal pH on the efficacy of controlled-releasePGE2vaginal insert and PGE2 gel for cervicalpriming/labour induction in which overall vaginal pH seemed to influence the PGE2release. The vaginal pH in pregnancy is known to be acidic and not much is known about the variations in vaginal pHthroughout pregnancy. There are studies that mention thatpH may change the degree of ionization of a drug and affect the absorption of the drug resulting in variableclinical responses. Vaginal pH changes also has a role in preterm deliverywhich suggests that it has a role in influencing cervical ripening.5 Nonetheless, the effect of vaginal pH on overall efficacy of the cervical ripening/labour induction with PGE₂ gel has not been well studied, thus this study is to evaluate the influence ofvaginal pH on the efficacy of PGE₂gel for cervicalripening/labour induction which would improve patient selection for PGE₂ gel induction and reduce the incidence offailed induction. The purpose of this study is to evaluate the influence of vaginal pH on the efficacy of PGE₂gel for cervical ripening/labour induction and assess its association with Various baseline characteristics of patientsand Labour outcomes.

cervical ripeningprocess has been indicated in cervical

Material And Method

Study Setting: Observational Prospective Study was done at Rajkiya Mahila Chikitsalaya, Jawaharlal Nehru Medical College situated at Ajmer, Rajasthan, India. Total number of 150subjects, for period of ten months from November

2016 to August 2017, who required induction, was enrolled in the study.Written and informed consent was obtained from all the patients after the study was approved.

Inclusion criteria: An unfavourable cervical Bishop score of < 6, Singletonpregnancy with vertex presentation, Reassuringfetal heart rate, Absence of spontaneous uterine contractions, no contraindications for induction.

Exclusion criteria :Known hypersensitivity to prostaglandins, Placenta Praevia, Suspected chorioamnionitis, Aprevious caesarean delivery or ahistory of uterine surgery ,Cephalopelvic disproportion.

- 1. Each participant underwent a speculum examination and vaginal pH value was assessed by using pH indicator paper (both broad &narrow spectrum) after performingcardiotocography to rule out uterine contractions andto assess fetalstatus. The indicator paper was placed on the lateral vaginal wall between the two valves of Cusco's speculum until it became Colour of the wet. change strip was immediatelycompared 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

Group II included vaginal pH >4.5.

 A vaginal examination was then performed to determine the Bishop's score. Bishop score was assessed:

SCORE	0	1	2	3
Cervical	0	1-2	3-4	>4
dilatation,(cm)	0	12	5 1	- 1
cervical	0- 30%	40-50%	60-70%	>80%
effacement	0 3070	+0 5070	00 / 0 / 0	20070
cervical	firm	medium	soft	

consistency				
cervical	anterior	mid	nosterior	
position	anterior	ma	posterior	
Fetal station	-3	-2	-1/0	+1/+2

The highest possible score is 13 and <6 is unfavourable that needs induction.

 After ruling out all contraindications Dinoprostone gel was applied endocervically. The patient is then continuously monitored.

Statistical Analysis

The data was coded and entered into Microsoft Excel spreadsheet. Analysis was done using SPSS version 20 (IBM SPSS Statistics Inc., Chicago, Illinois, USA) Windows software program.Descriptive statistics included computation of percentages, means and standard deviations. The independent t test (for quantitative data within two groups) was used for quantitative data comparison of all clinical indicators. Chi-square test used for qualitative data whenever two or more than two groups were used to compare. Level of significance was set at $P \leq 0.05$.

Results:

Atotal of 150 women with unfavourable cervix were enrolled with 75 cases in each group.

TABLE	1:	Vaginal	ph	and	subjects	baseline
character	ristic	s:				

Characteristics	Group I	Group Ii	Р
Characteristics	(<4.5)	(>4.5)	Value
Vaginal pH	3.72 ± 0.45	5.24±0.42	
Age(years)	24.08 ±	23.32 ±	0.208
	3.83	3.51	0.208
Gestational age (weeks)	39.53 ± 2.3	40.14 ± 1.2	0.09

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Obstetric score	55.5% primi	53.2%primi	0.02
Initial Bishop score	3.12±1.59	4.64±0.48	0.49

Table 1 showed that 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 0.49.



Figure 1: Vaginal ph and Indication of Induction.

PROM :prelabour rupture of membranes

TP: term pregnancy

Figure 1 showing Subjects with Post datism (56%) and term patient with Rh negative (28%) as indication of induction were found to have lower vaginal pH as compared to subjects with PROM (44% had higher vaginal pH.) Which would have been attributed due to basic nature of amniotic fluid.

Following induction, it was found that:

FIGURE 2: Vaginal Ph Andmean Bishop Change Over 12 Hr.





Figure 3: Vaginal Ph and Requirement of Augmentation:



 X^2 =12.85, df=2, p value=0.002 (S)

Figure 2 and 3 showing mean change in bishops score over 12hours after 1^{st} induction with PGE₂ gel was higher in subjects with higher vaginal pH(0.69 in group I vs 2.04 in group II) and responded to a single induction (41.45 % in group I vs 70.6% in groupII) Table 3 showing that the mean time between the initial induction by PGE₂ gel and delivery (irrespective of mode of delivery), was high in lower vaginal pH subjects (14.98

hours in group I vs 11.07 hours in group I) with p value = 0.001.

On assessment of delivery outcome among both the groups, it was found that:

Vaginal Ph and Mode of Delivery

VAGINAL pH		Mode of delivery			
		FTLSCS	FTVD		
GROUP I	N	42	33		
≤4.5		71.1%	36.3%		
GROUP II	Ν	17	58		
>4.5		28.8%	63.7%		
Total	Ν	59	91		
	%	100%	100%		

 X^2 =23.98, df=2, p value=0.001 (S)

Vaginal Ph and Indication of LSCS: Comparison of Groups

Vaginal	Failed	NPOL +	NRFHR	Total
pН	induction	NRFHR		
GROUP	9	15	18	42
Ι	(81.8%)	(65.2%)	(72%)	
≤4.5		· · ·		
GROUP	2	8	7	17
II	(18.1%)	(34.7%)	(28%)	
>4.5				
Total	11	23	25	59
	(100.0%)	(100.0%)	(100.0%)	

 X^2 =40.69, df=7, p value=0.04 (S)

Subjects with lower vaginal pH were associated with more number of LSCS(71.1% in group I vs 28.8% in group II). Among indications of LSCS, lower vaginal pH was more associated with failed induction (81.1% in group I vs 18.1% in group II).

Feto-maternal outcome: comparisons of group

Fetal outcome				Maternal outcom			me	
Vaginal pH	M/S	NICU	NNJ	Observati on	LSCS wound	Puerperal sepsis	РРН	
GROUPI	38	4	3	33	5	2	5	
≤4.5	44.0%	16.0%	4.0%	44.0%	6.0%	2.6%	6.0%	
GROUP II	57	2	3	13	0	3	4	
>4.5	76.0%	8.0%	4.0%	12.0%	0.0%	4.0%	5.3%	

X²=32.11,df=4,pvalue=0.09

 $X^2=17.14$, df=4, p value=0.09

Total there were only 6(4%) NICU admissions while 6 (4%) had neonatal hyperbilirubinemia , with overall 19 cases of post partum maternal complications , but none of fetomaternal outcome was associated with vaginal pH.

Discussion

Observations from the present study suggest that parity influences vaginal pH and vaginal pH itself has a significant effect on cervical ripening and the Bishop Score prior induction.With high vaginal pH, there is better chance of positive Bishops score change, often responds to a single induction and is more often associated with vaginal deliveries than LSCS and also reduced time to enter into active phase of labourand shorter delivery interval more so in multipara. . Lower vaginal pH is more associated with failed induction.

Vaginal pH has been investigated in several studies as a factor that may account for the variability observed clinically with prostaglandin used as cervical ripening/labor induction agents.

Johnson et al studied in vitro release of PGE from many commercially available preparations and reported higher release of prostaglandin in higher pH [6]

The first study was carried out in 2001 by Lyrenas et al, who evaluated the effect of vaginal pH and efficacy of a controlled-release PGE vaginal insert in 68 subjects with an unfavourable cervix who were undergoing labor induction and shown that the PGE2 release rate in women with PROM was not linear.[7]

Two in vitro studies by Johnson et al. and MacDonald and Weir describes an increased PGE2 release in solutions with a higher pH. (6.5 to 7.5) It was also reported that along with the increased release of PGE 2, it is also predominantly ionized at a pH of 7.5 (pKa, 4.9), which diminishes the potential of its systemic absorption.

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].

AVG Taylor in response to Johnson et al pointed out that the acidic environment encountered at term delays PGE release and a significant increase in pH could explain the occasional case of uterine hyperstimulation associated with this preparation [13].

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]

Conclusions

The findings of the present study showed that vaginal pH can be an important predictor for success of PGE2 gel induction.

The pH is important in terms of the design and the efficacy of vaginal drug delivery systems.[16] The effect of vaginal pH on the efficacy of sustained-release PGE vaginal insert could be better established if the vaginal insert had been moistened with solutions having different pH as in the previous studies.Hence knowing the vaginal pH prior induction could prove to be a useful tool in assessing the labour outcome of a patient undergoing labour induction with PGE2 gel.

Recommendation of This Study: Further research is a required to know about vaginal pH in pregnancy, cause of variation, and study of various agents that would increase the vaginal pH thereby creating a favourable environment for PGE_2 gel induction, thereby decreasing incidence of failed induction and associated maternal morbidity.

Abbreviations:

PGE₂: prostaglandins E₂

 PGE_1 : prostaglandins E_1

IL : interleukins

NO: nitric oxide

ACOG: American College of Obstetricians and Gynaecologists

WHO: World Health Organization

NPOL: non progression of labour

NRFHR: Non reassuring fetal heart rate

LSCS: lower segment cesarean section

MAS : meconium aspiration syndrome

PROM: Prelabour rupture of membrane

FTVD: full term vaginal delivery

References

- Cunningham FG, Leveno KJ, Bloom SL, Hoth 24td Edi. New York; McGrawHill: 2014 JC, Rouse DJ, Sponge CY. Williams Obstetrics.
- Vaisanen-Tommiska M, Nuutila M, Aittomaki K, Hiilesmaa V, Ylikorkala O. Nitric oxide metabolites in cervical fluid during pregnancy: further evidence

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for the role of cervical nitric oxide in cervical ripening. Am J Obstet Gynecol. 2003;188(3):779-85.

- Norman M, Ekman G, Ulmsten U, Barchan K Malmstrom A. Proteoglycan metabolism in the connective tissue of pregnant and non-pregnant human cervix. An in vitro study. Biochem. J. 1991;275:515-20.
- Marx SG. Effects of Progesterone on iNOS, COX-2, and Collagen Expression in the Cervix. Journal of Histochemistry & Cytochemistry. 2006;54(6):62339
- Hauth JC. Early pregnancy threshold vaginal pH and Gram stain scores predictive of subsequent preterm birth in asymptomatic women. Am J Obstet Gynecol. 2003;188(3):831-5.
- Johnson TA, et al. The effect of pH on release of PGE from vaginal and endocervical preparations for induction of labour. Br J Obstet Gynaecol. 1992; 99(11): 877-80.
- Lyrenas S, Clason I, Ulmsten U. In vivo controlled release of PGE from a vaginal insert (0.8 mm, 10 mg) during induction of labor. Br J Obstet Gynaecol. 2001; 108:169-78.
- Ramsey PS et al. Effect of vaginal pH on efficacy of the dinoprostone gel for cervical ripening/labor induction. Am J Obstet Gynecol. 2002; 187(4): 843-6.
- Basirat Z, et al. Does vaginal Ph affect the efficacy of dinoprostone in cervical ripening /labor? Clin Exp Obstet Gynecol. 2012; 39(4): 522-5.
- 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.
- RCOG. Royal College of Obstetricians and Gynaecologists. Induction of labour. 2008;1:112,5:45-68

- MacDonald IA, et al. The effect of pH on release of PGE from vaginal and endocervical preparations for induction of labour. Br J Obstet Gynaecol. 1993; 100(11): 1066-7.
- Taylor AVG, MacKenzi IZ. The effect of pH on release of PGE from vaginal and endocervical preparations for induction of labour. BJOG.1993; 100(5): 500–01.
- Marx SG. Effects of Progesterone on iNOS, COX-2, and Collagen Expression in the Cervix. Journal of Histochemistry & Cytochemistry. 2006;54(6):62339.
- Fusun Acarturk. Mucoadhesive Vaginal Drug Delivery Systems. Recent Patents on Drug Delivery & Formulation. 2009;3:193-205
- Choudhury A, Das S, Kar M. A Review on Novelty and Potentiality of Vaginal Drug Delivery. International Journal of Pharm-Tech Research. 2011; 3(2):1033-44.

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