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A prospective study for the effect of vaginal ph on dinoprostone gel for cervical ripening / labor induction

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Abstract
Induction of labor is the artificial initiation of labor before its spontaneous onset by means of various interventions. Now a days, about 10-30% obstetric cases required induction due to various indications. There are many surgical and medical methods available for induction of labor/cervical ripening. Of these cervical ripening using Prostaglandin Gel intracervically is most common practice in modern times. Prostaglandin gel is not only effective in cervical ripening, but also effective in activating myometrial contractility. There are many formulations available for Prostaglandin E2 for local administration, including vaginal tablets, endocervical gels, and vaginal gels and also in the form of slow release dinoprostone vaginal insert forms.
Prostaglandin E2 gel is an organic acid which has low solubility in aqueous solution with low pH. The aim of this study is to evaluate whether vaginal PH has any effect on Dinoprostone gel used for cervical ripening in labor induction.
Aim
1. The influence of vaginal PH on the efficacy of PGE2 gel which we commonly use for cervical ripening in labor induction. So it might improve patient selection and we can predict those cases which might go into failed induction with PGE2.
2. I will also try to study the changes in vaginal pH because of various factors e.g. age of the patient, gestational age, parity, draining per vagina etc.

Materials and Methods: This study was conducted on patients who were undergoing induction of labor with Dinoprostone (PGE2) gel at The Institute of social obstetrics, Government Kasturba Gandhi Hospital, Madras Medical College, Triplicane, Chennai, and Tamil Nadu during the academic year 2016-17. The study was done in 100 patients for duration of 1 year.
Study Designs: Prospective observational study. Sample size: 100
Results: 60% of the study populations are in the age group of 21 to 28 year.
33% pregnant women had vaginal pH >4.5.
66% women were primigravidae, while the remaining 34% are multigravidas.
Among 32 cases of draining P.V. vaginal pH >4.5 is seen in 20 cases, i.e. 62.5%.Among 100 cases of PGE2 gel induction, 83.7% cases show positive Bishops score changes after 6 hour of induction in pregnant women with higher vaginal pH of >4.5.If vaginal pH is >4.5, it was found that the time interval between gel to delivery is reduced to <12 hours in 77% of cases.
Conclusion: we can see that assessing vaginal pH before induction can be an useful parameter in predicting the outcome of labour in pregnant women who are undergoing labour induction with PGE2 gel. However further research with a well designed pharmacological study with bigger study population is necessary to study the role of vaginal pH in absorption and overall efficacy of Dinoprostone gel which in future could increase the efficacy and reduce unwanted outcomes.

Keywords: vaginal ph on dinoprostone gel, cervical ripening / labor induction

Introduction
Induction of labor is the artificial initiation of labor before its spontaneous onset by means of various interventions. Now a days, about 10-30% obstetric cases required induction due to various indications. There are many surgical and medical methods available for induction of labor/cervical ripening. Of these cervical ripening using Prostaglandin Gel intracervically is most common practice in modern times. Prostaglandin gel is not only effective in cervical ripening, but also effective in activating myometrial contractility. There are many formulations available for Prostaglandin E2 for local administration, including vaginal tablets, endocervical gels, and vaginal gels and also in the form of slow release dinoprostone vaginal insert forms.
Cervical ripening is a process in which cervix becomes soft and distensible to allow labor and delivery. The tissue in cervix consists of only few smooth muscle cells and most of it is collagen bundles surrounded by proteoglycans.

In pregnancy nearing term many factors induces enzymatic changes for e.g. collagenase in cervix resulting in breakdown of collagen fibers and rearrangements of extracellular matrix that cause cervix to be soft and distensible also known as cervical ripening.

There are agents that can induce these changes artificially if it has not occurred yet. At the level of internal os most of the remodeling occurs. The collagenase which is found in cervix is derived from neutrophils and the invading neutrophils play an important role in tissue remodeling in cervix. Collagenase is present in specific granules inside neutrophils. Variety of cytokines like IL-8 causes degranulation of these specific granules in neutrophils and so release of collagenase in the substance of cervix. This dual action of IL-8 by recruiting neutrophils and then exciting it is very powerful in initiating cervical ripening.

Prostaglandin is a well-established agent that acts synergistically with IL-8 in recruiting neutrophils. Also cervix can produce nitric oxide, an ultra-short acting free radical that act as an endogenous ripening substance through unknown mechanism. Nitric oxide and prostaglandin are the two pathways that cross activate each other and can bring the series of changes responsible for cervical ripening.

Prostaglandin induction also result in decrease in sulfated Glycosaminoglycan's leading to decrease in electrostatic interaction that would weaken interfibrillar interactions, so decrease in cervical resistance. Matrix Metalloproteinase i.e. MMP-2 and MMP-9 has also found to be a factor responsible for cervical ripening. So, the complex interaction among many cytokines brings profound changes in proteoglycans in the cervix that ultimately cause cervical ripening. Many studies were conducted on the safety and efficacy of various prostaglandin E2 preparations. But only few studies were done on the factors that affect the clinical efficacy of these vaginally administered PGE2 preparations. Generally vagina maintains a acidic pH of 3.8 -4.8 which is also influenced by many factors for example parity, frequency of coitus, presence of cervical mucus, vaginal transudate, lower genital tract infection, rupture of membrane, douching etc. The lactobacillus bacteria present in vagina plays an important role in maintaining acidic vaginal PH by producing lactic acid from glycogen store in vaginal cells. The acidity of vagina may be responsible for variable release of PGE2 gel in the vagina and responsible for variable clinical response among patients.

Prostaglandin E2 gel is an organic acid which has low solubility in aqueous solution with low pH. The aim of this study is to evaluate whether vaginal PH has any effect on Dinoprostone gel used for cervical ripening in labor induction.

Aim

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Materials and Methods

This study was conducted on patients who were undergoing induction of labor with Dinoprostone (PGE2) gel at The Institute of social obstetrics, Government Kasturba Gandhi Hospital, Madras Medical College, Triplicane, Chennai, and Tamil Nadu during the academic year 2016-17. The study was done in 100 patients for duration of 1 year.

Study Designs

Prospective observational study. Sample size: 100

Results

Table 1

Vaginal PH		Age Group					Total
		18-20 years	21-24 years	25-28 years	29-32 years	33-36 years	
<4.5	Count	15	19	14	7	2	57
	% within Vaginal PH	26.3%	33.3%	24.6%	12.3%	3.5%	100.0%
>4.5	Count	7	14	12	7	3	43
	% within Vaginal PH	16.3%	32.6%	27.9%	16.3%	7.0%	100.0%
Total	Count	22	33	26	14	5	100
	% within Vaginal PH	22.0%	33.0%	26.0%	14.0%	5.0%	100.0%

Chi-Square=2.102 p= 0.717 (no association). There is no statistical significance exists between Vaginal PH <=4.5 and >4.5 with respect to different age group.

Table 2: Crosstab

Vaginal PH		Change In Bishops Score After 6 hr#		Total
		No	Yes	
<4.5	Count	37	20	57
	% within Vaginal PH	64.9%	35.1%	100.0 %
>4.5	Count	7	36	43
	% within Vaginal PH	16.3%	83.7%	100.0 %
Total	Count	44	56	100
	% Within vaginal PH	44.0%	56.0%	100.0 %

Chi-Square=23.527** p<0.0001 (association). There is statistical significance exists between Vaginal PH <=4.5 and >4.5 with respect to change in bishop score after 6 hours.

Table 3: Crosstab

Vaginal ph		Gel to vaginal Delivery interval		Total
		<12 hrs	>12 hrs	
<4.5	Count	9	9	18
	% within Vaginal PH	50.0%	50.0%	100.0%
>4.5	Count	24	7	31
	% within Vaginal PH	77.4%	22.6%	100.0%
Total	Count	32	33	16
	% within Vaginal PH	65.3%	67.3%	32.7%

Chi-Square=3.893* p= 0.048 (association). There is statistical significance exists between Vaginal PH <=4.5 and >4.5 with respect to Gel to vaginal delivery interval.

Table 4: Crosstab

Vaginal PH		Outcome		Total
		Vaginal	Cesarean	
<4.5	Count	18	39	57
	% within Vaginal PH	31.6%	68.4%	100.0%
>4.5	Count	31	12	43
	% within Vaginal PH	72.1%	27.9%	100.0%
Total	Count	49	51	100
	% within Vaginal PH	49.0%	51.0%	100.0%

Chi-Square=16.099** p<0.0001 (association). There is statistical significance exists between Vaginal PH <=4.5 and >4.5 with respect to Vaginal and caesarean delivery.

Table 5

Vaginal PH		Draining P.V		Total
		Yes	No	
<4.5	Count	20	37	57
	% within Vaginal PH	35.1%	64.9%	100.0%
>4.5	Count	30	13	43
	% within Vaginal PH	69.8%	30.2%	100.0%
Total	Count	50	50	100
	% within Vaginal PH	50.0%	50.0%	100.0%

Chi-Square=11.7911** p<0.0001 (association). There is statistical significance exists between Vaginal PH <=4.5 and >4.5 with respect to Draining.

Discussion

In the present study, we have found out that vaginal pH play a very important role in predicting success of PGE2 gel induction.

60% of the study populations are in the age group of 21 to 28 year. 33% pregnant women had vaginal pH >4.5. 66% women were primigravidae, while the remaining 34% are multigravidas.

In the study, we have not seen much influence of age and parity to the level of vaginal pH. Among 32 cases of draining P.V. vaginal pH >4.5 is seen in 20 cases, i.e. 62.5%.

Among 100 cases of PGE2 gel induction, 83.7% cases show positive Bishops score changes after 6 hour of induction in pregnant women with higher vaginal pH of >4.5.

If vaginal pH is >4.5, it was found that the time interval between gel to delivery is reduced to <12 hours in 77% of cases.

Conclusion

The findings of the present study showed that vaginal pH can be an important predictor for success of PGE2 gel induction. It has been observed that if vaginal pH is high there is better chance of positive Bishops score change, higher chance of vaginal delivery interval and also reduced time to enter into active phase of labour and shorter delivery interval more so in multipara.

Higher vaginal pH has more chance of responding fast to single gel induction and higher chance of vaginal deliveries than caesarean section.

So, we can see that assessing vaginal pH before induction can be an useful parameter in predicting the outcome of labour in pregnant women who are undergoing labour induction with PGE2 gel. However further research with a well designed pharmacological study with bigger study population is necessary to study 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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