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Study on influence of vaginal pH on efficacy of dinoprostone gel for labour induction

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Abstract
Background: Induction of labour is one of the common interventions practiced in modern obstetrics. Overall, throughout the world, up to 20 percent of women have labour induced by one method or the other. Induction is indicated before the spontaneous onset of labour when the benefit to the mother or fetus is perceived to outweigh continuation of pregnancy.
Vaginal pH may be one such factor that may influence the efficacy of prostaglandins for cervical ripening /labour induction. Vaginal pH may alter PGE2 release from the delivery vehicle, alter PGE2 absorption or metabolism and modulate prostaglandin activity in the cervico vaginal environment, thus altering its clinical efficacy.
Aims & Objectives: To compare the efficacy of Dinoprostone gel for labour induction in patients with vaginal pH < 4.5 and pH >4.5.
2. To improve the patient selection for PGE2 gel induction which would reduce the incidence of failed induction and unwanted outcomes.
Materials Methods: After obtaining clearance from the hospital ethical committee, this cohort study was undertaken in the Department of Obstetrics and Gynaecology at Government Kilpauk Medical College and Hospital, Chennai from October 2017 to March 2018. Written informed consent was obtained from the women explaining it to them in their language they best understand. This hospital based study included 54 antenatal women attending labour ward of Kilpauk Medical College and Hospital, Chennai.
Inclusion Criteria: Singleton pregnancy with vertex presentation, unfavourable cervix and no contraindication to vaginal delivery with reactive NST.
Exclusion Criteria
- Hypersensitivity to prostaglandins
- Premature rupture of membranes
- Placenta previa
- Previous cesarean delivery or a history of uterine surgery
- Major cephalo pelvic disproportion.

The sample size should be minimum of 27 for each group and so total sample size is 54.
Results: A total of 54 cases with unfavourable cervix were enrolled in this study. They were divided into 2 groups based on the vaginal pH. Out of 54 there were 27 cases in group 1 (vaginal pH <4.5) and 27 cases in group 2 (vaginal pH>4.5).
Conclusion: This shows that vaginal pH has significant effect on cervical ripening and Bishop score change and may lead to improved clinical efficacy of Dinoprostone gel. 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.

Keywords: influence, vaginal pH, dinoprostone, labour induction

Introduction
Induction of labour is one of the common interventions practiced in modern obstetrics. Overall, throughout the world, up to 20 percent of women have labour induced by one method or the other. Induction is indicated before the spontaneous onset of labour when the benefit to the mother or fetus is perceived to outweigh continuation of pregnancy. Induction rates vary with practices and cultural backgrounds.
The reasons for the rising rate of induction of labour can be complex and multifactorial. Some of them are
1. Improved ability of physicians to determine the gestational age accurately with dating scans, thus avoiding the possibility of iatrogenic prematurity.
2. Widespread availability of cervical ripening agents.

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1. Improved ability of physicians to determine the gestational age accurately with dating scans, thus avoiding the possibility of iatrogenic prematurity.
2. Widespread availability of cervical ripening agents.
3. Improved knowledge of methods and indications for induction.
4. Litigation constraints.

As induction of labour is a common intervention in obstetrics, and failed induction contributes significantly to cesarean sections. The success of induction depends largely on the state of the cervix which can be assessed with Bishop's Score. When the cervix is unfavorable, preinduction cervical ripening reduces the time required for induction and reduces cesarean delivery. Prostaglandins are the first choice for cervical ripening in comparison to oxytocin, since oxytocin mainly affects the uterine contractions and not the cervix directly.

Since the discovery of prostaglandins in the early 1970s, they have contributed significantly to the practice of obstetrics. Prostaglandins are almost produced by every tissue in the body and serve as important messengers or effectors in a wide variety of functions. Prostaglandins are important mediators of uterine activity and play a pivotal role in the contraction of smooth muscle of the uterus and the biophysical changes associatd with cervical ripening.

The prostaglandins E and F are most important for labour, delivery and the postpartum period. Among this Prostaglandin E series are relatively more uteroslective and more effective in cervical ripening.

Prostaglndin E2 soften the cervix, induce gap junctions and further sensitizes the myometrium to Oxytocin, leading to progressive cervical dilatation.

While a large body of evidence of evidence exists documenting the clinical efficacy of these agents for cervical ripening and labour induction, only few studies have characterized the factors that influence the relative clinical efficacy of these prostaglandin preparations.

Vaginal pH may be one such factor that may influence the efficacy of prostaglandins for cervical ripening /labour induction. Vaginal pH may alter PGE2 release from the delivery vehicle, alter PGE2 absorption or metabolism and modulate prostaglandin activity in the cervico vaginal environment, thus altering its clinical efficacy.

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Inclusion criteria

Singleton pregnancy with vertex presentation, unfavourable cervix and no contraindication to vaginal delivery with reactive NST.

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The sample size should be minimum of 27 for each group and so total sample size is 54.

Results

Table 1: Comparison of labour outcomes

Change in bishop score over 12 hours	Group I	Group II
Mean	2.41	6.37
SD	1.01	0.97
p Value by 't' Test	<0.001	

The difference between the mean of change in Bishop score over 12 hours between the group I (2.41) and group II (6.37) was statistically significant($p<0.001$).

Table 2: Comparison of time for active labour:

Time for Active Labour	Group I	Group II
Mean	21.13	11.04
Sd	1.42	0.93
P Value By 'T' Test	<0.001	

The difference between the mean of time to entry into active labour between group I (21.13) and II (11.04) was satistically significant ($p<0.001$).

Table 3: Comparison of Augmentation required between two groups.

Augmentation Required (%)	Group I	Group II
Yes	23	5
No	4	22
P Value By 'T' Test	<0.001	
Odds Ratio	0.04 (0.01-0.17)	

The difference between need for augmentation between group I (23) and II (5) was satistically significant ($p<0.001$).

Table 3.1: Induction Delivery Interval.

Induction Delivery Interval	Group I	Group II
Mean	27.24	15.2
Sd	0.58	1.03
P Value By 'T' Test	<0.001	

The difference between the mean of induction to delivery interval between group I (27.24) and group II (15.2) was statistically significant ($p<0.001$).

Table: 4: Comparison of mode of delivery

Mode Of Delivery	Group I	Group Ii
Vaginal	9	23
Lscs	18	4
Total	27	27
P Value By X2 Test	0.0001	
ODDS Ratio (95% CI)	11.5 (3.04-43.46)	

The above table shows comparison of mode of delivery between the two groups. Group II had higher rate of vaginal delivery when compared to group.

Table 5: Comparison of Fetal Complications

Neonatal Hyperbilirubinemia	Group I	Group II
Yes	1	3
No	26	24
P Value By 'T' Test	0.2987	
Odds Ratio (95 % Ci)	0.31(0.03-3.16)	

The difference between the two groups was statistically insignificant (p=0.2987).

Table 6: Comparison of Apgar @ 5 Minutes

Apgar <7 @ 5 Minutes	Group I	Group II
Yes	1	1
No	26	26
Fisher Exact P Value	0.509	

The difference between the two groups was statistically insignificant (p=0.509)

Table 7: Comparison of maternal complications

Puerperal Pyrexia	Group I	Group Ii
Yes	1	0
No	26	27
Fisher Exact P Value	0.5	

The difference between the two groups was statistically insignificant (p=0.5)

Table 8: Postpartum Hemorrhage.

Postpartum Hemorrhage	Group I	Group II
Yes	0	2
No	27	25
Fisher Exact P Value	0.245	

The difference between the two groups was statistically insignificant (p=0.245).

Discussion

A total of 54 cases with unfavourable cervix were enrolled in this study. They were divided into 2 groups based on the vaginal pH. Out of 54 there were 27 cases in group 1 (vaginal pH <4.5) and 27 cases in group 2 (vaginal pH>4.5).

Table 9: Baseline Characteristics

Baseline Characteristics					
Characteristics	Group I		Group Ii		P Value By 'T' Test
	Mean	Std. Deviation	Mean	Std. Deviation	
Age (years)	25.11	3.38	25.07	3.86	0.97
Gestatinal age (weks)	39.13	1.28	39.25	1.27	0.727
Gravida(no)	1.48	0.64	1.67	0.83	0.364
Initial Bishop score	1.41	0.5	2.3	0.95	<0.001

Baseline characteristics were shown in table.1. There was no statistically significant association between the two groups with respect to maternal age, gestational age, gravidity.

The difference between the mean initial Bishop score was found to be statistically significant between the two groups (p<0.001).

Table 10: Labour Outcomes

Labour Outcomes					
Outcomes	Group I		Group Ii		P Value By 'T' Test
	Mean	Std. Deviation	Mean	Std. Deviation	
Bishop score change over 12 hours	2.41	1.01	6.37	0.97	<0.001
Time to active labour(hours)	21.13	1.42	11.04	0.93	<0.001
Augmentation required (%)	85.18%		18.51%		0.364
Induction delivery interval(hours)	27.24	0.58	15.2	1.03	<0.001

Comparison of labour outcomes between the two groups is shown in Table. 2. The Bishop score change over 12 hours, time to active labour, need for augmentation, induction delivery interval was significantly different between the two groups.

Out of 54 cases, 23 (85.18%) required augmentation with oxytocin belonged to group I and 5 (18.51%) belonged to group II. Out of the 26 cases who did not require augmentation 4 (14.81%) belonged to group I and rest 22 (81.48%) belonged to group II.

Table 11: Mode of Delivery

Mode Of Delivery	Group I	Group II	Total
Vaginal	9 (33.33%)	23(85.18%)	32(59.25%)
Lscs	18(66.66%)	4(14.81%)	22(40.74%)
Total	27(100%)	27(100%)	54(100%)
P Value By X2 Test	0.0001		
Odds Ratio (95% Ci)	11.5 (3.04-43.46)		

Table 3 shows comparison of mode of delivery between the two groups. Out of 54 cases, 32 (59.25%) had vaginal delivery of

which 9 (33.33%) belonged to group I and 23 (85.18%) belonged to group II. 22 (40.74%) had cesarean section of which 18 (66.66%) belonged to group I and 4 (14.81%) blonged to group II. Group II had higher rate of vaginal delivery when compared to group I.

Table 12: Maternal Complications

Maternal complications				
	Group I	**Group Ii**	**Total**	**P Value (Fisher Exact)**
Puerperal Pyrexia	1(3.7%)	0(0%)	1(1.85%)	0.5
Postpartum Hemorrhage	0(0%)	2(7.4%0	2(3.7%)	0.245

Table (4) shows the distribution of maternal complications between the two groups. There were totally 3 cases of postpartum maternal complications. Out of 54 cases, there was 1 (3.7%) case of puerperal pyrexia which was due to breast engorgement belonged to group I. There was 2 (7.4%) cases of postpartum hemorrhage, both of which belonged to group II.

Table 13: Neonatal complications

Neonatal complications				
Neonatal complications	**Group I**	**Group Ii**	**Total**	**P Value (Fisher Exact)**
Neonatal Hyperbilirubinemia	1(3.7%)	3(11.11%)	4(7.4%)	0.2987
Apgar Score <7 At 5 Mins	1(3.7%)	1(3.7%)	2(3.7%)	0.509

Table 5 shows distribution of neonatal complications between the two groups. There were totally 6 neonatal complications.

Out of 54 cases, there was 1 (3.7%) case of neonatal hyperbilirubinemia belongd to group I and 3 (11.11%) cases belonged to group II. Out of the 50 cases who did not develop neonatal hyperbilirubinemia, 26(96.29%) cases belonged to group I and 24 (88.88%) cases belonged to group II.

Out of 54 cases, there was 1 (3.7%) case of 5 min APGAR score <7 belonged to group I and the other 1 (3.7%) belonged to group II. Out of the 52 cases, who had an APGAR score >7, 26 (96.29%) cases belonged to group I and, 26 (96.29%) cases belonged to group II.

The difference between the two groups was statistically insignificant (p >o.o5).

Conclusion

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

Patients with higher vaginal pH has better change of Bishop's score (mean - 6.37, p value <0.001).

The duration of time to active labour was found to be shorter (mean -11.04, p value <0.001) in patients with higher vaginal pH.

The induction delivery interval (mean-15.2, p value<0.001) was also found to be shortened with higher vaginal pH.

Patients with higher vaginal pH is associated with more number of vaginal deliveries (85.18%) than LSCS (14.81%).

This shows that vaginal pH has significant effect on cervical ripening and Bishop score change and may lead to improved clinical efficacy of Dinoprostone gel. 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.

Further research is required to find various agents that would increase the vaginal pH thereby creating a favorable environment for PGE2 gel induction.

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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