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Original Research Article

A comparative study of single versus multiple instillations of intravaginal PGE2 gel for induction of labour

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ABSTRACT

Introduction: The aim of induction is to achieve successful vaginal delivery where continuation of pregnancy is not desirable. Unfavourable cervix is one of the main causes of failed induction. Introduction of prostaglandins has revolutionised the scenario of cervical ripening. More than one dose of Prosta glandin E2 (PGE2) gel may be necessary to facilitate cervical ripening and increase the chances of vaginal delivery.
Materials and Methods: This retrospective study was done to find the efficacy of multiple instillations of intravaginal Prostaglandin E_2 gel and to compare the maternal and fetal outcome between the single instillation group and multiple instillation group. The women who went into labour or achieved cervical ripening with a single instillation of Prostaglandin E_2 gel forms Group A. Those who required more than one instillation of prostaglandin E_2 gel forms Group B. Both groups were compared for specific parameters.
Results: Primigravidas required multiple instillations. Postdated pregnancy was the most common indication for Induction of Labour. 45.2% of primis had only single dose and 54.8% required multiple doses. About two third (77.8%) of multipara required only one dose and a third of multipara needed multiple doses. In Group A 90.7% had vaginal delivery, 9.3% had Caesarean section. Group B 95.7% had vaginal delivery and 4.3% had Caesarean section.
Conclusion: Though PGE2 0.5mg gel is recommended to be used intracervically, it is equally effective intravaginally. Three doses of intravaginal PGE2 can be safely used without the risk of uterine hyperstimulation. There is no increased fetal risk with multiple instillations of intravaginal PGE2 gel.

1. Introduction

Induction of labour has become an integral part of modern Obstetrics. The aim of induction is to achieve successful vaginal delivery where continuation of pregnancy endangers the life or wellbeing of the mother or the fetus. The infant should be born in good condition with less trauma within acceptable time frame and with least maternal complications. It is not possible to achieve 100% success when labour is induced. Several factors influence the outcome. Unfavourable cervix is one of the main causes of failed induction. In order to overcome this, cervix should be ripened. The physical and biochemical changes in the uterine cervix resulting in its softening and dilatation are recognized as cervical ripening. It is well recognized that induction of labour is more successful when attempted with a well ripened cervix.

Induction of labour in an unripe cervix is associated with frequent maternal complications and leads to induction failure in upto 20-50% and associated with high rates of Caesarean delivery.[1] Even when vaginal delivery is achieved these patients often have prolonged labour, with high incidence of instrumental delivery and fetal asphyxia.

In an attempt to ripen the cervix various pharmacological and physical agents have been evaluated such as breast stimulation, amniotomy, oxytocin infusion, estrogen gel, mechanical and electrical devices and local and systemic Prostaglandins. Introduction of Prostaglandins has revolutionised the scenario of cervical ripening. Several published studies have reported significant improvement of Bishop score, more vaginal deliveries, shorter duration of labour and fewer caesarean deliveries without affecting the

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neonatal outcome.[2,3]

Local use of prostaglandin E2 (PGE2) by extra-amniotic, intravaginal and intracervical route has been found to be effective in priming the cervix and inducing labour in patients at term with poor Bishop score. The recommended routes of application of Prostaglandins ($PGE_{2)}$ are intracervical and intravaginal as these have been reported to be most advantageous in terms of increased efficacy and diminished side effects.[4,5] A single dose PGE_2 of 0.5 mg has been found to be superior to placebo in ripening the cervix. However if the ripening effect is insufficient, failure of induction and caesarean rate are nearly as high as when the cervix has been ripened with placebo.[6] Various authors have reported success rates ranging from 83% to 90%.[7] The patients where attempts at cervical ripening failed often had failed induction. Multiple instillations (upto 4 doses) of Prostaglandin gel in patients who do not respond to one dose have been shown to increase the rates of vaginal delivery and decrease the Caesarean section rate.

Extra-amniotic use, besides being invasive is associated with increased risk of introducing infection. The intravaginal application though less invasive and easy to use requires larger dose of the drug and hence associated with gastrointestinal side effects and uterine irritability.[8] Besides its action is unpredictable and result often unsatisfactory. The intracervical use has fewer side effects.

Intravaginal application requires larger dose than intracervical dose and thus associated with side effects. However intracervical application has draw backs. The patient has to be in lithotomy position, necessitates using of instruments to visualize the cervix and there is risk of accidental placement of the gel into extraamniotic space. Intravaginal application is easy and causes less discomfort to the patient.

The present study is designed to see if multiple instillations of intravaginal prostaglandin E_2 0.5mg gel will improve the success of induction of labour and to compare the maternal and fetal outcome between the single instillation group and multiple instillation group.

2. Aims and Objectives

1. To evaluate the efficacy of instillation of more than one dose of intravaginal prostaglandin E_2 gel in cervical ripening.
2. To compare the maternal and fetal outcome between patients who had single instillation and multiple instillations.
3. To study the adverse effects, if any of multiple instillations of intravaginal prostaglandin E_2 gel.

3. Materials and Methods

It is a retrospective study. This study was conducted in the Department of Obstetrics and Gynaecology, SVS Medical College, Mahabubnagar. One hundred patients, who had induction of labour were included in this study after applying the following inclusion and exclusion criteria.

The inclusion criteria were:

Singleton pregnancy.

Vertex presentation.

Gestational age greater than or equal to 34 completed weeks.

Bishop score less than or equal to 6.

The exclusion criteria were:

Bishop score >6.

Previous uterine scar.

Non vertex presentation.

Medical conditions like glaucoma or asthma.

Antepartum haemorrhage.

3.1. Procedure

An informed consent was taken. All the patients were administered 0.5 mg prostaglandin gel intravaginally. The commercially available gel in a prefilled syringe (cerviprime) that contains 0.5mg of Prostaglandin E_2 in a 3 gmtylose base was used for all the patients. After administering the gel into the posterior fornix under aseptic conditions the woman was kept on the bed for 30 minutes and was observed for contractions, rupture of membranes, bleeding or foetal heart rate changes.

After 6 hours, if the patient had not gone into labour, a reassessment of the cervical status was done. If the Bishop score was less than 6, another instillation of intravaginal gel was done. Again the patient was assessed after 6 hours. This procedure was done either till onset of labour, change of Bishop score to 6 or more or till 3 instillations of prostaglandin gel. If labour did not occur spontaneously and Bishop score was 6 or more, oxytocin induction/augmentation was done if necessary.

The patients who went into labour or achieved cervical ripening with a single instillation of prostaglandin E_2 gel forms Group A. Those who required more than one instillation of prostaglandin E_2 gel forms Group B. Initial Bishop Score, change in score with each instillation of prostaglandin gel, onset of spontaneous labour, mode of delivery, side effects of prostaglandin and maternal and foetal complications were noted. The details obtained were used to compare between the groups A & B.

The data was analyzed using SPSS software version 17.0. Appropriate statistical tests were used to determine the efficacy of instillation of intra vaginal prostaglandin E_2 gel. Descriptive results are expressed as mean and SD of various parameters in different groups. Probability value (p value) was used to determine the level of significance p

value < 0.05 was considered as significant, p value < 0.01 was considered as highly significant.

4. Results

Out of 100 cases studied, there were 54 women who had single instillation and 46 women had more than one dose instilled. The majority of the women in both the groups were between 21-25 years of age. The mean age of the patients in the both groups was not significantly different from each other. There was no statistically significant deference in pattern of distribution of patients based on age group. Primis were 73 and multiparous were 27. Out of 73 primigravid women, 45% had single instillation and 55% had multiple instillation. It was observed that there were significantly more primi gravid patients i n Group B compared to group A p <0.05.

Out of 27 multi parous patients 21 patients (77.8%) required single instillation compared to 45.2% primi parous patients. Among multiparous women 21 (77.7%) required single instillation compared to 6 (22.3%) which is statistically significant.

The period of gestation was similar in both the groups. About 75% of patients in both the groups were between 40 and 42 weeks. The most common indication for induction of labour in both the groups was post dated pregnancy followed by Pregnancy induced Hypertension.

No of intravaginal PGE2 instillations: Among Primis, 45.2% had one dose, 37% had two doses and 17.8% had 3 doses. 77.8% of multipara had single instillation which is statistically significant compared to Primis and rest of the multiparous women equally had two and three doses.

The initial bishop score and the mean change in bishop score was analysed after single, two and three instillations of PGE2 gel and the percentage of patients who went into spontaneous labour was calculated for both primis and multis. 43 patients (79.6%) had spontaneous labour after single instillation, 21 patients (70 %) had spontaneous labour after two instillations and 14 patients (87.5%) after three instillations.

Mean change in bishop score was compared using ANOVA there was significantly higher mean change in bishop score after three instillations compared to one p =0.010. Multiple comparison ANOVA was done to compare the mean initial and change in bishop scores between primi and multi patients who required one, two or three doses, statistically significant observations were noted. Multiparous patients who required single dose had a higher mean initial bishop score comapared to primi patients who required one dose (p = 0.007), two dose (0.004) and three dose (0.002). Mean Change in Bishop score was significantly more primi patients who required three doses compared to primi patients with single instillation (p=0.001) and primi patients with two instillations (p = 0.028). multi patients with single instillation Mean Change in Bishop score was significantly more than primi patients with single instillation p = (0.008).

In Group A 61% of women received Oxytocin augmentation and in Group B 76% had Oxytocin. More than 90% of women in both groups had vaginal delivery and 9.3% in Group A, 4.3% in Group B underwent Caesarean section. Complications noted were premature rupture of membranes in both groups 11.1%, 4.3% and hyperstimulation in 1.9% and 2.2%. Fetal distress, Cephalo pelvic Disproportion and Non progression of Labour were the indications for Caesarean section.

The mean birth weight in group A was 2.8 ± 0.47 compared to 2.67 ± 0.34 in group B, there was no significant difference in mean birth weight in either groups, p >0.05. There was no significant difference in the mean interval in hours between primi and multi para in either group one or two p >0.05. there were no significant fetal/neonatal complications.

5. Discussion

Intravaginal instillation of PGE_2 gel has been accepted as a useful method of cervical ripening before induction of labour.[4,5] The dose required is much less and the side effects are often acceptable.[2,4,5]

A single application of PGE_2 gel has been reported to be successful in 83% to 96% of cases. Successful use includes both spontaneous onset of labour and improvement in Bishop score.[7] However in about 5% to 25% of patients, a single application may not achieve spontaneous labour or cervical ripening. These patients may end as failed inductions if labour is induced with oxytocin as such. Several workers have attempted to use multiple instillations to overcome the problem of failure with single instillations.[9–12] Hence in our institution we undertook this study to assess the efficacy of using multiple instillation of intravaginal PGE_2 gel instead of intracervically.

We attempted to compare our results with the studies where PGE2 gel was used intracervically as no study has been done with 0.5mg gel. Use of 3 or 4 mg of PGE2, although effective, has been reported to be accompanied by uterine hypertonus or fetal heart changes. Lower dose of PGE2 at 0.2 mg and 0.4 mg do not have the above-mentioned side effects but necessitate multiple applications. Chatterjee MS et al found that using 2 mg of PGE2 single dose intravaginally as a safe method of cervical ripening prior to induction of labor.$

Prolonged pregnancy was the commonest indication for induction in our study 76%, Bhatla et al,[12] had prolonged pregnancy in 36.25% and Mainprize et al[10] in 40%, Norchiet al[11] in their series had only 10% of induction for prolonged pregnancy. In our study most of our patients either had spontaneous labour or achieved a ripe cervix within 3 instillations of PGE_2 gel. This was similar to the finds of other studies[10–12] where PGE2 gel was used

Table 1: Spontaneous labour after PGE 2 gel instillation (In percentage)

Study		**1 st dose**	**2 nd dose**	**3 rd dose**
Prins et al (1986)		41.5	29	5.9
Mainprize et al (1987)		38	27.7	40
Norchi et al (1992)		32.2	45.2	81.8
Puliyat Geetha (2011)		36.8	50	13.04
Present study	Group A	37	-	-
	Group B	-	22	26.7

Table 2:

		Group-A		**Group B**	
		Number	**%**	**Number**	**%**
Age group in years	<20	16	29.6	11	23.9
	21-25	32	59.3	30	65.2
	26-30	5	9.3	4	8.7
	31-35	1	1.9	0	0
	> 35 yrs	0	0	1	2.2
	Total	54	100	46	100
Parity	Primi	33	61.1%	40	87
	Multi	21	38.9	6	13
Gestational age in wks	34-36	5	9.3	6	13
	37-39	8	14.8	5	10.9
	40-42	41	75.9	35	76.1

Table 3: Indication for Induction of labour

Indications	**Group A**		**Group B**	
	No	**%**	**No**	**%**
Post dated	41	75.9	35	76.1
Pregnancy induced hypertension	7	13	7	15.2
Premature rupture of membranes	3	5.6	2	4.3
Oligohydramnios	3	5.6	0	0
Intrauterine growth retardation	0	0	2	4.3
Total	54	100	46	100
Chi square	5.066	p value		0.281

Table 4: Number of intravaginal p rostaglandin instillations

No. of Instillations	**Primi**		**Multi**	
	No	**%**	**No**	**%**
One	33	45.2	21	77.8
Two	27	37	3	11.1
Three	13	17.8	3	11.1
Total	73	100	27	100
Chi square	8.82	P value		0.012

Table 5: Initial Bishop Score and outcome after instillation

	One dose (n=54)		**Two doses (n=30)**		**Three doses (n=16)**	
	Primi (n = 33)	**Multi (n = 21)**	**Primi (n = 27)**	**Multi (n = 3)**	**Primi (n = 13)**	**Multi (n = 3)**
Mean Initial bishop score	2.54	3.09	2.48	3	2.3	2.6
Mean Change in Bishop score	6.27	7.9	7.01	8.67	8.7	8
Spontaneous labour	28 (84.8%)	15 (71.4%)	19 (70.4%)	2 (66.7%)	11 (84.6%)	3 (100%)

Table 6: Comparison of mode of delivery

Mode of delivery	Group A		Group B	
	No.	%	No.	%
vaginal delivery	49	90.7	44	95.7
LSCS	5	9.3	2	4.3
Chi square	2.08		P value	0.354

Table 7: Comparison of mean interval in hrs based on parity in both groups

	Interval in hours			
	Mean	SD	t value	p value
Primi (grp 1)	18.56	5.09	1.1	0.274
Multi (grp 1)	17.02	4.79		
Primi (grp 2)	20.6	4.13	0.1	0.921
Multi (grp 2)	20.4	4.4		

intracervically.

A significant percentage of patients developed spontaneous labour with sequential intravaginal PGE_2 gel instillation.

Our study showed a significant difference between initial Bishop Score and post instillation score. Similar findings were observed by Mainprize et al[10] (1987), Norchi et al[11] (1992), Bhatla et al[12] (1997) and Puliyat Geetha[13] (2011). But Prins et al[9] (1986)opined that sequential gel application was no more effective than single application followed by an equal period of observation. In our study, prelabour rupture of membranes was the main complication observed. This was not reported by other workers. Norchi et al[11] (1992) observed hyperstimulation of uterus in 2.2% of patients. This was observed in 1.9% and 2.2% in both groups respectively in our study. Prins et al[9] (1986) did not have any case of hypertonus in their patients. Prins et al opined that hypertonus is usually seen with very ripe cervix (Bishop Score $>$ 8) or in grand multipara. About 60% of caesarean sections in our study were for fetal distress. Mainprize et al[10] (1987) and Bhatla et al[12] (1997) reported cesarean section for fetal distress in 33.3% of their patients. About 3% of the new borns in our study had APGAR less than 7. The incidence of asphyxia was not affected by multiple instillations of gel. Bhatla et al (1997)[12] found no infant to have APGAR score of less than 7 out of their 80 patients.

6. Conclusion

PGE2 0.5mg gel is recommended to be used Iintracervically. The dose required for vaginal use is higher and is known to cause uterine hyperstimulation and fetal heart rate abnormalities. In the present study PGE2 0.5mg gel is used intravaginally and found to be very effective for cervical ripening. Multiple instillations of gel was proven to have spontaneous labour mostly in primigravida more than Multiparous (P value significant) while in others Bishop score improved primis required more than one dose. The maternal risks like infection or hyperstimulation are not increased by multiple instillations. There is no increased fetal risk with multiple instillation and beneficial if used in appropriately selected cases.

7. Source of funding

None.

8. Conflict of interest

None.

References

1. Friedman EA, Niswander KR, Rivera BN, Sachleben MR. Relation of prelabour evaluation to inducibility and course of labor. *Obstet Gynecol*. 1966;28.
2. Sasikala A, Rani PR, Bhupathy RS, Endocervical A. PGE2 gel for cervical ripening before induction of labor - a preliminary report. *J Obstet Gynaecol Ind*. 1994;p. 379–383.
3. Bhattacharya SM. Study of use of PGE2 gel. *J Obstet Gynaecol Ind*. 1995;45:180–185.
4. Rayburn WF. PGE2 Gel for cervical ripening and induction of labor. *Am J Obstet Gynecol*. 1989;160:529–533.
5. Zanini A, Ghidini A, Norchi S. Beretta E and Bottinos Preinduction cervical ripening with PGE2 gel Intracervical Vs intravaginal route. *Obstet Gynecol*. 1990;76:681–683.
6. Bernstein P, Leyland N, Gurland P, Gare D. Cervical ripening and labour induction with PGE2 Gel. *Am J Obstet Gynecol*. 1987;156:336–340.
7. Noah ML, Decoster JM, Fraser TJ, Orr JD. Preinduction cervical ripening with endocervical PGE2 Gel. *Acta Obstet Gynecol Scand*. 1987;66:3–7.
8. Ekman G, Forman A, Marsl K, Ulmsten U. Intravaginal versus intracervical application of prostaglandin E2 in viscous gel for cervical priming and induction of labor at term in patients with an unfavorable cervical state. *Am J Obstet Gynecol*. 1983;147(6):657–61.
9. Prins RP, Neilson DR, Rn B, Mark III, Watson P. Pre Induction cervical ripening with sequential use of PGE2 ;.
10. Mainprize T, Nimrod C, Dodd G, Persuad D. Clinical utility of multiple dose administration of PGE2. *Am J Obstet Gynecol*. 1987;2:341–342.
11. Norchi S, Zanini A, Pollini A, Silva A. Cervical priming and labour induction by multiple dose of PGE2 Gel. *Int J Gynecol Obstet*. 1992;38:5–7.

12. Bhatla N, Verma A, Buckshee KA, K. Multiple dose intra cervical PGE2 Gel for cervical ripening. *J Obstet Gynaecol Ind*. 1997;p. 47–62.
13. Geetha P. Sponteneous Labour after PGE2. *Gel Middle East Fertil Soc J*. 2012;17(3):170–175.

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