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EFFICACY OF PROSTAGLANDIN E2 GEL IN THE INDUCTION OF LABOR AMONG PRIMIGRAVIDA AND MULTIGRAVIDA WOMEN

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ABSTRACT

Background and objectives*:* The use of an ideal inducing agent for cervical ripening is necessary to prevent adverse maternal and fetal outcomes. The present study aimed to assess the efficacy and safety of prostaglandin E2 (PGE2) in the induction of labor among primigravida and multigravida women at a hospital in Karad.

Materials and Method: A total of 110 primigravida and multigravida women were included in this observational study. Women were grouped into experimental and control groups with 35 primigravida mothers and 20 multigravida mothers each in both the groups. Subjects in the experimental group were subjected to intracervical application of PGE2.

Results: A significantly higher proportion ($p<0.001$) of women in the experimental group had poor Bishop scores. The most common complication responsible for labor induction was postdatism in primigravida (37.1%) and multigravida women (50%). The induction failure rate

was significantly low in primigravida (20%) and multigravida (5%) women who underwent PGE2 induction when in comparison with the control group. Mean duration from induction to delivery in primigravida was 9 hrs, 22 mins and 8 hr, 15 min in multigravida women. Nausea (primigravida=28.6%, multigravida=5%) and vomiting (primigravida=8.6%, multigravida=5%) were reported by significantly lesser number of primigravida and multigravida women in the PGE2 group

Conclusion: Prostaglandin E2 gel is effective in inducing labor in primigravida and multigravida women, with a shorter induction to delivery time, and low incidence of maternal and fetal adverse effects. Hence, prostaglandins can be routinely administered for smooth induction of labor in primigravida and multigravida women.

Keywords: Cervical ripening, Prostaglandin E2, Induced labor, Fetal outcome, Maternal outcome

INTRODUCTION

Labor induction has become an integral part of modern obstetrics and remains one of the main challenges in obstetrics **[1]**. It is the last resort when continuation of pregnancy may be hazardous to the fetus and mother **[2]**. The goal of modern obstetrics is to improve the safety of mother and fetus during the antenatal period as well as during parturition **[3]**.

The success of labor induction and subsequent vaginal birth is highly dependent on cervical ripening. For cervical ripening, various pharmacological and physical methods have been evaluated such as amniotomy, breast stimulation, oxytocin infusion, mechanical and electrical devices, estrogen gel, and various local and systemic prostaglandins **[4]**. Cervical ripening should be assessed before a regimen is selected. This assessment is accomplished by calculating the Bishop score. It is a pre-labor scoring system to assist in predicting whether labor induction will be required. Bishop score <6 recommends that cervical ripening agent is required for labor induction **[5]** .

Prostaglandin E2 (PGE2) has proved to be effective and safe for ripening of cervix and induction of labor at term **[6]**. It has also proved to improve Bishop scores and reduce induction to delivery duration in comparison to untreated controls **[7]**. The exact mechanism by which the PGE2 induces ripening of cervix is unknown, although PGE2 has demonstrated to regulate matrix metalloproteinases production providing the rationale for the use of PGE2 in pre-induction cervical ripening **[8]**. The human cervix usually has bundles of collagen fibers

which get easily split, separate and dissolve into more abundant ground substance after PGE2 therapy and thus facilitates further cervical ripening **[9]**.

Various studies conducted have proved the efficacy and safety of PGE2 for ripening of cervix and labor induction **[10]**. However, studies comparing the effect of PGE2 on labor induction between primigravida and multigravida women are limited. Therefore, the current study was conducted for the comparison of safety and efficacy of PGE2 in inducing labor between primigravida and multigravida women.

MATERIALS AND METHODS

This observational study was conducted in primigravida and multigravida mothers admitted to the labor ward at a tertiary care centre from October 2012 to November 2013. The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all the pregnant women meeting the study criteria. Sampling technique used for this study was non probability purposive convenient sampling also known as deliberate sampling.

A total of 110 primigravida and multigravida women were included in the study. Women with unripe cervix, postdatism, intrauterine growth restriction (IUGR), pregnancy induced hypertension (PIH), singleton pregnancy and patients consenting to take part in the study were divided into experimental (n = 55) and control (n = 55) groups with 35 primigravida and 20 multigravida mothers in each group. Women with preterm labor, twin pregnancy, any adverse systemic disease, or history of a surgery were excluded. Details regarding age, gravida, past medical history were recorded. Temperature, pulse, respiratory parameters, blood pressure, and edema were assessed. Per speculum/per vaginal examination was performed to calculate the Bishop score, which is a pelvic scoring system that evaluates cervical dilatation, effacement, station, consistency, and position. The scoring is done based on a provisional examination undertaken to predict the chances of normal delivery and Bishop score is mandatory during labor induction.

Nonstress test (NST) and ultrasound were performed for subjects in the experimental group. All the subjects in the experimental group were examined in the lithotomy position and with the help of Cusco's speculum the cervix was visualized. Prostaglandin E2 gel was applied from the internal os and around the cervix through a piston syringe and cannula. Cerviprime gel (manufactured by Astra IDL) containing 0.5

mg of prostaglandin E2 or dinoprostone for intracervical use were administered. The subjects were asked to lie down in the supine position for 30 min and fetal head station (FHS) was counted at 10 mins, 15 mins, and 30 mins. The mothers were advised liquid diet and ambulation. The control group received usual treatment whenever needed that is Oxytocin drip, instrumental delivery or sometime caesarean section. No NST was performed and no prostaglandin E2 gel was used for control group. A nonstress test is usually recommended when it's suspected that the baby is at an increased risk of death. However, as in control group no new intervention is used the NST could be skipped.

Subjects in both the groups were evaluated for the time elapsed since labor induction until onset of labor, time of dilatation of cervix and expulsion of fetus. Women were dispensed with pitocin to accelerate instrumental delivery or cesarean section. During delivery mothers were observed for perineal tear and supra-urethral tear. Baby was evaluated using the Apgar score and observed for respiratory distress and meconium aspiration.

Change in Bishop scores, induction failure rate, duration of 1^{st} and 2^{nd} stages of labor, mean duration of induction to delivery, maternal and fetal outcomes were recorded. Induction of failure was defined as the inability to achieve cervical dilatation >4 cm after 12 ± 3 h of administration of any labor inducer **[11]**.

Data was computed using statistical software R version 4.0.1. Chi-square test was employed to check the association between categorical variables. Fischer's exact test was applied when assumptions for Chi-square test were not met. Independent sample t-test and paired t-test were applied while comparing unpaired and paired quantitative data. $p < 0.05$ indicated statistical significance.

RESULTS

The mean age was 22.77±2.5 years in the experimental group which was not significantly different from the control group with 22.22±2.6 years in primigravida mothers. The mean age of multigravida mothers in the experimental group was 25.25±3 years and was not dissimilar from the mean age in the control group (24.25±3.1 years).

The complications reported in the primigravida women were postdatism (37.1%), PIH (37.1%), oligohydramnios (14.3%) an intra-uterine growth retardation (8.6%). The complications reported in multigravida women were postdatism (50%), PIH (25%), and oligohydramnios (20%).

Bronco spasm, diarrhea, postpartum hemorrhage (PPH), hyper stimulation, supraurethral tear, extension of episiotomy, cervical tear, puperal sepsis was not observed in both groups.

A significantly higher proportion of mothers with poor Bishop scores were observed in the experimental group in comparison to the control group in both primigravida ($p<0.001$) and multigravida mothers ($p<0.001$) **(Table 1)**. The induction failure rate was significantly higher in the control group in primigravida (71.42%, $p<0.001$) and multigravida women (35%, $p<0.05$) when compared to the experimental group **(Table 2)**.

The mean duration of first stage of labor ($p<0.05$) was shortened in the experimental group and the second stage

($p<0.01$) of labor was significantly prolonged in the primigravida women when compared to the control group. Duration of 1st and 2nd stages of labor between groups in multigravida women were observed to be insignificant **(Table 3)**.

Mean duration between induction and delivery in primigravida was 9 hrs, 22 mins. Whereas, in the multigravida women the mean duration between induction and delivery was 8 hrs, 15 mins.

Nausea (primigravida=28.6%, multigravida=5%) and vomiting (primigravida=8.6%, multigravida=5%) were reported by significantly lesser number of primigravida and multigravida women who underwent PGE2 induction when compared to the control group. No supraurethral or perineal tears were reported in primigravida women who underwent PGE2 induction while 50% of multigravida women reported perineal tear but significantly lesser than the control group (65%) **(Table 4)**.

Respiratory distress was observed in 3 (8.6%) babies and 2 (10%) babies from the control groups in primigravida and multigravida women, respectively. Meconium aspiration was seen in 6 babies (1 primigravida experimental group, 3 primigravida experimental group, 2 multigravida control group). However, none of the babies required NICU care **(Table 5)**.

Table 1: Results of chi-square test evaluating the association of Bishop score with PGE2 in primigravida and multigravida women

Bishop score	Primigravida women		Multigravida women	
	Experimental group n (%)	Control group n (%)	Experimental group n (%)	Control group n (%)
Good (6-13)	1 (2.86)	18 (51.43)	0 (0)	13 (65)
Poor (0-5)	34 (97.14)	17 (48.57)	20 (100)	7 (35)
p-value	$p < 0.001$*[C]		$p < 0.001$*[C]	

*C: Chi-square test; *p<0.05 considered statistically significant*

Table 2: Comparison of rate of induction failure between experimental and control group in primigravida and multigravida women

	Primigravida women		Level of significance*	Multigravida women		Level of significance*
	Experimental group	Control group		Experimental group	Control group	
Repeated induction	2 (5.71%)	0 (0%)		0 (0%)	0 (0%)	
Augmentation with oxytocin	3 (8.57%)	7 (20%)		1 (5%)	3 (15%)	
Instrumental delivery	0 (0%)	2 (5.71%)	p <0.001	0 (0%)	2 (10%)	p < 0.05
LSCS	2 (5.71%)	16 (45%)		0 (0%)	2 (10%)	
Total	7 (20%)	25		1 (5%)	7 (35%)	
		(71.42%)				

**Fischer's exact test, LSCS; Lower segment cesarian section*

Table 3: Comparison of duration of stages of labor between experimental and control groups in primigravida and multigravida women

Stages of labor	Primigravida women		Level of significanc e*	Multigravida women		Level of significanc e*
	Experimental group (M±SD)	Control group (M±SD)		Experimental group (M±SD)	Control group (M±SD)	
1st stage	6.05±2.44	7.417±3.26	t=1.99 p = 0.05	5.345±2.05	5.975±1.76	t=1.04 p = 0.30
2nd stage	33.31±16.27	21.714±21.24	t=2.56 p = 0.01	27.500±6.17	29.065±14.33	t=0.45 p = 0.65

** Independent sample t-test*

Table 4: Comparison of outcomes between experimental and control groups in primigravida and multigravida women

Variable	Primigravida women		p - value	Multigravida women		p - value
	Experiment n (%)	Control n (%)		Experiment n (%)	Control n (%)	
Nausea						
Present	10 (28.6)	19 (54.3)	0.03^{C}*	1 (5)	14 (70)	$<0.001^{C}$*
Absent	25 (71.4)	16 (45.7)		19 (95)	6 (30)	
Vomiting						
Present	3 (8.6)	15 (42.9)	0.001^{C}*	1 (5)	10 (50)	0.001^{C}*
Absent	32 (91.4)	20 (57.1)		19 (95)	10 (50)	
Perineal tear						
1°	0	1 (2.9)	1^{MC}	10 (50)	13 (65)	0.0555^{MC}
2°	-	-		0	3 (15)	
No	35 (100)	34 (97.1)		10 (50)	4 (20)	
Supra-urethral tear						
Present	0	1 (2.9)	1^{MC}	-	-	-
Absent	35 (100)	34 (97.1)		-	-	

*C – Chi square test, MC – Chi square test with Monte Carlo simulation *p<0.05 considered statistically significant*

Table 5: Comparison of fetal

Variable	Primigravida women		*p* - value	Multigravida women		*p* - value
	Experimental n (%)	Control n (%)		Experimental n (%)	Control n (%)	
Apgar Score @1 Min						
Good	**34 (97.1)**	**35 (100)**	**1^{MC}**	**20 (100)**	**19 (95)**	**1^{MC}**
Poor	**1 (2.9)**	**0 (0)**		**0**	**1 (5)**	
Apgar Score @5 Min						
Good	**34 (97.1)**	**35 (100)**	**1^{MC}**	**20 (100)**	**18 (90)**	**0.5002^{MC}**
Poor	**1 (2.9)**	**0**		**0**	**2 (10)**	
Respiratory Distress						
Present	**0**	**3 (8.6)**	**0.2459^{MC}**	**0**	**2 (10)**	**0.5002^{MC}**
Absent	**35 (100)**	**32 (91.4)**		**20 (100)**	**18 (90)**	
Muconium Aspiration						
Present	**1 (2.9)**	**3 (8.6)**	**0.2459^{MC}**	**0**	**2 (10)**	**0.5002^{MC}**
Absent	**34 (97.1)**	**32 (91.4)**		**20 (100)**	**18 (90)**	

outcomes between experimental and control group in primigravida and multigravida women; ***MC – Chi square test with Monte Carlo simulation***

DISCUSSION

Intracervical application of PGE2 gel has been widely accepted as an effective method of cervical ripening before labor induction. In the present study, the efficacy and safety outcomes of PGE2 gel in primigravida and multigravida women with complications such as unripe cervix, postdatism, intra-uterine growth restriction (IUGR), pregnancy-induced hypertension, and leaking were assessed.

The complications reported in the primigravida women were postdatism (37.1%), pregnancy-induced hypertension (37.1%), oligohydramnios (14.3%) an IUGR (8.6%). The complications reported in multigravida women were postdatism (50%), PIH (25%), and oligohydramnios (20%). The induction failure rate was lower in the group that underwent PGE2 gel induction as compared to control group **[9]**.

Deshmukh *et al* also reported similar results on successful labor induction with PGE2 gel in women with postdatism, IUGR and PIH **[12]**. Agrawal *et al* reported that higher percentage of mothers in the multigravida group required induction while in the current study we observed that higher number of primigravida women (20%) required induction when compared to multigravida women (5%) **[13]** .

The mean duration of first stage and second stage of labor was comparable between experimental and control groups in the multigravida group. Whereas mean duration of first stage was shortened and second stage c from the experimental group was significantly prolonged when compared to the control group. These findings are in

concurrence with the results by Ramaswamy *et al* that reported a second stage duration of 49 mins in the study group (p=0.01) as compared to 23.3 mins in the control group **[14]**. The prolonged second stage of labor in primigravida mothers could be attributed to the nulliparity, increased maternal weight, artificial induction of labor, increased birthweight, etc. **[13]**.

The mean duration from induction to delivery in primigravida and multigravida women was 9 hours, 22 mins and 8 hours, 15 mins, respectively. A study conducted by Najam *et al* reported a mean duration of induction to delivery as 11 hours, 2 minutes in the PGE2 administered group compared to 8 hours, 7 mins in the group receiving intravenous oxytocin. [15] Shorter duration from induction to delivery in the present study could be because of the use of intracervical application of PGE2 as opposed to vaginal insertion. Agrawal *et al* reported an induction to delivery time of 10-20 hours in 34% women (13/38) **[13]**. Samra *et al* reported an induction to delivery time of 12.18 hours **[16]**. Nausea (primigravida=28.6%, multigravida=5%) and vomiting (primigravida=8.6%, multigravida=5%) were reported by significantly fewer number of primigravida and multigravida mothers who experienced PGE2 induction in comparison to the control group.

No supraurethral or perineal tears were reported in primigravida women who underwent PGE2 induction while 50% of multigravida women reported perineal tear but was significantly lesser than the control group (65%). Similar results were reported by Najam *et al* where a lower incidence of maternal side effects with PGE2 gel were observed **[15]**. These results support the safe application of PGE2 for induction of labor with minimal maternal complications. Also, Samra *et al* reported no nausea and vomiting in women induced by PGE2 gel **[16]**. Dhillon *et al* reported fever and GI symptoms in 16% of women who experienced PGE2 induction **[17]**. No significant difference in the Apgar scores was observed between the experimental and control groups in the present study. These findings are in agreement with the studies by Samal *et al* and Ray *et al* that reported no adverse fetal outcomes **[18, 19]**.

The study reports good efficacy and safety outcomes of PGE2 gel use in inducing labor. However, as a result of the limited sample size of the present study, the results should be generalized with caution. Future studies should be carried out in larger samples.

CONCLUSION

Prostaglandin E2 gel is effective in inducing labor in primigravida and multigravida women, with a shorter induction to delivery time, and low rate of maternal and fetal adverse effects. Hence, prostaglandins can be routinely administered for smooth labor induction in primigravida and multigravida women.

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Conflicts of Interest: None

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