A Study of Intracervical PGE2 Gel for Cervical Ripening and Induction of Labour

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ABSTRACT

Introduction: Labor is a process through which the fetus moves from the intrauterine to extrauterine environment. Induction of labor is defined as the initiation and perpetuation of uterine contractions with the goal of producing progressive cervical effacement and dilatation. Induction of labor is common in obstetric practice**.** Study aimed to evaluate the efficacy of intracervical Prostaglandin E2 gel as a cervical ripening agent in unfavorable cervix for induction of labor.

Material and Methods: This study comprised of 180 women who required labor induction Singleton pregnancy between 37- 41 weeks live intrauterine fetus, Cephalic presentation, Bishop score of 1-6, Reactive FHR pattern were included. Those women who required only single induction and who delivered within 24 hours were categorized as Group 1. Women with persistent poor Bishop score < 6 after 24 h were re-induced and belonged to Group 2.

Results: Both the groups were comparable in demographic factors like age and period of gestation. The most common indication for induction was past dates followed by pre-labor rupture of membranes and gestational hypertension. In group 2, 48.4% was induced for past dates. Reinduction was required in 41.5% of primi and 18% of multigravida. Success rate in group 1 was71.6% and in group 2 was 42%. Maternal side effects were minimal and neonatal outcome was good.

Conclusion: The study showed that intracervical application of PGE2 is effective, safe and acceptable method for labor induction in women with unfavorable cervix. Dinoprostone gel application resulted in improved Bishops score and decreased caesarean delivery rate. All these effects were achieved without increasing maternal and neonatal morbidity.

Keyword: Intracervical prostaglandin E2, unfavorable cervix, Bishop score, induction of labour.

INTRODUCTION

Labor is a process through which the fetus moves from the intrauterine to the extrauterine environment. It is a clinical diagnosis defined as the initiation and perpetuation of uterine contractions with the goal of producing progressive cervical effacement and dilatation. Induction of labor is common in obstetric practice. It means deliberate termination of pregnancy beyond 28 weeks by any method which aims at the initiation of labor and vaginal delivery.[1-3] The goal of modern obstetrics is to improve the safety of the mother and the fetus during the antenatal period as well as parturition.[4,5] According to the most current studies, the induction rate varies from 9.5 to 33.7 percent of all pregnancies annually. The outcome of induced labor is highly dependent on the ripeness of cervix. In the absence of a ripe or favorable cervix, successful vaginal birth is less likely. To date, no medications have been proved ideal for the induction of labor in a patient with an unripe cervix. The drugs commonly available for induction are oxytocin, dinoprostone gel and recently misoprostol.[6] Cervical ripening or preparedness for induction should be assessed before a regimen is selected. Assessment is accomplished by calculating a Bishop score. When the Bishop score is less than 6, it is recommended that a cervical ripening agent is used before labor induction.[7] Nonpharmacologic approaches to cervical ripening and labor induction have included herbal compounds, castor oil, hot baths, enemas, sexual intercourse, breast stimulation, acupuncture, acupressure, transcutaneous nerve stimulation, mechanical and surgical modalities. Of these nonpharmacologic methods, only the mechanical and surgical methods have proven efficacy for cervical ripening or induction of labor. Pharmacologic agents available for cervical ripening and labor induction include prostaglandins, misoprostol, mifepristone, and relaxin.[8] Studies in vitro have revealed that prostaglandin E2 (PGE2) reduces cervical stiffness. Prostaglandin E2 placed intracervically is effective in improving unfavorable Bishop Scores. Tightly woven bundles of collagen fibers in the human cervix are thought to split, separate and dissolve into more abundant ground substance after prostaglandin therapy. In some cases, an early uterine activity may start as well. When the Bishop score is favorable, the preferred pharmacologic agent is oxytocin. Some reports have appeared in the international literature favoring the intracervical route, claiming the advantage of increased incidence of successful initial inductions, fewer side effects and minimal discomfort to the patient. The present study aimed to observe the administration of PGE2 gel, and the benefits and hazards of such therapy. Study aimed to evaluate the efficacy of intracervical Prostaglandin E2 gel as a cervical ripening agent in unfavorable cervix for induction of labor.

MATERIAL AND METHODS

This prospective clinical trial was carried out in the Department of Obstetrics and Gynecology at a tertiary care hospital. The purpose of this study was to evaluate the safety

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How to cite this article: Niloufur Syed Bashutheen, Minthami Sharon. A study of intracervical PGE2 gel for cervical ripening and induction of labour. International Journal of Contemporary Medical Research 2018;5(3):C4-C7.

and efficacy of intracervical PGE2 as an inducing agent in women with an unfavorable cervix, at term (Bishop score <=6). This study comprised of 180 women who required labor induction. Inclusion criteria: Singleton pregnancy between 37- 41 weeks live intrauterine fetus, Cephalic presentation, Bishop score of 1-6, Reactive FHR pattern. Exclusion criteria: Cephalopelvic disproportion, abnormal fetal heart rate patterns, uterine scar, hypersensitivity to prostaglandins. On admission, a detailed history of the subjects was taken. Complete general and obstetric examination was carried out. Under strict aseptic precautions, the vaginal examination was done. Bishop score was assessed. Once the inclusion criteria were fulfilled, the patient was counseled and written informed consent was obtained. Dinoprostone was instilled intracervically after ensuring a reactive FHR pattern. Repeat per vaginal examination was done at 6 hours, 12 hours and 24 hours depending upon the improvement in Bishop score. Women were divided into two groups depending on the number of inductions. Those women who required only single induction and who delivered within 24 hours were categorized as Group 1. Women with persistent poor Bishop score < 6 after 24 hours were reinduced and belonged to Group 2. Once in active labor, patients were managed as per routine protocol. From the start of induction, uterine activity and fetal heart rate were monitored clinically. Progress was monitored by using WHO portogram during the active phase. If the membranes were ruptured, the vaginal examination was done to assess the Bishop score and color of the liquor was noted. Maternal side-effects like hyperstimulation, nausea, vomiting, and fever were noted. The success of induction, in this study, was defined as achieving vaginal delivery within 24 hours of induction. Failed induction was defined as women who did not enter active phase of labor even after 3 inductions.

RESULTS

In group I Women who delivered within 24 hours (116 cases) were included, in group II: Women who required reinstillation (64 cases) were included (table-1). Group I had 66.4% of primi and 33.6% of multi, while Group II had 84.8% of primigravidae and 15.6% of multigravidae which was statistically significant. In Group I, 25.9% and in Group II, 32.8% had various antenatal complications which were comparable. The most common indication for induction in both the groups was past dates (accounting for 35.3% in Group I and 48.4% in Group II). The mean preinduction Bishop score in Group I was 4.09 compared to 2.89 in Group II (table-2,3). In Group I, 31.9% had Bishop Score of 4 while in Group II, 40.6% had Bishop Score of 2. Group, I required one induction and delivered within 24 hours. In Group II, 76.6% required two inductions, while 21.9% required three inductions, which was statistically significant. In Group I, the rate of improvement in Bishop score was

Indications for induction	Group I		Group II	
	No.	%	No.	%
Past dates	41	35.3	31	48.4
Oligohydramnios	7	6	3	4.7
Pre labor rupture of membranes	31	26.8	3	4.7
Gestational hypertension	13	11.2	9	14.1
Preeclampsia	3	2.6	5	7.8
Low normal liquor	11	9.5	10	15.6
Others	10	8.6	3	4.7
Total	116	100	64	100

Table-1: Indications for induction

Preinduction Bishop score	Group I		Group II	
	No.	%	No.	%
2	14	12.1	26	40.6
3	24	20.7	23	35.9
4	37	31.9	11	17.2
5	20	17.2	4	6.3
6	21	18.1	-	-
Total	116	100	64	100

Table-2: Preinduction Bishop Score

Number of inductions	Group I		Group II	
	No.	%	No.	%
1	116	100	-	-
2	-	-	49	76.6
3	-	-	14	21.9
4	-	-	1	1.6
Total	116	100	64	100

Table-3: Number of inductions

Post induction	Group I		Group II		P value
Bishop score	Mean	S.D	Mean	S.D.	
6 hours	7.79	2.19	4.02	1.41	0.0001
12 hours	9.5	2.34	5.53	2.6	0.0001
24 hours	10.26	2.18	7.66	3.5	0.0001

Table-4: Post induction Bishop score

Mode of delivery	Group I		Group II	
	No.	%	No.	%
Vaginal delivery	83	71.6	27	42.2
Outlet forceps	4	3.4	2	3.1
Vacuum delivery	3	2.6	-	-
Emergency cesarean	26	22.4	35	54.6
Total	116	100	64	100

Table-5: Mode of delivery

Indications for Cesarean	Group I		Group II	
	No.	%	No.	%
Secondary arrest of labor	1	3.8	-	-
CPD in labor	2	7.7	1	2.9
Failed induction	-	-	11	31.4
Fetal distress	12	46.2	10	28.6
Non progress of labor	2	7.7	4	11.4
Oligohydramnios	-	-	2	5.7
Prelabor rupture of membranes	3	11.5	1	2.9
Thick MSAF	2	7.7	.1_	2.9
Patient's request	1	3.8	5	14.3
Other reasons	3	11.5	-	-
Total	26	100	35	100

Table-6: Indications for cesarean

Complications		Group I		Group II	
		No.	%	No.	%
Intrapartum complications	Present	-	-	-	-
	Absent	116	100	64	100
Postpartum complications	Present	5	4.3	-	-
	Absent	111	95.7	64	100
Neonatal complications	Present	23	19.8	7	10.9
	Absent	93	80.2	57	89.1

Table-7: Complications of labor induction

Birth weight	Group I		Group II	
	No.	%	No.	%
< 2.5kg	15	12.9	6	9.4
≥ 2.5 kg	101	87.1	58	90.6
Total	116	100	64	100
Mean	2.94 ±0.43		2.96 ±0.4	
P value	0.9541			

Table-8: Birth weight (kg)

satisfactory, i.e., 9.5 at 12 hours and 10.26 at 24 hours. In Group II, the mean Bishop score was 5.53 at 12 hours and 7.6 at 24 hours (table-4). The success rate in Group I was 71.6% while in Group II was 42.2%. The rate of cesarean delivery in Group I was 22.4%, while in Group II, it was 54.6%. The mean induction delivery interval in Group I was 9 hours and in Group II, was 38.6 hours (table-5). The most common indication for cesarean delivery in' Group I was fetal distress while in Group II, it was failed induction. Negligible maternal and neonatal complications were seen in both the groups. The mean birth weight in both the groups was comparable (table 6-8).

DISCUSSION

Cervical ripening, prior to labor induction, in the presence of an unfavorable cervix reduces the likelihood of not being delivered in 12 and 24 hours, lowers the epidural analgesia rate, decreases cesarean delivery and operative vaginal delivery rates, but increases uterine hypertonus There is limited information on the dosing of prostaglandin (PGE2) gel, level of monitoring required and the use of oxytocin after PGE2 gel administration. The best dosing regimen of prostaglandin for labor induction with a favorable cervix is not known. When compared with oxytocin for labor induction, prostaglandin reduces the likelihood of operative delivery and failed induction. The data in the world literature seem to support the premise that the application of prostaglandin E2 gel into the cervix promotes cervical ripening and facilitates induction of labor. Induction should be considered when it is felt that the benefits of vaginal delivery outweigh the potential maternal and fetal risks of induction. These issues should be discussed with the woman before initiation of induction. Our study enrolled 180 women who required labor induction. All patients were induced with cervi prime gel after satisfying the inclusion criteria. The mean age in both the groups was comparable. There were 131 (64.5%) Primigravidae and 49 (35%) multigravidae. The subjects were divided into two groups: Group 1 - women who delivered within 24 hours and Group 2 - women who required reinstillation. The similar methodology was adapted by Warke HS et al. (1999) who divided the subjects into two groups.[9] Dinoprostone (PGE2) was instilled intracervically in our study. Ekman's group in Malmo, Sweden (1983) has demonstrated in a randomized study that patients with a highly unfavorable cervix apparently respond best to intracervical application of the prostaglandin E2 gel. The Ekman's group achieved cervical ripening, induction of labor and delivery with an 8% Cesarean rate.[10] In our study, the most common indication for induction was past dates (48.8%) Which is comparable with a study done by HS Warke et al, where the most common indication was past dates (52%).[9] The results were compared with the study done by Turner JE.[11] The categorization into groups in the present study was based upon the number of inductions. Reinduction was required in 41.5% of primigravidae and 18% of Multigravidae. Before and after induction, the cervical assessment was done using modified Bishop score (Calder)5 and rate of improvement in scores were observed. We found that a higher cervical score correlated with shorter labor and few induction failures. The success of induction of labor was found to be directly proportional to the Bishop score at instillation. In a study done by Calder et al. (1977), the cervical score had improved from a mean of 2.3 to 6.3 in 6 hours.[12]

The rate of improvement in Bishop score, in this study, was comparable to the results shown by Warke HS et al.[9] The first instillation in our study caused an increase in 2 -6 points in Group 1 while in Group 2 the increase was 2 points after the first instillation. Group 2 had a mean preinduction Bishop score of 2.8, and subsequent inductions resulted in poor improvement in scores (probably this group included more primis and the most common indication was past dates).

In our study success of induction refers to achieving vaginal delivery. Failed induction is defined as failure to enter active phase of labor even after three inductions. In this study, 71.6% had vaginal delivery compared to study done by Warke HS et al. which was 85.5%.[9] The rate of failed induction was 30% in Group 2. The largest reported study was conducted by Noah et al. in 1986 and involved a multicentre trial under a single protocol in 16 centers in Africa where successful induction was achieved in 83%. The induction delivery interval was shortened and fewer cesarean deliveries were performed (16%).31 Similarly, the success of induction in a study done by Calder et al. (1977) was 61% and 75% as per G. Mare Jackson et al.[13] The PGE2 gel has shown to shorten the induction delivery interval and thus

results in less fetal and maternal morbidity and mortality. The overall mean induction delivery time was 16.43 hours. Various studies have shown considerable variation as far as induction delivery time is concerned ranging from 9 hours (Noah et al.) to 17.9 hours (Thiery et al.) 13 to 20.2 hours in a study done by Jackson GM (1994) and 10 hours in a study by Calder et al. (1977).[13-15] The parity of the patients also influenced the duration of labor. In this study, mean induction delivery interval in primigravidae was 20.6 hours and in multigravidae was 10.8 hours. The success rate in Group 1 was 71.6% and in Group 2 was 42%. Group 2 had less success rate when compared to Group 1 because 84% were primigravidae 48.4% were induced for past dates Mean pre-induction Bishop score was only 2.8 The overall success rate regarding vaginal delivery was 71.6% in Group 1 and 42.4% in Group 2 in our study. Present data from worldwide prospective investigations strongly suggest that local PGE2 therapy has few maternal side effects and favorable neonatal outcomes. In our study, the side effects were minimal and neonatal outcome was good.

CONCLUSION

The study showed that intracervical application of prostaglandin E2 is an effective, safe and acceptable method for induction of labor in women with unfavorable cervix and indications for induction. Dinoprostone gel application resulted in improved Bishop score, facilitates the process of induction, increased number of successful inductions, shortened application delivery interval and decreased cesarean delivery rate. All these effects were achieved without increasing maternal and neonatal morbidity. Hence PGE2 gel can be recommended as a useful and potent method of induction of labor with an unfavorable cervix.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 20-02-2018; **Accepted:** 16-03-2018; **Published:** 10-04-2018