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Original Research Article

Pre- Induction Cervical Ripening with Unfavorable Bishop Score Using Two Different Dinoprostone Vaginal Preparation: A Prospective Randomized Comparative Study between Controlled Release Dinoprostone Gel & Dinoprostone Vaginal Insert

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Conflict of interest: Nil

Abstract

Background: The present study compares the safety and effectiveness of dinoprostone vaginal gel to dinoprostone vaginal insert for cervical ripening and induction of labour in pregnancies with poor Bishop score.

Materials & Methods: This prospective randomized comparative study was carried out in 200 pregnant mothers (100 mothers using dinoprostone vaginal gel and 100 mothers using dinoprostone vaginal insert) undergone labour induction with unfavorable Bishop score. Then the safety, efficacy and Bishop score changes over time in between the two groups were compared. Study outcomes included induction to vaginal delivery interval, mode of delivery and hospital stay following delivery. Statistical analysis was done by IBM SPSS Ver. 25 statistical software.

Results: Statistically significant difference was found between the two groups regarding the main outcome measures except cervical Bishop score changes at 24 hours. The probability of induction to vaginal delivery interval (p 0.03), successful vaginal delivery (p 0.03), hospital stay after delivery ($p < 0.001$) were more favourable to insert group.

Conclusion: Dinoprostone vaginal insert used for cervical ripening demonstrate a high degree of efficacy and safety for both mother & fetus as well as distinct superiority in terms of vaginal delivery within 24 hours along with shorter induction to delivery time and less duration of hospital stay following delivery. Single application is sufficient to achieve cervical ripening in majority of patients and adding to patient acceptability.

Keywords: Dinoprostone, gel, insert, unfavorable Bishop score.

Introduction

Labour induction is the intentional initiation of labour before it's spontaneous onset, for delivery of feto- placental unit safely, commonly practice around 20 % of all births in developed countries [1]. Induction of labour is one of the most abused procedure used in Obstetrics. Therefore one should cautious about the indications before induction. Post dated pregnancies & PIH accounts for 80% of all induction nowadays [2]. For successful induction in cases of unfavorable cervix, promoting cervical ripening is recommended automatically.

Dinoprostone is one of the synthetic prostaglandins commonly used for cervical ripening and labour induction, which can be administered via various routes like tablet, suppositories, vaginal or intra- cervical gel or as a controlled release intra-vaginal insert [3].

Commonly sequential method of induction is followed i.e. prostaglandins are used for ripening of cervix followed by oxytocin infusion for further augmentation of labour when Bishops score improves. Successful induction is related to the state of the cervix which is determined by Bishops score.

Dinoprostone gel has been used successfully for many years to achieve cervical ripening & labour induction in term mother with an unfavorable cervix while dinoprostone vaginal insert has also proved to be effective for cervical ripening and gradual onset of labour for women of full term pregnancy with suitable indications as a local application through consistently controlled release of 0.3 mg/ hours of dinoprostone [4].

The slow release vaginal insert has potential advantage compared to the other regimens like single and comparatively easy application, immediate termination of the drug effect can be achieved by removing it if uterine hyperstimulation and or abnormal fetal heart rate changes occur during ripening process [5].

Despite the frequency of induction around 20 %, the best way to proceed for induction in patient with unfavorable cervix is still controversial. Previous studies comparing PGE 2 vaginal insert to other prostaglandin preparations showed variable results [6]. These may be due to heterogeneities in terms of inclusion criteria, indications of labour induction, pre induction Bishops score, different primary outcome measures & various drug administration regimens.

As conflicting data exists concerning the most efficient and safe method, we aimed to compare two preparations of dinoprostone, gel and insert, for induction of labour in pregnancies with poor Bishop score for cervical ripening and induction of labour. Also the purpose of the study was to compare the effectiveness and safety of the insert to gel for induction of labour.

Material and Methods

This prospective randomized comparative study was conducted in the department of Obstetrics and Gynecology, VIMS & RKMSP, Kolkata. The study was carried out in 200 pregnant women undergone labour induction with unfavorable Bishops score for fetal and maternal indications for the duration of one year, among which 100 pregnant mother using controlled release dinoprostone vaginal insert and 100 pregnant mother using dinoprostone vaginal gel for induction. The study was conducted after approval of institutional ethics committee. Then the efficacy, safety & Bishops score changes over time in between the two groups were compared. Also the cost effectiveness regarding hospital stay after delivery was compared.

Inclusion criteria: 18 to 35 years old singleton primi-gravida mothers with cephalic presentation between 37 to 42 weeks gestational age with Bishops score less than equal to 5 were included in our study.

Exclusion criteria: Pregnant women with previous uterine surgery like caesarean section, myomectomy, metroplasty etc, known case of bronchial asthma, glaucoma, suspected CPD, fetal malpresentation, placenta praevia, rupture of membranes, known hypersensitivity to PGE2 or other conditions contraindicating vaginal delivery were excluded from the study.

Statistical analysis was done using IBM SPSS Ver.25 statistical software. Continuous variables were compared with unpaired t-test, categorical variables with Chi- square test. A repeated measures ANOVA analysis was done to detect difference in the change of Bishop scores among all & those with vaginal delivery in the two groups. Statistical significance was defined at p – value less than 0.05 with all 2- sided tests.

Result

This prospective randomized comparative study was conducted in 200 pregnant women undergone labour induction with unfavorable Bishop score for fetal and maternal indications for the duration of one year, among which 100 pregnant mother using controlled release dinoprostone vaginal insert & 100 pregnant mother using dinoprostone vaginal gel for induction.

Table 1: Demographic characteristics of the studied women. Statistically significant difference was there regarding maternal age but no significant difference was found in respect to weeks of gestation.

Variables	Dinoprostone Vaginal Gel Group (N=100)	Dinoprostone Vaginal Pessary Group (N=100)	P Value
Maternal Age(Years)	26.2+/- 3.5	25.2 +/- 3.4	0.04
Gestational Week	38.5 +/- 0.7	38.7 +/- 1	0.09
Medical Co-Morbidities	51(51%)	74(74%)	
Surgical Co-Morbidities	3(3%)	1(1%)	0.13
Bishop's Score Before Induction	3.6 +/- 0.5	3 +/- 0.5	<0.001

Table 2: Bishop score changes over time between the two groups. A repeated measures of ANOVA for change in mean Bishop score over time (6, 12, 18 & 24 hours) in all cases showed statistically significant difference between the two groups except at 24 hours.

Time	Mean Bishop's Score				P Value
	GEL		PESSARY		
	COUNT	MEAN	COUNT	MEAN	
0	100	3.6	100	3.02	<0.001
6	99	5.7	100	7.2	<0.001
12	64	5.9	85	9.2	<0.001
18	38	5.8	37	10.1	<0.001
24	30	7.6	11	7.8	0.79

Table 3: Labour data of participating mothers. There was no statistically significant difference between the two groups regarding time of ARM/SRM and oxytocin augmentation. Statistically significant difference was found in terms of Bishop score before induction, induction to vaginal delivery interval, rate of normal delivery & caesarean section and hospital stay following delivery between the two groups.

Variables	Dinoprostone Vaginal Gel Group (N=100)	Dinoprostone Vaginal Pessary Group (N=100)	P Value
Induction To Pessary Removal Time		14.4+/- 5	
Time Of Arm/Srm(Hrs)	13.9 +/- 8	13.7 +/- 4.7	0.83
Oxytocin Augmentation	59(59%)	65(65%)	0.38
Induction To Vaginal Delivery Interval (Hours)	19.9 +/- 8.8	<0.001	0.03
Mode Of Delivery			
Normal Delivery	60(60%)	73(73%)	0.03
Caesarean Delivery	40(40%)	26(26%)	
Outlet Forceps	0	1(1%)	
Hospital Stay After Delivery (Days)	3.5+/- 1.9	2.7+/- 1.3	<0.001

Table 4: Indicates proportion of patients with different indications for caesarean section between the two groups. Most common indication was thick meconium stained liquor followed by induction failure.

Indication	No of Mothers with Gel	No of Mothers with Pessary	Total	P Value
Deep Transverse Arrest	0	1	1	<0.001
Fetal Distress	8	1	9	
Induction Failure	11	7	18	
Non Progress Of Labour	2	8	10	
Pathological Ctg	6	2	8	
Second Stage Arrest	0	1	1	
Suspicious Ctg	0	4	4	
Thick Meconium	14	3	17	
Total	41	27	68	

Discussion

The success of induction is strictly depends on status of the cervix either assessed by Bishop score or by sonographic measurement of the length of the cervix as study conducted by Strobel E *et al*, Tan PC *et al* and Roman H *et al*. We decided to use the Modified Bishop score as it does not need any machinery assistance, hence making our observations more applicable. Dinoprostone (PGE2) has a dual action of cervical ripening and promotes uterine contraction. Most of the studies done were randomized control trial (RCT) type, similar to the present study. This prospective, randomized comparative study was conducted on 200 singleton pregnancies with Bishop score less than 5 & with no contraindications to vaginal delivery, which were randomly assigned into two groups (100

in insert & 100 in gel). The aim of this study was to compare the efficacy of two preparations of dinoprostone insert and gel, for induction of labour in pregnancy with unfavorable Bishop score.

Age was normally distributed in the two groups. Mean age of the mothers in gel group was 26.2+/- 3.5 years while that in pessary group was 25.2+/- 3.5 years (p = 0.04) . The mean period of gestation was 38.5+/- 0.7 weeks with median of 39.9 weeks in the gel group while it was 38.7+/- weeks with median of 38.6 weeks in the pessary group (p= 0.09). The reported result was similar to the present study as done by Kalkat RK *et al* [7].

Medical co- morbidities (most common were gestational diabetes mellitus & hypothyroidism) was found in 51% cases in gel group and 74% cases in pessary group. But surgical co – morbidities was found only in 3 % cases in gel group & 1% cases in pessary group, which was non significant.

Median Bishops score before induction was 4 in the gel group and 3 in the pessary group, the difference was statistically significant by Wilcoxon signed test. The Bishop score was calculated at 6 hours interval till 24 hours in all cases or till delivery whichever occurred earlier. There were more number of patients having higher Bishop score in pessary group at 6, 12, 18 and 24 hours compared to gel group. A repeated measures ANOVA for change in mean Bishop score over time in all cases showed statistically significant difference between the groups (p < 0.001). The difference was significant between groups at different times expect at 24 hours. Very few studies have specifically focused on women with an unfavorable Bishop score <4 but none was on <5 Bishop score. Miller *et al* showed an advantage of the pessary group in the induction of active labour compared to the gel group at 12 hours [8]. But in a prospective trial by Facchinetti *et al* requiring induction of labour at term with Bishop score <4 , found non-significant changes of Bishop score at 6 & 12 hours between the two groups [9]. Another study by Vollebregt A *et al*, where cervical ripening was achieved within 24 hours in 80% cases of pessary group, compared to 50% cases in cervical gel group [10].

The mean time of ARM/SRM in gel group was 23.9+/-8 hours vs 13.7+/-4.7 hours in pessary (p 0.083). Vollebregt A *et al* found that the application- membrane rupture interval was shorter in the pessary group compared to the gel group (22.7+/-21.3 hours vs 56.4+/- 77.7 hours, p 0.009).[10] In this study 59% mothers in gel and 65% mothers in pessary group required oxytocin augmentation. But in Contrary to the study done by Abdelaziz A *et al*, where 10% cases in gel & 5% cases in pessary group required oxytocin augmentation [11].

Mean duration from induction to delivery was 19.9+/- 8.8 hours in gel group compared to 17.3+/- 4.2 hours in pessary group for vaginal delivery in our study. Current study shows vaginal pessary patients had a shorter induction delivery time than the gel group, similar to the study done by others [12]. Vollebregt A *et al* also found that 62 % mothers in the pessary group delivered within 24 hours compared to 28 % in the gel group, which is quite comparable with the present study [10].

60% patient in the gel group & 73% patient in the pessary group had successful vaginal delivery, where as 40% patient in the gel group & 26% patient in insert group required caesarean section due to various indication, most common being thick meconium stained liquor followed by induction failure. In comparison to the present study, the rate of spontaneous vaginal delivery was significantly higher in the pessary group (72%) than the gel group (54%), paralleled by a lower rate of operative vaginal delivery (3% vs 15%) as study conducted by Aldelaziz A *et al* & Triglia MT *et al* [11-13]. The

dinoprostone vaginal insert was found to reduce cesarean section rate in nulliparous women by 24% compared to other ways of administration [14].

The current study also shows that the average duration of hospital stay after delivery was 3.5+/- 1.9 days for the gel group & 2.7+/- 1.3 days for pessary group ($p < 0.001$). Meta-analysis conducted by Zeng X *et al*, noticed that dinoprostone vaginal insert rather associated with shorter hospital stay compared to the gel group [15]. The result of this study was consistent with the present research.

Conclusion

Dinoprostone vaginal insert used for cervical ripening demonstrate a high degree of efficacy and safety for both mother & fetus as well as distinct superiority in terms of vaginal delivery within 24 hours along with less duration of hospital stay after delivery and shorter induction to delivery time.

Ethical Approval: The study was approved by the Institutional Ethics Committee.

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