Research Article

Role of Intracervical Dinoprostone Gel Administration versus Vaginal Administration of Oral Prostaglandin E2 Tablet for Induction of Labour

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Accepted on: 23-11-2014; **Finalized on:** 31-12-2014.

ABSTRACT

Our purpose was to compare the efficacy of two different dinoprostone delivery methods for induction of labour. In a prospective randomized study, 128 patients were randomly assigned to receive either one dose of intracervical prostaglandin E2 (PGE2) Gel 0.5 mg or 3 doses of vaginal administration of oral PGE2 Tablet (Primiprost) 0.5 mg for induction of labour during the period from April 2010 to March 2013. Outcomes were studied as changes in Bisop's score, induction to delivery interval, augmentation with oxytocin use or artificial rupture of membrane and vaginal delivery. Mean change in Bisop's score at 6 hours and 12 hours were 7.725 and 8.945 in cerviprime group versus 4.015 and 5.863 in primiprost group (p=0.0001). Induction delivery interval was shorter in the gel group with a mean of 12.66 hours where as 20.732 h in tablets group (p=0.0001). Out of total 128 patients 93 delivered vaginally of which 57 % belongs to gel group and 43% to tablet group (p=0.017). During course of labour 22 patients were augmented with syntocinon, artificial rupture of membrane or both, out of which 40.9% in gel group and 59% in tablet group required induction which is not statistically significant(p=0.483). Induction of labour with PG E2 gel results in better Bisop's score at 6 hours and 12 hours, shorter induction delivery interval and more vaginal delivery compared to oral dinoprostone tablet used vaginally. However there is no statistically significant difference in use of agents for augmentation of labour in both the groups.

Keywords: Induction of labour, Dinoprostone gel, Dinoprostone pessary, Primiprost tablet.

INTRODUCTION

Labor induction is a common obstetric intervention, occurring in approximately 16% of deliveries.[1] In developed world at least 19.8 % of all labours are induced.[2] Despite its frequency, the best way to proceed with induction of labor in the patient with an unfavourable cervix is still controversial. Multiple methods such as, oxytocin, various prostaglandin cervical ripening agents and cervical dilating agents have recently been studied.[3] Prostaglandins have been shown to induce cervical ripening and to stimulate uterine contractions and are effective in numerous clinical trial.[3-7] However, only two prostaglandin cervical ripening agents dinoprostone gel (Cerviprime) and dinoprostone vaginal pessary are currently approved by the Food and Drug Administration (FDA). Cerviprime gel is expensive, needs refrigeration for storage, requires endocervical administration and in most cases oxytocin is required for augmentation. However dinoprostone vaginal pessary does not require refrigeration and can be administered vaginally. But in India this vaginal pessary is not available. In India Prostaglandin E2 tablet Primiprost (0.5 mg) is available which is used as oral tablet. The tablet is soluble in water to the extent of 1-1.05 mg/ml at 25°C. The tablet is stable for 90 days in room temperature. However the most frequent adverse reaction of the tablet is vomiting with or without nausea and diarrhoea (21%-50%).[8] These adverse reactions can be avoided if the tablet is used vaginally.

The purpose of our prospective randomised study was to compare the efficacy of cerviprime gel and primiprost tablet in promoting cervical priming and achieving vaginal delivery.

MATERIALS AND METHODS

This prospective randomized study was carried out in consecutive patients requiring labour induction at department of Obstetrics and Gynaecology, IMS and Sum Hospital, Bhubaneswar, Odisha, India during April 2010 to March 2013. This study was approved by Institutional ethics committee of our hospital. The patients were selected with the eligibility criteria of singleton pregnancy >31weeks of gestation, vertex presentation, no previous uterine surgery, Bishop score <4 and absence of contraindications to vaginal delivery. Gestational age was calculated from the last menstrual period and confirmed by routine sonography before 20 weeks of gestation. On the other hand the exclusion criteria were previous uterine and cervical surgery, cephalo-pelvic disproportion, grand multipara, malpresentation, intra-uterine growth restriction, elderly primigravida, nonreassuring fetal surveillance, vaginal bleeding of any etiology, hepato-renal disorders, bronchial asthma, pyrexia and patients hypersensitive to prostaglandin.

A total of 128 cases met the inclusion criteria and selected randomly out of which 64 cases were instilled with 0.5 mg of cerviprime gel (Group A) and other 64 cases with vaginal application of oral dinoprostone tablet

(primiprost 0.5mg) (Group B). In all cases the patient consent was taken. Patients were randomly assigned to either the cerviprime gel group or primiprost tablet group by taking the next envelop that contained the group assignment. The envelopes were assigned to a group by means of a random numbers table and the assignment schedule was not known to the investigator making the random assignment. Detailed history, thorough physical and abdominal examination was done along with pelvic examination before induction of labour. Bishop's score was noted before start of procedure and also at 6th and 12th hour. Women had continuous fetal and uterine monitoring for at least 1 hour following induction in supine position. Labour was followed with partogram. Augmentation of labour with artificial rupture of membrane and/or oxytocin was done as and when required.

In group A, single dose of cerviprime gel was given intracervically for induction of labour and progress was assessed after 6 and 12 hours. Failure of induction was declared if there was no adequate uterine contraction even after 12 hour of induction. In group B, PGE2 tablet 0.5 mg was introduced into the posterior fornix of vagina and the doses were repeated every 4 hours for a maximum of 3 (Three) doses in case of inadequate uterine contraction or till the cervix is 3 cm dilated. If effective uterine contractions were not established even after 16 h of induction, then the process was abandoned as induction failure. In both the groups patients were closely monitored with cardiotochogram (CTG) and 4 hourly pervaginal examinations.

Artificial rupture of membrane was done once the cervix is 3cm dilated. Oxytocin was started if the patient was not in adequate labour after 12 hrs of induction with dinoprostone gel or 4 hours after the last dose of tablet or at any time that the cervix was dilated >3cm and there was arrest of dilatation for longer than 2 hours. Oxytocin was administered according to the institution protocol and dosing was started at 2 mIU/ min and increased by 1 to 2 mIU/min every 15 to 20 minutes up to 10 mIU/min, if contractions were not adequate. Once the patient was in active labour, the management of labour and delivery were determined by managing labour room doctor as per the partogram recording. Outcomes were changes in bisop's score at 6 and 12 hours, induction delivery time interval, need of augmentation and vaginal delivery.

The statistical analysis was done by using the Statistical Package for Social Sciences (SPSS 20) program. When a variable was distributed normally, the results were presented as Mean and Standard Deviation (SD); otherwise, results were shown as median and interquartile range. Qualitative variables are expressed as number and percentage. Groups were compared by using unpaired Student t test. To compare proportions (qualitative variables), λ^2 test was used.

RESULTS

There were 128 cases randomly assigned to receive either cerviprime gel (n=64) or primiprost tablet (n=64). According to the data, there were no statistically difference in maternal age (p=0.292), parity (p=0.849), socio-economic status (p=0.242), gestational age of fetus (p=0.062) and pre-induction Bisop's score (p=0.397). Bisop's score at the induction of labour was 2.01±0.51 (Mean ± SD) for cerviprime gel group and 1.98±1.05 (Mean ± SD) for tablet group. This is not statistically significant (p=0.397) (Table1 and 2). Indications for labour induction includes post dated pregnancy, pre-labour rupture of membrane, pregnancy induced hypertension, intrauterine death and eclampsia. According to our data there was no statistical significance among the group A and group B (p=0.875) (Table 3).

Table 1: Variability of age, GA and Bishop's score at induction of labour

Variability	group	N	Mean	SD	P value
Age (years)	Cerviprime	64	23.3281	3.77567	.292
	Primiprost	64	22.6094	3.91017	
GA (weeks)	Cerviprime	64	38.5313	3.67302	.062
	Primiprost	64	39.5469	2.27428	
Bishop's score (0 h)	Cerviprime	64	2.0156	.51922	.397
	Primiprost	64	1.8906	1.05586	

Note: GA; gestational age, N: Number of patients in each group, SD: Standard Deviation

Bisop's score was done manually at 6 and 12 hours for both groups. Two patients in cerviprime gel group delivered before 4 hours in contrast to none in tablet group. At 6 hours the Bisop's scores were 7.72±2.43 (Mean ± SD) and 4.01±1.30 (Mean ± SD) for gel and tablet group respectively (p=0.0001). Within 12 hour of induction 27 patients in gel group and 20 patients in tablet group delivered. At 12 hours of induction the Bisop's score were 8.94±1.87 (Mean ± SD) and 5.86±2.04 (Mean ± SD) for gel and tablet groups respectively at p=0.0001(Table 4 and 5). Among those, who have delivered vaginally, the mean interval from drug administration to delivery was significantly shorter in the gel group compared to those who received tablets 12.66±5.09 hours versus 20.73±7.00 hours, which is statistically significant at p= 0.0001(Table 4 and 5).

During course of labour 22 cases were augmented either with syntocinon, artificial rupture of membrane or both. Out of 22 cases 9 cases (40.9%) in gel group and 13 cases (59.1%) in tablet group required induction, and was not statistically significant at p=0.483 (Table 6).

Table 2: Socioeconomic status and Distribution cases as per parity of the patients

Group	SES		Parity		Total (N)
	BPL	APL	Primi	Multi	
Cerviprime	42 (46.2%)	22(59.5%)	45(51.1%)	19(47.5%)	64 (50.0%)
Primiprost	49(53.8%)	15(40.5%)	43(48.9%)	21(52.5%)	64(50.0%)
Total	91(100.0%)	37(100.0%)	88(100.0%)	40(100.0%)	128 (100.0%)

BPL: Below poverty line, APL: Above poverty line, Pearson chi square value = 1.863, df = 1, p=0.242 with SES; Pearson chi square= 0.145, df=1, p=0.849

Table 3: Indications for induction of labour

Variables	Indication					Total
	Post dated	PROM	PIH	IUD	Eclamsia	
Cerviprime	34(51.5%)	21(47.7%)	4(40.0%)	4(66.7%)	1(50.0%)	64(50.0%)
Primiprost	32(48.5%)	23(52.3%)	6(60.0%)	2(33.3%)	1(50.0%)	64(50.0%)
Total	66(100.0%)	44(100%)	10(100%)	6(100%)	2(100%)	128(100%)

Note: With Chi square test, it was found that there is no statistical significant with indications for induction of labour, df=4 and P=0.875

Table 4: Cervical priming at 6 h and 12 h with induction delivery interval

Variables	Group	N	Mean	Std. Deviation
Bishop's score at 6h	Cerviprime	62	7.7258	2.43047
	Primiprost	64	4.0156	1.30314
Bishop's score at 12h	Cerviprime	37	8.9459	1.87003
	Primiprost	44	5.8636	2.04133
Induction delivery interval n (h)	Cerviprime	53	12.6642	5.09608
	Primiprost	40	20.7325	7.00174

Table 5: Statistical analysis of cervical priming at 6 h and 12 h with induction delivery interval with SPSS 20 software

Variables		T- test for Equality of Means					95% Confidence Interval of the Difference	
		t	df	P	Mean Difference	Std. Error Difference	Lower	Upper
Bishop's score at 6h	Equal variances assumed	10.725	124	.000	3.71018	.34594	3.02547	4.39489
Bishop's score at 12h	Equal variances assumed	7.032	79	.000	3.08231	.43833	2.20983	3.95479
ID interval	Equal variances assumed	-6.434	91	.000	-8.06835	1.25407	-10.55940	-5.57730

Table 6: Augmentation of labour

Group	Augmentation		Total
	Yes	No	
Cerviprime	9(40.9%)	55(51.9%)	64(50.0%)
Primiprost	13(59.1%)	51(48.1%)	64(50.0%)
Total	22(100%)	106(100%)	128(100%)

Among 128 cases, 93 delivered vaginally of which 53 cases (57 %) belongs to gel group and 40 cases (43%) to tablet group. Out of 35 cases delivered by caesarean sections, 11 cases (31.4%) belong to gel group and 24 cases (68.6%) belong to tablet group. Which was statistically significant p=0.017 (Table 7). In gel group caesarean section was done due to foetal distress in 7 cases and non-progress of labour in 4 cases. In tablet group caesarean section was done due to foetal distress in 15 cases all occurred within 12 hours of induction and failure to progress in 9 cases.

Table 7: Mode of delivery

Group	Mode of Delivery		Total
	Normal	CS	
Cerviprime	53(57.0%)	11(31.4%)	64(50.0%)
Primiprost	40(43.0%)	24(68.6%)	64(50.0%)
Total	93(100.0%)	35(100.0%)	128(100.0%)

There was no statistical significance in augmentation of labour with Chi-square test (P=0.483), whereas, the mode of delivery is statistically significant at P=0.017.

In gel group 53 cases (82.81%) delivered vaginally, while in tablet group 40 cases (66.66%) delivered vaginally. Among those who delivered vaginally in gel group 27 patients (42.18%) delivered within 12 hours and 46 patients (71.87%) delivered within 18 hours of induction. Out of 53 patients 52 patients (98.11%) delivered vaginally within 24 hours of induction in gel group. In tablet group only 5 cases (7.81%) delivered within 12 hours of induction while at the end of 24 hours only 29 cases (45.31%) delivered vaginally. Out of 40 patients 39 patients (97.50%) delivered vaginally within 36 hours of induction in tablet group (Table 8).

Table 8: Application and vaginal delivery interval

Time in hrs	Cerviprime Gel		Primiprost Tablet	
	N=64	%	N=64	%
0-6	4	6.25	0	00
6-12	23	35.93	5	7.81
12-18	20	31.25	11	17.18
18-24	5	7.81	13	20.31
24-36	1	1.56	10	15.62
36-48	0	00	1	1.56
Total	53	82.81	40	66.66

DISCUSSION

Induction of labor is widely used obstetrical practice for different indications, the most frequent being prolonged pregnancy. The success of induction is strictly dependent on the cervical status either assessed by Bishop's score or by sonographic measurement of cervical length.[9-11] Various studies compared these two methods of cervical assessment, failing to consistently show an advantage of any of the two compared to the other in the prediction of vaginal delivery.[12-14]

In this study, unfavourable Bishop score < 4 was the criterion for entering into the study, and multiparae and nulliparae were equally represented in the two arms of the study. We decided to use the Bishop score as it does not need any machinery assistance, hence making our observations applicable to a larger number of clinical environments. Various studies have used bishop's score or ultrasound machine to predict the cervical favourability for induction of labor.[15-18] Very few studies have specifically focused on women with an unfavourable Bisop's score < 4. Miller et al.[19] compared the 12-hour dinoprostone pessary with 2.5-mg dinoprostone gel, with 20 women for each arm, showing an advantage of the pessary in the induction of active labor. Facchinetti et al [20] in a prospective trial of 144 consecutive nulliparous patients requiring induction of labour at term with bisop's score < 4, found that changes in bisop's score at 6 and 12 hours were not significantly affected by use of dinoprostone vaginal pessary or gel.

In a more recent comparison by Ottinger et al.[21] 90 women with an indication for labor induction were randomized to receive either intra-cervical gel (n=45) or controlled-release dinoprostone (n=45), and the advantages of controlled-release formulations were noted. The investigators found that controlled-release dinoprostone was associated with a greater mean change in Bishop's score (3.2±3.1 vs 1.8±1.9, P=0.01) than the gel. In this study, there was no significant difference between treatments in the percentage of deliveries within 24 h, and there was a non-significant decrease in the application to-delivery interval (28.3 and 24.0 h for gel and controlled-release formulations, respectively (p=0.19). [21] There are two meta-analyses on the efficacy of dinoprostone vaginal pessary for labor induction. Sanchez-Ramos et al. [22] concluded that the vaginal insert was less effective than other prostaglandins for cervical ripening and labor induction, whereas the conclusion reached by Hughes et al.[23] was that vaginal insert is equally effective as other prostaglandin routes of administration in terms of delivery by 24 hours, rate of uterine hyperstimulation with fetal heart rate changes and caesarean delivery rate.

In our study bisop's score at 6 hr and 12 hours were statistically favoured more towards gel group compared to tablet group. Two patients in cerviprime gel group delivered before 4 hours in contrast to none in tablet group. At 6 hours mean Bisop's score at cerviprime group was 7.72(SD = 2.43, SE = 0.30) contrast to 4.01 (SD=1.30, SE=0.16) in primiprost group (p=0.0001). Within 12 hours of cerviprime instillation another 23(35.93 %) women delivered vaginally while only 5(7.81%) cases in primiprost group delivered vaginally. Out of total 24 cases underwent Caesarean section in primiprost group 15 cases (62.5%) were within 12 hrs of induction in contrast to none in cerviprime gel group. In all cases the indication of caesarean section was foetal distress. Bisop's score at the end of 12 hours in gel group was 8.94 (SD=1.87, SE=0.30) contrast to 5.86 (SD=2.04, SE=0.30) in tablet group statistically significant (p=0.0001). So by the end of 12 hour in gel group 27/64 patients (42.18%) delivered vaginally in contrast to 5/64 cases (7.8%) in tablet group. Troostwijk et al in 1992 reported 35% of women delivered vaginally within 12 hours of gel application.[24] Within 18 hours of induction another 20 patients (31.25%) in gel group and 11 patients (17.18%) in tablet group delivered vaginally. Out of 53 patients delivered vaginally 52

patients (98.11%) delivered within 24 hours in gel group. In tablet group out of total 40 patients delivered vaginally 29 patients (72.50%) delivered within 24 hours. This shows the superiority of intracervical cerviprime gel over intravaginal primiprost tablet for cervical priming.

Facchinetti et al in a prospective, open-label trial of 144 consecutive nulliparous women with a Bishop score <4 who required induction of labour at term were randomised to receive either dinoprostone vaginal insert (10 mg over 12 h) or a cervical gel (0.5 mg, twice in 12 h). If labour did not start by 24 h after this pre-induction, patients received 2 mg vaginal dinoprostone gel followed 6 h later by oxytocin infusion. More women in the gel group (41.4% versus 24.3%) required the use of oxytocin (OR = 2.21; 95% CI = 1.07–4.55).[20] Abhijit Basu et al included 83 women who were eligible for inclusion, 44 in the Prostin (dinoprostone gel) group, and 39 in the Cervidil (dinoprostone pessary) group. The number of women requiring amniotomy and oxytocin infusion to cause effective contractions and delivery did not differ between the two groups.[25] In our study during course of labour 22 patients were augmented with syntocinon, artificial rupture of membrane or both. In gel group 40.9% and in tablet group 59% required induction which is not statistically significant (p=0.483).

Strobelt and colleagues randomized 107 patients with a Bishop score < 4 to either a 12-hour dinoprostone pessary or 0.5-mg dinoprostone cervical gel. Vaginal pessary patients had a shorter induction-to delivery time, (920±428 vs 1266±740 min, p< 0.01), with a mean difference of 5 hours and 46 minutes between the groups.[26] Facchinetti et al. randomized 144 nulliparous women with Bisop's score <4 either with dinoprostone vaginal insert 10 mg over 12 hours or cervical gel 0.5 mg twice in 12 hours. Interval from induction to vaginal delivery was similar in the vaginal insert (1374 ±609 min) and the cervical gel (1343±595 min) groups.[20]

A prospective multicenter German study found similar results. In this study, 158 pregnant women with a Bishop Score <4 were randomized to receive either controlled release dinoprostone (n=83) or intra-cervical application of 0.5 mg prostaglandin E2 gel (n=75). No significant difference in the mean induction to delivery interval (28 h for the gel and 21.5 h for the controlled-release pessary.[27] Anna Maria Marconi et al in a prospective randomised study compared the efficacy of dinoprostone gel and insert found that in multiparous the time to delivery interval was significantly shorter in the gel treated group (9.9± 4.9 h versus 13.1±5 h; $p < 0.001$) with more patients delivering vaginally ≤ 12 h (75% vs. 37.5%, $p < 0.001$), regardless of the pre-induction Bishop score.[28] Similarly, the results of Abhijit Basu et al, showed the mean time to delivery was significant difference, with women receiving Prostin (dinoprostone gel) delivering earlier on average than those having Cervidil(dinoprostone pessary) (21.1 versus 29.6 hrs $P = 0.018$) irrespective of the mode of delivery.[25] In our study the mean induction delivery time was 12.66±5.09 hrs in cerviprime gel group in contrast to 20.73±7.00 in tablet group which is statistically significant(p=0.0001). Cerviprime group patients delivered earlier in vaginal route because of favourable bisop's score at 6 and 12 hours.

Maria Teresa Triglia et al randomised 133 women for controlled release vaginal dinoprostone pessary or repeat doses of 2 mg vaginal dinoprostone gel. The spontaneous vaginal delivery rate was higher in the pessary group (72%) than in vaginal gel group (54%), with a significant difference (p = 0.03). However the difference in caesarean section rates between the pessary and gel groups (25 vs. 31%) was not significant.[29] The study by Facchinetti et al. compared cervical application of vaginal insert with gel for pre-induction cervical maturation in 144 nulliparous women with a bisop's score<4, found CS rate was lower in the vaginal insert group (22.9%) than in the cervical gel group (34.3%), though the difference did not reach statistical significance (Chi-square: 2.24, P =0.13). The rate of vaginal delivery within 12 h (18.5 % vs 15.2%) and 24 hours (57.4% vs 58.7%) was similar as was the rate of failure of induction.[20]

Anna Maria Marconi et al randomized 220 nulliparous and 100 multiparous with a Bishop score ≤7 to receive dinoprostone either gel or insert for cervical ripening. In nulliparous women no significant differences were found between the gel and insert groups in the rate of vaginal delivery (85.6% vs. 80.7%) delivery ≤12 (36.8% vs. 32.9%) and ≤24 h (85.3% vs. 93.4%) regardless of the pre-induction Bishop score.[27] Abhijit Basu et al found no difference in the incidence of caesarean section (RR 0.65, 95% CI 0.35–1.19, $P = 0.24$) between the Prostin and Cervidil groups. There was also no statistically significant difference in the number of women needing an operative delivery (either a caesarean section or assisted vaginal delivery) between the two groups (RR 1.12, 95% CI 0.76–1.66, $P = 0.72$).[25] In our study out of total 128 patients, 93 patients delivered vaginally of which 53 cases(57 %) belongs to gel group and 40 cases(43%) to tablet group (p=0.017) . In gel group within 12 hours of induction 27 patients (50.9%) out of total 53 patients delivered where as in tablet group 5 patients (12.5%) out of total 40 patients delivered vaginally, the difference reached statistical significance (Chi-square: 14.927, df=1, P <0.0001) with a odds ratio 7.27 (95%CI 2.47 – 21.42). As seen in table 4 the better Bisop's score at 12 hours (8.945 vs 5.863) in gel group resulted more vaginal delivery. Within 18 hours of induction 47/53(88.67%) in gel group and 16/40(40%) in tablet group delivered vaginally. Here again the difference reached statistical significance (Chi-square: 24.72, df = 1, p= 0.0001) with a odds ratio 11.75 (95% CI 4.07 – 33.89). Within 24 hours of induction 52/53 (98.11%) in gel group and 29/40(72.50%) in tablet group delivered vaginally. It is statistically significant (Chi-square: 13.30, df = 1, p = 0.0001) with a odds ratio 19.72 (95% CI 2.42 – 160.57).

CONCLUSION

Judicious and timely induction of labour has a vital role in the modern obstetric management. Intra cervical cerviprime gel is more superior to vaginally used oral dinoprostone in inducing the patients with unfavourable cervix. But Primiprost tablet which is used orally can be effectively used for cervical induction. For better effective result some more studies are required.

Acknowledgement: Authors would like to thank Prof. Dr. Manoj Ranjan Nayak, President, SOA University, Bhubaneswar for timely encouragement and extended facility. M C Sahu is Research Associate of this Institute.

REFERENCES

1. Ventura SJ, Martin JA, Curtin SC, Mathews TJ. Report of final natality statistics, 1995. Mo Vital Stat Rep 1997,45,1-84.
2. National Institute for Health and Clinical Excellence, Induction of Labour. NICE Clinical Guideline, RCOG Press, London,UK, 2nd edition, 2008.
3. O'Brien WF. Cervical ripening and labor induction: progress and challenges. Clin Obstet Gynecol 1995,38, 221-3.
4. Mukhopadhyay M, Lim KJH, Fairlie FM, "Is propess a better method of induction of labour in nulliparous women?" Journal of Obstetrics and Gynaecology, 22, 3, 294– 295, 2002.
5. Kho EM, Sadler L, McCowan L, "Induction of labour: a comparison between controlled-release dinoprostone vaginal pessary (Cervidil) and dinoprostone intravaginal gel (Prostin E2)," Australian and New Zealand Journal of Obstetrics and Gynaecology, 2008,48, 473–477.
6. El-Shawarby SA, Connell RJ, "Induction of labour at term with vaginal prostaglandins preparations: a randomized controlled trial of Prostin vs Propess". Journal of Obstetrics and Gynaecology, 26, 7, 627–630, 2006.
7. Keirse MJ. Prostaglandins in preinduction cervical ripening: meta-analysis of worldwide clinical experience. J Reprod Med, 1993, 38, 89-98.
8. Pfizer Canada Inc. Product monograph, Prostin E2 tablet, dinoprostone 0.5mg, Prostaglandin 2012.
9. Vankayalapati P, Sethna F, Roberts N, Ngeh N, Thilaganathan B, Bhide A. Ultrasound assessment of cervical length in prolonged pregnancy: prediction of spontaneous onset of labor and successful vaginal delivery. Ultrasound Obstet Gynecol, 2008, 31,328–31.
10. Rane S, Guirgis R, Higgins B, Nicolaides K. Pre-induction sonographic cervical measurement of cervical length in prolonged pregnancy: the effect of parity in the prediction of the need of Cesarean section. Ultrasound Obstet Gynecol, 2003, 22, 45–8.
11. Pandis GK, Papageorghiou AT, Ramanathan VG, Thompson MO, Nicolaides KH. Preinduction sonographic measurement of cervical length in the prediction of successful induction of labor. Ultrasound Obstet Gynecol, 2001, 18,623–8.
12. Vankayalapati P, Sethna F, Roberts N, Ngeh N, Thilaganathan B, Bhide A. Ultrasound assessment of cervical length in prolonged pregnancy: prediction of spontaneous onset of labor and successful vaginal delivery. Ultrasound Obstet Gynecol, 2008, 31,328–31.
13. Rane S, Guirgis R, Higgins B, Nicolaides K. Pre-induction sonographic cervical measurement of cervical length in prolonged pregnancy: the effect of parity in the prediction of the need of Cesarean section. Ultrasound Obstet Gynecol, 2003, 22, 45–48.
14. Pandis GK, Papageorghiou AT, Ramanathan VG, Thompson MO, Nicolaides KH. Preinduction sonographic measurement of cervical length in the prediction of successful induction of labor. Ultrasound Obstet Gynecol, 2001, 18, 623–628.
15. Strobel E, Sladkevicius P, Rovas L, De Smet F, Karlsson DE, Valentin L. Bishop score and ultrasound assessment of the cervix for prediction of time to onset of labour and time to delivery in prolonged pregnancy. Ultrasound Obstet Gynecol, 2006, 28,298–305.
16. Tan PC, Vallikkannu N, Suguna S, Quek KF, Hassan J. Transvaginal sonographic measurement of cervical length vs. Bishop Score in labor induction at term: tolerability and prediction of Cesarean delivery. Ultrasound Obstet Gyneco, 2007, 29,568–73.
17. Roman H, Verspyck E, Vercoustre L, Degre S, Col JY, Firmin JM, et al. Does ultrasound examination when the cervix is unfavorable improve the prediction of failed labor induction? Ultrasound Obstet Gynecol, 2004, 23, 357–62.
18. Rosenberg P, Chevret S, Chastang C, Ville Y. comparison of digital and ultrasonographic examination of the cervix in predicting time interval from induction to delivery in women with a low Bishop score. BJOG, 2005, 112,192–6.
19. Miller AM, Rayburn WF, Smith CV. Patterns of uterine activity after intravaginal prostaglandin E2 during preinduction cervical ripening. Am J Obstet Gynecol, 1991, 165, 1006–1009.
20. Facchinetti F, Venturini P, Verocchi G, Volpe A. Comparison of two preparations of dinoprostone for pre-induction of labour in nulliparous women with very unfavourable cervical condition: a randomised clinical trial, European Journal of Obstetrics & Gynecology and Reproductive Biology, 2005,119, 189-193.
21. Ottinger WS, MK Menard, BC Brost: A randomized clinical trial of prostaglandin E2 intracervical gel and a slow release vaginal pessary for preinduction cervical ripening. Am J Obstet Gynecol, 1998,179, 349.
22. Sanchez-Ramos L, Kaunitz AM, Delke I, Gaudier FL. Cervical ripening and labor induction with a controlled release dinoprostone vaginal insert: a meta-analysis. Obstet Gynecol, 1999, 94,878–883.
23. Hughes EG, Kelly AJ, Kavanagh J. Dinoprostone vaginal insert for cervical ripening and labor induction: a Meta analysis. Obstet Gynecol, 2001, 97,847–855.
24. Troostwijk AL, van Veen JBC, Doesburg WH. Pre-induction intracervical application of a highly viscous prostaglandin E_2 gel in pregnant women with an unripe uterine cervix: a double-blind placebo-controlled trial. European Journal of Obstetrics & Gynecology and Reproductive Biology, 1992, 43(2), 105–111.
25. Basu A, Elgey S, Haran M. Outcome of Induction of Labour in Nulliparous Women Following Replacement of Cervidil with Prostin, The Scientific World Journal, 2012, doi:10.1100/2012/325968.
26. Strobelt N, Meregalli V, Ratti M, Mariani S, Zani G, Morana S. Randomized study on removable PGE2 vaginal insert versus PGE2 cervical gel for cervical priming and labor induction in low-Bishop-score pregnancy. Acta Obstet Gynecol Scand, 2006, 85,302–305.
27. Werner Rath. A clinical evaluation of controlled-release dinoprostone for cervical ripening – a review of current evidence in hospital and outpatient settings. J. Perinat. Med, 2005, 33, 491–499.
28. Marconi AM, Bozzetti P, Morabito A, Pardi G. Comparing two dinoprostone agents for cervical ripening and induction of labor: A randomized trial. European Journal of Obstetrics & Gynecology and Reproductive Biology, 138, 2, 2008, 135–140.
29. Maria TT, Palamara F, Lojacono A, Prefumo F, Frusca T. A randomized controlled trial of 24-hour vaginal dinoprostone pessary compared to gel for induction of labor in term pregnancies with a bishopscore < 4. Acta obstetricia et gynecologica, 89, 2010, 651–657.

Source of Support: Nil, **Conflict of Interest:** None.