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Induction of Labour by Prostaglandin E_2 Intracervical Gel or Vaginal Suppository

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ABSTRACT

Objective To compare the effectiveness in induction of labour between prostaglandin E_2 intracervical gel and vaginal suppository.

Design Prospective, randomized study.

Setting Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University Hospital.

Subjects Nineteen pregnant women with unfavourable cervix (Bishop score ≤ 5) were randomized to receive either prostaglandin E_2 intracervical gel (0.5 mg) or vaginal suppository (3 mg) for induction of labour.

Main outcome measures Mode of delivery, time from initial application of PGE_2 unitil delivery, and adverse effect, Apgar score and immediate newborn status.

Results Caesarean section was performed in 5 out of 9 cases in intracervical gel group, comparing to 1 out of 10 cases in vaginal suppository group. The mean time of application of prostaglandins to labour (A-L) and application to delivery (A-D) in cases of successful vaginal delivery were significantly shorter in the intracervical gel than in the vaginal suppository group (A-L : 1 ± 0.71 hr vs 11.21 ± 9.29 hr ; A-D : 13.75 ± 3.63 hr vs 20.48 ± 6.74 hr, $P < 0.05$). The mean time from rupture of membranes to delivery was of no difference between the two groups (4.48 ± 2.46 hr vs 4.80 ± 2.88 hr respectively, $P = 0.85$) Neither uterine hyperstimulation nor other adverse effects both to the baby and mother was detected during the labour period.

Conclusion Prostaglandin E_2 vaginal suppository seemed to be simple and successful for induction of labour and delivery, though it required longer period of induction to delivery when compared to prostaglandin E_2 intracervical gel.

Key words : induction of labour, prostaglandin E_2, intracervical gel, vaginal suppository

Prostaglandins play a central role in the cervical ripening and, indeed, in initiating and maintaining labour. The role of prostaglandins in the natural process of cervical ripening provides the basic rationale for their use when cervical ripening is warranted.[1] Prostaglandins have been available for clinicians to assist in the cervical ripening process for more than two decades, however, the route of delivery has been changed from systemic to local. These changes have lowered the dose required for cervical ripening, and consequently, fewer side effects occurred.

Concerning prostaglandin E_2 (PGE_2) vaginal suppository, at present, the minimal dose available and commonly used is 3 mg. Many studies showed that this agent had better efficacy and safety when compared with oxytocin or placebo.[2-5] PGE_2 0.5 mg in the form of intracervical gel (2.5 ml) was first introduced in Thailand in 1992. Some suggested that this gel is used for induction of labour in pregnant women with low Bishop score when labour inducing is indicated. However, we have never had any experience in using this new route of PGE_2. To induce labour, therefore, we conduct this study to compare the effectiveness in induction of labour between this intracervical-application prostaglandin and the more commonly used intravaginal tablet. This will help us to obtain more information concerning the new pharmaceutical agents and have more alternatives in induction of labour.

Materials and Methods

This prospective randomized study was carried out at the Department of Obstetrics and Gynaecology, Faculty of Medicine, Chulalongkorn University Hospital from March 1993 to January 1995. Following the approval by our Institutional Review Board, nineteen women admitted for induction of labour, received either 0.5 mg of PGE_2 intracervical gel (Prepidil gel, Upjohn) or 3 mg of PGE_2 vaginal suppository (Prostin E_2, Upjohn). Inclusion criterias before informed consent and randomization were singleton pregnancy, vertex presentation, intact membranes, and cervical Bishop score of 5 or less. Patients with abnormal lie or presentation, premature rupture of membranes, oligohydramnios, previous uterine scars, history of allergy to prostaglandins or severe medical diseases such as asthma or heart diseases were excluded from the study. The gestational age was estimated with certainty by last menstrual period, early antenatal care or by ultrasonic findings that were compatible with the patients' own menstrual dates.

All procedures were performed in the labour room. Each patient was checked for cervical score and monitored over a period of 30 minutes to ensure that the fetal heart rate (FHR) were normal and few or no uterine contractions (fewer than three in 30 minutes). After an evaluation period, 0.5 mg of PGE_2 in a translucent, thixotropic sterile gel (2.5 ml) was administered into the cervical canal via a prefilled syringe with an accompanying introducer in the first group. Caution was taken not to push the gel above the level of the internal os.

In the other group, 3 mg of PGE_2 as a vaginal suppository was placed in the posterior fornix. Then, all the patients were asked to remain in flat position for at least 1 hour. In the first 2 hours, the patients were closely monitored for abnormal FHR and uterine hyperstimulation.

The Bishop score was assessed by the same obstetrician until delivery. After the first 2 hours, the routine labour care was carried out. Amniotomy was performed when cervical dilatation reached 3-4 cm unless membranes rupture spontaneously. Augmentation with oxytocin was done as indicated by arithmetic progression method. Route

and method of delivery was performed under obstetric indication.

We used the following indices to compare the outcome : time from initial application of PGE_2 until delivery, mode of delivery, incidence of uterine hyperstimulation, or other adverse effects, Apgar score and immediate newborn status.

The data were reported as mean and standard deviation and compared by unpaired t-test. $P < 0.05$ was considered significant.

Results

Nineteen cases with unfavourable cervix (Bishop score ≤ 5) were randomized to receive either PGE_2 intracervical gel or vaginal suppository. The patients' characteristics, shown in Table 1, were similar between the two groups.

Table 2 reveals the indications for induction of labour in both groups. Selected pregnancy outcome parameters are listed in Table 3. There were 2 cases of chorioamnionitis and 1 case of

Table 1. Patients' characteristics

	Gel (N = 9)	Suppository (N = 10)	P-value
Mother			
- Age (y)	25.33 ± 5.20	27.80 ± 5.35	0.32
- Parity	0.33 ± 0.71	0.70 ± 0.95	0.35
- Gestational age (wk)	39.44 ± 3.68	40.70 ± 1.57	0.36
- Initial Bishop score	3.33 ± 1.12	4.00 ± 0.94	0.18
Newborn			
- Birthweight (g)	3,022 ± 347	3,025 ± 308	0.99

Gel = Prostaglandin E_2 intracervical gel (Prepidil gel) 0.5 mg
Suppository = Prostaglandin E_2 vaginal suppository (Prostin E_2) 3 mg
y = year, wk = week, g = gram

Table 2. Indications for induction of labour

	Gel (N =9)	Suppository (N = 10)
1. Postterm	2	5
2. Fetal anomalies* or FDU	2	1
3. Poor weight gain	2	1
4. Mild preeclampsia	1	1
5. Others**	2	2

FDU = Fetal death in utero

* Fetal anomalies : Dandy-Walker syndrome, Hydrocephalus

** Decreased fetal movement, Thalassemia, Haemoglobinopathy, Systemic lupus erythematosus (SLE)

Table 3. Pregnancy outcome

	Gel (N=9)	Suppository (N=10)
Mother		
1. Route of delivery		
- Abdominal	5#	1@
- Vaginal	4	9
2. Augmentation with oxytocin	3	4
3. Analgesics given	8	7
4. Postpartum complication*	3	0
Newborn		
1. Sex (Male : Female)	4 : 5	6 : 4
2. Birthweight (g)	3,022 ± 347	3,025 ± 308
3. Apgar score (at 1 min < 7)	1	1
4. Neonatal jaundice	1	1

Reasons for caesarean section

Chorioamnionitis with fetal distress (1), Dandy Walker syndrome with chorioamnionitis (1), Fetal death in utero with cephalopelvic disproportion (1)-later developed endometritis, Failure to progress (2). The time of induction to delivery of the former 3 cases was 3 days.

@ Failure to progress (1)

* Chorioamnionitis (2), Endometritis (1)

Table 4. Mean time from application of PGE_2 to delivery in cases of successful vaginal delivery*

	Gel (N = 4)	Suppository (N = 8)	P-value
1. Application to labour (hr)	1 ± 0.71	11.21 ± 9.29	0.017
2. Application to delivery (hr)	13.75 ± 3.63	20.48 ± 6.74	0.049
3. Rupture of membranes to delivery (hr)	4.48 ± 2.46	4.80 ± 2.88	0.85

* Not included a case of hydrocephalus in the vaginal suppository group

postpartum endometritis in the gel group. In these cases, it took 3 days from induction of labour with PGE_2 until delivery. Birthweights were 2,990, 2,320 and 3,500 g respectively. The last two fetuses were Dandy Walker syndrome and fetal death in utero. In the other cases, delivery took place within 24 hours.

There was no uterine hyperstimulation found in both groups. Concerning the time-interval from labour to delivery, when considered only cases of successful vaginal delivery which also had similar patients' characteristics, the mean time interval of application to labour and application to delivery of the intracervical gel were significantly shorter than in the vaginal suppository group. However, the mean time of rupture of membranes to delivery had no statistical difference between the two groups (Table 4).

Discussion

The use of locally applied prostaglandin E_2 (PGE_2) has become a common intervention in the management of the unriped cervix in term pregnancy. Many studies have shown that induction of labour with prostaglandin E_2 vaginal suppositories was proved to be simple, safe and highly acceptable to patients and obstetricians alike in all cases in which a simple amniotomy would not suffice.[2,6-8] Nevertheless, in 1983 Stewart et al[9] found that extraamniotic prostaglandin E_2 produced a more reliable cervical ripening effect and rapid onset of labour in the cases of unriped cervix than vaginal prostaglandin E_2 group.The former route is relatively invasive when compared to vaginal application. When considering intracervical prostaglandin E_2 gel which is less invasive than the extraamniotic route, some studies have revealed that it is a safe and effective method of cervical ripening in parturients with highly unfavourable cervix.[10,11]

In this study, we compared pregnancy outcome between the two groups using intracervical prostaglandin gel or vaginal suppositories. It was found that the intracervical gel group had more caesarean section rate, partly due to chorioamnionitis, which is different from the studies of Legarthe et al[12] and Hales et al[13] which revealed no significant difference in the routes of delivery and reported no infection both intrapartum or postpartum. This might be due to the prolonged duration of the time interval from induction to delivery in 3 cases of the gel group which took 3 days. Moreover, the indication for induction of labour in this group were fetal death in utero in one case and Dandy Walker syndrome in another.

Regarding the mean time of application of prostaglandins to delivery, in cases of successful vaginal delivery, this study revealed that the intracervical gel had significant shorter time-interval of application to labour and application to delivery than the vaginal suppository group eventhough the mean time of rupture of membranes to delivery was not different. The results in this study are reversed to the study of Legarth et al[12] which found that in the suppository group the delivery time was significantly shorter than the cervical gel group, eventhough the study of Hales et al,[13] found no statistically significant difference. This might be due to the difference in form and dose of PGE_2 used in each study and also the frequency of repeated administration. Besides this, the instillation procedure of the intracervical gel is another key factor due to difference in depth of catheter insertion and amount of the gel spillage from the endocervical canal. This is only the first limited experience in our institute and further large scale studies are needed to clarify the appropriateness in using this new route in our population.

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References

1. Hayashi RH. Spontaneous and induced cervical ripening : natural dilatation and effacement process and current cervical ripening techniques. J Reprod Med 1993; 38: 66-72.
2. Shepherd JH, Bennett MJ, Laurence D, Moore F, Sims CD. Prostaglandin vaginal suppositories : a simple and safe approach to the induction of labor.

Obstet Gynecol 1981; 58: 596-600.

3. Kennedy JH, Stewart P, Barlow DH, Hillan E, Calder AA. Induction of labour : a comparison of a single prostaglandin E_2 vaginal tablet with amniotomy and intravenous oxytocin. Br J Obstet Gynaecol 1982; 89: 704-7.
4. Ekman G, Granstrom L, Ulmsten U. Induction of labor with intravenous oxytocin or vaginal PGE_2 suppositories : a randomized study. Acta Obstet Gynecol Scand 1986; 65: 857-9.
5. Legarth J, Lyndrup J, Dahl C, Philipsen T, Eriksen PS. Prostaglandin E_2 vaginal suppository for induction of labour : an efficient, safe and popular method. Eur J Obstet Gynecol Reprod Biol 1987; 26: 233-8.
6. Theppisai H, Taechakraichana N. Effects of prostaglandin E_2 on the cervix in complicated pregnancy. Chula Med J 1990; 34: 143-51.
7. Kenedy JH, Gordon-Wright AP, Stewart P, Calder AA, Elder MG. Induction of labor with a stable-based prostaglandin E_2 vaginal tablet. Eur J Obstet Gynecol Reprod Biol 1982; 13 : 203-8.
8. Elder MG. Intravaginal prostaglandins for cervical ripening and induction of labour. In : Egarter C, Husselin P, editors. Prostaglandins for cervical ripening and/or induction of labour. Wien. Facultas-Universitatsverlag. 1988: 46-52.
9. Stewart P, Kennedy JH, Hillan E, Calder AA. The unriped cervix : management with vaginal or extra-amniotic prostaglandin E_2. J Obstet Gynaecol 1983; 4: 90-3.
10. Rayburn WF Gosen R, Ramadei C, Woods R, Scott Jr J. Outpatient cervical ripening with prostaglandin E_2 gel in uncomplicated postdate pregnancies. Am J Obstet Gynecol 1988; 158: 1417-21.
11. Trofatter KF. Endocervical prostaglandin E_2 gel for preinduction cervical ripening : clinical trial results. J Reprod Med 1993; 38: 78-82.
12. Legarth J, Guldbaek E, Scher NJ. The efficacy of prostaglandin E_2 vaginal suppositories versus intracervical prostaglandin gel for induction of labor in patients with unfavorable inducibility prospects. Eur J Obstet Gynecol Reprod Biol 1988; 27: 93-8.
13. Hales KA, Rayburn WF, Turnbull GL, Christensen HD, Patatanian E. Doubleblind comparison of intracervical and intravaginal prostaglandin E_2 for cervical ripening and induction of labor. Am J Obstet Gynecol 1994; 171: 1087-91.