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Induction of labor by vaginal prostaglandin E2 (PGE2):a randomized study comparing gel with the suppository

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Objective : *To compare the efficacy and safety of prostaglandin E2 delivered as a vaginal gel and as a suppository.*

Methods : *Healthy term pregnant women with an unfavorable cervix (Bishop score < 5) and requiring induction of labor were admitted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University. All were randomly assigned to receive 2 mg PGE2 vaginal gel or a 3 mg PGE2 vaginal suppository. Failed induction was defined as no uterine contraction and/or cervical change within 24 hours of administration.*

Results : *Thirty five cases received PGE2 either as a vaginal gel (group I, n=17) or as a vaginal suppository (group II, n=18). Both groups were similar in terms of maternal age, gravida, gestational age and initial Bishop score. PGE2 vaginal gel and suppositories were equally effective in ripening the cervix. The mean changes of Bishop score were not different (3.53 versus 3.83; p=0.59). Although the mean induction-to-labor, induction-to-amniotomy, induction-to-full dilatation and induction-to-delivery intervals in group I seemed to be shorter, the differences did not reach statistical significance. No uterine hyperstimulation or other complications were recorded during this study.*

Conclusion : *Induction of labor with PGE2 vaginal gel or suppositories is equally effective and safe.*

Key words : *Prostaglandin E2, Cervical ripening, Labor induction.*

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สมชาย ธนวัฒนาเจริญ. ประสิทธิภาพในการชักนำให้เกิดการเจ็บครรภ์คลอดของพรอสตาแกลนดิน อี2 แบบสอดช่องคลอดชนิดเยลและชนิดเม็ด. จุฬาลงกรณ์เวชสาร 2540 พ.ย; 41 (11): 797-803

วัตถุประสงค์ : *เพื่อเปรียบเทียบประสิทธิภาพและความปลอดภัยระหว่างพรอสตาแกลนดิน อี2 แบบสอดช่องคลอดชนิดเยลและชนิดเม็ด ในการชักนำให้เกิดการเจ็บครรภ์คลอด*

วิธีการวิจัย : *สตรีตั้งครรภ์ครบกำหนดซึ่งมีข้อบ่งชี้ในการชักนำให้เกิดการเจ็บครรภ์คลอด และภาวะของปากมดลูกไม่พร้อม (Bishop score < 5) ได้เข้ารับการรักษาที่ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย และถูกแบ่งโดยการสุ่มออกเป็น 2 กลุ่ม กลุ่มที่ 1 ได้รับพรอสตาแกลนดิน อี2 แบบสอดช่องคลอดชนิดเยล ขนาด 2 มก. กลุ่มที่ 2 ได้รับพรอสตาแกลนดิน อี2 แบบสอดช่องคลอดชนิดเม็ด ขนาด 3 มก. การพิจารณาว่าการชักนำให้เกิดการเจ็บครรภ์คลอดล้มเหลวดูจากการตรวจไม่พบการหดรัดตัวของมดลูก และ/หรือ ไม่มีการเปลี่ยนแปลงภาวะของปากมดลูก ภายหลังบริหารยา 24 ชั่วโมง*

ผลการวิจัย : *สตรีตั้งครรภ์จำนวน 35 รายถูกแบ่งเป็นกลุ่มที่ 1 จำนวน 17 ราย และกลุ่มที่ 2 จำนวน 18 ราย โดยไม่มีความแตกต่างในเรื่องอายุ จำนวนการตั้งครรภ์ อายุครรภ์ และภาวะของปากมดลูกก่อนทำการศึกษา ประสิทธิภาพในการชักนำให้เกิดการเจ็บครรภ์คลอดของพรอสตาแกลนดิน อี2 แบบสอดช่องคลอดทั้งสองชนิดไม่แตกต่างกัน ค่าเฉลี่ยการเปลี่ยนแปลงภาวะของปากมดลูกก่อนและหลังบริหารยาระหว่างยาทั้งสองไม่แตกต่างอย่างมีนัยสำคัญทางสถิติ (3.53 และ 3.83; $p = 0.59$) ระยะเวลาตั้งแต่บริหารยาจนกระทั่งเจ็บครรภ์คลอด ถุงน้ำคร่ำแตก ปากมดลูกเปิดหมด และคลอดบุตร ในกลุ่มที่ 1 สั้นกว่ากลุ่มที่ 2 แต่ความแตกต่างดังกล่าวไม่มีนัยสำคัญทางสถิติในการศึกษานี้ไม่พบภาวะมดลูกหดรัดตัวมากเกินไปหรือภาวะแทรกซ้อนอื่น ๆ*

สรุป : *พรอสตาแกลนดิน อี2 แบบสอดช่องคลอดชนิดเยลและชนิดเม็ด มีประสิทธิภาพและความปลอดภัยในการชักนำให้เกิดการเจ็บครรภ์คลอดใกล้เคียงกัน*

Induction of labor in a patient with an unfavorable cervix always poses a formidable challenge to clinicians. The introduction of prostaglandin (PG) compounds, especially PGE2, has significantly reduced this challenge. PGE2 is proven effective and clinically acceptable.[1-6] Various routes of application and doses of the drug have been tried, but topical application in low doses has gained the most widespread acceptance.

Several studies have shown that a low-dose intracervical PGE2 gel appears to be an effective and safe cervical priming agent,[7,8] but the intravaginal preparation has the advantage of ease in application. Therefore, a lower dose intravaginal gel preparation with better absorption qualities has been developed.

The aim of the present study was to compare the efficacy and safety of prostaglandin E2 delivered as 2 mg vaginal gel and as a 3 mg vaginal suppository.

Material and methods

The study was carried out at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University. Healthy term pregnant women with Bishop scores < 5 with a fetus in cephalic presentation and not contraindicated to prostaglandin administration were admitted for induction of labor. All subjects gave their informed consent to take part in the investigation. They were all singleton pregnancies and had intact membranes prior to induction of labor. Exclusion criteria were patients with chronic medical illness, those suspected of cephalopelvic disproportion (CPD), abnormal lie or presentation, a history of cervical conization and serious obstetric complications.

Each patient underwent electronic fetal heart rate monitoring and had a reactive nonstress test (NST). Thereafter, the women were randomly allocated to receive either PGE2 gel (2 mg Dinoprostone gel) (group I) or a PGE2 suppository (3 mg Dinoprostone tablet) (group II). The cervical status was assessed before and 12 hours after drug administration or at the onset of labor. In both groups, amniotomy was performed when cervical dilatation reached 3 cm or more. After 12 hours of PGE2 administration, if the uterine contraction was inadequate, augmentation with oxytocin was administrated until adequate uterine contraction was achieved.

Failed induction was defined as no uterine contraction and/or cervical change after 24 hours of administration. A failed induction did not necessitate cesarean section. The clinical team made an evaluation and a subsequent induction or other treatment were prescribed as appropriate.

Continuous data were reported as a mean ± standard deviation. Statistical analysis was performed using an unpaired t-test or Fisher's exact test when it was appropriate. A p value < 0.05 was considered significantly different.

Results

A total of 37 cases were enrolled, but two were later excluded because one had a significant change of Bishop score at the time of administration and the other had unsuspected ruptured membranes. Thus 35 women received PGE2 intravaginally either gel (N = 17) or suppository (N = 18). Table 1 shows the patient characteristics of each group. Both groups were statistically similar with respect to age, gravida, gestational age and initial Bishop score. The indications for induction of labor were comparable between the groups as shown in Table 2. The most common indication was prolonged pregnancy.

Table 1. Patient characteristics.

	Group I* (N = 17)	Group II** (N = 18)	Significance
Age (Year)	24.5 ± 5.7	25.8 ± 4.8	NS
Gravida	1.3 ± 0.5	1.2 ± 0.4	NS
Gestational age (Days)	280.7 ±14.4	280.9 ±11.3	NS
Initial Bishop score	3.2 ± 0.8	3.3 ± 0.8	NS

* Group I = PGE2 vaginal gel

** Group II = PGE2 vaginal suppository

Table 2. Indications for induction of labor.

	Group I (N = 17)	Group II (N = 18)	Significance
Uncertain date	1	0	NS
Prolonged pregnancy	12	11	NS
Pregnancy induced hypertension	3	5	NS
Intrauterine growth retardation	1	2	NS

There was no significant difference in mean Bishop score change between both groups. Three patients in group I and one in group II was considered failed induction of labor. Time from induction to labor in successful induction of group I was shorter than group II, however the difference did not reach statistical significance. Two patients in each group underwent cesarean section. The indications for cesarean section are shown in Table 3.

Table 3. The outcomes of induction of labor.

	Group I (N = 17)	Group II (N = 18)	Significance
Bishop score change	3.53 ± 1.4	3.83 ± 1.9	NS
Failed induction of labor	3	1	NS
Cesarean section	2	2	NS
(Indications)	(CPD)	(Fetal distress)	

The outcomes during the intrapartum and neonatal periods are shown in Table 4. Although the mean induction-to-labor, induction-to-amniotomy, induction-to-full dilatation and induction-to-delivery intervals in group I seemed to be shorter, nevertheless, the differences did not reach statistical significance. In addition, no significant differences was found between the two groups regard to infant sex, birthweight and APGAR score at 1 and 5 minutes. No uterine hyperstimulation or other complications were encountered in this study.

Table 4. Intrapartum and neonatal outcomes.

	Group I (N = 12)*	Group II (N = 15)*	Significance
Time from induction (minutes)			
to labor	276.2 ±237.4	373.0 ±155.9	NS
to amniotomy	634.2 ±255.3	743.0 ±220.3	NS
to full dilatation	924.2 ±372.8	1,086.3 ±468.6	NS
to delivery	965.4 ±404.7	1,162.2 ±473.9	NS
Infant sex (male/female)	4/8	7/8	-
Birthweight (grams)	3,208.3 ±261.5	3,034.7 ±383.6	NS
APGAR score			
at 1 minute	9.0 ± 0.0	8.8 ± 0.7	NS
at 5 minutes	10.0 ± 0.0	10.0 ± 0.0	NS

* The analysis included only cases who carried on until full dilatation and delivery.

Cesarean sections in this study were infrequent. Two cesarean sections in group I were performed because of cephalopelvic disproportion. Two in group II were performed because of fetal distress (one intrauterine growth retardation and one prolonged pregnancy).

Discussion

Induction of labor is often necessary when the benefits to either the mother, fetus, or both outweigh those of continuing the pregnancy. The cervical status is clearly related to the success of a labor induction. In 1964, Bishop designed a scoring system in multiparous patients and determined that when the cervical score exceeded 8, the incidence of vaginal delivery subsequent to labor was not significantly lower than that observed after spontaneous labor.[9] The American College of Obstetricians and Gynecologists determined that a cervical score of at least 6 is favorable and more likely to result in successful labor induction.[10] Those patients with a poor cervical score are more likely to have failed induction, prolonged labor, and increased likelihood of cesarean section.[11]

Prostaglandins have been shown to be effective in the artificial inducement of cervical

ripening as assessed by the Bishop score prior to the induction of labor. The safest and most effective route of administration remains a source of debate.

Several studies with PGE2 have been performed comparing success with cervical ripening when it is given intracervically or intravaginally. Rix P et al, found that cervical ripening and induction of delivery by local administration of PGE2 gel or tablets was equally effective.[12] Comparing PGE2 intracervical and intravaginal gel, Hales KA, et al, concluded that both preparations were safe, but intravaginal gel was better because of its ease of administration and higher likelihood of cervical change.[7]

This study aimed to compare the efficacy and safety of PGE2 delivered as vaginal gel and as a suppository. Smith CV, et al, using 2.5 mg PGE2 gel compared with a 3 mg PGE2 suppository, concluded that both methods were effective, however a lower incidence of uterine hyperstimulation was noted with the gel.[8] Our study also found that the efficacy in induction of labor with PGE2 vaginal gel and suppositories were similar. But we encountered no uterine hyperstimulation or other complications in either group.

In conclusion, this study supports the efficacy and safety of PGE2 as a cervical ripening agent, either as a vaginal gel or as a suppository. However, due to the small sample size of this study, it might not have enough statistical power to detect a difference in efficacy and adverse effects between these two groups. Hence, further investigation in a larger scale clinical trial is ultimately required to determine any difference of these two preparations.

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References

1. Neilson DR Jr, Prins RP, Bolton RN, Mark C 3rd, Watson P. A comparison of prostaglandin E2 gel and prostaglandin F2 gel for preinduction cervical ripening. Am J Obstet Gynecol 1983 Jul 1; 146 (5):526-30
2. Prins RP, Bolton RN, Mark C 3rd, Neilson DR, Watson P. Cervical ripening with intravaginal prostaglandin E2 gel. Obstet Gynecol 1983 Apr; 61 (4):459-62
3. Prins RP, Neilson DR Jr, Bolton RN, Mark C 3rd, Watson P. Preinduction cervical ripening with sequential use of prostaglandin E2 gel. Am J Obstet Gynecol 1986 Jun; 154 (6): 1275-9
4. Rayburn W, Gosen R, Ramadei C, Woods R, Scott J Jr. Outpatient cervical ripening with prostaglandin E2 gel in uncomplicated post-date pregnancies. Am J Obstet Gynecol 1988 Jun; 158 (6 pt 1):1417-23
5. Rayburn WF. Prostaglandin E2 gel for cervical ripening and induction of labor: a critical analysis. Am J Obstet Gynecol 1989 Mar; 160 (3):529-34
6. Trofatter KF Jr. Endocervical prostaglandin E2 gel for preinduction cervical ripening, Clinical trial results. J Reprod Med 1993 Jan; 38 (Suppl):78-82
7. Hales KA, Rayburn WF, Turnbull GL, Christensen HD, Patatanian E. Double-blind comparison of intracervical and intravaginal

prostaglandin E2 for cervical ripening and induction of labor. Am J Obstet Gynecol 1994 Oct; 171 (4):1087-91

8. Smith CV, Rayburn WF, Connor RE, Fredstrom GR, Phillips CB. Double-blind comparison of intravaginal prostaglandin E2 gel and "chip" for preinduction cervical ripening. Am J Obstet Gynecol 1990 Sep; 163 (3):845-7
9. Bishop EH. Pelvic scoring for elective induction. Obstet Gynecol 1964 Aug; 24 (2):266-8
10. American College of Obstetricians and Gynecologists. Induction and augmentation of labor. Washington, DC: American College of Obstetricians and Gynecologists, November 1987; technical bulletin no 110
11. Lange AP, Secher NJ, Westergraard JG, Skovgard I. Prelabor evaluation of inducibility. Obstet Gynecol 1982 Aug; 60 (2):137-47
12. Rix P, Ladehoff P, Moller AM, Tilma KA, Zdravkovic M. Cervical ripening and induction of delivery by local administration of prostaglandin E2 gel or vaginal tablets is equally effective. Acta Obstet Gynecol Scand 1996 Jan; 75 (1):45-7