A Randomized Comparison of One Single Dose of Vaginal 50 μg Misoprostol with 3 mg Dinoprostone in Pre-Induction Cervical Ripening

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Abstract

Objective: To compare the efficacy and safety of one single dose of 50 μg misoprostol to one single dose of 3 mg dinoprostone administered vaginally for pre-induction cervical ripening in term-pregnant women, who had indications for induction of labor with unripe cervices.

Study design: A randomized double-blind controlled trial.

Setting: Bangkok Metropolitan Administration Medical College and Vajira Hospital, Bangkok, Thailand.

Subjects: One hundred and forty-three singleton pregnant women of ≥ 37 weeks of gestation, who had indications for termination of pregnancy. All patients had a Bishop score of 0-6, without contraindications for labor induction.

Intervention: The subjects were stratified by parity to nullipara and multipara group. The subjects in each stratum were allocated by randomization to receive a single dose of 50 μg misoprostol or 3 mg dinoprostone, administered vaginally. Twenty-four hours after medication, oxytocin augmentation was given to both groups.

Main outcome measure: The Bishop score of cervix at 24 hours after insertion of the studied drugs, the occurrence of abnormal uterine contraction, and the number of vaginal deliveries within 24, 48 hours.

Results: The demographic data and the initial Bishop score (median score 3.5 *versus* 4.0) were comparable in both groups. The change of score at 24 hours was one unit higher in misoprostol-treated patients compared with dinoprostone-treated patients (mean change score 6.5 *versus* 5.5, with 95 per cent CI 0.04 to 2.1, p=0.042) but was not of clinical importance. There was a higher frequency of hyperstimulation syndrome in the misoprostol group (6.9% *vs* 0%) during 8 hours of cervical ripening. Although the difference was not statistically significant (p=0.058), it was clinically important. Comparing vaginal deliveries between the misoprostol and dinoprostone groups, the frequencies of delivery within 24 hours were 46.3 per cent *versus* 35.7 per cent (p=0.350), and within 48 hours were 88.9 per cent *versus* 89.3 per cent (p>0.05), non-significantly different. No significant differences were noted between misoprostol and dinoprostone in terms of interval from start of medication to vaginal delivery and neonatal outcomes.

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Conclusion: The efficacy of a single 50 μg dose of vaginally administered misoprostol, is not clinically different to 3 mg dinoprostone in cervical ripening. Although the study was not sufficiently large to detect the differences in abnormal uterine contractions between the two groups, there was a higher frequency of hyperstimulation syndrome in the misoprostol group compared to the dinoprostone group. Close utero-fetal monitoring in misoprostol-treated patients is needed.

Key word : Pre-induction Cervical Ripening, Misoprostol, Dinoprostone

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Labor induction is a necessary procedure for the completion of pregnancy in 10 per cent - 20 per cent of patients. Half of these patients have cervices that are unfavorable for the induction of labor. It is well known that labor induction in the presence of an unfavorable cervix is often prolonged, tedious and may lead to induction failure[1]. Due to the potential increase in unnecessary cesarean deliveries in patients with an unfavorable cervix, cervical ripening agents including Laminaria tents, prostaglandins are often applied before oxytocin is initiated[2]. The only agent approved for pre-induction cervical ripening and for induction of labor in patients with an unripe cervix is prostaglandins E_2 (PGE_2)[3]. Misoprostol, a synthetic prostaglandin E_1 analogue used for the prevention and treatment of gastro-duodenal ulcers has been recently studied. Many recent reports, including a meta-analysis, have revealed that misoprostol safely and effectively ripens the cervix in patients with an unfavorable cervix[4,5]. Misoprostol decreases the cesarean delivery rate and increases the incidence of vaginal delivery within 24 hours of its administration.

Most studies have shown an increased incidence of uterine tachysystole and hyperstimulation with the use of misoprostol[6,7]. However, the proportion of poor neonatal outcomes, as a consequence of the increased uterine activity, does not significantly increase.

The majority of dosing regimens, which has been studied till the present, is the multiple administrations of misoprostol with various doses and intervals that safely ripen the cervix and induce labor[3-10]. The proper dosage of misoprostol for cervical ripening without any adverse effect on the fetus has not been established. Adverse effects on the uterus potentially occur due to the frequent administration of misoprostol. There are a few studies of one single dosing regimen for pre-induction cervical ripening. The objective of this study was to compare one single dose of 50 μg misoprostol to 3 mg of dinoprostone (PGE_2), administered vaginally for pre-induction ripening in patients with unripe cervices, in terms of efficacy and safety.

SUBJECTS AND METHOD

The study was performed from November 1998 to December 1999, at Bangkok Metropolitan Administration Medical College and Vajira Hospital. This study was a randomized, double – blind, controlled clinical trial and approved by the Institutional Review Board. The enrolled patients were singleton pregnant women of $\geq$ 37 weeks of gestation with indications for termination of pregnancy and with an initial Bishop score less than seven. All eligible patients were stratified by parity into nullipara and multipara groups and patients in each stratum were randomly allocated to receive a single dose of 50 μg misoprostol or 3 mg dinoprostone, administered vaginally. Excluded criteria consisted of suspected cephalo–pelvic disproportion, estimated fetal weight > 4000 grams, parity > 5, previous cesarean section and other uterine surgeries, suspected chorioamnionitis, contraindications to vaginal delivery, contraindications to the use of prosta-

glandins, and moderate to severe pre-existing medical diseases.

For the preparation of 50 μg misoprostol, a Cytotec oral tablet (200 mg, Searle, U.S.A.) was weighed on an electronic balance "Ohaus – model AP210S" (Ohaus Corporation, U.S.A.). Each tablet was composed of an active ingredient, misoprostol 200 μg, and supporting inactive powder. After weighing, Cytotec was bisected almost equally into two pieces. Each piece was gradually trimmed and weighed until its weight reached one – fourth of the initial tablet. The dinoprostone vaginal tablet was put in the original foil (Prostin E2, Upjohn, U.S.A.)

After the determination of indication for induction, each patient underwent a digital cervical examination to assess the Bishop score. Informed consent was signed after proper counselling. An intravenous line was placed, and the external cardiotocometer was started 30 minutes before the drug administration in order to ensure a normal fetal heart rate tracing and absence of regular uterine contraction. The investigator assessed the initial Bishop score at 8.00 a.m.. A resident, who was not involved in the outcome assessment, inserted the randomized drugs into the posterior vaginal fornix. The patient was left in supine or lateral position for at least one hour. Vital signs and side effects were monitored every hour. The cardiotocometer continuously monitored fetal heart activity and uterine contraction for 8 hours. Pelvic examination and oxytocin infusion as well as amniotomy were not employed within the 24 hours of prostaglandin insertion, except in a necessary situation.

The cardiotocograph was evaluated for uterine tachysystole, hypertonus, hyperstimulation syndrome[11]. Tachysystole was defined as ≥5 uterine contractions in ten minutes for two consecutive 10 – minute periods. Hypertonus was defined as a single uterine contraction that persisted for ninety seconds or more. Hyperstimulation syndrome was defined as tachysystole or hypertonus accompanied with any one of non-reassuring fetal heart rate patterns: fetal tachycardia (>160 beats per minute), late deceleration, bradycardia, moderate to severe variable deceleration and /or loss of short – term variability. The treatment of uterine contraction abnormality was given in both groups when there was tachysystole or hypertonus of pressure amplitude >30 mm Hg with or without non – reassuring fetal heart rate. Terbutaline 250 μg was administered intravenously and repeated if there were recurrent episodes of abnormal uterine contractions. Intrauterine resuscitation was given in patients having non-reassuring fetal heart rate pattern, consisting of a change in maternal position, administration of oxygen and close observation. Patients with abnormal contractions would be monitored continuously until delivery. Twenty-four hours after medication, the investigator reassessed the cervical Bishop score, and oxytocin was given to augment the labor.

For the primary outcome, change of Bishop score at 24 hours, a sample size of 66 per group was calculated by using a two tailed α=0.05, β=0.10, and pooled variance derived from the results of our pilot study. Standard deviation in the misoprostol group was 2.13 units and in the dinoprostone group was 3.33 units. The mean change difference of the 24-hour score of 1.5 units was considered to be clinically important according to the concensus of investigators.

The data were analyzed on an intention-to-treat basis by both parametric and non-parametric statistics, using statistical program SPSS 7.5. Continuous variables were examined for normal distribution (Kolmogorov-Smirnov test) before using parametric statistics. Differences among continuous variables were evaluated with the unpaired *t* test for variables that were normally distributed, and with the Mann-Whitney U tests for variables that were not normally distributed. Categorical variables were evaluated appropriately with the Chi square (χ^2) test or Fisher's exact test. The primary outcome measure was considered significantly only when $p \leq 0.05$. The significance for all secondary outcomes was $p \leq 0.001$ to account for multiple testing, a conservative approach.

RESULTS

During the study period, 143 pregnant women who had indications for induction of labor and fulfilled the eligible criteria were enrolled in the study. They were randomly allocated to receive misoprostol in 72 cases and dinoprostone in 71 cases. Demographic baseline data were similar in both groups as shown in Table 1. The indications for labor inductions were not significantly different between the groups, as shown in Table 2.

There were four vaginal deliveries and one cesarean delivery for fetal distress within 8 hours after the insertion of misoprostol. In the dino-

Table 1. Demographic data of patients.

	Misoprostol (n=72)	Dinoprostone (n=71)	P
Age(yr)			
Median (range)	24(15-38)	24(16-37)	0.902**
Height (cm)			
Mean (SD)	154.6(6.38)	154.4(5.40)	0.831*
Weight (kg)			
Median (range)	65.1(54.7-94.3)	63.3(50.0-106.0)	0.566**
Hct (vol%)			
Mean (SD)	34.3(3.26)	34.8(3.42)	0.428*
Gestational age (wk)			
Median (range)	41(37-42)	41(38-42)	0.278**
Number of primigravidae	42(58.3%)	36(50.7%)	0.454#
Number of nulliparae	47(65.3%)	48(67.6%)	0.906#
Initial Bishop score			
Median (range)	3.5(0-6)	4.0(0-6)	0.481**
Score less than 4	36(50.0%)	33(46.5%)	0.800#

*Unpaired *t* test. ** Mann-Whitney *U* test. # χ^2 with continuity correction.

Table 2. Indications for labor induction.

	Misoprostol (n=72)	Dinoprostone (n=71)	P
Gestational age ≥41 wk	46(63.9%)	50(70.4%)	0.549#
Oligohydramnios	18(25.0%)	13(18.3%)	df=2
Pre-eclampsia	8(11.1%)	6(8.5%)	
Chronic hypertension	0	1(1.4%)	
Diabetes mellitus	0	1(1.4%)	

#χ^2, P by gestational age, oligohydramnios and pre-eclampsia.

prostone group, there were two vaginal deliveries and one cesarean delivery performed due to fetal distress. Cesarean section for fetal distress in both groups was related to oligohydramnios. The score of subjects, whose labor went through the active phase or delivered vaginally within 24 hours after insertion, were arbitrarily assigned to be 13 units. Therefore, 71 misoprostol - treated patients and 70 dinoprostone – treated patients were assessed for Bishop score 8 hours after medication. Table 3 shows the Bishop score and changes of score at 8 and 24 hours after medication. The median score and the change of score at 8 hours after medication in the misoprostol group, were similar to those of the dinoprostone group. Between 8 to 24 hours, there were three cesarean sections in the misoprostol group and two cesarean sections in the dinoprostone group of which labor did not go through the active phase. Consequently, there were 68 cases in both groups to which the Bishop score was assessed 24 hours after medication. The mean change of score in the misoprostol group was one unit more than that of the dinoprostone group, a statistically significant difference.

Abnormal uterine contractions between the two groups was not significantly different, as shown in Table 4. All cases of abnormal uterine contraction responded to conservative treatment. In three of seven cases of the misoprostol group, an abnormal contraction developed later than four hours. The latest occurrence was seven hours after drug insertion. All five cases with abnormal contractions in the dinoprostone group occurred within four hours.

Table 3. Bisphop score at 8 and 24 hours.

	Misoprostol	Dinoprostone	Difference(95%CI)	P
8-hour score	(n=71)	(n=70)		
Median score (range)	7(0-13)	7(1-13)		0.294**
Median change of score (range)	3(0-10)	2(0-7)		0.169**
24-hour score	(n=68)	(n=68)		
Median score (range)	10(3-13)	10(1-13)		0.173**
Mean change of score (SD)	6.5(3.01)	5.5(2.93)	1.0(0.04 to 2.1)	0.042*
95%CI	5.8 to 7.2	4.8 to 6.2		

*Unpaired *t* test. ** Mann-Whitney *U* test.

Table 4. Abnormal uterine contraction within 8 hours.

	Misoprostol (n=72)	Dinoprostone (n=71)	OR(95%CI)	P
Abnormal uterine contraction	7(9.7%)	5(7.0%)	1.4(0.4 to 4.7)	0.782#
Tachysystole*	2	4		
Hypertonus*	0	1		
Hyperstimulation syndrome**	5	0		0.058##

* Without abnormal felal heart tracing. ** With abnormal fetal heart tracing.
# χ^2 with continuity correction. ## Fisher's exact test.

The delivery rate within 24 hours in the misoprostol group was higher than the delivery rate in the dinoprostone group, as shown in Table 5. However, the difference was not statistically significant. Vaginal and cesarean deliveries between the two groups were not statistically significant. Two patients in the dinoprostone group withdrew from the study after 24 hours of drug insertion. Both refused further treatment when they did not enter true labor after two days of admission. After 24 hours, vaginal and cesarean deliveries were not significantly different in both groups, as shown in Table 5. All cesarean sections for fetal distress were not related to the uterine hyperactivity in both groups. The number of patients with vaginal delivery in the misoprostol group and dinoprostone group were 54, 56 respectively. The incidences of vaginal delivery within 24 hours, during 24 to 48 hours and after 48 hours were not significantly different between both groups, as shown in Table 6. The vaginal delivery rate within 24 hours was 46.3 per cent *versus* 35.7 per cent (P=0.350) and within 48 hours was 88.9 per cent *versus* 89.3 per cent (P>0.05). This table also shows the time interval from the administration of the studied drugs to vaginal delivery. In the misoprostol group, the median interval was 2.8 hours shorter than in the dinoprostone group, a non-significant difference.

In both groups, there were no maternal adverse events in terms of nausea, vomiting, diarrhea, pyrexia and the postpartum course during hospitalization. The neonatal outcomes in both groups were evaluated and revealed no significant difference, as shown in Table 7. There were no poor neonatal outcomes in both groups.

DISCUSSION

Prostaglandins are the agents of choice to ripen the cervix before the induction of labor. However, they are expensive and usually not available in many developing countries. Misoprostol, on the other hand, is quite cheap, available in over 70 countries and more stable than PGE_2 (dinoprostone) tablets[12].

The accumulative effects of multiple doses of misoprostol may cause a dangerous degree of uterine hyperactivity and are potentially prone to

Table 5. Deliveries within 24 hours and after 24 hours.

	Misoprostol (n=72)	Dinoprostone (n=71)	OR(95%CI)	P
Delivery within 24 hours	32(44.4%)	23(32.4%)	1.7(0.9 to3.3)	0.191#
- Vaginal delivery	25(34.7%)	20(28.2%)		0.494##
- Cesarean delivery	7(9.7%)	3(4.2%)		
Fetal distress	5	3		
CPD/arrest pattern	2	0		
Delivery after 24 Hours	40(55.6%)	46(64.8%)*		
- Vaginal delivery	29(40.3%)	36(50.7%)		0.712#
- Cesarean delivery	11(15.3%)	10(14.1%)		
CPD/arrest pattern	8	7		
Failed induction	2	3		
Fetal distress	1	0		

* Two patients withdrew after 24 hours. CPD = cephalo-pelvic disproportion
# χ^2 with continuity correction. ## Fisher's exact test,

Table 6. Vaginal delivery and start to vaginal delivery time.

	Misoprostol (n=54)	Dinoprostone (n=56)	P
Vaginal delivery within 24 hours	25(46.3%)	20(35.7%)	0.486#
Vaginal delivery during 24 - 48 hours	23(42.6%)	30(53.6%)	df=2
Vaginal delivery after 48 hours	6(11.1%)	6(10.7%)	
Median start to vaginal delivery time (h)	25.8(4.8-77.5)	28.6(7.8-85.0)	0.155*

#χ^2 . *Mann-Whitney *U* test.

Table 7. Neonatal outcomes.

	Misoprostol (n=72)	Dinoprostone (n=69)	P
Birth weight (g)			
Median (range)	3170(2250-4500)	3250(2450-4150)	0.336**
Meconium stained			
(moderate to thick)	3(4.2%)	2(2.9%)	>0.05##
Apgar score 1 min			
Median (range)	9(6-10)	10(5-10)	0.508**
<7	2(2.8%)	5(7.2%)	0.268# #
Apgar score 5 min			
Median (range)	10(9-10)	10(8-10)	0.622**
<7	0	0	
NICU admission	0	1(1.5%)	0.489# #

NICU = neonatal intensive care unit.
** Mann--Whitney *U* test. ## Fisher's exact test.

adverse effects[13]. The one-time dose of misoprostol for cervical ripening before labor induction with oxytocin should reduce the complications, which may occur during the administration of a multiple dosing regimen. A few studies in the literature have reported a single dose of 100 µg misoprostol for pre-induction cevical ripening[13,14]. The duration of ripening of the studies varied from 6, 12 to 24 hours. The 24-hour cervical ripening might yield more efficacy, although with a longer waiting period.

The primary goal of this study was to compare the efficacy of a single dose of 50 µg of intravaginal misoprostol, assessed 24 hours after drug insertion, to the standard cervical ripening agent. With a one-time dose of 50 mg of intravaginal misoprostol and 3 mg of dinoprostone, the findings supported the improved efficacy in cervical ripening of prostaglandins during 24-hour waiting. The mean change of 24-hour score in the misoprostol group was one unit more than that of the dinoprostone group. This difference was statistically significant but without clinical importance.

The meta-analysis and systematic review confirmed that misoprostol was an effective agent for cervical ripening and labor induction in patients at term, showing an increase in the incidence of vaginal delivery within 24 hours of its administration[4]. The trials, using a single dose of 100 µg misoprostol for 6-24 hours of cervical ripening and being further augmented by oxytocin, reported 80 per cent to 95 per cent delivered vaginally within 24 hours and mean start to vaginal delivery time of 16 to 19 hours[13,15]. In this study, vaginal delivery within 24, 48 hours in the misoprostol group was 46.3. per cent and 88.9 per cent respectively, with the median start to vaginal delivery time of 25.8 hours. There were no significant differences in the frequencies of vaginal delivery within 24, 48 hours between the misoprostol and dinoprostone group.

Uterine hyperactivity is mainly relevant to the use of misoprostol. Wing et al[6] reported the highest rate of uterine tachysystole at 36.7 per cent with a hyperstimulation rate of 7.4 per cent with the use of a dose of 50 µg, repeated every 3 hours for the maximum of six doses. The accumulative effects of multiple doses of misoprostol reported in other series may cause an increase in uterine tone. The studies using a single dose of 100 mg misoprostol and being further augmented by oxytocin reported tachysystole rates of 4.2 per cent to 37 per cent and uterine hyperstimulation rates of 0 to 9.4 per cent[13-17]. In this study, with the use of a single 50 mg dose of intravaginal misoprostol, there was an abnormal uterine contraction rate of 9.7 per cent, which was 2.8 per cent uterine tachysystole and 6.9 per cent hyperstimulation syndrome occurring within 8 hours. Although the study did not show any difference in abnormal uterine contractions between the two studied drugs, the higher frequency of hyperstimulation syndrome in the misoprostol group was clinically important. However, patients receiving a ripening agent including misoprostol and dinoprostone require close observation. As the abnormal uterine contraction is encountered, it can be normalized by conservative management. This study did not show any differences in neonatal outcome between the misoprostol and dinoprostone groups, but the power of the study was not sufficient to eliminate the possibility of type II error.

This trial studied the ripening efficacy of the drugs administered only by single dose with 24-hour waiting. The result would not be applicable for women who need urgent termination of pregnancy or whose indications for induction of labor cannot wait beyond 24 hours.

A single dose of 50 µg misoprostol was not clinically different from 3 mg dinoprostone for ripening the unfavorable cervix. Misoprostol shows promise as an effective, inexpensive and convenient agent. One tablet of 3 mg dinoprostone costs 550 baht, whereas, one tablet of 200 µg misoprostol costs 11 baht. However, the increase in hyperstimulation syndrome following misoprostol is a matter of concern and needs close utero-fetal monitoring. Further trials examining dosage, intervals and routes of administration with large power for the detection of fetal and maternal morbidity are needed.

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REFERENCES

1. Bishop EH. Pelvic scoring for elective induction of labor. Obstet Gynecol 1964; 24:266-8.
2. Wilson PD. A comparison of four methods of ripening the unfavorable cervix. Br J Obstet Gynecol 1978; 85:941-4.
3. Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cevical ripening and labor induction. Am J Obstet Gynecol 1995; 172:1811-6.
4. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labor induction: a meta-analysis. Obstet Gynecol 1997; 89:633-42.
5. Hofmeyr GL. Misoprostol administered vaginally for cervical ripening and labour induction with a viable fetus. The Cochrane Library 1998;2:1-15.
6. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. Am J Ostet Gynecol 1995; 172:1804-10.
7. Varaklis K, Gumina R, Stubblefield PG. Randomized controlled trial of vaginal misoprostol and intracervical prostaglandin E2 gel for induction of labor at term. Obstet Gynecol 1995;86:541-4.
8. Buser D, Mora G, Arias F. A randomized comparison between misoprostol and dinoprostone for cervical ripening and labor induction in patients with unfavorable cervices. Obstet Gynecol 1997; 89:581-5.
9. Wing DA, Ortiz-Omphroy G, Paul RH. A comparison of intermittent vaginal administration of misoprostol with continuous dinoprostone for cervical ripening and labor induction. Am J Obstet Gynecol 1997;177:612-8.
10. Sanchez-Ramos L, Peterson DE, Delke I, Gaudier FL, Kaunitz AM. Labor induction with prostaglandin E1 misoprostol compared with dinoprostone vaginal insert: a randomized trial. Obstet Gynecol 1998;91:401-5.
11. Curtis P, Even S, Resnick J. Uterine hyperstimulation. The need for standard terminology. J Reprod Med 1987;32:91-5.
12. Toppozada MK, Anwar MYM, Hassan WS, El-gazaerly WS. Oral or vaginal misoprostol for induction of labor. Int J Gynecol Obstet 1997;56: 135-9.
13. Gottsschall DS, Borgida AF, Mihalek JJ, Sauer F, Rodis JF. A randomized clinical trial comparing misoprostol with prostaglandin E2 gel for preinduction cervical ripening. Am J Obstet Gynecol 1997;177:1067-70.
14. Herabutya Y, O-Prasetsawat P, Pokpirom J. A comparison of intravaginal misoprostol and intracervical prostaglandin E2 gel for ripening of unfavorable cervix and labor induction. J Obstet Gynaecol Res 1997;23:369-74.
15. Srisomboon J, Piyamongkol W, Aiewsakul P. Comparison of intracervical and intravaginal misoprostol for cervical ripening and labor induction in patients with an unfavorable cervix. J Med Assoc Thai 1997;80:189-93.
16. Fletcher H, Mitchell S, Simeon D, Frederick J, Brown D. Intravaginal misoprostol as a cervical ripening agent. Br J Obstet Gynecol 1993;100: 641-4.
17. Fletcher H, Mishell DR, Simeon D, Frederick J, Brown D. Intravaginal misoprostol *versus* dinoprostone as cervical ripening and labor-inducing agents. Obstet Gynecol 1994;83:244-7.

เปรียบเทียบยามัยโสพรอสทอล 50 ไมโครกรัม กับ ยาไดโนพรอสโทน 3 มิลลิกรัม สอดทางช่องคลอดครั้งเดียวในการเตรียมปากมดลูกเพื่อการคลอดโดยการทดลองทางคลินิกแบบสุ่มทดลอง

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วัตถุประสงค์ : เพื่อเปรียบเทียบประสิทธิผลและความปลอดภัยของการใช้ยามัยโสพรอสทอล 50 ไมโครกรัมกับยาไดโนพรอสโทน 3 มิลลิกรัม สอดทางช่องคลอดครั้งเดียว ในการเตรียมปากมดลูกเพื่อการคลอดในสตรีตั้งครรภ์ครบกำหนด ซึ่งมีข้อบ่งชี้ในการคลอดแต่ปากมดลูกยังไม่พร้อม

รูปแบบการทดลอง : การทดลองทางคลินิกแบบสุ่มทดลอง

สถานที่ทำการวิจัย : วิทยาลัยแพทยศาสตร์กรุงเทพมหานครและวชิรพยาบาล กรุงเทพมหานคร

กลุ่มตัวอย่าง : สตรีตั้งครรภ์เดี่ยวที่มีอายุครรภ์ตั้งแต่ 37 สัปดาห์ขึ้นไป จำนวน 143 ราย ที่มีข้อบ่งชี้ให้สิ้นสุดการตั้งครรภ์ มีคะแนนบิช็อบ 0–6 ไม่มีข้อห้ามในการคลอดทางช่องคลอด

การกระทำ : ผู้ป่วยทั้งที่ไม่เคยคลอดและเคยคลอด แต่ละกลุ่มแบ่งผู้ป่วยเป็น 2 กลุ่มการศึกษาโดยวิธีการสุ่มแบ่งกลุ่ม โดยกลุ่มแรกได้รับยามัยโสพรอสทอล 50 ไมโครกรัม ในกลุ่มที่สองได้รับยาไดโนพรอสโทน 3 มิลลิกรัม ทั้งสองกลุ่มได้รับการบริหารยาโดยการสอดทางช่องคลอดครั้งเดียว หลังจากนั้น 24 ชั่วโมง ให้ยาอ็อกซิโทซิน

การวัดผล : คะแนนบิช็อบของปากมดลูกที่ 24 ชั่วโมงหลังได้รับยา การหดรัดตัวผิดปกติของมดลูก การคลอดทางช่องคลอดใน 24 และ 48 ชั่วโมง

ผลการวิจัย : ข้อมูลพื้นฐานและคะแนนบิช็อบเริ่มต้น (คะแนนมัธยฐาน 3.5 เทียบกับ 4.0) ของผู้ป่วยทั้ง 2 กลุ่มไม่แตกต่างกัน ผู้ป่วยที่ได้ยามัยโสพรอสทอลมีคะแนนที่เพิ่มขึ้นเมื่อชั่วโมงที่ 24 มากกว่าผู้ป่วยที่ได้ยาไดโนพรอสโทนหนึ่งหน่วย (คะแนนเพิ่มเฉลี่ย 6.5 เทียบกับ 5.5 ; 95% CI 0.04 ถึง 2.1 ; p=0.042) แต่ไม่มีความสำคัญทางคลินิก อัตราการเกิดกลุ่มอาการมดลูกหดรัดตัวมากกว่าปกติภายใน 8 ชั่วโมงในกลุ่มได้รับยามัยโสพรอสทอลสูงกว่า (6.9% เทียบกับ 0%) แม้ว่าไม่มีนัยสำคัญทางสถิติ (p=0.058) แต่มีความสำคัญทางคลินิก เมื่อเปรียบเทียบการคลอดทางช่องคลอดในผู้ป่วยที่ได้รับยามัยโสพรอสตอลและไดโนพรอสโทน พบว่าอัตราการคลอดใน 24 ชั่วโมงเท่ากับ 46.3% เทียบกับ 35.7% (p=0.350) และอัตราการคลอดใน 48 ชั่วโมงเท่ากับ 88.9% เทียบกับ 89.3% ซึ่งแตกต่างอย่างไม่มีนัยสำคัญ (p>0.05) ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติในระยะเวลาเริ่มให้ยาจนคลอดทางช่องคลอดและผลต่อทารก

สรุป : ยามัยโสพรอสทอล 50 ไมโครกรัมสอดทางช่องคลอดครั้งเดียวมีประสิทธิผลทางคลินิกในการเตรียมปากมดลูกเพื่อการคลอด ไม่แตกต่างจากยาไดโนพรอสโทน 3 มิลลิกรัม แม้ว่าจำนวนผู้ป่วยที่ศึกษายังไม่มากพอที่จะตรวจความแตกต่างของอัตราการเกิดมดลูกหดรัดตัวผิดปกติระหว่างผู้ป่วยทั้ง 2 กลุ่ม แต่ผู้ป่วยที่ได้ยามัยโสพรอสทอลเกิดกลุ่มอาการมดลูกหดรัดตัวมากกว่าปกติมากกว่าผู้ป่วยที่ได้รับยาไดโนพรอสโทน จึงจำเป็นที่จะต้องเฝ้าระวังการหดรัดตัวของมดลูกและเสียงหัวใจทารกในผู้ป่วยที่ได้รับยามัยโสพรอสทอล

คำสำคัญ : การเตรียมปากมดลูก, มัยโสพรอสทอล, ไดโนพรอสโทน

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