Therapeutic Termination of Second Trimester Pregnancy with Vaginal Misoprostol

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Abstract

Objective : To evaluate the efficacy of vaginal misoprostol in therapeutic termination of second trimester pregnancy with a live fetus.

Design : Prospective descriptive study.

Setting : Maharaj Nakorn Chiang Mai Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University.

Subjects : Pregnant women meeting the inclusion criteria including 1) pregnancy with a live fetus, 2) gestational age of 14-28 weeks, 3) having an indication for therapeutic termination, 4) Bishop's score of ≤ 4, 5) absence of uterine contraction and leakage of amniotic fluid, 6) no previous classical uterine scar and 7) no contraindication for misoprostol such as hypersensitivity.

Intervention : 400 microgram misoprostol gel intravagina every 12 hours.

Main outcome measures : Mean induction-delivery time, mean abortion time, maternal side effects.

Results : Sixty eight pregnant women were recruited into the study. The mean induction-delivery time was 35.58 ± 34.13 hours, mean abortion time was 35.80 ± 34.13 minutes. Fever was the most common side effect occuring in about two-third of the patients, but no serious maternal complication was observed.

Conclusion : 400 microgram vaginal misoprostol is effective for therapeutic termination of second trimester pregnancy with no serious side effects. However, the response to this treatment was markedly varied from patient to patient.

Key word : Misoprostol, Therapeutic Termination, Induction-Delivery Time, Mean Abortion Time

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J Med Assoc Thai 2001; 84: 515-519

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Termination of pregnancy in the second trimester is one of the most common problems in obstetric practice. Although various methods for termination of pregnancy are now available, such as several forms of prostaglandins, hypertonic saline solution and mifepristone, each of them has some disadvantage despite the comparable efficacy[1-4]. For example PGE2 or PGF2α are very expensive, mifepristone is not available in Thailand, and hypertonic solution technique is invasive, less effective and carries significant side effects, i.e. DIC. Misoprostol (Cytotec^{R}), a synthetic PGE1 analogue[5], used for treatment of peptic ulcer induced by NSAIDS, has currently been used for this purpose. Based on preliminary reports, misoprostol was effective in therapeutic abortion[5-8]. Due to its high efficacy, drug stability in room temperature, convenience in application and low cost, misoprostol has become more popular, though the efficacy and safety have not completely been studied. Although several preliminary reports suggested that misoprostol is highly effective, the optimal dosage, interval and route of administration were not evaluated. The objective of this study was to evaluate the efficacy and side effects of intravaginal misoprostol with a dosage of 400 microgram every 12 hours.

MATERIAL AND METHOD

Sixty-eight pregnant women were enrolled into the study because of medical reasons for therapeutic termination. Gestational age was based on reliable menstrual history, clinical estimation, and/or ultrasound examination. Cervical assessment for Bishop score was done just before insertion of misoprostol gel. Each of them met the inclusion criteria including 1) pregnancy with a live fetus, 2) gestational age of 14-28 weeks, 3) having an indication for therapeutic termination, 4) Bishop's score of $\leq$ 4, 5) absence of uterine contraction and leakage of amniotic fluid, 6) no previous classical uterine scar and 7) no contraindication for misoprostol such as hypersensitivity.

Two tablets of 400 micrograms misoprostol were crushed in a sterile container and mixed with 3 ml of 1 per cent CMC gel (carboxyl methyl cellulose prepared by the hospital pharmacists). Misoprostol gel was drawn into a 5 ml. plastic syringe and then was pushed deep into the posterior vaginal fornix. The patient was left in the supine position from 30 minutes to 1 hour. Vital signs, uterine contractions and side effects were monitored. Acetaminophen (500-1000 mg), diphenoxylate HCL (5 mg) and metoclopamide HCL (10 mg) were given orally in case of fever, diarrhea and nausea/vomiting, respectively.

Progression of labor was evaluated by cervical examination prior to subsequent dosage at 12 hourly intervals. If a favourable cervix was attained but uterine contraction was inadequate (less than 3 contractions in 10 minutes), oxytocin infusion would be started. Meperidine 50 mg and promethazine HCL 25 mg were intravenously given on demand as narcotic analgesic for uterine pain.

Induction-delivery time was defined as the time from initial administration of misoprostol to complete delivery of the fetus. Complete abortion was defined as complete expulsion of the placenta. If the conceptive products were not completely delivered either instrumental or manual evacuation was then carried out and this condition was considered to be an incomplete abortion. Abortion time was defined as the time from initial administration of the drug to complete expulsion of the placenta.

RESULTS

Sixty eight pregnant women were recruited into the study. Indications for therapeutic termination and baseline characteristics of the patients are shown in Table 1 and Table 2 respectively. The most common indication was Hb Bart's disease prenatally diagnosed by cordocentesis. The mean (±SD) maternal age was 29.21 ± 7.03 years and the mean (±SD) gestational age was 20.72 ± 3.22 weeks. Half of them were nuliparous and the other half were parous. The mean (±SD) cervical Bishop scores prior to intervention was 1.94 ± 0.98. The mean (±SD) induction-delivery time and the mean (±SD) abortion time were and 35.58 ± 34.13 hours and 35.80 ± 34.13 hours, respectively. (Table 3) About 83.9 per cent had complete abortion within 48 hours, and nearly 60 per cent had complete abortion within 24 hours. Side effects are presented in Table 4. Fever was the most common side effect, occurring in two-third of the patients but no serious maternal complication was noted.

DISCUSSION

The results of this study demonstrated the mean induction delivery time was 35.58 ± 34.13 hours and the mean abortion time was 35.80 ± 34.13 hours which were slightly longer than the

Table 1. Indications for therapeutic termination.

Indication	Number	%
Hb Bart's disease	19	27.9
ß-thal major	10	14.7
ß-thal E	7	10.3
Maternal HIV (+) ve	6	8.8
Fetal Down syndrome	6	8.8
Others	20	29.41
- holoprosencephaly	3	
- anencephaly	2	
- hydranencephaly	1	
- hydrocephalus	1	
- Dandy-Walker syndrome	1	
- cystic hygroma	1	
- spina bifida	1	
- thanatophoric dysplasia	1	
- trisomy 9	1	
- conjoint twins	1	
- hemophilia	1	
- fetal warfarin syndrome	1	
- maternal DM class R	1	
- pulmonary hypertension	1	
- maternal CA stomach	1	
- rape	1	
- multiple anomaly	1	

Table 2. Baseline characteristics of the patients.

Characteristics		
Maternal age (years),	mean ± SD	29.21 ± 7.03
	range	12 - 42
Gestational age (weeks),	mean ± SD	20.72 ± 3.22
	range	14 - 28
Bishop score,	mean ± SD	1.94 ± 0.98
	range	1 - 4
Parity		
0	number (%)	34 (50)
1		26 (38.2)
2		6 (8.8)
3		2 (2.9)

Table 3. Results of the treatment.

Results			
Induction-delivery time,	mean ± SD	35.58 ± 34.13	
(hours)	range	3.10 - 150.65	
Abortion time (hours),	mean ± SD	35.80 ± 34.13	
	range	3.12 - 150.70	
Complete abortion within			%
12 hours,	number	25	36.8
24 hours,	number	40	58.9
48 hours,	number	57	83.9
72 hours,	number	60	88.3
Oxytocin augmentation,	number	33	48.5
Analgesic requirment,	number	30	44.1
Complete abortion,	number	61	89.7
Mean doses of misoprostol,	mean ± SD	2.94 ± 2.73	
	range	1 - 14	

Table 4. Maternal side effects.

Side effects	Number	%
Fever (temperature > 38°C)	46	67.6
Chill	43	63.2
Diarrhea	14	20.6
Nausea	8	11.8
Vomiting	3	4.4
Post partum hemorrhage	0	
Uterine rupture	0	

study by Herabutya[9]. (33.4 hours, 400 mcg vaginal misoprostol every 12 hours)

Srisomboon[10] presented the mean abortion time of a live fetus (14-28 weeks of gestation by intracervicovaginal administration of 400 mcg misoprostol every 12 hours) was 27 hours 7 minutes. This time is obviously shorter than in our study eventhough a smaller dose of misoprostol was used. It can be explained that intracervical administration is highly effective, but this technique requires greater skill.

When compared to the study of Nuutila [11] the induction-abortion time was 27.8 ± 11.8 and 23.1 ± 12.3 hours in the group of misoprostol 200 mcg intravagina every 12 hours and 100 mcg intravagina every 6 hours, respectively. The time interval was shorter than our study, in spite of a smaller dose of misoprostol being given. With thorough review, we found that fetal death was not excluded, so it can shorten the mean time. The fact that 100 mcg misoprostol was more effective than 200 mcg, the time interval may be influenced by different treatment interval. According to the study by Nuutila[11] the administration interval might be more important than dosage to achieve complete abortion. Therefore, we might have achieved a better outcome if we had shortened the interval from 12 to 6 hours.

Our study confirmed that an intravaginal misoprostol regimen of 400 microgram every 12 hours was effective with no serious complications,

but the abortion time was rather longer than that in previous reports. Therefore, a more appropriate regimen with more shortened interval should be carried out. Furthermore, randomized controlled trials to compare the efficacy between different dosages and different intervals should be conducted.

Side effects were found to be transient but not serious. The most common side effect was fever followed by chill. No patient was complicated by a total blood loss of more than 500 ml.

Response to misoprostol was varied highly from person to person and unpredictable.

In conclusion, 400 mcg vaginal misoprostol every 12 hours is effective for therapeutic termination of second trimester pregnancy but optimal dose and time interval require further study.

(Received for publication on December 14, 1999)

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การยุติการตั้งครรภ์ในไตรมาสที่สองของการตั้งครรภ์ในกลุ่มทารกมีชีพ โดยมิโซ-โปรสตอลแบบเจลสอดทางช่องคลอดทุก 12 ชั่วโมง

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การศึกษาครั้งนี้มีวัตถุประสงค์เพื่อศึกษาประสิทธิภาพของการใช้ยามิโซโปรสตอล สองทางช่องคลอดเพื่อยุติการตั้งครรภ์ในไตรมาสที่สองในกลุ่มทารกมีชีพ โดยเป็นการวิจัยเชิงพรรณนา ทำการศึกษาที่ภาควิชาสูติศาสตร์และนรีเวชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ โดยคัดเลือกสตรีตั้งครรภ์ 68 ราย ที่มีเกณฑ์การคัดเลือกเข้าสู่การศึกษาดังนี้

1. ตั้งครรภ์และทารกมีชีพ
2. อายุครรภ์ 14–28 สัปดาห์
3. มีข้อบ่งชี้ให้ยุติการตั้งครรภ์
4. Bishop score น้อยกว่าหรือเท่ากับ 4
5. ไม่มีเจ็บครรภ์คลอดและน้ำเดิน
6. ไม่มีแผลผ่าตัดที่ตัวมดลูกแบบ classical scar
7. ไม่มีข้อบ่งห้ามต่อการใช้มิโซโปรสตอล เช่น แพ้ยา

บริหารยาโดยสอดยามิโซโปรสตอล ครั้งละ 400 ไมโครกรัม ในรูปแบบเจล เข้าไปในช่องคลอดซ้ำทุก 12 ชั่วโมง

ผลการศึกษาพบว่า :

ระยะเวลาเฉลี่ยตั้งแต่เริ่มบริหารยา–คลอดทารก = 35.58 ± 34.13 ชั่วโมง,

ระยะเวลาเฉลี่ยตั้งแต่เริ่มบริหารยา–คลอดรกครบ = 35.80 ± 34.13 ชั่วโมง

และผลข้างเคียงที่พบมากที่สุด คือ ไข้

สรุปว่า : มิโซโปรสตอล 400 ไมโครกรัมในรูปแบบเจล บริหารยาทางช่องคลอดทุก 12 ชั่วโมงมีประสิทธิภาพดีในการยุติการตั้งครรภ์ในไตรมาสที่สองในกลุ่มทารกมีชีพ แล้วไม่มีผลข้างเคียงใด ๆ ที่รุนแรง แต่อย่างไรก็ตามการตอบสนองต่อยาในสตรีตั้งครรภ์แต่ละคนมีความแปรปรวนมาก

คำสำคัญ : มิโซโปรสตอล, การยุติการตั้งครรภ์, เวลาชักนำคลอด, เวลาเฉลี่ยในการแท้ง

สายพิณ พงษธา, ธีระ ทองสง, อรวรรณ สุวรรณวุฒิ
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