Second Trimester Pregnancy Termination with 800 mcg Vaginal Misoprostol

SAIPIN PONGSATHA, M.D.*,
THEERA TONGSONG, M.D.*

Abstract

Objective : To demonstrate the efficacy of 800 microgram vaginal misoprostol tablet for second trimester pregnancy termination.

Design : Prospective descriptive study.

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

Subject : Pregnant women meeting the inclusion criteria including (1) singleton pregnancy with live fetus, (2) gestational age of 14-28 weeks, (3) indication for therapeutic termination, (4) closed and uneffaced cervix, (5) absence of uterine contraction and leakage of amniotic fluid, (6) no previous classical uterine scar, (7) no contraindication for misoprostol such as hypersensitivity.

Intervention : 800 microgram misoprostol tablet intravagina every 12 hours.

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

Results : The mean induction delivery time was 21.38 $\pm$ 13.68 hours, mean abortion time was 21.56 $\pm$ 13.68 hours. Diarrhea was the most common side effect occuring in 40 per cent of patients.

Conclusions : 800 mcg vaginal misoprostol every 12 hours is effective but if we want high efficacy along with fewer side effects, lower dose and interval should be further studied.

Key word: Misoprostol, Second Trimester Pregnancy Termination, Induction-Delivery Time, Mean Abortion Time

PONGSATHA S & TONGSONG T
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* Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

As we know there are several techniques for termination of second trimester pregnancy. Some of which are invasive and some are not effective. At the present time most physicians prefer to use prostaglandins because their efficacy and techniques for administration are invasive[1]. But there are some problems of prostaglandins use such as unstable at room temperature and high cost. These are the reasons they are inappropriate for use in our country. Misoprostol (Cytotec^{R}), a synthetic PGE_1 analogue, used for treatment of peptic ulcer induced by NSAIDS, has been widely used for this purpose. In previous studies have shown that misoprostol is effective in termination of second trimester pregnancy, drug stability in room temperature, low cost and safe[2-5]. However, the optimal dose and interval have not been concluded. The doses varied between 200 - 800 mcg every 3 - 12 hours. This study was carried out to evaluate the efficacy and maternal side effects of 800 mcg misoprostol tablet intravagina every 12 hours.

MATERIAL AND METHOD

Twenty pregnant women with indications for second trimester pregnancy termination were recruited into the study. Gestational age was confirmed by reliable menstrual history, clinical examination and / or ultrasound examination. Cervical assessment was evaluated just before insertion of the misoprostol tablets. Each patient met the inclusion criteria including 1) singleton pregnancy with live fetus diagnosed by ultrasound 2) gestational age of 14-28 weeks, 3) indication for therapeutic termination 4) closed and uneffaced cervix, 5) absence of uterine contraction and leakage of amniotic fluid, 6) no previous classical uterine scar, 7) no contraindication for misoprostol such as hypersensitivity.

Four tablets of 200 mcg misoprostol were placed deep in the posterior vaginal fornix. The patients were left in the supine position for 30 minutes. Vital signs, uterine contraction and side effects were closely observed. In cases of fever, diarrhea, nausea and vomiting, acetaminophen (500-1,000 mg) was given orally.

Progression of labor was assessed by cervical examination prior to the next dose at 12 hourly intervals. If a favourable cervix was attained but uterine contraction was inadequate (less than 3 contractions in 10 minutes), oxytocin infusion was started. Meperidine 50 mg and promethazine hydrochloride 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 the complete expulsion of placenta. Incomplete abortion was defined if the conceptive products were not completely delivered and in this situation the next step was instrumental or manual evacuation. Abortion time was defined as the time from initial administration of misoprostol to complete expulsion of placenta.

RESULTS

The baseline characteristics of 20 patients and indications for therapeutic termination are demonstrated in Table 1 and 2, respectively. The mean (± SD) maternal age was 28.55 ± 7.26 years, the mean (± SD) gestational age was 20.6 ± 3.69 weeks. Two patients had previous uterine scar.

The most common indication for termination was Hb Bart's disease (40%) prenatally diagnosed by cordocentesis. Results of the treatment are shown in Table 3. Mean (± SD) induction delivery time and mean (± SD) abortion time were 21.38 ± 13.68 and 21.56 ± 13.68 hours, respectively. Side effects are presented in Table 4. Diarrhea was the most common side effect followed by chills. No serious maternal side effects occurred.

Table 1. Baseline characteristics of the patients.

Characteristics	mean ± SD (range)	number	%
Maternal age (years)	28.55 ± 7.26 (18 - 40)	-	
Gestational (weeks)	20.6 ± 3.69 (14 - 28)	-	
Parity 0	-	12	60
Parity 1	-	5	25
Parity 2	-	2	10
Parity 3	-	0	
Parity 4	-	1	5
Previous cesarean section	-	2	10

Table 2. Indication for therapeutic termination.

Indications	Number	%
Hb Bart's disease	9	45
β- thal major	4	20
β- thal E	3	15
Trisomy 18	2	10
Down syndrome	1	5
Maternal HIV +	1	5

Table 3. Results of the treatment.

Results	Mean ± SD (range)	Number	%
Induction-delivery time (hours)	21.38 ± 13.68 (8.5 – 66.7)	-	
Abortion time (hours)	21.56 ± 13.68 (8.6 – 66.7)	-	
Complete abortion within			
12 hours	-	4	20
24 hours	-	15	75
48 hours	-	19	95
72 hours	-	20	100
Oxytocin augmentation	-	6	30
Analgesic requirement	-	9	45
Complete abortion	-	18	90
Mean dose of misoprostol	1.9 ± 1.26 (1-6)	-	

Table 4. Maternal side effects.

Side effects	Number	%
Diarrhea	8	40
Fever (temperature > 38°C)	7	35
Chill	3	15
Nausea	2	10
Vomiting	1	5
Post partum hemorrhage	0	
Uterine rupture	0	

DISCUSSION

Although several studies have demonstrated the efficacy of misoprostol for second trimester pregnancy with live fetus, there were different doses and intervals. Misoprostol can be used with or without mifepristone, when it was used with mifepristone high efficacy was shown. As mifepristone is not available in Thailand, study of misoprostol alone for this purpose was necessary to establish the efficacy.

The results in this study showed the mean induction delivery time and the mean abortion time were 21.38 ± 13.68 and 21.56 ± 13.68, respectively. When compared to the study of Bulgalho[6], in which 800 microgram intravaginal misoprostol followed by 400 mcg 18 hours later was used, it was found that the mean induction-delivery time in this study was significantly longer (21.38 ± 13.68 *vs* 11.8 ± 5.4 hours). Neither Bishop score of the cervix prior to intervention status of the fetus (live or dead) was mentioned. These factors may influence the time interval.

Herabutya[7] showed the mean induction abortion time with misoprostol 400 mcg intravagina every 12 hours was 22.3 ± 14.3 hours. This is slightly longer than our study (21.56 ± 13.68). Noticibly, a higher dose of misoprostol was better, but side effects were more common.

A smaller dose of misoprostol was studied in other studies for second trimester termination of pregnancy such as 400 mcg intravagina every 3 hours[8] and 200 mcg intracervicovagina every 12 hours[9], the mean induction-abortion time was 23.6 ± 33.1 hours and 27 hours 7 minutes, respectively. The time was comparable to our study, so a shorter interval and intracervical route influenced the shorter time.

The combination of mefipristone single dose with 200 mcg intravaginal misoprostol every 3 hours[10], showed a significantly shorter interval (induction abortion time was 14.8 ± 18.2 hours). Mefipristone is an interesting drug for this purpose and the interval of 3 hours may be better than a longer interval.

Complete abortion occurred in most cases (90%), so routine curettage was not recommended. The most common side effect was diarrhea followed by chills. No patient was complicated by uterine rupture even though 2 cases had had prior low transverse cesarean section. However, we could not confirm whether 800 mcg was safe for patients with uterine scar, because there was a small number of patients.

In conclusion, 800 mcg misoprostol intravagina every 12 hours was effective but a lower dose and interval should be further studied.

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การยุติการตั้งครรภ์ในไตรมาสที่สองด้วยมิโสพรอสตอล 800 ไมโครกรัม สอดทางช่องคลอด

สายพิณ พงษธา, พ.บ., ธีระ ทองสง, พ.บ.**

วัตถุประสงค์ : เพื่อศึกษาประสิทธิภาพของ Misoprostol 800 ไมโครกรัม สอดทางช่องคลอดเพื่อยุติการตั้งครรภ์ในไตรมาสที่สอง

รูปแบบการวิจัย : Prospective descriptive study

สถานที่ศึกษา : โรงพยาบาลมหาราชนครเชียงใหม่ ภาควิชาสูติศาสตร์และนรีเวชวิทยา คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

ผู้เข้าร่วมการศึกษา : สตรีตั้งครรภ์ที่มีเกณฑ์คัดเลือกเข้าสู่การศึกษา ดังนี้

1. ตั้งครรภ์เดี่ยว และทารกมีชีวิต
2. อายุครรภ์ 14-28 สัปดาห์
3. มีข้อบ่งชี้ให้ยุติการตั้งครรภ์
4. ปากมดลูกปิดและไม่มีการบางตัว
5. ไม่มีการหดรัดตัวของมดลูกและการแตกรั่วของถุงน้ำคร่ำ
6. ไม่เคยมีแผลผ่าตัดที่มดลูกแบบ classical มาก่อน
7. ไม่มีข้อห้ามต่อการใช้ misoprostol เช่น การแพ้

วิธีบริหารยา : ค่าเฉลี่ยระยะเวลาตั้งแต่ให้ยาจนคลอดทารก, ค่าเฉลี่ยตั้งแต่ให้ยาจนคลอดรกครบ, ภาวะแทรกซ้อนในมารดา

ผลการศึกษา : ค่าเฉลี่ยตั้งแต่ให้ยาจนคลอดทารก = 21.38 $\pm$ 13.68 ชั่วโมง, ค่าเฉลี่ยตั้งแต่ให้ยาจนคลอดรกครบ = 21.56 $\pm$ 13.68 ชั่วโมง, ท้องเดินพบมากที่สุดในภาวะแทรกซ้อนของมารดาโดยพบใน 40%

สรุป : การให้ misoprostol 800 ไมโครกรัม สอดทางช่องคลอดทุก 12 ชั่วโมง มีประสิทธิภาพดีในการยุติการตั้งครรภ์ในไตรมาสที่สอง แต่ถ้าต้องการประสิทธิภาพที่ดียิ่งขึ้นร่วมกับผลข้างเคียงที่ลดลง อาจพิจารณาการให้ยาในขนาดที่ต่ำและบ่อยกว่านี้ และควรมีการศึกษาเพิ่มเติมต่อไปเพื่อพิสูจน์ผล

คำสำคัญ : มิโสพรอสตอล, การตั้งครรภ์ไตรมาสที่สอง, การชักนำการคลอด, ค่าเฉลี่ยในการยุติการตั้งครรภ์

สายพิณ พงษธา, ธีระ ทองสง
จดหมายเหตุทางแพทย์ ฯ 2544; 84: 859-863

* ภาควิชาสูติศาสตร์-นรีเวชวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่, เชียงใหม่ 50200