Success Rate of Second-Trimester Termination of Pregnancy Using Misoprostol

Natthinee Prachasilpchai MD*,
Kusol Russameecharoen MD*, Dittakarn Borriboonhirunsarn MD, MPH, PhD*

** Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University*

Objective: *To evaluate the efficacy and maternal side effects of misoprostol usage for second trimester termination in Siriraj Hospital.*
Study design: *Descriptive cross sectional study.*
Setting: *Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University*
Material and Method: *The medical records of 94 pregnant women, between 14-28 weeks of gestation, who were admitted for medical termination of pregnancy, were reviewed. Each patient received 400 g of misoprostol vaginally every 12 hours as recommended by RTCOG for termination of pregnancy. Main outcome measures included success rate of abortion within 48 hours, induction to abortion interval and maternal side effects.*
Results: *The success rate of abortion within 48 hours was 89.46%. Mean induction to abortion interval was 22.1 hours. The most common maternal side effect was fever (24.5%). The rate of incomplete abortion was 28.6% of successful cases. No factor, including age, parity and viability of fetus affected the success rate significantly. No serious maternal complication was detected.*
Conclusion: *Misoprostol 400 g vaginally every 12 hours can be used effectively and safely for second trimester pregnancy termination.*

Keywords: *Misoprostol, Second trimester termination*

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The termination of second trimester pregnancy is a common problem in obstetric practice because of its complications and psychic trauma to patients. Although various methods for second-trimester termination are effective, there are many risks of patients. Intraamniotic hypertonic saline infusion induces risks to heart failure, septic shock, water intoxication and consumptive coagulopathy[1]. Evacuation and curettage are associated with infection, uterine perforation and cervical trauma. Various methods for second trimester termination of pregnancy have been investigated to find more effective methods with fewer complications to the patients.

Misoprostol (Cytotec), a synthetic prostaglandin E_1 analog, has become an important drug in obstetric and gynecological practice because of its ability for cervical ripening and uterotonic action. One of its usages is for second trimester termination of pregnancy. Although various doses and routes of administration have been studied, the optimal dosage and route have not been defined. Zieman et al[2] demonstrated oral administration of misoprostol is absorbed more rapidly and resulting in higher peak serum concentrations than vaginal administration. Although the peak serum concentration of vaginal administration is lower, the decline of serum concentration is slower. Overall exposure to the drug through vaginal administration increased. Currently, the Royal Thai College of Obstetricians and Gynecologists (RTCOG) has recommended the protocol for medical termination of second trimester pregnancy with misoprostol is 400 g vaginally every 12 hours.

The objectives of the present study were to assess the success rate and maternal side effects of

Correspondence to : Prachasilpchai N, Department of Obstetrics and Gynecology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

misoprostol 400 g vaginally every 12 hours for termination of pregnancy at 14-28 weeks of gestation.

Material and Method

This retrospective study was established by reviewing the medical records between June 1, 2003 and April 30, 2005 at the Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital. Ninety four pregnant women at 14-28 weeks of gestation with indications for pregnancy termination were enrolled. All patients had received authorization by the Abortion Committee of Siriraj Hospital. All were counseled about the method for termination, side effects and complications. Following the counseling, a consent form was signed by all patients. Medical and obstetric history was taken and physical examination was performed. Gestational age was assessed by reliable last menstrual history, physical examination and/or ultrasonography. Exclusion criteria included previous classical uterine scar, cervical dilation of more than 3 centimeters, and maternal history of hypersensitivity to prostaglandins.

All patients received misoprostol 400 g intravaginally every 12 hours. The misoprostol tablets were placed in the posterior vaginal fornix by an obstetric resident. No additional co-interventions were used. Cervical progression was evaluated by vaginal examination before insertion of the next dose of misoprostol. Patients would receive intramuscular or intravenous narcotic agents for pain control. If the side effects of misoprostol such as fever occurred, patients would receive acetaminophen 500-1,000 mg orally.

Treatment success was defined as expulsion of the fetus within 48 hours after the initial dosage of misoprostol. Induction to abortion interval was defined as the time from the initial dosage of misoprostol to the expulsion of the fetus. Factors possibly affecting the success rate and the maternal side effects such as abdominal pain, fever (temp $\geq$ 37.8 C), nausea-vomiting, diarrhea and rupture of uterus were recorded. Uterine curettage was performed if the placenta was not expelled within 30 minutes.

Various baseline characteristics were described using mean, standard deviation, number and percentage. Comparison was made between success and failure groups using student's t test and chi-square test as appropriate. Statistical significance was considered when p value < 0.05.

The present study has been reviewed and approved by the Ethics Committee, Faculty of Medicine Siriraj Hospital, Mahidol University.

Results

Medical records were reviewed between June 1, 2003 and April 30, 2005. Ninety four pregnant women indicated for termination of pregnancy during the second trimester were recruited. Demographic data are shown in Table 1. Mean maternal age was 29.4 years. The mean gestational age was 20.3 weeks. The majority of the women were nulliparous (60.6%), 37 women were multiparous (39.4%), 27 of 37 had a previous vaginal delivery (73.0%), 10 of 37 had previous cesarean delivery (27%). Seventy two (76.6%) pregnant women had viable fetuses, and the others had intrauterine fetal death (23.4%).

Table 1. Demographic data (n = 94)

Demographic dat	Number (%)
Mean Age $\pm$ SD (years)	29.4 $\pm$ 6.6
Mean GA $\pm$ SD (weeks)	20.3 $\pm$ 3.3
Parity	
: Nulliparous	57 (60.6)
: Previous vaginal delivery	27 (28.7)
: Previous C/S	10 (10.6)
Viability of the fetus	
: Viable	72 (76.6)
: DFIU	22 (23.4)
Maternal indication	
: HIV seropositive	17 (18.1)
: Rape	3 (3.2)
: Other*	3 (3.2)
Fetal indication	
: DFIU	22 (23.4)
: β-thal or β/E	14 (14.9)
: Chromosome abnormality	10 (10.6)
: Hydrops fetalis	10 (10.6)
: Other**	15 (16.0)

* HIV seropositive with Eisenmenger, VSD with Eisenmenger, Schizophrenia

** multiple anomalies 7 cases, Anencephaly 5 cases, Preterm PROM 3 cases

Table 2. Success rate and mean induction to abortion time (n = 94)

	Number (%)
Success rate at 48 hours	
Success	84 (89.4%)
Failure	10 (10.6%)
Mean induction to abortion time $\pm$ SD (hours)	
Success	17.07 $\pm$ 10.0
Failure	64.04 $\pm$ 12.4

Table. 3 Comparison of various factors between the success group and the failure group (n = 94)

Factor	Success (n = 84)	Failure (n = 10)	p-value
Age (years) mean ± SD	29.3 ± 6.6	30.1 ± 7.1	0.723
GA (weeks) mean ± SD	20.4 ± 3.4	19.1 ± 2.4	0.23
Parity			0.56
: Nulliparous (n = 57)	52 (91.2%)	5 (8.8%)	
: Previous vaginal delivery (n = 27)	24 (88.9%)	3 (11.1%)	
: Previous C/S (n = 10)	8 (80.0%)	2 (20.0%)	
Viability			
0.44			
: Viable (n = 72)	63 (87.5%)	9 (12.5%)	
: DFIU (n = 22)	21 (95.5%)	1 (4.5%)	

The common maternal indications were HIV seropositive (18.1%), rape (3.2%) and severe maternal illness (3.2%) such as HIV seropositive with Eisenmenger syndrome, ventricular septal defect with Eisenmenger syndrome and schizophrenia.

The most common cause of fetal indications was intrauterine fetal death (23.4%), followed by fetal anomalies, not compatible with life (16%) such as multiple anomalies (7 of 15), anencephaly (5 of 15) and preterm premature rupture of membranes (3 of 15).

At 48 hours, the success rate was 89.4% (84 of 94). The mean induction to abortion interval in this group was 17.07 ± 9.96 hours (range 4-45 hours). Of 84 successfully treated cases, 24 (28.6%) had incomplete abortion and required uterine curettage. For 10 (10.6%) women who did not abort within 48 hours, all were continued with the same misoprostol regimen and/or added oxytocin infusion. All of them expelled the fetus successfully and none required hysterotomy. The mean induction to abortion interval of this group was 64.0 ± 12.4 hours (range 53-92 hours). The results are shown in Table 2.

Comparison was made between success and failure groups and the results are shown in Table 3. No significant differences were observed between groups with regard to various characteristics.

From Table 4, the most common maternal side effects were fever defined as temperature ≥ 37.8 C (24.5%), followed by abdominal pain (16%), and nausea-vomiting (5.3%). No uterine rupture or postpartum hemorrhage occurred in the present study.

Table 4. Side effects (n = 84)

Side effects	Number (%)
Fever	23 (24.5)
Abdominal pain	15 (16)
Nausea/vomiting	5 (5.3)
No side effects	51(54.2)

Discussion

Termination of second-trimester pregnancy can be accomplished by various methods. Misoprostol is known to be safe and effective for such a purpose. Other prostaglandins such as prostaglandins E_2 vaginal suppositories and prostaglandins F_2 injections are also effective, but associated with side effects such as severe nausea-vomiting, diarrhea and fever[3,4]. Previous studies demonstrated that the side effects of misoprostol were better tolerated than other prostaglandins for pregnancy termination in the second trimester. Several studies have been conducted to determine the optimal dosage and route of administration of misoprostol. Comparison between vaginal and oral administration of misoprostol for the induction of labor at term had shown that vaginal administration was more effective, because of its pharmacokinetics[5,6]. In a previous study comparing misoprostol 200, 400 and 600 g vaginally every 12 hours for second trimester termination found that although the rate of successful abortion at 48 hours increased with increasing dosage, the frequency of side effects also increased[7]. The protocol of misoprostol 400 g vaginally every 12 hours is recommended by the Royal Thai College of Obstetricians and Gynecologists (RTCOG) for medical termination in second-trimester pregnancy.

The present study found that the success rate was 89.4%, the mean induction to abortion interval was 17.1 ± 9.9 hours, shorter than that of the previous study using a similar regimen from the University of Connecticut Health Center (26 ± 14.5 hours)[3].

Herabutya et al demonstrated using misoprostol 400 g every 12 hours for second-trimester termination, the success rate was 82% and the mean induction to abortion interval was 33.4 ± 34.9 hours[7].

The incidence of uterine rupture during second-trimester termination with misoprostol is unknown. There were two case reports of uterine rupture in the second-trimester induced abortion. One woman had a history of two prior cesarean sections and received one dose of misoprostol 200 g for induction at 23 weeks of gestation due to chorioamnionitis, and whether the infection may be predisposing to dehiscence of uterine scars is unknown[8].The other woman had placed laminaria in the cervical os before the administration of misoprostol 400 g vaginally followed by misoprostol 400 g orally, and it was possible that laminaria caused the increase in uterine pressure sufficiently to rupture the scars[9]. However, several other studies reported no uterine rupture from misoprostol use for second-trimester termination among patients with previous cesarean delivery[10-12]. Friel el al performed meta-analysis of published studies demonstrated that misoprostol is safe and effective for induction between 13 and 28 weeks of gestation in patients with a history of previous cesarean section[13]. In the present study, there were 10 pregnant women with the history of previous uterine surgery and none had uterine rupture. However, extreme precaution must be paid in this group of women that vital signs and uterine contractions must be closely and continuously monitored.

It is well known that induction of labor is more easily performed in multiparous compared with nulliparous women and a previous study showed that misoprostol is less effective for termination of pregnancies with live fetuses than those with dead fetuses[5,14]. In the present study, no factors affected the success rate significantly. However, the number of patients was still too small to make definitive conclusions with this regard. Further study should be established to find the factors affecting the success rate.

The most common maternal side effects found in the present study was fever (24.5%) followed by abdominal pain (16%) and nausea-vomiting (5.3%). However, these side effects were only minor and transient. No uterine rupture occurred in the present study.

In summary, misoprostol 400 g vaginally every 12 hours is an effective method for termination of pregnancy at 14-28 weeks of gestation, is easy to use and has no serious maternal side effects.

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อัตราการประสบความสำเร็จของการใช้ยาไมโสพรอสทอลในการตั้งครรภ์ในไตรมาสที่สอง

ณัฏฐินี ประชาศิลป์ชัย, กุศล รัศมีเจริญ, ดิฐกานต์ บริบูรณ์หิรัญสาร

วัตถุประสงค์: *เพื่อศึกษาถึงประสิทธิภาพและผลข้างเคียงของยาไมโสพรอสทอลในการยุติการตั้งครรภ์ในไตรมาสที่สองในโรงพยาบาลศิริราช*

รูปแบบการศึกษา: *การศึกษาเชิงพรรณนาแบบตัดขวาง*

สถานที่: *ภาควิชาสูติศาสตร์และนรีเวชวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล*

วัสดุและวิธีการ: *ทำการค้นข้อมูลย้อนหลังจากบันทึกผู้ป่วยในที่เข้ารับการรักษาในโรงพยาบาลศิริราชเพื่อยุติการตั้งครรภ์ ระหว่างอายุครรภ์ 14-28 สัปดาห์ มีทั้งหมด 94 ราย แต่ละรายจะได้รับการเหน็บยาไมโสพรอสทอล 400 ไมโครกรัม ทางช่องคลอดทุก12ชั่วโมง ตามคำแนะนำในการใช้ยาไมโสพรอสทอลเพื่อยุติการตั้งครรภ์ของราชวิทยาลัยสูตินรีแพทย์แห่งประเทศไทย ผลการศึกษาประเมินจากอัตราความสำเร็จของการแท้งภายใน 48 ชั่วโมง, ระยะเวลาที่ใช้ในการทำแท้ง และผลข้างเคียงต่อมารดา*

ผลการศึกษา: *อัตราความสำเร็จของการแท้งภายใน 48 ชั่วโมง เท่ากับ ร้อยละ 89.4 ระยะเวลาที่ใช้ในการทำแท้งเท่ากับ 22.1 ชั่วโมง ผลข้างเคียงต่อมารดาที่พบบ่อยที่สุด คือ ไข้ ร้อยละ 24.5 อัตราการเกิดการแท้งไม่ครบ เท่ากับร้อยละ 28.6 จากการศึกษาไม่พบว่ามีปัจจัยอื่น เช่น อายุมารดา, ประวัติการคลอด และการมีชีวิตของทารกในครรภ์ที่มีผลต่ออัตราความสำเร็จของการใช้ยาไมโสพรอสทอลอย่างมีนัยสำคัญ ไม่พบภาวะแทรกซ้อนที่รุนแรงต่อมารดา*

สรุป: *ยาไมโสพรอสทอล ขนาด 400 ไมโครกรัม เหน็บทางช่องคลอดทุก 12 ชั่วโมง สามารถใช้เพื่อยุติการตั้งครรภ์ในไตรมาสที่สองได้อย่างมีประสิทธิภาพและปลอดภัย*