Outcomes of Pregnancy Termination by Misoprostol at 14-32 Weeks of Gestation: A 10-Year-Experience

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Objective: *To review outcomes of pregnancy termination between 14-32 weeks of gestation based on a10-year-experience of misoprostol use at Maharaj Nakorn Chiang Mai Hospital.*
Study design: *A retrospective, descriptive study*
Material and Method: *Based on the authors' prospective database, all pregnancy terminations by misoprostol between 14-32 weeks of gestation between 1998 and 2008 were reviewed. The main outcomes included success rate of termination, mean induction-to-abortion time, and complication rate. In addition, regimens and routes of drug administration as well as indications for termination of pregnancy were also analyzed.*
Results: *Seven hundred forty one pregnancy terminations were performed using misoprostol with dosage varied from 50 mcg to 800 mcg, mostly 400 mcg intravagina every three hours. The most common indication for pregnancy termination was severe fetal thalassemia (35.8%). The majority of cases were pregnancies with live fetuses and only 18.2% were associated with a dead fetus in utero. Success rate of termination within 48 hours was 85.9%. Pregnancies with previous cesarean section accounted for 8.6% of cases. The mean gestational age was 20.94 weeks. The mean abortion time was 25.35 hours, ranging from 1.25 to 247.88 hours. The two most common adverse effects were chill and fever (43.7% and 34.3%). The rate of analgesia needed was 39.3%. No serious adverse complications such as uterine rupture were found.*
Conclusion: *This experience suggests that misoprostol has a high efficacy for pregnancy termination with acceptable minor side effects and it is relatively safe when used with precaution.*

Keywords: *Misoprostol, Pregnancy termination, Abortion time*

J Med Assoc Thai 2011; 94 (8): 897-901
Full text. e-Journal: *http://www.mat.or.th/journal*

Second trimester termination of pregnancy is one of the challenging problems for obstetricians since it is more difficult and more dangerous than that in the first trimester[1]. Traced back for more than 10 years in Maharaj Nakorn Chiang Mai hospital, the surgical methods such as condom balloon technique, surgical evacuation, or even hysterotomy were mainly performed for second trimester pregnancy termination. During the last two decades, the use of prostaglandins either PGE2 or PGF2a vaginally has replaced the surgical methods due to its ease of administration, high effectiveness and fewer complications. However, the high expense of the medicine and instability in room temperature are the barriers especially in developing countries[2]. Recently, misoprostol (prostaglandin E 1 analog) has been widely used and appears to replace the older methods and the expensive prostaglandins[3,4]. To the authors' best knowledge, misoprostol is much cheaper, stable in room temperature and very potent to stimulate cervical ripening and uterine contraction. However, the regimens for clinical use were varied, depending on the period of studies since the appropriate dose and route of administration were not well established. For about 10 years, in Maharaj Nakorn Chiang Mai hospital misoprostol has become a primary technique for termination of pregnancy in the second trimester because of the outstanding property mentioned above[3,5-10]. Even though misoprostol combined with mifepristone may give a better outcome in terms of shorter abortion time[11,12], misoprostol alone is still the standard protocol worldwide, especially in the developing countries.

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The objective of the present study was to assess the outcomes of pregnancy termination between 14-32 weeks of gestation based on a 10-year-experience of misoprostol use at Maharaj Nakorn Chiang Mai Hospital.

Material and Method

A retrospective descriptive study was conducted at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand. It was approved by the ethics committee of the Faculty of Medicine, Chiang Mai University. The author developed a prospective database of pregnancy termination with misoprostol for more than 10 years. All data of pregnancy termination in 14-32 weeks of gestation with misoprostol use were prospectively collected as a computerized storage system. All of the data over the period of ten years (1998-2008) were accessed and reviewed for routes (oral, vaginal or combined), dosage (starting dose or interval of administration), viability of the fetuses and pregnancy outcomes in terms of success rate, mean abortion time, and adverse effects. In addition, all baseline data such as demographic characteristics of pregnant women, time interval of misoprostol use, analgesia use, need of oxytocin, as well as blood loss were also evaluated. The main outcomes of measurement included success rate, induction-to-abortion time and adverse effects. The qualitative data were presented as proportion or percent while the quantitative data were expressed as mean $\pm$ SD or median and range. The statistical analysis was analyzed using software SPSS version 17 (Chicago, IL).

Results

All data of 741 pregnant women who had pregnancy termination at 14-32 weeks of gestation with misoprostol were assessed and analyzed. The starting dosage of misoprostol varied from 50 to 800 mcg, administration interval varied from every three hours to 12 hours.

The mean ($\pm$ SD) age of participants was 30.15 $\pm$ 6.91 years and the mean ($\pm$ SD) gestational age was 20.94 $\pm$ 3.92 weeks. The most common indication for pregnancy termination was severe fetal thalassemia. Concerning fetal viability, most of the pregnancies (81.8%) had live fetuses and only 18.2% had a dead fetus in utero. Sixty-four women (8.6%) had cesarean section in the previous pregnancies. All data are presented in Table 1. While the regimen of misoprostol use is presented in Table 2.

Table 1. Baseline characteristics and indication for pregnancy termination of the participants (n = 741)

Characteristics	
Age (years): mean $\pm$ SD	30.15 $\pm$ 6.91
Median(range)	30.0 (12-47)
GA (weeks): mean $\pm$ SD	20.94 $\pm$ 3.92
Median (range)	20.0 (14-32)
Nulliparous: number (%)	363 (48.9)
Previous cesarean: number (%)	64 (8.6)
Indications	**Number (%)**
Hb Bart's disease	134 (18.1)
Other severe fetal thalassemia	131 (17.7)
Fetal chromosome abnormalities	102 (13.8)
Severe fetal anomalies	177 (23.9)
Maternal medical complication	20 (2.7)
Maternal HIV	4 (0.5)
Dead fetus	136 (18.2)
Others	37 (5.0)

Table 2. Regimen of misoprostol use (n = 741)

	Number (%)
400 mcg oral q 4 hr	69 (9.3)
400 mcg vaginal then 400 mcg oral q 4 hr	32 (4.3)
400 mcg vagina q 3 hr	415 (56.0)
400 mcg vagina q 6 hr	140 (18.9)
800mcg vagina q 12 hr	20 (2.7)
Others	65 (8.8)

The two most common adverse effects of misoprostol use were chill and fever (43.7% and 34.3%). Adverse effects of misoprostol are shown in Table 3.

The rates of oxytocin and analgesia use were 23.9% and 39.3% respectively. The mean abortion time was 25.35 hours (1.25-247.88 hours), while the serious adverse complications such as uterine rupture, amniotic fluid embolism, or severe postpartum hemorrhage were not found in the present study. Success rate of termination within 48 hours was 85.9%. However, 14 (1.9%) women had some degree of postpartum hemorrhage with no need of surgical intervention or blood transfusion. In addition, none ended up with hysterotomy or hysterectomy (Table 4).

Most cases (96.4%) of pregnancy termination were successful by misoprostol use alone, whereas

Table 3. Adverse effects of misoprostol use (n = 741)

	Number (%)
Chill	324 (43.7)
Fever	254 (34.3)
Diarrhea	111 (14.9)
Nausea	64 (8.6)
Vomitting	40 (5.4)

Table 4. Various outcomes of pregnancy termination (n = 741)

	Number (%)
Oxytocin use	177 (23.9)
Analgesia use	291 (39.3)
Complete abortion	631 (85.2)
PPH	14 (1.9)
Uterine rupture	0
Misoprostol use alone	714 (96.4)
Additional use of condom balloon technique	24 (3.2)
Additional use of other methods	3 (0.4)
Hysterotomy	0
Mean dose of misoprostol (mcg)	1,407.36 $\pm$ 1,164.23
Median (range)	1,200 (50-8,800)
Mean blood loss (ml)	155.39 $\pm$ 130.74
Median (range)	100 (10-1,000)
Mean abortion time (hr)	25.35 $\pm$ 29.04
Median (range)	16.33 (1.25-247.88)

the remainder needed the additional method to achieve successful termination, such as condom balloon technique or additional course of misoprostol after a day of rest. Some cases of failure, which was defined by no abortion within 48 hours after the initiation of misoprostol, were given the additional misoprostol. Finally, all cases successfully aborted. Uterine curettage was performed in 14.8% of women for incomplete abortion or retained pieces of placenta. All various outcomes of pregnancy termination are presented in Table 4.

Discussion

Since misoprostol has been widely used in the authors' institute, the incidence of septic abortion has significantly declined. The success rate of termination has significantly improved and the rate of oxytocin use is less. The current evidence suggests dilatation, and evacuation (D&E) is preferable to skilled personnel in medical abortion for pregnancy termination in the second trimester because the rate of incomplete abortion and infection seems to be lower in the D&E group[13]. However, the evidence shows that misoprostol is effective and carries only a few adverse effects in the early second trimester pregnancy termination. Moreover, D&E has a higher theoretical risk in termination of pregnancy in advanced gestational age. In such cases, D&E is not easy to perform even in an experience hand and carries the risk of immediate complication (uterine perforation bleeding, infection) or late complication (cervical incompetence, placenta previa, placenta accreta. So in advanced gestational age, medical abortion may be the prefer method. However, there is no adequate data of misoprostol use in the late second trimester (23-26 weeks) in terms of effectiveness and safety, especially uterine rupture[14].

In the past, condom balloon technique was commonly used for second trimester pregnancy termination in the authors' institute. From experience, this method is effective and inexpensive but need skilled personnel to perform it. It also has a theoretical risk of infection. Cases of failure usually ended up with intramniotic hypertonic saline or hysterotomy. Since the introduction of misoprostol, the authors and attending physicians have rarely used the condom balloon technique in cases of failure with misoprostol. Moreover, no case at all needed hysterotomy. Based on an impressive experience of misoprostol use in the authors' institute, therefore, misoprostol has replaced the older methods nearly completely.

Some evidence indicates that misoprostol combined with mefipristone is more effective than misoprostol alone in terms of second trimester pregnancy termination[11,12]. However, misoprostol alone is still a primary technique in Maharaj Nakorn Chiang Mai hospital either in early or late second trimester pregnancy termination. The outstanding properties of misoprostol is not only very cheap and effective but also convenient to administer. Its use needs no trained personnel either physicians or nurses. It is practical in the real situation in both developing and developed countries. The authors adjusted its dosage depending mainly on gestational age and the background knowledge at that time period. Different routes, dose, interval of its use also depend on other conditions such as previous uterine scar and survival of the fetus.

In women with uterine scar, there is more theoretical risk of uterine rupture with misoprostol use especially for more than one previous cesarean

section[15]. However, misoprostol can still be safe and effective for this condition[9,15]. It is unnecessary to avoid misoprostol use in such a condition by switching to an invasive method like hysterotomy. However, extreme safety precaution must be taken with termination of pregnancy in these cases with either misoprostol or other methods.

The 10-year-experience in the present study demonstrates that misoprostol is effective and safe in second trimester pregnancy termination. Nearly all were successfully aborted with misoprostol alone, though a few cases needed other methods for fetal expulsion. Despite the descriptive nature of the present study without a comparison of various regimens of misoprostol, the data shows most cases successfully aborted within 48 hrs after the initiation of misoprostol. Furthermore, none of the failed cases needed hysterotomy or hysterectomy. Of note, failure of termination in this study was defined by no abortion after 48 hrs of misoprostol administration. In cases of failure, attending physicians can switch to other methods for example; condom balloon technique, intraamniotic hypertonic saline, or additional course of misoprostol after temporary rest. The longest abortion time in the present study was 10.33 days. This case was nulliparous, at 22 weeks of gestation, it ended up with intramniotic hypertonic saline plus additional misoprostol plus intravenous oxytocin. The total dose of misoprostol use was 8,800 mcg. No serious adverse complication or postpartum hemorrhage was found. Finally, complete expulsion was accomplished without curettage.

Most published papers, but few[9,16], on misoprostol do not mention the management of the failed cases. Therefore, the attending physician should have the alternative method and keep it in mind in the part of counseling.

The most common adverse effects of misoprostol were chill (43.7%) and fever (34.3%). These effects were temporary and then spontaneously resolved. However, they can be relieved by supportive care and medication as necessary.

Some centers may provide feticide before pregnancy termination especially in the late second trimester. The purpose is to avoid the signs of fetal life and may enhance the success rate of termination. However, the authors' institute does not perform this procedure because of the religious concern and to avoid the invasive procedure.

In conclusion, misoprostol is highly effective for pregnancy termination either in early or late second trimester. Misoprostol is also safe in the case of uterine scar if used with precaution. For safety, the patient must be closely monitored during and after drug administration. In failed cases with misoprostrol, other methods can be used or combined with misoprostol again. In the summary, misoprostol should be the first line treatment for late second trimester pregnancy termination.

Acknowledgement

The authors wish to thank the National Research University Project under Thailand's Office of the Higher Education Commission for financial support.

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ผลลัพทธ์ของการยุติการตั้งครรภ์ด้วย misoprostol ในอายุครรภ์ 14-32 สัปดาห์:ประสบการณ์ 10 ปี ในโรงพยาบาลมหาราชนครเชียงใหม่

สายพิณ พงษธา, ธีระ ทองสง

วัตถุประสงค์: *เพื่อนำเสนอผลลัพธ์ของการตั้งครรภ์ด้วย misoprostol ในช่วงอายุครรภ์ 14-32 สัปดาห์ ในโรงพยาบาลมหาราชนครเชียงใหม่โดยเป็นประสบการณ์ 10 ปี*

วัสดุและวิธีการ: *Retrospective, descriptive study โดยเป็นการรวบรวมข้อมูลที่มีอยู่แล้วโดยสตรีตั้งครรภ์ทุกรายที่ได้รับการยุติการตั้งครรภ์ในช่วงอายุครรภ์ 14-32 สัปดาห์ด้วย misoprostol ด้วยขนาดและรูปแบบของการบริหารยาทุกรูปแบบ ตั้งแต่ปี พ.ศ. 2541-2551 ได้นำข้อมูลมาวิเคราะห์ โดยผลลัพธ์ที่สำคัญที่ต้องการทราบคือความสำเร็จในการยุติการตั้งครรภ์ภายใน 48 ชั่วโมง ระยะเวลาเฉลี่ยตั้งแต่เริ่มให้ยาจนกระทั่งทารกคลอด และภาวะแทรกซ้อนที่เกิดขึ้น*

ผลการศึกษา: *สตรีตั้งครรภ์ทั้งหมดที่รวบรวมได้จำนวน 741 ราย มีการใช้ misoprostol เพื่อยุติการตั้งครรภ์ในขนาดตั้งแต่ 50 mcg-800 mcg ส่วนใหญ่มักเป็นขนาด 400 mcg สอดทางช่องคลอดบริหารยาทุก 3 ชั่วโมงข้อ บ่งชี้ของการยุติการตั้งครรภ์ที่พบบ่อยที่สุดคือทารกเป็นโรคเลือดธาลัสซีเมียชนิดรุนแรง (35.8%) และทารกที่มายุติการตั้งครรภ์ส่วนใหญ่ยังมีชีวิตอยู่มีทารกเพียง 18.2% เท่านั้นที่เสียชีวิตในครรภ์แล้วสตรีตั้งครรภ์ที่เคยผ่าตัดคลอดมาก่อนแล้วครรภ์นี้ต้องมายุติการตั้งครรภ์มี 8.6% อายุครรภ์เฉลี่ยขณะที่มายุติการตั้งครรภ์คือ 20.94 สัปดาห์ ระยะเวลาเฉลี่ยตั้งแต่ให้ยาจนกระทั่งทารกคลอดคือ 25.35 ชั่วโมง (1.25-247.88 ชั่วโมง) อัตราการประสบผลสำเร็จในการยุติการตั้งครรภ์ภายใน 48 ชั่วโมง คือ 85.9% ผลข้างเคียงที่พบได้บ่อยที่สุด 2 อันดับแรกคือ หนาวสั่นและไข้ (43.7% และ 34.3% ตามลำดับ) อัตราการใช้ยาระงับอาการปวดในระหว่างที่ยุติการตั้งครรภ์ คือ 39.3% ไม่พบผลข้างเคียงที่เป็นอันตรายที่รุนแรงและไม่พบการแตกของมดลูกเลย*

สรุป: *ประสบการณ์ที่นำเสนอมาบ่งชี้ว่าการใช้ misoprostol เพื่อยุติการตั้งครรภ์ในช่วงอายุครรภ์ 14-32 สัปดาห์มีประสิทธิภาพสูง พบผลข้างเชียงเพียงเล็กน้อยซึ่งยอมรับได้มีความเหมาะสมในการนำมาใช้เพื่อยุติการตั้งครรภ์เมื่อมีข้อบ่งชี้ และภายใต้การดูแลด้วยความระมัดระวัง*