
OBSTETRICS

Medical Abortion at Gestational Age \leq 24 weeks at Songklanagarind Hospital

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ABSTRACT

Objectives: To determine the success and complication rates of medical abortion at gestational age \leq 24 weeks, and to identify their associated factors.

Materials and Methods: A retrospective study was conducted from January 2006 to December 2017.

Medical records of pregnant women at gestational age \leq 24 weeks, who were admitted for medical abortion, were reviewed. Spontaneous abortion was excluded. Multivariate logistic regression analysis was used to identify factors associated with success and complications. A p value of < 0.05 was considered statistically significant.

Results: A total of 717 cases were reviewed. Two medical regimens were used, including misoprostol alone (84.7%) and mifepristone-misoprostol (MM) (15.3%). The overall success rates in the first and second trimester were 65.8% and 79.3%. The highest success rate was observed in women at gestational age of \leq 9 weeks, with the MM regimen (92.0%). The overall complication rate was 5.3%, including hemorrhage requiring blood transfusion (4.7%) and infection (0.6%). The complication rates in the first and second trimester were 2.5% and 5.6%, respectively. One factor associated with success in the first trimester was the drug regimen (MM); while that in the second trimester was maternal age. Multivariate analysis showed that factors associated with complications in the second trimester were multigravida and having an underlying disease.

Conclusion: Medical abortion at gestational age \leq 24 weeks had low complications. Multigravida and having an underlying disease were factors associated with complications in the second trimester.

Keywords: medical abortion, mifepristone, misoprostol, complication.

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การยุติการตั้งครรภ์โดยการใช้ยาที่อายุครรภ์ไม่เกิน 24 สัปดาห์ ณ โรงพยาบาลสงขลา นครินทร์

วรรณพร สุดสาย, จิตเกษม สุวรรณรัชต์, ธนาพันธ์ ชูนุญ

บทคัดย่อ

วัตถุประสงค์: เพื่อศึกษาอัตราความสำเร็จ ภาวะแทรกซ้อน และปัจจัยที่มีผลต่อความสำเร็จและภาวะแทรกซ้อน ของการยุติการตั้งครรภ์โดยการใช้ยาที่อายุครรภ์ไม่เกิน 24 สัปดาห์

วัสดุและวิธีการ: เป็นการศึกษาวิจัยแบบย้อนหลัง โดยเก็บข้อมูลจากเวชระเบียนของสตรีที่ตั้งครรภ์ไม่เกิน 24 สัปดาห์ ที่นอนโรงพยาบาลเพื่อใช้ยา_yติการตั้งครรภ์โดยไม่รวมสตรีตั้งครรภ์ที่มีภาวะแท้บบุตรองตามธรรมชาติตั้งแต่เดือนมกราคม พ.ศ.2549 ถึงธันวาคม พ.ศ.2560 วิเคราะห์ข้อมูลโดยใช้สถิติเชิงพรรณนาและการวิเคราะห์การทดสอบพหุแบบโลจิสติกส์ เพื่อหาปัจจัยที่มีผลต่อความสำเร็จและภาวะแทรกซ้อนจากการใช้ยาในการยุติการตั้งครรภ์โดยกำหนดค่า p value < 0.05 ถือว่ามีนัยสำคัญทางสถิติ

ผลการศึกษา: ผู้ป่วยทั้งหมด 717 ราย ได้รับการยุติการตั้งครรภ์โดยใช้ยา 2 สูตรได้แก่ misoprostol อย่างเดียว (ร้อยละ 84.7) และ mifepristone ร่วมกับ misoprostol (MM) (ร้อยละ 15.3) อัตราความสำเร็จรวมของยาทั้ง 2 สูตรในไตรมาสแรก และไตรมาสที่สองคือร้อยละ 65.8 และร้อยละ 79.3 ตามลำดับ อัตราความสำเร็จพบมากที่สุดในผู้ป่วยที่ใช้ยาสูตร MM ที่มีอายุครรภ์ไม่เกิน 9 สัปดาห์ (ร้อยละ 92) ภาวะแทรกซ้อนโดยรวมคิดเป็นร้อยละ 5.3 ได้แก่ ตกเลือดและต้องได้รับส่วนประปอบของเลือด (ร้อยละ 4.7) และติดเชื้อ (ร้อยละ 0.6) ภาวะแทรกซ้อนในไตรมาสแรกและไตรมาสที่สองพบร้อยละ 2.5 และร้อยละ 5.6 ตามลำดับ ปัจจัยที่มีผลต่อความสำเร็จในไตรมาสแรกได้แก่ สูตรยาที่ใช้ ส่วนในไตรมาสที่สองได้แก่ อายุ ส่วนปัจจัยที่มีผลต่อภาวะแทรกซ้อนในไตรมาสที่สองได้แก่ การตั้งครรภ์หลังและการมีโรคประจำตัว

สรุป: การใช้ยา_yติการตั้งครรภ์ที่อายุครรภ์ไม่เกิน 24 สัปดาห์ มีภาวะแทรกซ้อนต่ำ การตั้งครรภ์หลัง และการมีโรคประจำตัว เป็นปัจจัยที่สัมพันธ์กับการเกิดภาวะแทรกซ้อนในไตรมาสที่สอง

คำสำคัญ: การใช้ยาในการยุติการตั้งครรภ์, mifepristone, misoprostol, ภาวะแทรกซ้อน

Introduction

Since 1960, surgical abortion has been a method of choice for early pregnancy termination. Until 1970, medical abortion had become an alternative method with the use of prostaglandins, and then with anti-progesterone in 1980⁽¹⁾. Medical abortion is an effective, acceptable and safe method. It can be used in early pregnancy, up to 24 weeks of gestation^(2, 3). The most effective medical abortion regimen is a combination of mifepristone and misoprostol^(1, 4), as this has higher efficacy, shorter duration of abortion and lower complications than the use of misoprostol alone^(4, 5). However, high variation in doses, timing and route of administration still exists. The World Health Organization (WHO) recommends a 200 mg of mifepristone, followed by 800 mcg of misoprostol in pregnancies up to 63 days of gestation⁽⁶⁾. This regimen is highly effective, with low failure rates (2%-5%)^(1, 7). Recent studies have demonstrated acceptable efficacy and low complications in more advanced gestational ages with higher efficacy for repeated dosages of misoprostol⁽⁸⁾.

Our institution, Songklanagarind Hospital, a university hospital in Southern Thailand, has provided safe abortions for women with maternal and fetal indications for a long period. The database from the Medical Statistics Unit, Department of Obstetrics and Gynecology, Songklanagarind Hospital has shown an increasing trend of medical abortion during the past ten years: from 30 cases to 130 cases per year. Situation analysis of medical abortion in our hospital has never been studied. Therefore, we conducted this research to determine the success and complication rates of medical induced abortion at gestational age ≤ 24 weeks, and to identify their associated factors. These results can be used for improvement of quality of abortion care, and close surveillance in women at risk for serious complications.

Materials and Methods

The retrospective descriptive study was conducted after approval by the Institutional Review Board of Faculty of Medicine, Prince of Songkla University (REC.62-262-12-4).

Medical records of women who were admitted for induced abortion at Songklanagarind Hospital, from January 2006 to December 2017 were reviewed. Data were retrieved from the database of the Medical Statistics Unit, Department of Obstetrics and Gynecology, and the Hospital Information System of Songklanagarind Hospital. The inclusion criteria were 1) gestational age ≤ 24 weeks, and 2) admitted for medical abortion. The exclusion criteria were 1) spontaneous abortion, 2) medical use for cervical preparation before surgical procedure, and 3) surgical abortion.

Maternal age, gestational age at termination, gravidity, underlying diseases, history of previous uterine surgery and curettage, indications for termination of pregnancy, drug regimens for termination of pregnancy, status of abortion (success or failure), complications, requirement of blood transfusion and duration of hospital stay were collected.

The primary outcome was complication rate of medical abortion at gestational age ≤ 24 weeks. The secondary outcomes were success rate and factors associated with complications and success of medical abortion.

Success of medical abortion was defined as complete expulsion without additional treatment⁽⁹⁾ within 72 hours. Failure of medical abortion was defined as ongoing pregnancy, need for additional treatment or no abortion after five doses of misoprostol⁽⁹⁾. Complications included major adverse outcomes, such as hemorrhage requiring blood transfusion, infection (related to abortion, such as endometritis or metritis) and uterine rupture⁽¹⁰⁾. Duration of termination was defined as time from first dose of misoprostol to expulsion of conceptus or fetus⁽¹¹⁾. First trimester was defined as gestational age < 13 weeks⁽¹²⁾. Early first trimester was defined as gestational age ≤ 63 days^(5, 6). Late first trimester was defined as gestational age 64-90 days. Second trimester was defined as gestational age 13-24 weeks⁽¹²⁾.

Sample size was calculated using a formula for a prevalence study; with $p = 0.067^{(10)}$ (the prevalence of complications associated with medical abortion),

alpha = 0.05 and d = 0.02; a total of 601 cases being required. We added 15% more cases for missing data, so at least 692 eligible cases were recruited.

Descriptive statistics and multivariate logistic regression were used for data analysis. A p value of < 0.05 was considered statistically significant.

Results

During a 12-year period, there were 1,227 cases admitted for termination of pregnancy. We excluded 510 cases who did not meet the criteria, including: gestational age > 24 weeks, spontaneous abortion, medical use for cervical preparation before surgical procedure and admitted for surgical abortion.

Finally, a total of 717 cases were studied. There were two regimens used: misoprostol alone (84.7%) and a combination of mifepristone-misoprostol (15.3%). Regarding route of administration of misoprostol: vaginal route was the most common (77.4%) with the remaining being sublingual (22.6%). The regimens and routes were selected by an obstetrician in-charge.

The MM regimen consists of 200 mg of

mifepristone and 800 mcg of misoprostol, provided by the Department of Health, Ministry of Public Health, Thailand. It is free of charge. Mifepristone was taken first and followed by misoprostol within the next 24-48 hours. This regimen was used for gestational ages of up to 63 days.

In the second trimester, the MM regimen was administered, followed by repeated doses of misoprostol until expulsion. Between 2006 and 2014, there was only misoprostol alone regimen in use, with MM regimen becoming available in 2015. Dosage of misoprostol use (200 mcg or 400 mcg every 3, 6, 8, 12 or 24 hours) depended on the preference of the obstetrician in-charge, with a maximum of five doses.

Demographic and obstetric data are shown in Table 1. About two-thirds of cases were below 35 years of age. Most women were in their second trimester. Approximately one-third of cases had underlying diseases, which were: hypertension (5.9%), heart diseases (4.9%), psychiatric disease (3.2%), systemic lupus erythematosus (2.4%), diabetes mellitus (1.4%) and hyperthyroidism (1.3%).

Table 1. Demographic characteristics and obstetric data (n = 717).

	Median (IQR)	n	Percent
Age (years)	31 (24, 37)		
< 35		458	63.9
≥ 35		259	36.1
Religion			
- Buddhism		598	83.4
- Islam		116	16.2
- Christianity		3	0.4
Primigravida		344	48.0
GA ≥ 13 weeks		638	89.0
Underlying diseases		201	28.0
Hospital stay (days)	2 (2, 3)		

IQR: interquartile range

The indications for pregnancy termination are shown in Table 2, and they show higher rates of fetal indication than that of maternal. Three-fourths of cases with fetal indications were due to abnormal

chromosomes or congenital anomalies. For maternal indications, socioeconomic problems were the leading cause, followed by medical diseases and sexual assaults.

Table 2. Indication for induced abortion (n = 717).

Indication	n	percent
Maternal indications	290	40.5
Medical diseases	71	9.9
Psychiatric disorder	19	2.6
Teratogen exposure	7	1.0
Socioeconomic problems	161	22.5
Sexual assault	32	4.5
Fetal indications	427	59.5
Dead fetus in utero	111	15.5
Abnormal chromosomes	155	21.6
Fetal anomalies	161	22.4

Of the 717 cases, 79 were in the first trimester and 638 were in the second trimester. Table 3 shows drug regimens used for pregnancy termination, success rates and duration of termination. With regard

to first trimester abortions, approximately 60% of cases were in the late first trimester. The highest success rate was noted in the MM regimen at gestational age ≤ 63 days.

Table 3. Drug regimens for medical abortion, success rates and duration of termination.

Drug regimen	n	percent	Success rate (%)	Duration of termination (hours) median (IQR)
First trimester	79	100	65.8	
Gestational age ≤ 63 days	33	41.8	75.8	
Mifepristone-misoprostol	25	75.8	92.0	4.0 (2.7,6.1)
Misoprostol	8	24.2	25.0	15.5 (6.0,23.3)
Gestational age 64 - 90 days	46	58.2	58.7	
Mifepristone-misoprostol	23	50.0	73.9	4.5 (3.2,6.8)
Misoprostol	23	50.0	43.5	10.3 (5.5,15.7)
Second trimester	638	100	79.3	
Mifepristone-misoprostol	62	9.7	82.3	6.2 (4.1,8.6)
Misoprostol alone	576	90.3	79.0	15.4 (10.0,29.0)
- Misoprostol 200 mcg every 3 hours	4	0.7	50.0	
- Misoprostol 400 mcg every 3 hours	54	9.4	79.6	12.2 (8.3,18.3)
- Misoprostol 400 mcg every 6 hours	151	26.2	83.4	15.4 (9.6,30.0)
- Misoprostol 400 mcg every 8 hours	100	17.4	71.0	18 (11.0,30.4)
- Misoprostol 400 mcg every 12 hours	183	31.8	82.0	16.4 (11.5,29.0)
- Misoprostol 400 mcg every 24 hours	3	0.5	66.7	
Others	81	14.1	75.3	

IQR: interquartile range

Focusing on 576 cases in the second trimester terminated by the misoprostol alone regimen, there was wide variations of dosage and intervals of misoprostol administration, depending on the obstetricians' preference. A dosage of 400 mcg every 12 hours was the most commonly used regimen, followed by 400 mcg every 6 hours and 400 mcg every 8 hours, respectively, with success rates of approximately 70-80%. (Table 3). Dosage of 400 mcg every 3 hours had the shortest duration of termination.

Regarding 27 failure cases in the first trimester: 20 cases (all in late first trimester) received second cycle of misoprostol alone with success, five cases ended up with manual vacuum aspiration and two cases had spontaneous abortion within few days. With regard to 132 failure cases in the second trimester, 118 cases underwent surgical evacuation, nine cases received second cycle of misoprostol alone regimen with success, four cases had spontaneous abortion and one case ended up with

hysterotomy.

To identify factors associated with success of medical abortion in the first trimester, univariate analysis was performed and showed that only drug regimen (MM) was significant. However, in the second trimester, there were two significant factors: maternal age (< 35 years) and gravidity (primigravida) (Table 4). Multivariate analysis showed that only maternal age (< 35 years) was significant in the second trimester (adjusted odds ratio 1.78, 95% confidence interval 1.23-2.59, $p = 0.002$), adjusted by gravidity.

Regarding complications of abortion, there were only two cases (2/79, 2.5%) in the first trimester and 36 cases (36/638, 5.6%) in the second trimester. The overall complication rate was 5.3%, including hemorrhage requiring blood transfusion (4.7%), and infection (0.6%). No maternal death or uterine rupture was reported in this study. Since there were only 2 cases with complications in the first trimester, multivariate analysis could not be performed.

Table 4. Univariate analysis of factors associated with success of medical abortion.

Factor	First trimester (n = 79)			Second trimester (n = 638)		
	n	Percent of success	p value	n	Percent of success	p value
Age (years)			0.954			< 0.001
< 35	53	66.0		405	84.0	
≥ 35	26	65.4		233	71.2	
Gravidity			0.509			0.029
Primigravida	34	61.8		310	82.9	
Multigravida	45	68.9		328	75.9	
Regimen			< 0.001			0.546
Mifepristone-misoprostol regimen	47	81.6		62	82.3	
Misoprostol alone	30	40.0		576	79.0	
Underlying diseases			0.296			0.404
Yes	61	55.6		173	81.5	
No	18	68.9		465	78.5	
Indication for induced abortion			0.206			0.573
Maternal indication	62	69.4		226	80.5	
Fetal indication	17	52.9		412	78.6	

To identify factors associated with complications in the second trimester, a univariate analysis was performed. It was found that four variables including maternal age, gravidity, a history of uterine curettage and having an underlying disease, were significant (Table 5). A history of uterine surgery and drug regimen were not statistically significant. Multivariate logistic regression analysis was performed with six

variables in the final model: maternal age (< 35 vs > 35 years), gravidity (primigravida vs multigravida), a history of uterine curettage (yes/no), a history of uterine surgery (yes/no), drug regimen (MM vs misoprostol alone) and having underlying diseases (yes/no). The only two significantly associated factors were gravidity and having an underlying disease (Table 5).

Table 5. Multivariate logistic regression analysis of factors associated with complications in the second trimester (n = 638).

Variables	Crude odds ratio (95% confidence interval)	p value	Adjusted odds ratio	p value
			(95% confidence interval)	
Maternal age ≥ 35 years	2.0 (1.0-4.0)	0.040	1.5 (0.7-3.0)	0.300
Multigravida	3.0 (1.4-6.5)	0.005	2.4 (1.0-5.5)	0.046
Underlying disease	2.3 (1.2-4.5)	0.019	2.1 (1.1-4.2)	0.037
History of uterine surgery	2.0 (0.9-4.1)	0.073	1.2 (0.5-2.7)	0.680
History of uterine curettage	2.8 (1.2-6.4)	0.016	2.3 (0.9-5.4)	0.065
Medical regimens (misoprostol alone)	1.9 (0.4-8.0)	0.393	1.8 (0.4-8.0)	0.426

Discussion

Medical abortion at gestational age ≤ 24 weeks was effective and safe. Low complication rate was noted. Factors associated with complications in the second trimester were multigravida and having an underlying disease. Factors associated with success in the first trimester was the drug regimen (MM), whilst in the second trimester, it was maternal age (< 35 years).

In our study, the success rate of the MM regimen at gestational age ≤ 63 days (92%) was comparable to previous studies, ranging from 92-99.6%⁽¹³⁻¹⁶⁾. With regard to late first trimester abortions, the overall success rate of this study (58.7%) was lower than previous reports (78.6%-94.6%)⁽¹³⁾. This could be explained by 1) we declared failure of medical abortion quite early, and urgently proceeded to manual vacuum aspiration to ensure complete abortion, and 2) repeated doses of misoprostol were rarely administered in the MM regimen, especially in the early period of drug implementation. However, we had a very low success

rate for the misoprostol alone regimen due to unavailable protocols for drug use, especially before 2012. In addition, we had only a few cases terminated by misoprostol alone. We preferred manual vacuum aspiration for early pregnancy termination to medical abortion, especially before 2015, when the MM regimen was not available. The MM regimen had higher success rates and shorter duration of termination than misoprostol alone, similar to previous studies⁽¹⁾.

Regarding second trimester abortions, the overall success rate (79%) was quite low, compared to previous studies (82-92%)^(11,17). It could be explained by that we did not have a protocol for medical abortion. Wide variations of dosage of misoprostol were used depending on obstetrician in-charge. Median duration of termination for MM regimen in our study (6.2 hours) was comparable to previous studies (5.9-6.6 hours)⁽¹¹⁾. International Federation of Gynecology and Obstetrics (FIGO) (2017) recommends the regimen of misoprostol 400 mcg every 3 hours⁽¹²⁾. However, we had only 10%

of cases using the FIGO (2017) regimen. We were afraid of uterine rupture, so most obstetricians preferred longer intervals of misoprostol administration. Even though we had longer intervals of misoprostol administration than that recommended by FIGO, all prescribed regimens had a median duration of termination of 15.6 hours (12-18 hours), comparable to previous studies (10-15 hours)⁽¹⁸⁻²¹⁾. We found the longer intervals of misoprostol administration, the longer the duration of termination. We capped the number of misoprostol doses to a maximum of five. However, recent studies recommended continuous dosing of misoprostol until expulsion rather than capping the number of doses⁽⁸⁾.

Drug regimen was the only factor associated with success in the first trimester. This is not surprising, because the mechanism of action of the MM regimen was better than that of misoprostol alone. The mifepristone blocked the progesterone receptor, leading to a change in the endometrial lining and detachment of the decidua, softening and dilation of the cervix and increased uterine sensitivity to prostaglandin. In addition, misoprostol acted by softening the cervix and uterine contractility, resulting in the expulsion of the product of conception⁽²²⁾. However, in the second trimester, only maternal age (< 35 years) was a significant factor of success. This was similar to previous study⁽²³⁾.

Multigravida and having an underlying disease were significant factors associated with complications in the second trimester. For multigravida, increased complications were also found in previous study⁽²⁴⁾. Since common complications in our study were hemorrhage and infection, therefore, it might be related to other factors which were higher rates in multigravida, such as coexisting genital tract infection, advanced maternal age, history of uterine scar and history of uterine curettage. Women with underlying diseases, such as heart disease, hypertension, autoimmune disease and diabetes mellitus, were at risk for hemorrhage and/or infection due to low immunity and/or receiving anti-coagulant.

The strengths of this study were: 1) an adequate sample size, 2) reliable and complete data, and 3)

determination of factors associated with success and complications. The limitations of the study were: 1) it was a retrospective design, 2) no protocol of medical abortion management was available, and 3) declaration of failure depended on the judgement of obstetrician in-charge.

Conclusion

In conclusion, medical abortion at gestational age \leq 24 weeks was safe. Obstetricians should pay special attention to multigravida women, and those having an underling disease for close surveillance, so as for early detection of serious complications.

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Potential conflicts of interest

The authors declare no conflict of interest.

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