MONITORING MEDICAL ABORTION USING MIFEPRISTONE/MISOPROSTOL COMBINATION WITH ULTRASONOGRAM AND SERUM HUMAN CHORIONIC GONADOTROPIN

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SUMMARY

Objective: The oral mifepristone/misoprostol combination (MMC) is safe for medical abortion in early pregnancy. The abortion status in MMC-treated pregnancies at Taipei Medical University–Wan Fang Medical Center was determined by ultrasonography, serum β-human chorionic gonadotropin (β-HCG), and histopathology.

Methods: All women at less than 49 days since the last menstruation who asked for legal abortion were evaluated by ultrasonography. They then received 600 mg of oral mifepristone followed 48 hours later by 600 μg of misoprostol. Women who had vaginal spotting or bleeding after 14 days were included in this study and underwent transvaginal ultrasonography, serum β-HCG measurement and vacuum aspiration or therapeutic dilatation and curettage (D&C) on day 14. Specimens were identified by histopathology. Abortion status was determined from linear regression of serum β-HCG and endometrial thickness.

Results: Of 35 women who underwent vacuum aspiration or therapeutic D&C, histopathology showed that 20 had decidual tissue and 15 had gestational tissue. Logistic regression showed that the distance measurement to the logistic regression line differed significantly between complete and incomplete abortion (p < 0.05).

Conclusion: In this study, serum β-HCG assays in addition to ultrasonographic evaluation helped to discriminate abortion status after oral MMC. [Taiwanese J Obstet Gynecol 2006;45(1):48–52]

Key Words: early pregnancy, incomplete abortion, mifepristone, misoprostol

Introduction

Mifepristone is a synthetic steroid that acts as a competitive blocker of both progesterone and cortisone receptors [1]. Misoprostol is a prostaglandin analog used to prevent gastric ulcers induced by nonsteroidal anti-inflammatory drugs [2]. The mifepristone/misoprostol combination (MMC) is an effective method to terminate early pregnancy [1–3], because mifepristone increases myometrial sensitivity to prostaglandin in pregnant women [4]. Taking oral misoprostol 36–48 hours after mifepristone is the most common regimen used to terminate a pregnancy of up to 49 days’ gestation [1]. With this regimen, complete abortion rates of 87% [5] and 96% have been reported [6]. Mild vaginal spotting or bleeding on day 14 after administering MMC may suggest the presence of products of conception, which are prone to infection. Our study, per-

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formed at the Taipei Medical University–Wan Fang Medical Center (TMU-WFMC), Taipei, Taiwan, was intended to predict complete abortion status after administering MMC, using serum β-human chorionic gonadotropin (β-HCG) and ultrasonographic measurement of endometrial thickness.

Methods

We studied patients who requested legal termination of pregnancy at TMU-WFMC from October 1, 2004, to January 30, 2005. We excluded heavy cigarette smokers (>10/day), all patients with cardiovascular disease, asthma, possible ectopic pregnancy, and hematologic disorders, and patients with ultrasonographic proof of pregnancy of more than 49 days’ gestation (crown–rump length or gestational sac). Written informed consent was obtained from each patient before being enrolled in the study.

Patients were given 600 mg of oral mifepristone (Apano; Lotus Pharmaceutical Co Ltd, Taipei, Taiwan) followed by 600 μg of misoprostol (Cytotec; Searle, Morpeth, Northumberland, UK) 48 hours later. A 24-hour on-call telephone number was provided to answer any questions. All patients were instructed to return for a post-treatment ultrasound examination on day 14 after taking the first pills. We enrolled patients who complained of vaginal spotting or bleeding and evaluated endometrial thickness and serum β-HCG on day 14. All enrolled patients underwent vacuum aspiration or therapeutic dilatation and curettage (D&C).

Enrolled patients underwent ultrasonic examination with real-time ultrasound equipment (Image Point; Hewlett Packard, Andover, MA, USA) and using a 5–10-MHz transducer to measure endometrial thickness by identifying the long axis (anterioposterior dimension or “height”) of the uterus, including both opposing layers of the endometrium [7]. All specimens removed by vacuum aspiration or therapeutic D&C were sent for pathologic examination. Patients were considered to have an incomplete abortion if the pathologic findings of the specimens revealed trophoblasts or chorionic villae.

Statistical analyses

We used logistic regression to correlate patients’ serum β-HCG and endometrial thickness with the abortion status, and to estimate coefficients of regression to discriminate whether the pregnancy was successful.

We used the β-HCG and endometrial thickness values as risk factors for gestational age, and built logistic models with different risk factors for improved discrimination between complete and incomplete abortion.

Results

In this study, 35 patients with a mean age of 31.7 ± 3.6 years and a mean gestational age of 5.3 ± 1.1 weeks had an intrauterine pregnancy visible on transvaginal ultrasonography. Of these women, 31.4% were nulliparous and 68.6% multiparous.

Figure 1 shows serum β-HCG and endometriotic thickness against pregnancy outcome for all 35 patients. Through logistic regression, we calculated the distance to the logistic regression line relative to the probability of success (Table 1). We defined the odds ratio of being a “case” at follow-up for those who were a “case” at the first examination compared to those who were a “non-case” at baseline. The estimated coefficients showed that βHCG was significantly associated with abortion. β-HCG = β-human chorionic gonadotropin.

![Figure 1. Patients with complete (●) and incomplete (○) abortion. β-HCG = β-human chorionic gonadotropin.](image)

<table>
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<tr>
<th>Parameter</th>
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<th>Standard error</th>
<th>Pr &gt; Z-</th>
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<td>1.782502</td>
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Pr = probability; Z = normal distributed random variable.

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Table 1. Results of fitting logistic regression model
the presence of gestational tissue, and logistic regression showed that the measurement result was significantly different between complete and incomplete abortion ($p < 0.05$).

We performed discriminant analysis to determine whether the abortion was complete (Table 2). With this analysis, we classified the patient correctly in 97.14% of patients. Using logistic regression, the influence of different variables on the complication was studied. Therefore, we were assured that the discriminant method, including endometrial thickness and $\beta$-HCG, was better than that determined simply by serum $\beta$-HCG concentration.

### Discussion

MMC used according to the manufacturer’s protocol [8] is an alternative to vacuum aspiration to terminate an early pregnancy, after all possible contraindications are considered. Patients who undergo vacuum aspiration are more likely have heavier vaginal bleeding, infection, and mechanical trauma than those who receive MMC [2]. Based on the results of this study, we suggest the use of ultrasonography and serum $\beta$-HCG assays to help prompt diagnosis and management [9] if patients have an uncertain outcome or suspected ectopic pregnancy.

Rulin et al found that when the endometrial stripe is about 10 mm wide, products of conception are unlikely to be detected [10]. In other studies, an endometrial stripe of 8 mm or less was used for diagnosis of complete abortion [11].

Honkanen et al reported that by day 14, serum HCG concentrations have declined by 99.4 ± 10% and that the route of medication administration (oral or vaginal) has no effect on the kinetics of serum $\beta$-HCG in patients treated for medical abortion [12]. Another study reported that failed or incomplete abortion occurs when pregnancy tests with sensitivities of at least 1,000 mIU/mL are positive within 2 weeks after surgical abortion [13].

In France, MMC is often used to terminate a pregnancy before 50 days of amenorrhea, which is calculated from the first day of the last menstrual period, with a complete abortion rate of about 95% [8]. In a previous study, we reported that most Taiwanese patients who asked for legal abortion before 49 days from the last menstruation were evaluated ultrasonographically. The study showed that the complete abortion rate was only 78.5% [14]. This discrepant finding suggests that the optimal MMC regimen in Taiwan needs to be established [15].

Some studies have revealed that oral misoprostol is less effective in causing abortion and produces more side effects than vaginal misoprostol [3]. Oral misoprostol is licensed to prevent gastric ulcers induced by nonsteroidal anti-inflammatory drugs. The misoprostol tablet is inexpensive, stable, and effective for medical abortion [2], but it was not developed and manufactured for vaginal use. We chose to use 600 μg of oral misoprostol in MMC because the vaginal route is uncomfortable and painful for the patient [16]. Studies to develop a drug that can be administered by different routes are also needed. Thus, more studies on the best MMC protocol for the legal termination of early pregnancy are needed in different populations. Based on the results of our study, we suggest a new protocol for most Taiwanese women (Figure 2).

Previous studies on patient satisfaction with medical abortion revealed two disadvantages: the need for many office visits and the prolonged time of waiting until the abortion is over [17,18]. Based on the findings of this study, mild vaginal spotting or bleeding on day 14 after administration of MMC does not guarantee the absence of products of conception, which are at high risk of infection, and serum $\beta$-HCG assays can help ultrasonographic evaluation of abortion status after oral MMC.

### Acknowledgment

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### References

Figure 2. Block diagram of the new protocol for most Taiwanese women.

Day 1: Gestational age confirmation by ultrasound (≤ 49 days), then mifepristone 600 mg orally

Day 3 (36–48 h): Misoprostol 600 μg orally

Day 14: Transvaginal ultrasonographic evaluation of endometrial thickness and speculum examination of the vagina

Endometrial thickness < 10 mm

Without spotting or bleeding

Complete abortion

Without spotting or bleeding

Speculum examination of the vagina (Day 21)

Vacuum aspiration of endometrial contents

With spotting or bleeding

Serum β-HCG < 400 mIU/mL

Serum β-HCG ≥ 400 mIU/mL

Check serum β-HCG

Endometrial thickness ≥ 10 mm with or without spotting or bleeding

Serum β-HCG < 400 mIU/mL

With spotting or bleeding

With spotting or bleeding

Without spotting or bleeding

Vacuum aspiration of endometrial contents

Without spotting or bleeding

Serum β-HCG ≥ 400 mIU/mL

Speculum examination of the vagina (Day 21)

Check serum β-HCG


abortion, clinically thought to be complete: a prospective study. 


