CONCURRENT USE OF MIFEPRISTONE AND MISOPROSTOL FOR EARLY MEDICAL ABORTION

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SUMMARY

Objective: This study was designed to evaluate the efficacy of using mifepristone and misoprostol concurrently for early medical abortion.

Materials and Methods: A total of 90 women with undesired pregnancies ≤ 49 days’ gestation were enrolled. All women concurrently received oral mifepristone 200 mg and vaginal misoprostol 800 μg. Follow-up evaluation with transvaginal ultrasonography was performed 4 days and 2 weeks after treatment.

Results: The complete abortion rate was 97.8% (88/90 women). The mean induction to abortion interval was 5.5 hours. The mean bleeding duration was 11.8 days. Patients found the side effects acceptable and reported a 91.1% (82 patients) satisfaction rate.

Conclusion: Concurrent administration of oral mifepristone and vaginal misoprostol is an efficacious regimen for medical abortion of pregnancies ≤ 49 days of gestation. [Taiwanese J Obstet Gynecol 2006;45(4):325–328]

Key Words: concurrent medical abortion, mifepristone, misoprostol

Introduction

For early medical abortion, many reports recommend oral administration of mifepristone (RU 486) 600 mg, followed by oral administration of misoprostol 400 μg 36–48 hours later, which results in a 87–96.9% complete abortion rate [1–4].

When orally administered, mifepristone is quickly absorbed and reaches its peak serum concentration in 1–2 hours. With a half-life of 24–48 hours, mifepristone is best administered orally once only. Studies also show that the peak serum concentration of mifepristone is more or less invariable for a dose that ranges between 100 and 800 mg [5,6]. Hence, many early medical abortion regimens use a dose of 200 mg mifepristone [7].

Research has shown that vaginal administration of misoprostol is characterized by slow absorption but long duration of high serum concentration. Hence, vaginal bioavailability of misoprostol is three times greater than oral bioavailability of misoprostol; thus, vaginal administration of misoprostol has a relatively higher success rate of abortion than oral administration [8].

A recent study shows that the success rate of complete abortion remains unchanged even if the interval between administration of mifepristone and subsequent administration of misoprostol decreases from 36–48 hours to 6–8 hours [9]. Also, research reveals that the therapeutic effect is good when the two drugs are used concurrently. We studied the efficacy of mifepristone and misoprostol used concurrently for early medical abortion.

Materials and Methods

Between October 2005 and September 2006, a total of 90 early pregnant women requested medical abortion. The program had the approval of the ethics committee of Kuo General Hospital, Tainan, Taiwan.

Before receiving medical abortion, a patient had to meet the following criteria: (1) patient requests medical abortion; (2) gestational age ≤ 49 days, as confirmed by vaginal ultrasonography; (3) patient signs

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an agreement of consent and is informed of the advantages and risks of medical abortion and the necessity of receiving surgical abortion in case of medical abortion failure; and (4) patient promises to attend follow-up appointments.

No medical abortion was performed on pregnant women with any of the following: (1) allergy to mifepristone or prostaglandins; (2) symptoms of threatened abortion; (3) medical history of diseases related to the heart, respiratory system, kidneys, liver, or adrenal gland; (4) medical history of thromboembolism, hypertension, coagulopathy, or diabetes mellitus; (5) medical history of ultrasonographic or uterine pathology; and (6) active pelvic infection.

Three clinic visits were scheduled. At visit 1 (day 1), each female patient concurrently received oral mifepristone 200 mg and vaginal administration of misoprostol 800 μg (in the form of four 200 μg tablets), and stayed in the hospital for 1 hour of observation before being discharged. Participants were given three 500 mg tablets of acetaminophen that they could take every 6 hours if they had lower abdominal pain.

At visit 2 (day 4), patients visited the hospital again for transvaginal ultrasonography. Patients were instructed to be alert to the expulsion of the conceptus and to note the amount of bleeding. All symptoms, such as abdominal pain, shivering, vomiting, nausea, headache, diarrhea or other symptoms, were to be recorded. If a patient had menses as usual or complained of menorrhagia, and the gestational sac was no longer visible on ultrasound, the patient was scheduled to visit the hospital 10 days later. If the gestational sac was intact, surgical abortion was recommended, and the patient received gynecologic examination when necessary.

At visit 3 (day 14), the patient was asked if she had had bleeding, and underwent transvaginal ultrasonography again. Normal ultrasonographic findings indicated the end of therapy, but a follow-up appointment in 1 week was made when necessary. The definition of a successfully induced complete medical abortion was one that occurred without surgery to evacuate the uterus.

At the end of therapy, patients filled out a questionnaire designed to determine whether they agreed that the medical abortion was performed to their satisfaction; the questionnaire consisted of multiple choice questions with the following choices: strongly disagree; disagree; neutral; agree; strongly agree.

Results

The mean age of the 90 women was 23.6 years (range, 17–42 years), and the mean gestational age was 44.8 days (range, 36–49 days); 50 (55.6%) were nulliparous, 16 (17.8%) were primiparous, and 24 (26.7%) were multiparous. A total of 88 (97.8%) patients had complete abortion; two (2.2%) had incomplete abortions and received dilatation and curettage to evacuate the uterus. The mean induction to abortion interval was 5.5 hours (range, 4–8 hours). The mean duration of bleeding was 11.8 days (range, 9–32 days).

Side effects included abdominal pain in 56.7% (51 women), nausea in 17.8% (16), fever in 15.6% (14), shivering in 14.4% (13), headache in 13.3% (12), diarrhea in 8.9% (8), and vomiting in 4.4% (4), and were mostly mild and required no medication except for analgesics. No patient had infection, severe hemorrhage or any need for blood transfusion. Regarding how much patients agreed that the therapy they had received were performed to their satisfaction, the following answers were received: strongly agree 72.2% (65 women), agree 18.9% (17), neutral 6.7% (6), disagree 2.2% (2); resulting in a satisfaction rate of 91.1% (82 patients).

Discussion

To achieve medical abortion, patients typically take misoprostol 36–48 hours after taking mifepristone. We evaluated the effects of taking the two drugs simultaneously, wherein vaginal administration of misoprostol resulted in a 97.8% success rate of complete abortion with side effects similar to those previously reported, and a high satisfaction rate of 91.1%.

As affirmed by many studies, administration of higher doses of mifepristone within the range 100–800 mg does not increase the serum peak concentration of mifepristone. The reason for this is as follows: the serum kinetics of mifepristone in humans is regulated by the transport protein α1-acid glycoprotein (AAG), and the saturation of the binding capacity of serum AAG might explain the similar levels of serum concentrations of mifepristone after doses exceeding 100 mg [7]. There is no difference between administration of 600 mg and 200 mg of mifepristone in terms of the success rate of complete abortion [7]. Hence, we used 200 mg of mifepristone.

Since vaginal bioavailability of misoprostol is three times greater than oral bioavailability of misoprostol, vaginal administration of misoprostol is more efficacious than oral administration. Citing several papers, Kahn et al assert that oral administration of misoprostol has an incomplete abortion rate of 6.4%, while the rate for vaginal administration is 2.1% [3]; thus, vaginal administration of misoprostol is more efficacious than oral administration. Accordingly, we also adopted
vaginal administration of misoprostol, and used 800 μg as recommended in the literature.

The success rate of complete abortion will remain unchanged even if the interval between administration of mifepristone and subsequent administration of misoprostol decreases from 36–48 hours to 6–8 hours [9]. Inasmuch as a shorter interval of administration of mifepristone and subsequent administration of misoprostol is an available option, and considering that vaginal administration of misoprostol results in strong uterine contractions, the vaginal administration of misoprostol alone is crucial to a high success rate of complete abortion. However, studies have indicated that the combined use of mifepristone and misoprostol leads to a higher success rate of abortion than with misoprostol alone. Jain et al, in a randomized double-blind controlled trial, studied 250 pregnant women (gestational age <56 days) [10]. Group 1 women received mifepristone and vaginal administration of misoprostol 800 μg, and Group 2 women received vaginal administration of misoprostol 800 μg only. Group 1 had a successful abortion rate of 95.7% (114/119), and Group 2 had a successful abortion rate of 88.0% (110/125); the difference was statistically significant (p < 0.05). Therefore, we also used both mifepristone and misoprostol.

In 2005, Murthy et al reported that in 40 women with pregnancies <7 gestational weeks who received oral mifepristone 200 mg and vaginal administration of misoprostol 800 μg, a complete abortion rate of 98% was achieved in 2 weeks, with only one woman requiring suction and curettage because of incomplete abortion [11]. Their conclusion was that combined administration of mifepristone and misoprostol to pregnant women <7 gestational weeks is an efficacious way of achieving medical abortion. Our rate of 97.8%, achieved with the same dosages, is similar to that of Murthy et al's.

Also in 2005, Schreiber et al studied 40 pregnant women in their 8th gestational week (Group 1) and 40 pregnant women in their 9th gestational week (Group 2) who received oral mifepristone 200 mg and vaginal administration of misoprostol 800 μg, and who underwent vaginal ultrasonography 24 hours and 2 weeks afterwards [12]. They found that by the second week, the success rates of complete abortion were 93% and 90% in Groups 1 and 2, respectively. They concluded that mifepristone and misoprostol are efficacious in women with pregnancies of 8–9 gestational weeks, whether administered concurrently or one after the other 36–48 hours later. However, these results are slightly unsatisfactory when compared to those of Murthy et al [11], because Schreiber et al's study involved pregnant women at 50–56 days' gestation (8 weeks) and 57–63 days' gestation (9 weeks), compared to <49 days' gestation in Murthy et al's study.

More recently, in 2006, Kapp et al studied the effects of oral mifepristone 100 mg and vaginal administration of misoprostol 800 μg in 39 pregnant women at 56 days' gestation (9th gestational week), who received follow-up consultation 2–7 days and phone-based evaluation of symptoms and acceptability 3 weeks afterwards [13]. The success rate of complete abortion was 90%, and four women needed uterine aspiration. Abortion occurred at a mean of 7 hours after taking the drugs. Most of the participants (92%) considered it appropriate to take all the drugs during a single consultation visit.

In conclusion, for medical abortion, women in their 7th week of gestation or earlier can receive oral mifepristone and vaginal administration of misoprostol concurrently; the rate of successful abortion is high, although an insight into the optimal timing, method of administration, and dosage of misoprostol can only be gained by further research.

References


