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Original Research

A Randomized Comparison of Misoprostol 6 to 8 Hours Versus 24 Hours After Mifepristone for Abortion

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OBJECTIVE:

To demonstrate equivalence between mifepristone 200 mg followed 6 to 8 hours later and 24 hours later by misoprostol 800 μg vaginally for abortion in women up to 63 days of gestation.

METHODS:

Mifepristone 200 mg was swallowed by 1,080 women after which they were randomly assigned to self-administer misoprostol intravaginally 6 to 8 hours later (group 1) or 23 to 25 hours later (group 2) at home. Participants returned for an evaluation, including transvaginal ultrasonography, 7 ± 1 days after initiating treatment. Subjects who had not aborted were offered a second dose of misoprostol. All participants returned approximately 2 weeks after receiving mifepristone. Telephone contact was also attempted approximately 5 weeks after treatment. Treatment was considered a failure if a suction aspiration was performed for any indication.

RESULTS:

Complete abortion rates for groups 1 and 2 were 503 of 525 (95.8%, 95% confidence interval 93.7%, 97.3%) and 521 of 531 (98.1%, 95% confidence interval 96.6%, 99.1%), respectively, which were statistically equivalent. Side effects were significantly more common after mifepristone administration for women in group 2. Nausea, vomiting, and heavy bleeding were also significantly greater for women in group 2 after misoprostol treatment. Pain and subject acceptability were similar between groups.

CONCLUSION:

Mifepristone 200 mg followed 6 to 8 hours later by misoprostol 800 μg vaginally is as effective for abortion and has significantly fewer side effects as compared with regimens using a 24-hour dosing interval. Women receiving mifepristone and vaginal misoprostol for abortion can have the flexibility to administer the misoprostol as soon as 6 hours after using the mifepristone.

LEVEL OF EVIDENCE:

I

Mifepristone is a synthetic antiprogestin currently used in combination with a prostaglandin analog for medical abortion. Misoprostol is the most commonly used prostaglandin analog throughout the world in medical abortion regimens. The U.S. Food and Drug Administration–approved regimen of mifepristone and misoprostol is based on long-standing experience with this drug combination in Europe and China. In gestations up to 49 days, mifepristone is administered in a dose of 600 mg to a woman no more than 49 days gestation. She then returns in 36 to 48 hours to receive misoprostol 400 μg orally, after which she can be observed for 4 hours or return home; approximately 60–70% of women will abort within 4 hours, and 90% abort within 24 hours.[1] The woman returns in approximately 2 weeks for a follow-up evaluation. If the abortion is not considered complete at the time of this visit, a suction curettage is performed.

Multiple investigators have evaluated alternative medical abortion regimens to simplify the treatment process and extend the gestational age range. These regimens have included using lower doses of mifepristone, home administration of the misoprostol, varying the dose of misoprostol, use of vaginal misoprostol, and decreasing the dosing interval between mifepristone and misoprostol. Regimens with a shorter interval between mifepristone and misoprostol administration, if effective, would shorten the amount of time necessary for a medical abortion to occur and, potentially, increase acceptability. Accordingly, Schaff et al[2,3] demonstrated that misoprostol 800 μg vaginally administered 24 hours after 200 mg of mifepristone mg is effective for abortion through 63 days of gestation and is more acceptable to women compared with waiting 48 or 72 hours between the medications.

A further reduction in the time interval was evaluated in 2 pilot studies at the University of Pittsburgh.[4,5] These trials included 40 women in each of the gestational age ranges of less than or equal to 49 days, 50 to 56 days, and 57 to 63 days using 200 mg of mifepristone followed 6 to 8 hours later by 800 μg of misoprostol administered vaginally. Abortion rates at 24 hours were 88% to 92%. On the basis of the results of these pilot studies, we performed this trial to compare the efficacy, side effects, and acceptability of the administration of 200 mg of mifepristone followed 6 to 8 hours later or 24 hours later by 800 μg of misoprostol administered vaginally in women up to 63 days gestation.

MATERIALS AND METHODS

We conducted a prospective, multicenter, randomized comparative trial in 1,080 pregnant women who were up to 63 days of gestation and desiring an abortion. The study was reviewed and approved by the Institutional Review Boards of the respective institutions and by the U.S. Food and Drug Administration. The University of Pittsburgh/Magee–Womens Hospital served as the sponsoring institution; all protocol changes were submitted and approved by the Magee–Womens Hospital Institutional Review Board before submission to other institutions.

Healthy women were included if they were requesting an elective abortion, had an intrauterine pregnancy less than or equal to 63 days of gestation on the day of mifepristone administration as confirmed by vaginal ultrasound, were willing to comply with the visit schedule, were willing to have a surgical abortion if indicated, and had access to a telephone. Potential subjects were excluded if they had any contraindication to mifepristone, including chronic systemic corticosteroid administration or adrenal disease; had any contraindications to misoprostol, including glaucoma, mitral stenosis, sickle cell anemia, poorly controlled seizure disorder, or known allergy to prostaglandin; had a hemoglobin level less than 10 g/dL; had cardiovascular disease, including angina, valvular disease, arrhythmia, or cardiac failure; had a known coagulopathy or were receiving treatment with anticoagulants; had a pregnancy with an intrauterine device in utero; had active cervicitis on examination; were breastfeeding; had previously participated in the trial; or if their ultrasound examination results demonstrated any evidence of an early pregnancy failure.

After obtaining informed consent, a medical history was obtained, hemoglobin and blood type were obtained, and pelvic and transvaginal ultrasound examinations performed. Only women with a visible intrauterine gestational sac were enrolled. Mean sac diameter ([length + width + depth]/3) was used to determine estimated gestational age (EGA) only when an embryonic pole was absent. The gestational age was estimated by using mean sac diameter (EGA [days] = mean sac diameter [mm] + 30)[6] or embryonic pole (EGA [days] = embryonic pole [mm] + 42).[7] Last menstrual period was used to determine EGA if the last menstrual period was within 3 days of the ultrasound EGA; however, the ultrasound estimate was used if it differed by 4 days or more from the EGA by last menstrual period.

At the University of Pittsburgh, subjects returned for enrollment at least 24 hours after signing informed consent as required by the Pennsylvania Abortion Control Act. At all other sites, screening and enrollment occurred at the same visit. Once entry criteria were confirmed, each woman swallowed 200 mg of mifepristone and was given 4 tablets of misoprostol (200 μg each) to take home. Women were instructed to insert the misoprostol tablets as high up as possible into their vagina either 6 to 8 hours (group 1) or 23 to 25 hours (group 2) after taking the mifepristone. Group assignment was performed in a randomized fashion by using sequentially numbered opaque envelopes containing a card with computer-generated assignment information and prepared for each center by the Data Coordinating Center. Randomization was stratified by center with equal frequency to the 2 treatment arms. Random allocations were performed in a permuted block design with varying block sizes as described by Pocock.[8]

Rh-immune globulin (50 μg) was administered intramuscularly to all subjects who were Rh-negative. Participants were given a prescription for or supply of 20 tablets of codeine phosphate (30 mg), oxycodone (5 mg), acetaminophen with codeine (300 mg/30 mg, with instructions not to take more than 13 tablets in a 24-hour period), or acetaminophen with hydrocodone (500 mg/5 mg, with instructions not to take more than 8 tablets in a 24-hour period). Subjects were instructed to use ibuprofen or acetaminophen initially and to use the prescribed narcotic only if necessary. Subjects were asked to maintain a diary of medication use and side effects throughout the study. At each follow-up visit, the diary was reviewed and data collected regarding bleeding, cramping, other side effects, and medication use since the previous visit. An investigator was available 24 hours a day in the case of emergency and to answer subjects' questions.

Participants were scheduled to return for follow-up examinations 7 (± 1) days and 14 (± 2) days after taking mifepristone. Transvaginal ultrasound examinations were performed at each visit. Women who had not expelled the gestational sac at the first follow-up visit were offered a repeat dose of misoprostol. Subjects who missed the first follow-up visit and were not seen again until 12 or more days after receiving the mifepristone could not receive a second dose of misoprostol. Subjects who had not aborted by the second follow-up and had a viable gestation were offered a surgical abortion. Women with a nonviable persistent gestation at the second follow-up were offered a

surgical abortion or scheduled to return again in another 3 weeks. If the abortion had not been completed by this final follow-up visit, subjects were offered a surgical abortion or weekly follow-up. Suction aspiration was also performed if it was clinically necessary because of uterine hemorrhage or incomplete abortion or at the subject's request. We attempted to contact all subjects with a complete abortion by the second follow-up visit by telephone 5 weeks after initiating the study to review if there had been any problems since the abortion. The procedure was considered successful if a complete abortion occurred without requiring a suction aspiration.

Immediately before enrollment, subjects completed a questionnaire regarding their prior experience with abortion and a visual analog scale (VAS)[9–11] measuring the amount of pain and bleeding they anticipated. At the subject's final follow-up visit, she was questioned about her satisfaction with this medical abortion regimen and completed a VAS measuring the amount of perceived bleeding and pain experienced during the abortion process and her preference for medical or surgical abortion if she needed an abortion again in the future. On a 100-mm line with 0 equaling no bleeding and 100 equaling heavy bleeding, subjects were asked to mark the amount of bleeding they experienced. In a similar fashion, pain was recorded with 0 equaling no pain and 100 representing severe pain. Likewise, preference for abortion method was recorded with 0 equaling medical abortion and 100 representing surgical abortion.

On-site monitoring was performed by staff from the Data Coordinating Center at a minimum of every 4 weeks or upon request of the principal investigator. The monitor reviewed the center's documents to ensure appropriate institutional review board approval and communication as well as accurate and appropriate reporting of source data.

Sample size was estimated to demonstrate equivalence of the 2 treatment methods. The complete abortion rate in the standard care group (group 2) was set at 97%, based on reported complete abortion rates using mifepristone followed by vaginal misoprostol ranging from 95% to 99%.[2,3,12–16] By using a 1-sided, 2-group test of equivalence, 528 subjects per group were required to prove equivalence within a 3% observed difference (upper 95% confidence interval [CI] of 5%). To allow for 2% of subjects to not have documentation of a final outcome, the total sample size was increased to 1,080 women. Because individual side effects in medical abortion regimens using these agents typically occur at a rate exceeding 10%,[4,5,12,14–17] this sample size had 80% power to detect at least a 60% difference in the rates of side effects between the 2 treatment groups. For side effects occurring at rates of 20%, this study had 80% power to detect at least a 45% difference between the 2 groups.

For all analyses, 2-tailed *P* values less than .05 were considered statistically significant. Baseline demographic data were compared according to treatment group by using the Student *t*, Fisher exact, or χ^2 test, where appropriate, to assess for clinically significant differences. An intent-to-treat analysis was primarily performed to include the study population who had at least 1 follow-up visit or contact, stratified by assigned treatment group. The status of participants at the end of the study (eg, completed study, lost to follow-up, or discontinued) in both treatment groups was compared by using Mantel–Haenszel tests, stratified by study site. All other calculations and statistical analyses were conducted on the intent-to-treat population.

The primary objectives of this study was to compare the complete abortion rates in women who received mifepristone followed by vaginal misoprostol 6 to 8 hours later (experimental group) and 24 hours later (standard care group) by using a 1-sided equivalence test of proportions with an equivalence limit of 5%. Unlike other statistical tests, the null hypothesis for the test of equivalence is that 2 treatments are not equivalent. Rejecting the null hypothesis, indicated in this study by a $P \leq .05$, implies that the 2 treatments are equivalent.[18] A planned interim analysis of the primary objective (complete abortion rate) was conducted when 300 women (approximately 25% of the study population) completed their follow-up visits. This interim analysis reduced the α for the final analysis to .04991 according to the O'Brien and Fleming method.[19]

Secondary outcomes included side effects, bleeding, and acceptability data. The rate of side effects (nausea, vomiting, and pain medication use) and bleeding between the 2 abortion regimens was compared by using the Fisher exact test. The rate of side effects between site and gestational age was evaluated by using the overall χ^2 test and χ^2 test for linear trend, respectively; when differences were detected, multivariable logistic regression was performed to assess for potential confounding.[20] The length of bleeding after treatment and the pre- and posttreatment VAS assessments were compared between treatment groups by using the Mann–Whitney *U* test because these data did not appear to be normally distributed when their frequency distributions were graphically displayed. The acceptability of the 2 abortion regimens, as measured by positive or negative answers, was compared by using the Fisher exact test.

RESULTS

Between April 2002 and June 2003, 1,080 subjects were enrolled (Figure 1). Both groups were similar in demographic characteristics (Table 1). The gestational age was set by last menstrual period and confirmed by ultrasonography in 46% and 45% of women in groups 1 and 2, respectively; the remaining women had their gestational age adjusted by the ultrasound examination. Ninety-eight percent of women in both groups used the misoprostol at the correct time, defined as within 30 minutes before or after their assigned time interval. The median time of misoprostol administration was 6.5 and 24 hours after mifepristone in groups 1 and 2, respectively. Only 5 (0.5%) women used the misoprostol incorrectly, including 3 who crossed over in study group assignment (1 woman in group 1 and 2 women in group 2) and 2 women in group 2 who did not use the misoprostol (both expelled the pregnancy by the first follow-up visit).

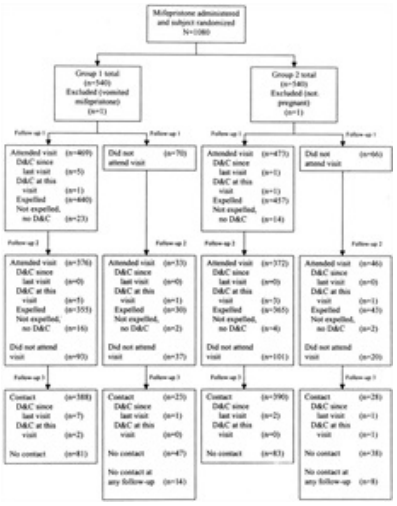

Figure 1:

Figure 1.Creinin. Medical Abortion in 1 Day. Obstet Gynecol 2004.

Table 1. Baseline Demographics of Study Population

	Study treatment, interval 6–8 hours (n = 539)	Standard treatment, interval 23–25 hours (n = 539)
Gestational age (days)	50 ± 7	50 ± 8
≤ 49	251 (47)	262 (49)
50–56	159 (29)	159 (29)
57–63	129 (24)	118 (22)
Age (y)	25 ± 6	25 ± 5
Gravidity		
1	98 (18)	102 (19)
2	115 (21)	119 (22)
3	99 (18)	112 (21)
4	93 (17)	72 (13)
≥ 5	134 (25)	134 (25)
Parity		
0	191 (34)	193 (34)
1	136 (25)	133 (25)
2	119 (22)	133 (25)
≥ 3	92 (17)	66 (12)
Race		
Caucasian	209 (39)	209 (39)
African American	177 (33)	164 (30)
Asian	11 (2)	17 (3)
Other	7 (1)	1 (0.2)
None of these	135 (25)	148 (27)
Ethnicity		
Hispanic	138 (26)	131 (24)
Non-Hispanic	401 (74)	408 (72)
Marital status		
Single	429 (80)	421 (78)
Married	69 (13)	60 (11)
Divorced	17 (3)	22 (4)
Separated	22 (4)	34 (6)
Widowed	2 (0.4)	2 (0.4)
Living with partner	214 (40)	191 (35)
Prior elective abortion	271 (50)	273 (51)

Data are presented as n (%) or mean ± standard deviation.

Table 1:

Baseline Demographics of Study Population

A final outcome was established for 1,056 women with 22 (2.0%) women lost to follow-up (Figure 1). A small number of women (32, 3.0%) had follow-up only by phone contact but had histories consistent with expulsion and no signs of a continuing pregnancy. The efficacy of both treatment groups, as demonstrated in Table 2, was equal based on an equivalence limit of 5% ($P = .005$). The complete abortion rate did not vary significantly by treatment group, gestational age, or study site. Reasons for suction aspiration in groups 1 and 2 included viable pregnancy at follow-up 2 (2 and 1 women, respectively), persistent nonviable pregnancy at follow-up 2 (2 and 0 women, respectively), persistent nonviable pregnancy at follow-up 3 (1 and 1 women, respectively), incomplete abortion (12 and 7 women, respectively), prolonged bleeding (2 and 0 women, respectively), and subject request (3 and 1 women, respectively).

Table 2. Complete Abortion Rate With Mifepristone 200 mg Followed by Misoprostol 800 μg Vaginally*

	Study treatment, interval 6–8 hours (n = 525)	Standard treatment, interval 23–25 hours (n = 531)
By misoprostol dose		
Total	95.8 (93.7, 97.3)	98.1 (96.6, 99.1)
With single dose misoprostol	94.9 (92.6, 96.6)	97.2 (95.4, 98.4)†
By days post mifepristone		
7 days (± 1 day [follow-up 1])	440 (94)	457 (97)†
	n = 469	n = 473
14 days (± 2 days [follow-up 2])	479 (95)	509 (96)
	n = 502	n = 519
By gestational age		
≤ 49 days	97.1 (94.2, 98.8)	98.4 (96.3, 99.4)
	n = 243	n = 258
50–56 days	94.2 (89.2, 97.3)	97.3 (93.6, 99.3)
	n = 154	n = 157
57–63 days	95.2 (89.9, 98.2)	98.3 (93.9, 99.8)
	n = 126	n = 116

Data are presented as % (95% confidence interval) or n (%).

* Women who were lost to follow-up are excluded.

† Includes 2 subjects who did not use misoprostol and aborted before the first follow-up visit.

Table 2:

Complete Abortion Rate With Mifepristone 200 mg Followed by Misoprostol 800 μg Vaginally

Cramping and bleeding began after a median of 2 hours (range, 0–87.5) and 3 hours (range, 0–72.5), respectively, after the first dose of misoprostol in group 1. In group 2, cramping and bleeding began after a median of 1.5 hours (range, 0–35.75 hours) and 2 hours (range, 0–43.1 hours), respectively, after the first dose of misoprostol. None of these times was significantly different. Bleeding and spotting duration also was not different between groups, lasting a median of 7 and 5 days, respectively, for women in group 1, and 7 and 6 days, respectively, for women in group 2. Pad count data were available for 519 (99%) and 517 (97%) subjects in groups 1 and 2, respectively. For these women, 45% and 49% reported that the heaviest amount of bleeding they experienced was soaking at least 2 pads in 1 hour ($P = .2$). However, the difference in heavy bleeding was significant when comparing women who reported their heaviest flow soaked at least 3 pads in 1 hour (13% and 19%, respectively, $P = .007$).

Side effects are presented in Table 3. Women in group 2 reported a significantly higher rate of side effects during the interval between mifepristone and misoprostol than the women in group 1. Additionally, women in group 2 had significantly more nausea and vomiting after misoprostol administration. Although a few of the side effects differed by gestational age (Table 4) or study site, regression analysis did not change the statistical difference of these effects.

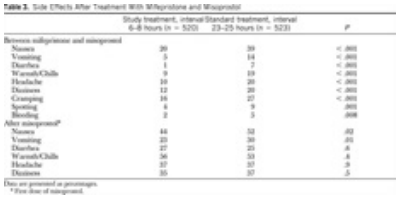

Table 3:
Side Effects After Treatment With Mifepristone and Misoprostol

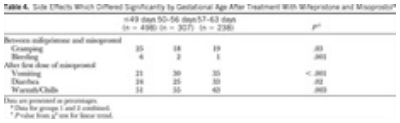

Table 4:
Side Effects Which Differed Significantly by Gestational Age After Treatment With Mifepristone and Misoprostol

Complete pre- and posttreatment VAS assessments were available for 404 (75%) and 419 (79%) women in groups 1 and 2, respectively. The median levels of pain reported on the posttreatment questionnaires were 57 mm and 58 mm, respectively. The indicated level of pain was 2 mm lower than that anticipated on pretreatment VAS assessment in both groups. The findings were similar for bleeding with a median posttreatment severity of bleeding of 64 mm and 65 mm for the 2 groups, and the differences as compared with pretreatment estimation of bleeding 5.5 mm and 2 mm lower, respectively.

Serious adverse events occurred in 6 (0.6%) women. Two women (0.2%) received a transfusion, 1 in each treatment group. Two women (0.2%) in group 1 were hospitalized and treated with intravenous antibiotics for postabortal pelvic inflammatory disease. Two other women were hospitalized for indications that were not felt to be a direct result of the medical abortion. One woman in group 1 had a laparoscopic cholecystectomy for acute cholecystitis, and 1 woman in group 2 had a symptomatic ovarian cyst for which she was hospitalized for 1 day for observation and pain management. Last, there were 3 other women who were diagnosed with acute pelvic infection after the medical abortion but were treated as outpatients; as these women were not hospitalized, these infections were not considered serious adverse events.

Posttreatment acceptability questionnaires were available from 478 (89%) and 481 (89%) of women in groups 1 and 2, respectively. Results were identical between groups. In group 1, 452 (95%; 95% CI 92%, 96%) would recommend this method of abortion to a friend, and 425 (89%; 95% CI 86%, 92%) would choose medical abortion using this regimen again if they were to have another abortion. Similarly, for group 2, the results were 457 (95%; 95% CI 93%, 97%) and 431 (90%; 95% CI 87%, 92%), respectively.

DISCUSSION

We have demonstrated in a prospective, randomized, multicenter trial that using mifepristone and vaginal misoprostol as early as 6 hours apart is as effective as waiting 24 hours between administration of the 2 medications. Importantly, this equivalent efficacy is achieved with fewer side effects. Regardless, women found both treatment regimens equally acceptable. The high efficacy in the 6- to 8-hour group is not a reflection solely of misoprostol action because studies using misoprostol alone achieve much lower rates of efficacy when administered in a single dose vaginally.[17,21]

We had estimated having missing data in 24 women; this estimation was very close as our total number of women with no follow-up data was 22 (2.0%). Unfortunately, a small percentage of women did not attend any follow-up visits although we were able to make some contact by phone to confirm that the pregnancy had not continued. The number of women who attended scheduled visits after the first visit decreased, as we would likely expect. Even though this was a study, women who had expelled the pregnancy had no impetus to return for a second follow-up visit. Still, the drop-off in the number of women attending these visits did not affect the primary outcome as we had documented expulsion at a prior visit.

Although the study was not blinded, there was little potential for bias in our results. When a dilation and curettage (D&C) was performed for a persistent sac, no bias could be introduced because this was an objective finding. It is possible that bias could be present when performing a “clinically indicated” D&C for incomplete abortion or prolonged bleeding. However, it is more likely that the investigators would have been biased against performing a D&C. Given the overall outcome with relatively few medically necessary D&C procedures, it is unlikely that any bias was present.

The finding of fewer side effects between mifepristone and misoprostol administration in the 6- to 8-hour interval group was unexpected, especially because many of the side effects are commonly attributed to administration of the prostaglandin analog. Our study demonstrates that women do experience side effects that are attributable solely to the mifepristone, and the longer the interval between the mifepristone and misoprostol is, the more side effects that women experience from the mifepristone. We also were surprised to find that women in the 6- to 8-hour group experienced less severe side effects (nausea, vomiting, and heavy bleeding) after misoprostol administration as compared with women in the 24-hour interval group. Ironically, at the onset of the study, we were concerned that a shorter interval between the 2 medications may result in more pain and side effects, given that the mifepristone had less time to act. The VAS assessments actually demonstrated that subjects in both groups rated their pain and bleeding experiences identically. The similarity of the assessments to

pretreatment projections also indicates that subjects received appropriate counseling and had realistic expectations of their pain and bleeding. Although a few of the side effects were statistically different based on gestational age (Table 4), we did not have any data on the presence of these complaints before treatment. It is possible that some symptoms (ie, vomiting) were more prevalent in women at later gestational ages. Regardless, these differences are unlikely to be clinically relevant.

On the basis of the findings of our study, we postulate that both the time-dependent effect of mifepristone side effects and the finding of fewer misoprostol-related side effects in the 6- to 8-hour group may be related to the effects of mifepristone on endogenous prostaglandin production and action. In animal models, antiprogestins, including mifepristone, do not increase uterine prostaglandin synthesis or release but do increase the sensitivity of the uterus to prostaglandin actions during early pregnancy.[22–24] Our findings suggest the plausibility that the sensitivity increases in a time-dependent manner. As such, the longer mifepristone acts before the abortion, the more that side effects, especially those that are mediated by prostaglandin, are likely to occur. Additionally, the shorter the interval between medications, the lower the sensitivity to the exogenous prostaglandin analogue, which results in fewer side effects after misoprostol administration.

Mifepristone's known actions on a pregnant uterus include decidual necrosis, cervical softening, and increasing both uterine contractility and prostaglandin sensitivity.[25,26] Human studies have suggested that uterine contractility does not increase until 24 to 36 hours after mifepristone administration.[25] At this point, the myometrium is 5 times more sensitive to the stimulatory effects of exogenous prostaglandins.[25] However, our study suggests that some or all of these actions occur sooner, and that a longer interval between mifepristone and prostaglandin analog administration is not necessary for the medical abortion to be successful, tolerable and acceptable to the patient. Further investigations are needed to better understand which of mifepristone's actions are important and necessary for its abortifacient activity.

The onset of bleeding and cramping for women in both groups was quite variable, although clinically similar. It is possible that the differences could be related to variable absorption of the misoprostol or differences in the point at which mifepristone's actions are sufficient to effect abortion. Regardless of the reason, using the misoprostol vaginally with this shortened interval between medications is important; Creinin et al[27] reported only a 50% 24-hour success rate when the administration of 200 mg of mifepristone was followed 6 to 8 hours later by the oral administration of misoprostol.

The adverse events that occurred in our trial are similar in nature and incidence to what has been reported in the literature. Schaff et al[2] reported 2 women (0.1%) were hospitalized for treatment with intravenous antibiotics for pelvic infections. In both cases, the women had a failed medical abortion that had required a suction aspiration for completion of the abortion. Transfusion rate in a large series in the medical literature is 0.2%,[13,28] which is the same rate that was found in our current study.

On the basis of the results of this study, a 24-hour or longer interval between mifepristone and misoprostol administration is not necessary to achieve complete abortion. Additionally, women are less likely to experience side effects the earlier the misoprostol is used. Women can now have more flexibility when using mifepristone and vaginal misoprostol for medical abortion. Because misoprostol can be used as soon as 6 hours after mifepristone administration, women can now have a medical abortion in a single day with a high level of efficacy, safety, and acceptability.

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APPENDIX

The following institutions and persons participated in the Medical Abortion in One Day (MOD) Study Trial. The principal investigators at each center are indicated by asterisks. Data Coordinating Center (Magee–Womens Research Institute): M. Creinin,* L. Meyn, E. Sain; University of Pittsburgh: M. Fox,* B. Harwood, A. Murthy, C. Potter, M. Holovanisin; Columbia University: S. Teal,* C. Westhoff, A. Davis, D. Kaufman; Boston University: A. Chen,* L. Borgatta, O. Vragovic; and University of Rochester: E. Schaff,* A. Anderson, M. Scahill.

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