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Comparing two early medical abortion regimens: mifepristone+misoprostol vs. misoprostol alone☆

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Abstract

Background: Nonsurgical abortion methods have the potential to improve access to high-quality abortion care. Until recently, availability and utilization of mifepristone medical abortion in low-resource countries were restricted due to the limited availability and perceived high cost of mifepristone, leading some providers and policymakers to support use of misoprostol-only regimens. Yet, this may not be desirable if misoprostol-only regimens are considerably less effective and ultimately more costly for health care systems. This study sought to document the differences in efficacy between two nonsurgical abortion regimens.

Study Design: This double-blind randomized placebo-controlled trial enrolled women with gestational ages up to 63 days seeking early medical abortion from August 2007 to March 2008 at a large tertiary hospital in Ho Chi Minh City, Vietnam. Eligible consenting women received either (1) two doses of 800 mcg buccal misoprostol 24 h apart or (2) 200 mg mifepristone and 800 mcg buccal misoprostol 24 h later. Participants self-administered all study drugs and returned to the hospital for follow-up 1 week later. The trial is registered at ClinicalTrials.gov as NCT00680394.

Results: Four hundred women were randomized to either misoprostol-only (198) or mifepristone+misoprostol (202). Complete abortion occurred for 76.2% (n=147) of women allocated to misoprostol-only vs. 96.5% (n=194) of those given mifepristone+misoprostol (RR 0.79, 95% CI 0.73–0.86). Ongoing pregnancy was documented for 16.6% (32) of misoprostol-only users and 1.5% (3) of mifepristone +misoprostol users (1.62, 0.68–3.90). Side effects were generally similar for both groups, although significantly more women allocated to misoprostol-only reported diarrhea.

Conclusions: Mifepristone+misoprostol is significantly more effective than use of misoprostol-alone for early medical abortion. The number of ongoing pregnancies documented with misoprostol-only warranted an early end of the trial after unblinding of the study at interim analysis. Policymakers should advocate for greater access to mifepristone. Future research should prioritize misoprostol-only regimens with shorter dosing intervals.

Keywords: Medical abortion; Medication abortion; Mifepristone; Misoprostol

1. Introduction

Nonsurgical abortion methods using the drugs mifepristone and misoprostol have the potential to improve abortion care. Medical methods have several advantages over surgical evacuation, particularly for use in low-resource settings, including reducing the need for surgery, sterilization of instruments, specific clinic rooms and surgically trained personnel. In countries where demand for abortion has overwhelmed surgical abortion services or where access to surgical services may be restricted to higher level facilities, medical abortion could reduce the workload for providers and facilities currently providing surgical abortion care. Widespread adoption of mifepristone medical abortion has been limited due to lack of access to the drug and its perceived high cost in many low-resource countries [1]. Misoprostol, on the other hand, is widely available and

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inexpensive, and has therefore been promoted as an alternative to the combined regimens. In recent years, a host of new mifepristone and misoprostol products have become available which has reduced the cost of both drugs and facilitated access to medical abortion methods [2,3]. The mifepristone pill continues to cost considerably more than the misoprostol pill and alone represents the most significant portion of the cost of any medical abortion regimen.

Mifepristone and misoprostol have been used by millions of women for early pregnancy termination. Several refinements from the original protocol [4] have reduced the dose of mifepristone [5–7], introduced home use of misoprostol [1,4,5], shortened the time between mifepristone and misoprostol administration [8–11], and tested alternative doses and routes of misoprostol [5,12–15]. Providers have come increasingly interested in regimens using buccal misoprostol after mifepristone for medical abortion. Results from the large randomized trial in the United States comparing misoprostol 800 mcg given orally or buccally 24 to 36 h after 200 mg mifepristone through 63 days since the last menstrual period (LMP) showed 96.2% efficacy with buccal misoprostol (vs. 91.3% with oral) [12]. These results contributed to a policy change in the United States in favor of the 200 mg mifepristone+800 mcg buccal misoprostol as standard care for early abortions through 63 days LMP at Planned Parenthood affiliate clinics [16].

Misoprostol-alone has been used to induce abortions for over a decade. Its first use for this indication was documented in Brazil in the early 1990s, where women learned of the drug's abortifacient properties and began to use it clandestinely. Dozens of studies have examined various misoprostol regimens in an effort to determine the best regimen for this indication [14]. The most widely used regimen in studies includes repeated 800 mcg vaginal doses over a period of hours or days until a complete abortion is achieved. Research testing vaginal administration of misoprostol-alone for abortions up to 63 days LMP has reported success rates ranging from 66% to 90% [14,17–23]. Oral routes of misoprostol administration have proven less effective [18]. The largest randomized controlled trial examined two vaginal and sublingual misoprostol regimens composed of 800 mcg misoprostol administered at either 3- or 12-h intervals, resulting in a four-arm trial [22]. Dosing interval had a more important effect with the sublingual route: women given 800 mcg sublingual misoprostol at 3-h intervals had 84% efficacy vs. 78% efficacy with 12-h intervals, while 800 mcg vaginal misoprostol worked similarly regardless of dosing interval: 85% efficacy at 3 h vs. 83% at 12 h. Ongoing pregnancy rates ranged from 4% to 9% across study arms. A trial by Jain et al. [23] randomized women to either 200 mg mifepristone followed 24 h later by 800 mcg vaginal misoprostol or repeated doses (three maximum) of 800 mcg vaginal misoprostol in gestations through 56 days LMP and reported 95.7% efficacy with mifepristone+vaginal misoprostol vs. 88% with vaginal misoprostol-alone.

Although there is limited information on buccal misoprostol for medical abortion, the route appears promising given the pharmacokinetic evidence. The pharmacokinetic profile of buccal and vaginal misoprostol is similar, suggesting that the buccal route might work similarly to the vaginal route when administered alone for early medical abortion [24,25]. Previous research has documented regular and sustained uterine contractility with both routes [26].

Abortion has been legal in Vietnam since 1965 and widely available since the 1980s [27]. In 2002, mifepristone medical abortion was approved by the Ministry of Health and included in the National Reproductive Health Standards and Guidelines. For now, the method is only offered to women with gestations through 56 days LMP at tertiary level facilities, although there are plans to broaden access to other levels of the health care system in the future.

This double-blinded RCT compares two regimens for early medical abortion, one with and one without mifepristone to determine whether a misoprostol-alone regimen has a comparable safety, efficacy and acceptability profile to a combined regimen.

2. Methods

From August 2007 through March 2008, 400 women presenting for early medical abortion with gestational ages up to 63 days by LMP and living or working within an hour from the hospital were determined eligible to participate in the study and recruited at a large tertiary facility in Ho Chi Minh City, Vietnam. Gestational age was determined primarily by clinical examination and transvaginal ultrasound. Additional inclusion criteria were intrauterine pregnancy, general good health, able to provide informed consent and willing to return for follow-up. Exclusion criteria included known allergy to either mifepristone or misoprostol, suspicion of ectopic pregnancy, chronic adrenal failure, concurrent long-term corticosteroid therapy, history of hemorrhagic disorders, concurrent anticoagulant therapy or inherited porphyria.

After providing written informed consent, participants were randomized to either (1) 200 mg mifepristone followed 24 h later by 800 mcg buccal misoprostol followed by placebo 24 h later, or (2) placebo followed by two 800 mcg buccal misoprostol repeated 24 and 48 h later (1600 mcg total). On the day of recruitment, women received one envelope containing three packets of pills to be taken *at home*. After leaving the hospital, they were instructed to swallow the pill in Study Packet 1 [either one 200-mg tablet mifepristone (Mifestad®, Stada, Vietnam) or placebo]. Twenty-four hours later (Study Day 2), all participants were instructed to buccally administer the four tablets contained in Study Packet 2 (800 mcg misoprostol, Gymiso®, HRA Pharma, France). On Study Day 3, participants were instructed to buccally administer the four tablets contained in Study Packet 3 (either placebo or

800 mcg misoprostol). Treatment group was assigned by a computer-generated random sequence in blocks of 10 created at Gynuity Health Projects in New York.

Participants were informed that buccal administration entailed placing the tablets between the cheek and gum for approximately 20 min and then swallowing the remainder of the tablets. They were also instructed to take all of the study medications even if they believed that their abortion was complete beforehand. Participants were given eight 500-mg paracetamol tablets (with or without codeine) to manage any pain, counseled about potential side effects, scheduled for follow-up 1 week later and asked to record any side effects and use of pain medication. Side effects, including nausea, vomiting, diarrhea, fever and chills, were recorded on a diary card by participants. They were also told that they could return to the hospital or contact their providers if they had any additional questions or concerns.

At follow-up, each woman's abortion status was assessed by clinical examination and ultrasonography as needed. Women with ongoing pregnancy, confirmed by transvaginal ultrasound, were offered immediate surgical evacuation. Women with persistent nonviable pregnancy or gestational sac were offered the option to take an additional dose of 800 mcg buccal misoprostol and wait one more week to see whether the uterus would evacuate spontaneously. Women not wanting to wait or take an additional dose of misoprostol were given an immediate surgical evacuation. Women with retained products at the second follow-up visit confirmed by transvaginal ultrasound were given surgical evacuation. After the abortion was complete, women were interviewed to gauge acceptability and satisfaction with the treatment.

This study initially planned to enroll 700 women from two hospitals in Vietnam and Tunisia. The primary outcome measure was complete uterine evacuation without recourse to surgical intervention for any reason. Based on a review of the literature, mifepristone+buccal misoprostol was estimated to be approximately 95% effective [12]. The efficacy of buccal misoprostol-alone at 24-h intervals was unknown, but recent unpublished reports suggested that rates of 80–90% had been achieved in some circumstances. When used alone vaginally, misoprostol had efficacy rates around 88% and some reports indicated rates above 90% [4]. The study team determined that a 5% difference in efficacy between the two regimens would be clinically meaningful and therefore planned to enroll 664 cases (334 per arm) for an alpha=0.05, a one-sided test and 80% power. To account for possible dropouts, 700 cases were sought. The study was stopped early due to the unexpectedly high number of ongoing pregnancies which caused concern in the study team, particularly among the Vietnamese providers. An interim analysis was conducted examining outcomes by study arm after this high number of ongoing pregnancies. This article presents data from 400 women enrolled in Vietnam before stopping the study. Enrollment in Tunisia had just begun, with nearly a dozen pilot cases enrolled at the time the trial was stopped. Those data are not reported in this article.

Data entry and analysis were done with Standard Program for Social Scientists v. 15 (SPSS, Inc., Chicago, IL, USA). Characteristics of the two treatment groups were compared using χ^2 or Fisher's Exact Test for categorical variables and *t* tests or Mann–Whitney *U* test for continuous variables. The level of statistical significance was set at $p<.05$. The primary outcomes of this study were to assess efficacy, safety and acceptability of the regimens to women. Secondary outcomes included assessment of side effects and pain. Relative risks (RR) with 95% confidence intervals (CI) were calculated to measure treatment effects for main study outcomes. Ethical approval was obtained from the institutional review board at Hung Vuong Hospital, Ho Chi Minh City, Vietnam, and the trial is registered at ClinicalTrials.gov as NCT00680394.

3. Results

3.1. Participant characteristics and treatment group

Table 1 details participants' baseline characteristics. Four hundred women were enrolled and assigned to either misoprostol-only (*n*=198) or mifepristone+misoprostol (*n*=202). Participants averaged 28 and 29 years of age in the misoprostol-alone and mifepristone+misoprostol arms, respectively, with the majority reporting having completed

Table 1
Participant characteristic

	Misoprostol-only (*n*=198)	Mifepristone+misoprostol (*n*=202)
Age, years; mean±SD (range)	28±6.2 (17–45)	29±6.3 (17–45)
Level of education, % (*n*)		
None	0.5 (1)	0.0 (0)
Primary	0.5 (1)	2.0 (4)
Secondary	80.8 (160)	78.2 (158)
University or higher	18.2 (36)	19.8 (40)
Married, % (*n*)	81.3 (161)	82.7 (167)
Gravidity, mean±SD	2.5±1.3	2.6±1.5
Primigravida, % (*n*)	27.8 (55)	26.2 (53)
Number of previous surgical abortions, mean±SD (range)	0.41±0.74 (0–4)	0.48±0.81 (0–5)
Number of previous medical abortions, mean±SD (range)	0.13±0.35 (0–2)	0.15±0.38 (0–2)

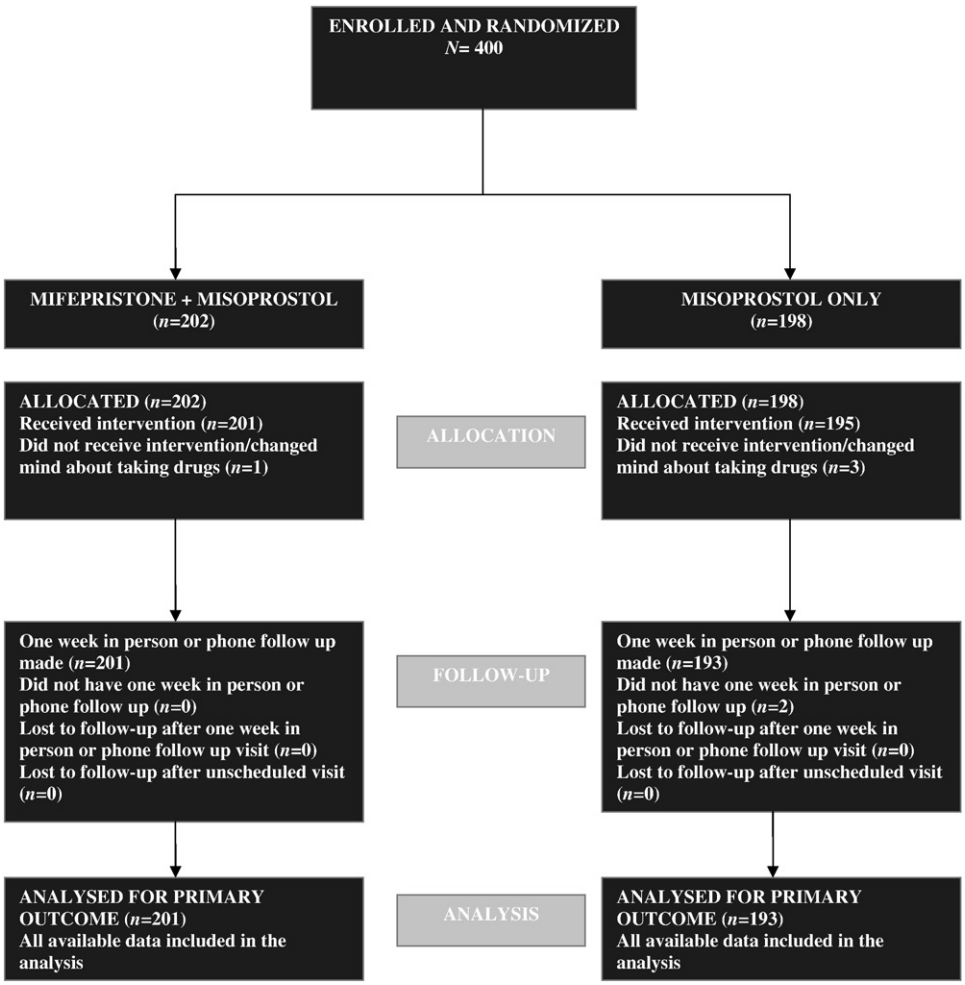

Fig. 1. Treatment flowchart.

secondary level education; 80% were married. This was the first pregnancy for approximately a quarter of participants. This trial is reported according to the CONSORT guidelines (Fig. 1) [28,29].

3.2. Efficacy

Two women allocated to misoprostol-only and no woman given mifepristone+misoprostol were lost to follow-up. All available data for these participants is shown. Three women in the misoprostol-alone arm and one woman in the mifepristone+misoprostol arm changed their mind about the abortion and did not take any of the allocated pills. One woman in the mifepristone+misoprostol arm took the first pill but changed her mind subsequently and opted for surgery.

Complete abortion without recourse to surgical evacuation, determined by clinical exam and confirmed by ultrasound in a large majority of women, was recorded for 76.2% (147) of misoprostol-only users and for 96.5% (194) of mifepristone+misoprostol users (RR 0.79, 95% CI 0.73–0.86) (Table 2). Ongoing pregnancy at follow-up, defined as a viable pregnancy showing presence of a fetal heart beat on ultrasound, was significantly more common among misoprostol-only users: 16.6% (32) vs. 1.5% (3) with mifepristone+misoprostol (RR 11.27, 95% CI 3.51–36.22). Nonviable pregnancy or gestational sac was found among 6.7% (13) of misoprostol-only users and among 0.0% (0) of mifepristone+misoprostol users. One woman allocated to misoprostol-only and four women allocated to mifepristone +misoprostol had surgical evacuations for other reasons, including woman's request and retained products of conception at study end. Two women, one in each arm, received study drugs and after taking the first set of pills opted to have a surgical completion at another hospital.

Although the study was not designed to assess efficacy by gestational age grouping, these data do reveal that at each gestational age interval, mifepristone+misoprostol is significantly more likely to result in complete abortion compared to the misoprostol-only group (Table 2). However, the data do show a trend towards increased likelihood of ongoing pregnancy with the misoprostol-only regimen at more advanced gestational ages.

An additional misoprostol dose was given to 29 women given misoprostol-only (14.7%) and to 12 women allocated

Table 2
Outcomes, % (*n*)

	Misoprostol-only (*n*=198)	Mifepristone+misoprostol (*n*=202)	RR (95% CI)
Lost to follow-up	1.0 (2/198)	0.0 (0/202)	
	(*n*=193)	(*n*=201)	
Complete abortion without surgical evacuation[a]	76.2 (147)	96.5 (194)	0.79 (0.73–0.86)
Type of failure[a]	23.8 (46)	3.5 (7)	
Ongoing pregnancy	16.6 (32)	1.5 (3)	11.27 (3.51–36.22)
Nonviable pregnancy or gestational sac	6.7 (13)	0.0 (0)	
Other[b]	0.5 (1)	2.0 (4)	
Complete abortion without surgical evacuation, by gestational age group[a]			
≤49 days LMP	81.8 (121/148)	97.5 (158/162)	0.84 (0.77–0.91)
50–56 days LMP	61.8 (21/34)	89.3 (25/28)	0.69 (0.52–0.93)
57–63 days LMP	45.5 (5/11)	100.0 (11/11)	0.45 (0.24–0.87)
Ongoing pregnancy, by gestational age group			
≤49 days LMP	12.2 (18/148)	0.6 (1/162)	19.70 (2.66–145.78)
50–56 days LMP	29.4 (10/34)	7.1 (2/28)	4.12 (0.98–17.27)
57–63 days LMP	36.4 (4/11)	0.0 (0/11)	–
Nonviable pregnancy or sac or other reason for surgical evacuation, by gestational age group			
≤49 days LMP	6.1 (9/148)	1.9 (3/162)	3.28 (0.91–11.90)
50–56 days LMP	8.8 (3/34)	3.6 (1/28)	2.47 (0.27–22.46)
57–63 days LMP	18.2 (2/11)	0.0 (0/11)	–

[a] Does not include two women lost to follow-up in the misoprostol-alone group and four women who changed their mind about the study and did not take any study medication (one in the mifepristone–misoprostol group, three in the misoprostol-alone group).

[b] Includes one woman who requested surgery in the misoprostol-alone group; one surgery due to incomplete abortion and three surgeries due to woman's request in the mifepristone–misoprostol group.

Table 3
Women's reports of side effects, % (*n*)

	Misoprostol-only (*n*=193)	Mifepristone+misoprostol (*n*=200)	RR (95% CI) or p value
Nausea	51.3 (99)	56.5 (113)	.175
Mild	82.8 (82)	85.8 (97)	
Moderate	12.1 (12)	13.3 (15)	
Severe	5.0 (5)	0.9 (1)	
Vomiting	19.2 (37)	26.0 (52)	.067
Mild	81.1 (30)	84.6 (44)	
Moderate	16.2 (6)	11.5 (6)	
Severe	2.7 (1)	3.8 (2)	
Diarrhea	71.0 (137)	58.5 (117)	.006
Mild	68.4 (93)	78.6 (92)	
Moderate	25.7 (35)	15.4 (18)	
Severe	5.9 (8)	6.0 (7)	
Fever	24.9 (48)	24.5 (49)	.513
Mild	83.3 (40)	89.8 (44)	
Moderate	14.6 (7)	8.2 (4)	
Severe	2.1 (1)	2.0 (1)	
Chills	36.3 (70)	32.5 (65)	.248
Mild	77.1 (54)	83.1 (54)	
Moderate	18.6 (13)	12.3 (8)	
Severe	4.3 (3)	4.6 (3)	
Bleeding			
More than expected	32.1 (59)	48.7 (97)	0.66 (0.51–0.85)
Same as expected	34.2 (63)	36.7 (73)	
Less than expected	33.7 (62)	14.6 (29)	
Pain			
More than expected	31.1 (60)	30.5 (61)	1.04 (0.77–1.40)
Same as expected	26.4 (51)	33.0 (66)	
Less than expected	39.9 (77)	36.0 (72)	
Overall experience with side effects			
Very acceptable	36.8 (71)	41.7 (82)	0.90 (0.70–1.16)
Acceptable	61.1 (118)	56.5 (113)	
Neutral	0.5 (1)	1.0 (2)	
Very unacceptable	0.0 (0)	0.5 (1)	

Table 4
Women's reports of acceptability and satisfaction, % (*n*)

	Misoprostol-only (*n*=193)	Mifepristone+misoprostol (*n*=200)	RR (95% CI)
Time required for procedure	*(n=148)*	*(n=192)*	
More than expected	20.9 (31)	12.5 (24)	1.68 (1.03–2.73)
Same than expected	46.6 (69)	52.6 (101)	
Less than expected	32.4 (48)	34.9 (67)	
Characterization of the procedure	*(n=185)*	*(n=198)*	
Not difficult	83.9 (162)	95.0 (190)	0.91 (0.86–0.97)
Slightly difficult	9.8 (19)	3.5 (7)	
Moderately difficult	1.6 (3)	0.5 (1)	
Very difficult	0.5 (1)	0.0(0)	
Overall satisfaction	*(n=193)*	*(n=200)*	
Very satisfied	30.1 (58)	43.0 (86)	0.70 (0.53–0.91)
Satisfied	43.0 (83)	53.5 (107)	
Neutral	24.9 (48)	3.5 (7)	
Unsatisfied	2.1 (4)	0.0 (0)	
Method of abortion selected for future	*(n=193)*	*(n=200)*	
Medical	76.7 (148)	92.0 (184)	0.83 (0.76–0.91)
Surgical	7.8 (15)	2.5 (5)	
Don't know	15.5 (30)	5.5 (11)	

to mifepristone+misoprostol (6.0%) at the 1-week follow-up visit. One woman allocated to mifepristone+misoprostol made an unscheduled visit prior to follow-up and received an additional dose of misoprostol at that time.

Unscheduled visits due to concerns about bleeding, anxiety and/or pain were relatively uncommon, occurring among 3.6% (*n*=7) of misoprostol-only users and among 5% (*n*=10) of mifepristone+misoprostol users. Extended follow-up visits were given to 16.8% (*n*=33) of misoprostol-only users and to 15.9% (*n*=32) of mifepristone+misoprostol users who were diagnosed with an incomplete abortion at their first follow-up visit.

3.3. Experience with pain and side effects

Diarrhea was significantly more common among women allocated to misoprostol-only (71%, *n*=137) and occurred among 58.5% (*n*=117) of women given mifepristone +misoprostol (p=.006). There were no differences in occurrences of the other side effects between women allocated to one of the two treatment arms as shown in Table 3. Women characterized the severity of each side effect similarly regardless of study regimen, with the majority indicating that side effects were either "very acceptable" or "acceptable". Women allocated to mifepristone+misoprostol were more likely to characterize bleeding as "more than expected" [misoprostol-only=32.1% (59), mifepristone+misoprostol=48.7% (97), RR 0.66, 95% CI 0.51–0.85]. Pain was similarly characterized by women in both groups (Table 3).

3.4. Acceptability and satisfaction with the assigned method

In general, participants were either "very satisfied" or "satisfied" with the medical abortion method they were given (Table 4). Satisfaction was correlated with complete abortion, and all of the unsatisfied reports were recorded among women for whom the method had failed. Women given mifepristone+misoprostol were more likely to report that the procedure was not difficult [misoprostol-only=83.9% (162), mifepristone+misoprostol=95% (190), RR 0.91, 95% CI 0.86–0.97]. Participants were more likely to report that the misoprostol-only method took longer than expected [misoprostol-only=20.9 (31), mifepristone+misoprostol=12.5% (24), RR 1.68, 95% CI 1.03–2.73]. When asked to state their desired method if another abortion might be needed in the future, participants resoundingly voiced a preference for medical over surgical abortion: medical method preferred by misoprostol-only users=76.7% (148), medical method preferred by mifepristone+misoprostol users=92% (184) (RR 0.83, 95% CI 0.76–0.91).

4. Discussion

This study explored two regimens for early medical abortion, one with mifepristone+misoprostol and another with misoprostol-alone. Both regimens are widely used in a range of settings, with the combined mifepristone +misoprostol regimen having been used by millions of women worldwide. Use of misoprostol-alone has been advocated in the absence of mifepristone availability in many regions, particularly sub-Saharan Africa and Latin America. Yet, the results from the present trial clearly document the inferiority of misoprostol-only compared to a combined regimen. While the combined regimen led to complete abortion in 96.5% of women, the misoprostol-alone regimen tested had a success rate of 76.2%. The rate of ongoing pregnancy was 1.5% with the combined regimen and 16.6% with misoprostol-alone. This means that for every seven women treated with misoprostol-alone as opposed to the combined mifepristone+misoprostol regimen, one ongoing pregnancy would occur.

The high failure rate was unexpected given more positive results from other published trials using 800 mcg vaginal misoprostol repeated at 24 h; however is consistent with results from the large trial by von Hertzen and colleagues examining both vaginal and sublingual regimens of misoprostol-alone that was published after the launch of the present trial [22]. As there are no published reports on misoprostol-only using buccal misoprostol, no direct comparisons can be made.

Side-effect reports from previous trials also indicated a trend towards more fever and shivering resulting from misoprostol-only regimens and more nausea and vomiting with the combined regimens. In the current trial, these trends were not observed. The rate of fever and chills was not statistically different between the two study groups and was reported for 25–35% of participants. Diarrhea was the most commonly reported side effect and was documented for 70% of misoprostol-only users. In contrast, in the study by von Hertzen et al. [22], diarrhea was recorded for about 30% of misoprostol-only users. Interestingly, in the current trial, mifepristone +misoprostol users were more likely to characterize bleeding as "more than expected". This was likely a result of the fact that women with ongoing pregnancy (predominantly misoprostol-only users) did not experience much, if any, bleeding.

In low-resource settings with limited access to affordable mifepristone, the misoprostol-only method may be clinically acceptable and perceived as cost-efficient. Yet, there is sufficient reason to believe that it may not be as cost-efficient as presumed. Indeed, as noted by Creinin et al. [1] in their cost analysis of mifepristone+misoprostol vs. misoprostol alone, the indirect costs of providing the two medical abortion services could outweigh the cost of the drugs and, ultimately, favor systematic provision of the combined regimen. Given the significantly higher rate of failed terminations observed with misoprostol-only, additional care, including ultrasonography, additional clinic/provider visits, more time away from work/family; and the cost of surgical evacuations after failed medical abortion procedures should be included into cost estimates as well. Furthermore, given that there are now nearly a dozen mifepristone products being marketed worldwide, some at a unit cost of approximately US$4 for a 200-mg tablet, the argument favoring misoprostol-only as inexpensive and more widely available is becoming less relevant. Other service delivery issues should also be considered. For example, misoprostol-only has been recommended for use in settings with limited access to surgical terminations and where legal abortions may be restricted [30,31]. Yet, misoprostol-only regimens are associated with a significantly higher need for surgical terminations and require more follow-up care to ensure complete abortion, issues that may be complicated in the very settings for which the method is now being promoted. When designing programs for medical abortion, both the monetary costs and programmatic feasibility must be considered.

The present study has several weaknesses. It is conceivable that the rate of ongoing pregnancy would have been minimized if shorter intervals between misoprostol doses had been explored. However, at the time the study was conceived, there was limited evidence to suggest that shorter intervals (vs. total dose and/or route of administration) might be a defining factor in the overall effectiveness of the method. Had the study by von Hertzen et al. [22] been available at the time the study was launched, different dosing regimens might have been tested.

Furthermore, the efficacy of both study regimens could be lower when either regimen is used in regular clinical practice by inexperienced providers. Staff at Hung Vuong Hospital have used mifepristone and misoprostol in clinical settings for nearly two decades and provided more than 10,000 medical abortions in 2008. They are highly skilled and less prone to misinterpret ultrasound reports or to intervene surgically in the event of retained products and/or incomplete abortion. Effectiveness of both regimens in a typical service delivery setting may be lower.

This study documents several important innovations to medical abortion provision in Vietnam. First, it provides the first clinical evidence of 800 mcg buccal dose of misoprostol following mifepristone in Vietnam. It also demonstrates the feasibility of extending the national guidelines for medical abortion in Vietnam to 63 days LMP with this safe and effective regimen. Furthermore, mifepristone followed by misoprostol 1 day later shortened the medical abortion procedure, strengthening the evidence base for quicker abortion procedures with mifepristone. Lastly, the study documents a first attempt to provide mifepristone at home. Participants were instructed to both swallow the mifepristone and take the misoprostol at home and were able to do so quite easily. Given that there are few side effects after mifepristone administration, it seems feasible that the method could be provided with the option of taking both medicines at home.

In conclusion, this study reaffirms that mifepristone +misoprostol is the gold standard for early medical abortion. While new research on shortened time intervals between misoprostol doses may decrease the ongoing pregnancy rate found in this study with misoprostol-only regimens, mifepristone+misoprostol regimens should be advocated by providers and policymakers as the optimal early medical abortion method.

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