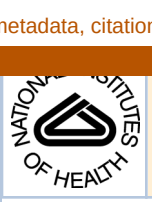

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Effectiveness of medical abortion with mifepristone and buccal misoprostol through 59 gestational days

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Abstract

Background—From 2001 to March 2006, Planned Parenthood Federation of America (Planned Parenthood) health centers throughout the U.S. provided medical abortion principally by a regimen of oral mifepristone followed 24–48 h later by vaginal misoprostol. In late March 2006, analyses of serious uterine infections following medical abortions led Planned Parenthood to change the route of misoprostol administration and employ additional measures to minimize subsequent serious uterine infection. We conducted an extensive audit in August 2006 of medical abortion with the new buccal misoprostol regimen so that patients could be given accurate information about the success rate of the new regimen.

Objectives—We sought to evaluate the effectiveness of the buccal medical abortion regimen and examine correlates of its success during routine service delivery.

Methods—Audits at 10 large urban service points were conducted in 2006 to estimate success rates of the buccal regimen. Success was defined as medical abortion without vacuum aspiration. These audits also permitted an estimate of success rates with oral misoprostol following mifepristone in a subset in which 98% of the subjects stemmed from 2 sites.

Results—Effectiveness of the buccal misoprostol-mifepristone regimen was 98.3% for women with gestational ages below 60 days. The oral misoprostol-mifepristone regimen, used by 278 women with a gestational age below 50 days, had a success rate of 96.8%.

Conclusion—In conjunction with 200 mg of mifepristone, buccal use of 800 mcg of misoprostol up to 59 days of gestation is as effective as vaginal use of 800 mcg of misoprostol up to 63 days of gestation.

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1. Introduction

From January 2001 to March 2006, Planned Parenthood Federation of America (Planned Parenthood) health centers throughout the U.S. provided medical abortion principally by a regimen of 200 mg oral mifepristone followed 24–48 h later by 800 mcg of misoprostol administered vaginally, at home, by the woman herself. An in-depth retrospective chart audit was conducted in 2003 of 11,290 clients in which the overall success rate of medical abortion with mifepristone and vaginal misoprostol through 63 days since the start of the last menstrual period was 98.5%. Over the years, data consistently informed us that medical abortion with mifepristone and vaginal misoprostol had a rate of ongoing pregnancy of about 0.5% and that an additional 1% of patients had uterine evacuation for various reasons including problematic bleeding, persistent gestational sac, clinician judgment or patient request. Although its national guidelines permitted delivery of medical abortion through 63 days of gestation, by the time PPFA suspended the vaginal route, some clinics in the system had adopted more restrictive gestational age criteria.

Healthcare organizations providing medical abortion have been interested in alternatives to vaginal administration of misoprostol for several reasons. One is a frequently reported patient dislike of vaginal self-manipulation, particularly in women from cultures where tampon and diaphragm use have low prevalence. In countries in which abortion is severely legally restricted, should patients need hospital care, having remnants of misoprostol tablets in the vagina could put the patient and the provider in legal jeopardy. In addition, there was conjecture, but no evidence, that the vaginal route of misoprostol contributed to the incidence of rare but serious infection among women having medical abortion. One alternative to the vaginal route has been the oral administration of misoprostol, the regimen on which U.S. Food and Drug Administration (FDA) approval was based. A more recent regimen is buccal administration of misoprostol. An open-label randomized U.S. trial through 56 days from last menses (n=429) compared self-administered buccal with vaginal misoprostol 800 mcg taken 1 or 2 days after 200 mg of mifepristone. The success rates were not significantly different for the two different routes of administration: 95.0% in the buccal group and 93.0% in the vaginal group (X^2=.043, p=0.51 [1].

The vaginal misoprostol option was suspended by Planned Parenthood at the end of March 2006. We present below evaluation of the effectiveness of the new regimens that began in April 2006.

2. Methods

From April 2006, patients with gestational age ≤49 days were offered 200 mg of mifepristone followed either 24 h later (at home) by 800 mcg of oral misoprostol or 24–48 h later by 800 mcg of buccal misoprostol. Women at gestational ages of 50–56 days were offered only the latter regimen. In all cases, gestational age was determined by transvaginal ultrasound. The buccal misoprostol regimen required patients to place two pills (200 mcg each) in each cheek for 30 min, and then swallow any remaining pill fragments. The oral regimen required swallowing the pills immediately after placement in the mouth. The Planned Parenthood protocol permits a second dose of misoprostol to be administered 12–24 h after the first dose if a woman fails to bleed. None of the participating sites in this study routinely gave patients two doses of misoprostol to take home.

A follow-up appointment is scheduled for patients within two weeks of taking mifepristone in the center, and the importance of this follow-up visit is emphasized to patients. Staff members are required to make three contact attempts with patients who fail to return for follow-up by the end of two weeks. An unpublished audit of follow-up at Planned

Parenthood affiliates was conducted using records from a convenience sample of 16 affiliates in 2005. On average, 80% of patients returned for a post-abortion visit. After the three attempts to contact them by telephone or mail, 10% of all patients having medical abortion remain uncontacted.

The sample size for estimating the effectiveness of the new buccal misoprostol-mifepristone regimen was calculated from this anticipated follow-up rate and the anticipated magnitude of the failure rate of the mifepristone and buccal misoprostol procedure. Failure rates of no more than a few percent were anticipated using the buccal route. With a follow-up rate of 90% and an anticipated failure rate of 2%, a sample size of 1,000 would yield a 95% confidence interval of width 1.8%. A geographically stratified sample of 10 Planned Parenthood health centers was selected to provide information on characteristics and outcomes of an estimated 1,000 patients with the buccal misoprostol regimen from the time period May through July 2006.. A team including the first author and three experienced Planned Parenthood nurse practitioners under her supervision conducted the audit at 10 metropolitan sites. The study protocol and design were submitted to and approved by Allendale Investigational Review Board.

Descriptive statistics of key sample characteristics were computed. Univariate and multivariate logistic regression analyses were used to examine whether individual or clinic characteristics were related to the success (no surgical intervention required) of the abortion procedure. The Kolmogorov-Smirnoff test was used to test for the uniform distribution of gestational age in days. Fisher's exact test was used to test for differences between two proportions. All calculations were preformed in SAS (SAS Institute Inc, Cary North Carolina) or Cytel Studio 7 (Cytel Inc, Boston Massachusetts).

3. Results

The 10 health centers selected to establish success rates were largely situated in urban areas across the United States. (Table 1). In Quarter Two of 2006, these 10 sites performed 1,638 medical abortions with known outcomes. The center volume during this period ranged from 59 to 268 procedures per site, with a mean of 164 per site. In 11 cases, the documentation did not establish whether oral or buccal administration had been used. Buccal misoprostol was the known route of administration in 1,349 cases; the remaining 278 cases employed oral misoprostol. Altogether, 15.7% of women provided no follow-up information (range 2–22% across sites).

Only 2.4% of women received a second dose of misoprostol; and in all cases, the second dose of misoprostol was administered at the follow-up visit for retained gestational sac or pronounced endometrial thickness accompanied by problematic bleeding. Because early success obviates the need for a second dose, the use of a second dose was not evaluated as a risk factor for successful abortion.

The Planned Parenthood Medical Standards and Guidelines in place during the period of this study stated that women could receive mifepristone with buccal misoprostol through 56 days of gestation or mifepristone with oral misoprostol through 49 days of gestation. However, there were a few women above these gestational age cut-offs who received medical abortions.

4. Effectiveness of the mifepristone-buccal misoprostol regimen

The mean number of cases per site was 135 (Table 2). The mean age of the women using the regimen with buccal administration of mifepristone was 25.8 years. Mean reported gestational age was 47 days (range 21–59 days).

Both higher age of the woman and the presence of multiple fetuses at the date of mifepristone administration were associated with reduced success rates (Table 2). The volume of medical abortions per site in the quarter and gestational age in days proved not to be significant, but had pvalues below 0.15. In the multiple regression analysis based on the same 4 factors, only the woman's age at presentation and the presence of multiple fetuses were significant; an increase in the woman's age moderately increased the risk of failure, while a multiple gestation increased the risk almost 6-fold. To equal the increased risk of failure for a multiple gestation compared with a singleton gestation would require an increase in a woman's age of 21.5 years.

The overall success rate of medical abortion using buccal misoprostol was 98.3% (95% exact CI 97.5%–99.0%) (Table 3). We explored further whether there was a trend toward decreased effectiveness with increased gestational age by examining effectiveness by gestational age cohorts in weeks separately for all pregnancies and for singleton pregnancies. In neither case did effectiveness decrease with increasing gestational age. However, for all pregnancies, the success rate (99.1%) at gestations below the median (44 days) was significantly higher than the success rate (97.6%) at gestations of 44 days and higher (p=0.028, one-sided test). For singleton pregnancies, the difference was not statistically significant (p=0.056, one-sided test).

There were 19 multiple-gestation pregnancies, one of which was triplets and the others were twins. None of the multiple-gestation pregnancies were ongoing after medical abortion but two patients with twin pregnancies had uterine evacuation, one for problematic bleeding and the other for a persistent retained gestational sac. Therefore, women with multiple fetuses experienced successful medical abortion 89.5% of the time (95% exact CI 97.6%–99.0%). If detection of a twin pregnancy is considered a contraindication to the buccal regimen, the overall success rate would be 98.4% (95% exact CI 97.6%–99.0%) rather than 98.3% (Table 3).

3.2 Effectiveness of the mifepristone-oral misoprostol regimen

In the 10-site sample, four sites had employed the oral misoprostol regimen, which requires women to swallow the tablets immediately, rather than keep them in their cheeks. A total of 278 women used this regimen. Maximum gestational age for any patient in this group was recorded as 54 days. The sites had 138, 134, 5 and 1 oral clients each in the audited period. Nine failures occurred, all at the two larger sites. The success rate was 96.8% (95% exact CI 94.4%–98.8%). Gestational age was the only tested variable significantly related to success (Table 4), with success declining with increasing gestational age. There were 5 multiple-gestation pregnancies, all of which were aborted successfully. Table 5 displays success rates by gestational age cohorts in weeks. There is a marked fall-off in success with the oral regimen during the sixth and seventh weeks. The trend toward lower success with increasing gestational age is significant (p=0.04).

5. Discussion

Planned Parenthood accumulated over five years of experience providing medical abortion with vaginal misoprostol. Based on several data collection mechanisms, we were confident that the success rate using this route up to 63 days of gestation was 98.5%. When the vaginal route was discontinued, clinicians wanted accurate data to inform patients of the success rate that could be expected with medical abortion using buccal misoprostol up to 56 days of gestation. The audit of 10 metropolitan centers in August 2006 demonstrated a success rate of 98.3% for medical abortion with the regimen of 200 mg of mifepristone combined with 800 mcg of misoprostol self-administered by the buccal route at home within 24 to 48 h.

If women with multiple pregnancies are omitted, the effectiveness of the buccal misoprostol regimen is 98.4%. One published abstract examined the effectiveness of medical abortion using vaginal misoprostol for multiple pregnancies; treatment success was not statistically different for twin and singleton pregnancies [2].

Limitations of the study are those inherent in retrospective service-delivery research. The outcomes of about 16% of patients who did not return for follow-up and were not contacted by phone are unknown. However, it is likely that almost all of these were successes, since women are strongly advised to contact the clinic if they experience problems, and treatment for a failure is included in the cost of a medical abortion.

If the experience among affiliates of the Planned Parenthood and sales figures from the US manufacturer, Danco Laboratories, LLC, (personal communication, Danco Laboratories, LLC) are indicative, use of medical abortion continues to grow in numbers and as a percentage of first-trimester abortions in the United States. By the end of 2007, about 50% of medically-eligible Planned Parenthood patients up to 56 days of gestation chose medical abortion (representing 26% of all first-trimester abortions), despite the loss of a critical week of eligibility when medical abortion with buccal misoprostol could be provided only through 56 days of gestation. The officially mandated switch from vaginal to buccal misoprostol resulted in no reduction in uptake of the method and no reduction in effectiveness. In February 2008, based on results of a recent clinical trial [3], Planned Parenthood resumed offering medical abortion from 57 through 63 days of gestation, employing the buccal route.

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Table 1

Cities and states of the 10 metropolitan centers which were audited

Annapolis MD
Baltimore MD
St. Louis MO
Bronx NY
Brooklyn NY
Boston MA
Chicago IL
San Francisco CA
Nashville TN
Phoenix, AZ

Table 2

Characteristics affecting outcome of buccal misoprostol-mifepristone abortions

				Univariate		Multivariate	
Characteristic	**Mean**	**S.D.**	**Median**	**Odds ratio for success**	**p-value**	**Odds ratio for success**	**p-value**
Woman's age in years	25.8	6.2	24	.925	.011	.922	.009
Gestational age in days	43.6	7.2	44	.954	.124	.945	.079
Multiple pregnancy (%)	1.4	11.8		.136	.011	.175	.027
Buccal caseload/site	135.0	43.6	164	.991	.075	.992	.107

Table 3

Success rate (%) by week of gestation of buccal misoprostol-mifepristone abortions

Week	N	All pregnancies	N	Singleton pregnancies
All weeks	1,349	98.3%	1,330	98.4%
Weeks grouped in days *beginning* in multiples of 7				
Week 4 (days 28–34)	149	99.3%	145	99.3%
Week 5 (days 35–41)	342	98.8%	342	98.8%
Week 6 (days 42–48)	467	98.1%	458	98.3%
Week 7 (days 49–55)	342	98.3%	337	98.5%
Week 8 (days 56–59)	46	95.7%	45	95.6%
p-value for linear trend in weeks in logistic regression				
Univariate		0.346		0.474
Multivariate		0.254		0.380

Notes:

[1] The multivariate model includes the woman's age and buccal caseload/site as well as gestation in weeks.

[2] Weeks with three or fewer cases are not shown; therefore, the sum of the number of cases grouped by weeks does not add up to the total number of cases. However, all cases are included in the logistic regression analyses used to assess the p-value for a linear trend in weeks.

Table 4

Characteristics affecting outcome of oral misoprostol-mifepristone abortions

				Univariate		Multivariate	
Characteristic	**Mean**	**S.D.**	**Median**	**Odds ratio for success**	**p-value**	**Odds ratio for success**	**p-value**
Woman's age in years	25.6	6.2	24.0	.995	.920	.985	.781
Gestational age in days	41.1	6.1	42.0	.856	.035	.854	.033

Table 5

Success rate (%) by week of gestation of oral misoprostol-mifepristone abortions

Week	N	All gestations	N	Singleton gestations
All weeks	278	96.8%	273	96.7%
Weeks grouped in days *beginning* in multiples of 7				
Week 4 (days 28–34)	47	100.0%	47	100%
Week 5 (days 35–41)	74	98.7%	71	98.6%
Week 6 (days 42–48)	127	95.3%	126	95.2%
Week 7 (days 49–54)	28	92.9%	27	92.6%
p-value for linear trend in weeks in logistic regression				
Univariate		0.039		0.039
Multivariate		0.037		0.036

Notes:

[1] The multivariate model includes the woman's age as well as gestation in weeks.

[2] Weeks with one or fewer cases are not shown and one case was missing data on gestational age; therefore, the sum of the number of cases grouped by weeks does not add up to the total number of cases. However, all cases are included in the logistic regression analyses used to assess the p-value for a linear trend in weeks.