

# What is the most effective management of first trimester miscarriage?

A Cochrane network meta-analysis reported that both uterine aspiration and medication management are more effective than expectant management for the treatment of miscarriage. The summary statistics from the meta-analysis may be helpful for patient counseling.



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First trimester miscarriage, the presence of a nonviable intrauterine pregnancy before 13 weeks' gestation, is a common complication occurring in approximately 15% of clinical pregnancies.<sup>1,2</sup> The goals for the holistic management of first-trimester miscarriage are to 1) reduce the risk of complications such as excessive bleeding and infection, 2) ensure that the patient is supported during a time of great distress, and 3) optimally counsel the patient about treatment options and elicit the patient's preferences for care.<sup>3</sup> To resolve a miscarriage, the intrauterine pregnancy tissue must be expelled, restoring normal reproductive function.

The options for the management of a nonviable intrauterine pregnancy include expectant management, medication treatment

*The author reports no conflict of interest related to this article.*

doi: 10.12788/obgm.0276

with mifepristone plus misoprostol or misoprostol-alone, or uterine aspiration. In the absence of uterine hemorrhage, infection, or another severe complication of miscarriage, the patient's preferences should guide the choice of treatment. Many patients with miscarriage prioritize avoiding medical interventions and may prefer expectant management. A patient who prefers rapid and reliable completion of the pregnancy loss process may prefer uterine aspiration. If the patient prefers to avoid uterine aspiration but desires control over the time and location of the expulsion process, medication treatment may be optimal. Many other factors influence a patient's choice of miscarriage treatment, including balancing work and childcare issues and the ease of scheduling a uterine aspiration. In counseling patients about the options for miscarriage treatment it is helpful to know the success rate of each treatment option.<sup>4</sup> This editorial reviews

miscarriage treatment outcomes as summarized in a recent Cochrane network meta-analysis.<sup>5</sup>

## Uterine aspiration versus mifepristone-misoprostol

In 2 clinical trials that included 899 patients with miscarriage, successful treatment with uterine aspiration versus mifepristone-misoprostol was reported in 95% and 66% of cases, respectively.<sup>6,7</sup>

In the largest clinical trial comparing uterine aspiration to mifepristone-misoprostol, 801 patients with first-trimester miscarriage were randomly assigned to uterine aspiration or mifepristone-misoprostol.<sup>6</sup> Uterine aspiration and mifepristone-misoprostol were associated with successful miscarriage treatment in 95% and 64% of cases, respectively. In the uterine aspiration group, a second uterine aspiration occurred in 5% of patients. Two patients in the uterine aspiration group needed

a third uterine aspiration to resolve the miscarriage. In the mifepristone-misoprostol group, 36% of patients had a uterine aspiration. It should be noted that the trial protocol guided patients having a medication abortion to uterine aspiration if expulsion of miscarriage tissue had not occurred within 8 hours of receiving misoprostol. If the trial protocol permitted 1 to 4 weeks of monitoring after mifepristone-misoprostol treatment, the success rate with medication treatment would be greater. Six to 8 weeks following miscarriage treatment, patient-reported anxiety and depression symptoms were similar in both groups.<sup>6</sup>

### **Uterine aspiration versus misoprostol**

Among 3 clinical trials that limited enrollment to patients with missed miscarriage, involving 308 patients, the success rates for uterine aspiration and misoprostol treatment was 95% and 62%, respectively.<sup>5</sup>

In a study sponsored by the National Institutes of Health, 652 patients with missed miscarriage or incomplete miscarriage were randomly assigned in a 1:3 ratio to uterine aspiration or misoprostol treatment (800 µg vaginally). After 8 days of follow-up, successful treatment rates among the patients treated with uterine evacuation or misoprostol was 97% and 84%, respectively.<sup>8</sup> Of note, with misoprostol treatment the success rate increased from day 3 to day 8 of follow-up—from 71% to 84%.<sup>8</sup>

### **Mifepristone-misoprostol versus misoprostol**

The combined results of 7 clinical trials of medication management of missed miscarriage that included

1,812 patients showed that successful treatment with mifepristone-misoprostol or misoprostol alone occurred in 80% and 70% of cases, respectively.<sup>5</sup>

Schreiber and colleagues<sup>9</sup> reported a study of 300 patients with an embryonic gestation or embryonic demise that were between 5 and 12 completed weeks of gestation and randomly assigned to treatment with mifepristone (200 mg) plus vaginal misoprostol (800 µg) administered 24 to 48 hours after mifepristone or vaginal misoprostol (800 µg) alone. Ultrasonography was performed 1 to 4 days after misoprostol administration. Successful treatment was defined as expulsion of the gestational sac plus no additional surgical or medical intervention within 30 days after treatment. In this study, the dual-medication regimen of mifepristone-misoprostol was more successful than misoprostol alone in resolving the miscarriage, 84% and 67%, respectively (relative risk [RR], 1.25; 95% CI, 1.09–1.43). Surgical evacuation of the uterus occurred less often with mifepristone-misoprostol treatment (9%) than with misoprostol monotherapy (24%) (RR, 0.37; 95% CI, 0.21–0.68). Pelvic infection occurred in 2 patients (1.3%) in each group. Uterine bleeding managed with blood transfusion occurred in 3 patients who received mifepristone-misoprostol and 1 patient who received misoprostol alone. In this study, clinical factors, including active bleeding, parity, and gestational age did not influence treatment success with the mifepristone-misoprostol regimen.<sup>10</sup> The mifepristone-misoprostol regimen was reported to be more cost-effective than misoprostol alone.<sup>11</sup>

Chu and colleagues<sup>12</sup> reported a study of medication treatment of missed miscarriage that included

more than 700 patients randomly assigned to treatment with mifepristone-misoprostol or placebo-misoprostol. Missed miscarriage was diagnosed by an ultrasound demonstrating a gestational sac and a nonviable pregnancy. The doses of mifepristone and misoprostol were 200 mg and 800 µg, respectively. In this study, the misoprostol was administered 48 hours following mifepristone or placebo using a vaginal, oral, or buccal route; 90% of patients used the vaginal route. Treatment was considered successful if the patient passed the gestational sac as determined by an ultrasound performed 7 days after entry into the study. If the gestational sac was passed, the patients were asked to do a urine pregnancy test 3 weeks after entering the study to conclude their care episode. If patients did not pass the gestational sac, they were offered a second dose of misoprostol or surgical evacuation. At 7 days of follow-up, the success rates in the mifepristone-misoprostol and misoprostol-alone groups were 83% and 76%, respectively. Surgical intervention was performed in 25% of patients treated with placebo-misoprostol and 17% of patients treated with mifepristone-misoprostol (RR, 0.73; 95% CI, 0.53–0.95;  $P=.021$ ).<sup>12</sup> A cost-effectiveness analysis of the trial results reported that the combination of mifepristone-misoprostol was less costly than misoprostol alone for the management of missed miscarriages.<sup>13</sup>

### **Expectant management versus uterine aspiration**

The combined results of 7 clinical trials that included a total of 1,693 patients showed that successful treatment of miscarriage with

expectant management or uterine aspiration occurred in 68% and 93% of cases, respectively.<sup>5</sup> In one study, 700 patients with miscarriage were randomly assigned to expectant management or uterine aspiration. Treatment was successful for 56% and 95% of patients in the expectant management and uterine aspiration groups, respectively.<sup>6</sup>

The Cochrane network meta-analysis concluded that cervical preparation followed by uterine aspiration may be more effective than expectant management, with a reported risk ratio (RR) of 2.12 (95% CI, 1.41–3.20) with low-certainty evidence.<sup>5</sup> In addition, uterine aspiration compared with expectant management may reduce the risk of serious complications (RR, 0.55; 95% CI, 0.23–1.32), with a wide range of treatment effects in reported trials and low-certainty evidence.<sup>5</sup>

In the treatment of miscarriage, the efficacy of expectant management may vary by the type of miscarriage. In one study, following the identification of a miscarriage, the percent of patients who have completed the expulsion of pregnancy tissue by 14 days was reported to be 84% for incomplete miscarriage, 59% for pregnancy loss with no expulsion of tissue, and 52% with ultrasound detection of a nonviable pregnancy with a gestational sac.<sup>14</sup>

### Expectant management versus mifepristone-misoprostol

Aggregated data from 3 clinical trials that included a total of 910 patients showed that successful treatment with expectant management or mifepristone-misoprostol was reported in 48% and 68% of cases, respectively.<sup>5</sup> The Cochrane network meta-analysis concluded that



When caring for patients with miscarriage, key goals are to communicate medical information with empathy and to provide emotional support.

mifepristone-misoprostol may be more effective than expectant management, with a risk ratio of 1.42 (95% CI, 1.22–1.66) with low-certainty evidence. In addition, mifepristone-misoprostol compared with expectant management may reduce the risk for serious complications (RR, 0.76; 95% CI, 0.31–1.84) with wide range of treatment effects and low-certainty evidence.<sup>5</sup>

### Expectant management versus misoprostol

The combined results of 10 clinical trials that included a total of 838 patients with miscarriage, showed that successful treatment with expectant management or misoprostol-alone occurred in 44% and 75% of cases, respectively.<sup>5</sup> Among 3 studies limiting enrollment to patients with missed miscarriage, successful treatment with expectant management or misoprostol-alone occurred in 32% and 70%, respectively.<sup>5</sup>

The Cochrane analysis concluded that misoprostol-alone may be more effective than expectant

management, with a reported risk ratio of 1.30 (95% CI, 1.16–1.46) with low-certainty evidence. In addition, misoprostol-alone compared with expectant management may reduce the risk of serious complications (RR, 0.50; 95% CI, 0.22–1.15) with a wide range of treatment effects and low-certainty evidence.<sup>5</sup>

### Patient experience of miscarriage care

Pregnancy loss is often a distressing experience, which is associated with grief, anxiety, depression, and guilt, lasting up to 2 years for some patients.<sup>15,16</sup> Patient dissatisfaction with miscarriage care often focuses on 4 issues: a perceived lack of emotional support, failure to elicit patient preferences for treatment, insufficient provision of information, and inconsistent posttreatment follow-up.<sup>17–19</sup> When caring for patients with miscarriage, key goals are to communicate medical information with empathy and to provide emotional support. In the setting of a miscarriage, it is easy for patients to perceive that the clinician is insensitive

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and cold.<sup>15</sup> Expressions of sympathy, compassion, and condolence help build an emotional connection and improve trust with the patient. Communications that may be helpful include: “I am sorry for your loss,” “I wish the outcome could be different,” “Our clinical team wants to provide you the best care possible,” and “May I ask how you are feeling?” Many patients report that they would like to have been offered mental health services as part of their miscarriage care.<sup>15</sup>

The Cochrane network meta-analysis of miscarriage concluded that uterine aspiration, misoprostol-mifepristone, and misoprostol-alone were likely more effective in resolving a miscarriage than expectant management.<sup>5</sup> The strength of the conclusion was limited because of

significant heterogeneity among studies, including different inclusion criteria, definition of success, and length of follow-up. Clinical trials with follow-up intervals more than 7 days generally reported greater success rates with expectant<sup>14</sup> and medication management<sup>8</sup> than studies with short follow-up intervals. Generally, expectant or medication management treatment is more likely to be successful in cases of incomplete abortion than in cases of missed miscarriage.<sup>5</sup>

In a rank analysis of treatment efficacy, uterine aspiration was top-ranked, followed by medication management. Expectant management had the greatest probability of being associated with unplanned uterine aspiration. Based on my analysis of available miscarriage

studies, I estimate that the treatment success rates are approximately:

- uterine aspiration (93% to 99%)
- misoprostol-mifepristone (66% to 84%)
- misoprostol-alone (62% to 76%)
- expectant management (32% to 68%).

Although there may be significant differences in efficacy among the treatment options, offering patients all available approaches to treatment, providing information about the relative success of each approach, and eliciting the patient preference for care ensures an optimal patient experience during a major life event. ●



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