

## Mifepristone and misoprostol in the management of early pregnancy loss

By Amy J. Levi, PhD, CNM, WHNP

*Womens Healthcare.* 2023;11(2):42-44. doi: 10.51256/WHC042342  
© 2023 HealthCom Media. All rights reserved.

**E**arly pregnancy loss (EPL), or what is commonly referred to as miscarriage, refers to a nonviable pregnancy diagnosed before the end of the 13th week of gestation. Bleeding in early pregnancy may be the first sign of EPL, although up to 50% of pregnancies with bleeding in early pregnancy go on to successful continuation culminating in birth.<sup>1</sup> The loss of the pregnancy may be diagnosed by the lack of a fetal heartbeat on ultrasound, falling serum levels of B-hCG (beta-human chorionic gonadotropin), vaginal bleeding, or passage of tissue. Women's health nurse practitioners (WHNPs) must initially rule out the possibility of an ectopic pregnancy prior to engaging in any further activities to manage resolution of an EPL. Following the identification of an early intrauterine pregnancy that will not successfully continue, WHNPs have several options for addressing successful uterine evacuation.<sup>1</sup>

### Patient-centered early pregnancy loss care

Patients experiencing early pregnancy loss may present with a variety of concerns about the resolution of the pregnancy. Especially when a pregnancy is desired, responding to the patient's emotional wellbeing should be a primary goal. Even when a pregnancy is unplanned or unwelcome, the experience of a miscarriage can be emotionally challenging. Ensuring adequate support for the patient is paramount, meaning that sometimes waiting to address the management of resolution of symptoms becomes secondary to ensuring the patient's emotional wellbeing.<sup>2</sup>

Women's health nurse practitioners have the opportunity to use shared decision making about how best to address the patient concerns related to the resolution of the pregnancy because of the variety of approaches available to support the evacuation of uterine contents. Prior to engaging in any activity to assist with the com-



pletion of the process of emptying the uterus, the needs and desires of the patient should be considered.<sup>3</sup>

Following an initial assessment of the patient to determine that they are hemodynamically stable and not at risk for infection, the approach to next steps needs to include a discussion with the patient to assess their preferences related to their care. These preferences may include a desire for privacy, fear of pain, need for expediency, economic considerations, previous experience with induced abortion or miscarriage management, ability to manage symptoms independently, and risk of complications.<sup>2</sup> Each of these considerations will have an impact on the best choice of early pregnancy loss management for an individual patient. Multiple resources are available to help guide the conversation with the patient about what is the best approach to resolve the miscarriage.<sup>3</sup>

### Approaches to early pregnancy loss management

The three approaches to EPL management are: expectant management, medication administration, and uterine evacuation by aspiration, with and without dilatation and curettage (D&C). Expectant management is watchful waiting. Without any intervention, up to 80% of women will naturally expel the products of conception within 8 weeks.<sup>1</sup> This may seem the most natural outcome for some women and avoids the use of medication or surgical intervention. It allows the patient to maintain privacy about their pregnancy and may not require any further engagement with the healthcare system. Patients electing to follow expectant management need to be able to monitor their symptoms for completion of the process, as well as for infection, and to recognize that intervention

may be required if uterine evacuation is not complete.

Uterine evacuation with aspiration with or without D&C is what most patients associate with EPL management. Uterine evacuation can be an inpatient or outpatient procedure, and can afford the patient the comfort of various methods of pain management including general anesthesia. This approach requires greater access to medical facilities and is the least cost-effective method, but it requires the least amount of time from diagnosis to resolution of symptoms.<sup>4</sup>

Medication management is a route to uterine evacuation that can be provided within the context of primary care provision, making it more widely accessible than surgical management.<sup>5</sup> The use of mifepristone in connection with misoprostol for miscarriage management has expanded the effectiveness and accessibility of the medication management regimen and provides another option for patients who want to avoid the costs and inconvenience of a surgical resolution, especially if it is not readily available. The most important difference between the two approaches, however, is related to the management of pain. Patients should be counseled that like expectant management, the use of medication to effectuate the completion of the miscarriage process will involve the experience of cramping and passage of tissue. The uterine cramping that accompanies the passage of tissue can be very painful for some patients, and visualizing the products of conception can be upsetting. Although embryonic tissue in the first trimester is somewhat amorphous, it can still be startling and is usually accompanied by blood clots, which some patients find alarming.<sup>6</sup> Providing adequate access to pain relief is an important consideration when initiating medical management.<sup>1</sup>

## Medication management regimens

There are three different regimens for medication management of early pregnancy loss: misoprostol alone, mifepristone and misoprostol, and methotrexate, which is used in the management of ectopic pregnancies.<sup>7-9</sup> It is important to note that none of these medications has been labeled for this use and patients need to be so advised when they are being counseled. The use of misoprostol alone to resolve an early pregnancy loss has been studied extensively since the 1990s and has been found to be as effective as both expectant management and surgical management, but it is often overlooked because of the side effects. Misoprostol is a synthetic prostaglandin analogue and creates uterine contractions to cause the contents of the uterus to be expelled. Misoprostol

also may create a significant gastrointestinal response in patients including nausea, diarrhea, and/or vomiting.<sup>1</sup> Patients should be counseled about the potential for these side effects, and offered antiemetics for relief if they occur. Similarly, access to pain medication should be addressed, with a preference for nonsteroidal analgesia over opioids.<sup>1</sup>

There are three different routes of administration of misoprostol alone: oral, sublingual, and vaginal. Vaginal administration reduces the gastrointestinal side effects of misoprostol, and although it does not peak until 4 hours after administration, has no impact on the eventual outcome. Oral and sublingual administration may act more quickly, but both produce the same effect as vaginal administration.<sup>7</sup>

The most efficacious dosage for misoprostol alone is an initial dose of 800 ug, with a subsequent 800 ug dose if there is no response after 4 hours.<sup>1</sup> Recent studies have confirmed that initiating the process of managing early pregnancy loss with a 200 mg dose of mifepristone taken orally 24 hours prior to administration of misoprostol may increase the efficacy of the medication management approach, reducing the time to complete uterine evacuation and decreasing the need for subsequent aspiration for retained products of conception. Both of these medications can be taken in the privacy of one's home.<sup>8</sup>

Mifepristone is a progestin agonist and binds to progestin receptors. In viable pregnancies, it destabilizes the implantation site, which is believed to be similar to the mode of action in miscarriages. The use of mifepristone is most widely connected to medication abortion, which has limited its availability for miscarriage management due to variations in abortion legislation across the United States. The current package labeling does not include an indication for miscarriage management, although efforts are under way to address this by the US Food and Drug Administration.<sup>10</sup> As with methotrexate and misoprostol, this represents an off-label use of these medications, which has created uncertainty about using them for miscarriage management as states have begun enforcement of antiabortion legislation that would limit their use.<sup>11</sup>

## Patient follow-up

Each of these approaches to managing EPL requires careful patient follow-up, especially if heavy bleeding (> 2 super sanitary pads/hr) or severe cramping and pain occur without passage of tissue. Patients need to have access to consultation 24 hours/7 days a week for support and evaluation of concerns, as well as information related to where to go for emergency care. With each medication

regimen, passage of tissue may occur within 4 hours or be delayed for up to 3 days.<sup>7</sup> Referral for aspiration may be required in up to 15% of cases, so a source for this kind of care needs to be identified before initiation of incorporating medication management of EPL into outpatient care. Ideally, patients should be seen 2 to 4 weeks after passage of tissue to ensure appropriate involution of the uterus, and if applicable, for ultrasound confirmation of completion.<sup>1</sup> Quantitative B-hCG levels also may be assessed to ensure that they continue to decrease, with the most rapid decline by day 10 and an expected return to 0 in 7 weeks.<sup>12</sup>

Recent research to understand the importance of the administration of Rho(D) immune globulin to Rh-negative women undergoing medication abortion has shed light on the actual potential for isoimmunization following termination of pregnancy in the first trimester. The potential for exposure to fetal red blood cells following EPL is well below the level that would require its administration for the prevention of maternal isoimmunization.<sup>13</sup> The elimination of Rh testing and the storage of Rho(D) immune globulin may make it more feasible to incorporate EPL management with medication in some settings.

The availability of medications that can be used for EPL management, although off label, has increased the number of options that women have for care. For patients who are not at risk for hemorrhage or infection, assessment of the need for psychosocial support should be paramount, after which WHNPs can determine the patient's preference for an appropriate management approach. Access to a higher level of care, pain management, duration of symptoms, need for privacy, cost, and past abortion or miscarriage experiences may all be considerations when discussing resolution of the EPL. Patients may be unfamiliar with their options, so clinicians should be ready to answer questions and support their choices. ■

**Amy J. Levi is Leah L. Albers Endowed Professor of Midwifery at the University of New Mexico, College of Nursing, in Albuquerque, New Mexico. The author has no actual or potential conflicts of interest in relation to the contents of this article.**

## References

1. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin no. 200. Early pregnancy loss. *Obstet Gynecol.* 2018;132(5):e197-e207.
2. Schreiber CA, Chavez V, Whittaker PG, et al. Treatment decisions at the time of miscarriage diagnosis. *Obstet Gynecol.* 2016;128(6):1347-1356.
3. Lee L, Ma W, Davies S, Kammers M. Toward optimal emotional care during the experience of miscarriage: an integrative review of the perspectives of women, partners, and health care providers. *J Midwifery Womens Health.* 2022 Nov 12. Online ahead of print.
4. Nagendra D, Gutman SM, Koelper NC, et al. Medical management of early pregnancy loss is cost-effective compared with office uterine aspiration. *Am J Obstet Gynecol.* 2022 Jun 30:S0002-9378(22)00530-0. Online ahead of print.
5. Srinivasulu S, Riker L, Maldonado L, Breitbart V. Evaluation of the miscarriage care initiative: a program to integrate comprehensive early pregnancy loss management in primary care settings. *Fam Med.* 2020;52(10):707-715.
6. Noor P. What a pregnancy actually looks like before 10 weeks – in pictures. *The Guardian.* October 19, 2022. <https://www.theguardian.com/world/2022/oct/18/pregnancy-weeks-abortion-tissue>.
7. Kim C, Barnard S, Neilson JP, et al. Medical treatments for incomplete miscarriage. *Cochrane Database Syst Rev.* 2017;1(1):CD007223.
8. Schreiber CA, Creinin MD, Atrio J, et al. Mifepristone pretreatment for the medical management of early pregnancy loss. *N Engl J Med.* 2018;378(23):2161-2170.
9. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology. ACOG Practice Bulletin no. 193. Tubal ectopic pregnancy. *Obstet Gynecol.* 2018;131(3):e91-e103.
10. Gerson J. Label change for mifepristone could reduce barriers to care for miscarriages, advocates say in petition to FDA. The 19th. October 4, 2022. <https://19thnews.org/2022/10/mifepristone-miscarriage-label-change-fda-petition/>.
11. Tal E, Paul R, Dorsey M, Madden T. Comparison of early pregnancy loss management between states with restrictive and supportive abortion policies. *Womens Health Issues.* 2022 Nov 12;S1049-3867(22)00114-1. Online ahead of print.
12. Choobun T, Maneeon R. Trend of serum beta-human chorionic gonadotropin levels after medical abortion in the early first trimester of pregnancy. *J Obstet Gynaecol Res.* 2022 Oct 2. Online ahead of print.
13. Horvath S, Tsao P, Huang Zhen-Yu, et al. The concentration of fetal red blood cells in first-trimester pregnant women undergoing uterine aspiration is below the calculated threshold for Rh sensitization. *Contraception.* 2020;102(1):1-6.