

Managing miscarriage: How the options stack up

Surgery is no longer the only choice, though some women may prefer it

CASE Can surgery be avoided for incomplete miscarriage?

"G.A." is a 34-year-old gravida 3, para 1 who presents to the emergency room at 9 weeks' gestation complaining of vaginal bleeding and cramping that began the night before. A transvaginal scan and speculum examination reveal minimal cervical dilatation with expulsion of a small quantity of gestational tissue, with most of the conceptus still inside the uterus.

When the patient is informed that she has had an incomplete miscarriage, she worries about the prospect of surgical evacuation, since she experienced difficult recovery from anesthesia in a previous first-trimester termination of pregnancy.

She wants to know what other options she may have.

iscarriage is an abiding problem. Fifteen to 20 of every 100 clinically recognized pregnancies end in miscarriage—most of them requiring treatment to ensure complete evacuation of the uterus. Surgery has been the usual approach.

Recent years have brought a shift to less invasive methods, and there is "strong evidence" supporting expectant management as a "realistic alternative to surgical evacuation."

This article explores the 3 treatment

options for miscarriage—surgery, drugs, and watchful waiting—and describes the most recent data on each.

The latest terminology

The most recent terminology for the classification of miscarriage, as proposed by the European Society for Human Reproduction and Embryology, is listed below.² Note that the term "miscarriage" is the standard in Europe, whereas "spontaneous abortion" is preferred in the United States.

The different types of miscarriage probably reflect diverse causes, as well as different stages of the phenomenon. Not surprisingly, the type of miscarriage also influences management.

- Threatened miscarriage vaginal bleeding during the first half of pregnancy
- Empty sac (formerly termed "anembryonic miscarriage" or "blighted ovum") – gestational sac with absent structures or minimal embryonic debris without heart-rate activity
- **Delayed miscarriage** (formerly termed "missed" miscarriage) absence of heart activity in a fetus more than 6 mm long
- **Incomplete miscarriage** passage of tissue with some products of conception retained in the uterus
- Complete miscarriage dilated cervix with complete expulsion of conception products

CONTINUED

Alexandros Sotiriadis, MD Specialist ObGyn and Research Fellow, Department of Obstetrics and Gynecology, University Hospital of Ioannina, Greece

IN THIS ARTICLE

- Commonly used misoprostol regimens
 Page 24
- An uncommon, unhappy event Page 31



TABLE 1

Commonly used misoprostol regimens

- 600 µg misoprostol in the posterior fornix4
- 800 µg misoprostol vaginally 17-19
- 400 μg misoprostol orally every 4 hours up to a total of 1,200 μg²⁰
- 600 μg misoprostol sublingually every 3 hours up to a maximum of 3 doses²¹
- 600 μg misoprostol vaginally every 3 hours up to a maximum of 3 doses⁸

Option #1 Surgical evacuation

This approach to spontaneous abortion has been the mainstay of management for many years, except in cases of spontaneous complete miscarriage.

The uterus can be evacuated via dilatation and aspiration or sharp curettage, using local or general anesthesia. Success rates—defined as complete evacuation—approach 100%.

What the data show. A recent Cochrane review³ indicates that vacuum aspiration is superior to sharp curettage in terms of blood loss, pain, and duration of the procedure.

Risks. Apart from failure, which may sometimes be related to structural abnormalities of the uterus, surgical evacuation carries the theoretical risk of cervical trauma, uterine perforation, bleeding, and infection. In their Cochrane review,³ Forna and Gülmezoglu found that the overall risk of uterine perforation with surgical evacuation was 1 in 450, the risk of sepsis 1 in 30, and the risk of blood loss exceeding 100 mL about 1 in 15.

1 in ing 1

Option #2 Medical management

Prostaglandins are the most commonly used agents, owing to their ability to induce uterine contractions and thus expel the products of conception. Prostaglandins can be given orally, vaginally, or rectally, and administration is often preceded by

oral mifepristone, which primes the uterus by allowing local production of prostaglandins (normally suppressed by progesterone).

No single best regimen. Although several regimens have been used in clinical trials (TABLE 1), none are specifically advocated by the Royal College of Obstetricians and Gynaecologists (RCOG) or the American College of Obstetricians and Gynecologists.

Option #3 Watchful waiting

This option requires supervision of the patient until the retained products of conception are spontaneously expelled, usually after a few days or weeks. Surgery may be necessary if bleeding is prolonged or complications develop (eg, fever or pain), or if the patient requests it.

What the data show. Although data are limited, expectant management appears to be more successful in patients with incomplete—as opposed to delayed—abortion.^{4,5}

I How the options stack up

A recent metaanalysis⁶ of randomized, controlled trials compared surgical, medical, and expectant management. It also highlighted striking weaknesses in the quality of the data. A reanalysis of these data, in which the options were assessed independently (ie, not pairwise), found success rates (and 95% confidence intervals) for surgical, medical, and expectant management of 97.4% (96.2–98.5), 71.3% (68.9–73.7), and 59.4% (55.3–63.5), respectively.

Complication rates are given in **TABLE 2**.

When compared as pairs, surgery topped the options

Surgery was 1.44 times more effective than medical management, which in turn was 2.77 times more effective than expectant

FAST TRACK

Vacuum aspiration is superior to sharp curettage in terms of blood loss, pain, and duration of the procedure

TABLE 2

Complications common to surgical, medical, and expectant management

	MANAGEMENT MODALITY		
COMPLICATION	SURGICAL (95% CI)	MEDICAL (95% CI)	EXPECTANT (95% CI)
Pelvic inflammatory disease	5.4% (3.6–7.2)	2.5% (1.3–3.7)	4.8% (2.8–6.8)
Moderate-to-severe hemorrhage	3.3% (1.9–4.6)	17.6% (15.2–19.9)	0.9% (0–1.8)
Blood transfusion	3.0% (1.6–4.4)	1.9% (0.9–2.8)	1.1 % (0–2.5)
Emergency curettage	2.6% (0.5–4.7)	3.4% (1.5–5.3)	4.3% (2.1-6.5)
Diarrhea	2.5% (0-7.3)	28.7% (25.2–32.2)	7.3% (2.4–13.2)
Vomiting	1.6% (0.3–2.9)	7.2% (5.6–8.8)	1.1 % (0–2.5)

CI = confidence interval

Based on data from Sotiriadis et al6

This table lists only complications that are common to all 3 modalities. Those restricted to a single modality (eg, uterine perforation in surgery) are not included.

management. The comparison between surgical and expectant management failed to reach significance, probably because of bias in the selection of women.

Other forms of bias seem likely. The reporting of side effects may have been biased as well. For example, diarrhea rates were low when prostaglandins were compared with surgical or expectant methods, but surprisingly higher when 2 different routes of misoprostol administration (vaginal versus oral) were compared to each other. In addition, the incidence of moderate-tosevere bleeding with medical management was 1.5% in studies comparing it to other management options, but increased to about 18% when data from a single study comparing vaginal and oral misoprostol were incorporated.

All 3 methods carry risk of sepsis

Traditionally, surgical evacuation of the uterus was preferred because retention of the products of conception was thought to increase the risk of infection in the preantibiotic era.7 It now is clear that each modality carries its own set of risks. For example, surgical evacuation carried a 3% rate of sepsis in the Cochrane review,3 and there are reports of severe sepsis with prostaglandin use as well.8

In a retrospective series, Hurd et al⁹ found the risk of complications with expectant management to increase significantly (37%) with the amount of intrauterine tissue—and 1 in 24 women with sac diameter greater than 10 mm required emergency curettage for septic abortion.

Nevertheless, taken collectively, the rates of pelvic inflammatory disease do not appear to differ significantly between the different modalities.6

Avoid prostaglandins if molar pregnancy is suspected

Molar pregnancy sometimes presents as a first-trimester loss. For this reason, the use of oxytocics in general and prostaglandins specifically is discouraged in cases with suspected molar pregnancy because of the theoretical concern of dissemination of trophoblastic tissue through the venous system.10

Ultrasound has imperfect accuracy when it comes to diagnosing molar pregnancies presenting as miscarriages, but may be useful in some cases.

Circumstances often determine best method

Surgical evacuation may fail when there are uterine abnormalities that distort the endometrial cavity. In such cases, medical treatment may be a good alternative.

As noted earlier, expectant management carries a good chance of success

FAST TRACK

The risk of complications with expectant management increases with the amount of intrauterine tissue when miscarriage is incomplete, but poorer results in cases of delayed miscarriage.6 Randomized studies indicate a success rate for expectant management of 85% in cases of incomplete abortion, but only 33% when miscarriage is delayed.4

Vaginal bleeding at presentation may predict successful evacuation with nonsurgical methods.1

Don't overlook patient's desires

When viewed collectively, data from randomized controlled trials indicate similar satisfaction rates for the 3 management options, although there is substantial heterogeneity between studies.6

However, miscarriage is a stressful event for almost every woman. Some populations are especially vulnerable, such as older women with longstanding infertility, and women with a history of recurrent abortion. Losing a pregnancy may trigger feelings of helplessness, and some women may seek to overcome that loss of control by choosing to avoid surgery.7

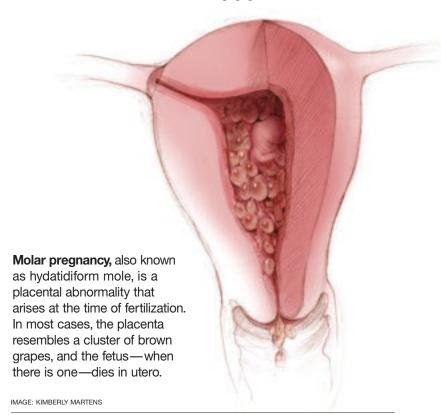
Another important point: The efficacy of a method, in terms of uterine evacuation rates, does not always predict the degree of satisfaction. Wieringa-de Waard and colleagues11 found that women randomized to expectant management had better mental health scores than those randomized to surgery, and Moodliar et al12 reported satisfaction rates of 94% in women randomized to medical treatment versus 40% in those randomized to surgical evacuation.

Past success influences a woman's choice. Preference rates of 55% were documented among women allocated to expectant management in a randomized controlled trial, but rose to 71% in the subset of women who had undergone expectant management successfully in the past.13

Women who do not respond to nonsurgical management and eventually have to undergo surgical evacuation appear to have the most profound anxiety- and depressionrelated reactions.14

Freedom of choice may be most important factor. Wieringa-de Waard et al13 found that 84% to 88% of women who were

An uncommon, unhappy event



managed according to their choice of treatments maintained their favorable opinion of that choice, compared with 55% to 74% of women who accepted randomization. In addition, women who chose curettage had better mental health scores than those randomized to this method.12

Women may prefer speed of surgery

Many women who choose surgical evacuation do so because it is the fastest method. Surgical treatment is a one-time event that does not usually require additional resources.

In contrast, medical and expectant management require longer stretches of time, and prolonged vaginal bleeding is common. Among women treated successfully with medical management, 88% and 100% present with complete evacuation of the uterus by days 2 and 7, respectively. For those treated by expectant management, the rates are 33% and 100%, respectively.^{4,18}

FAST TRACK

84-88% of women managed with their choice of treatments maintained a favorable opinion of that choice, vs 55-74% of women who accepted randomization

Offer medical or expectant management only when backup is available. Pain or the appearance of clots or side effects (eg, fever or diarrhea) with medical therapy may spur women to seek assistance, and the RCOG recommends that medical and expectant management be offered only when women have access to round-theclock telephone advice and immediate hospitalization, if needed.7

The RCOG also emphasizes the importance of an organized unit dedicated to early pregnancy assessment, with suitably trained staff, ultrasound and laboratory back-up, clear diagnostic and therapeutic algorithms, and easy access for primary care providers.7

Other recommendations at the time of treatment

Besides careful management of the abortion, the RCOG advocates the following:

- Screen for chlamydia in all at-risk women undergoing surgical evacuation
- Consider cervical priming before surgical evacuation
- Do histologic analysis of expelled tissue to exclude ectopic or molar pregnancy
- Offer psychological support and follow-up, with referrals, as necessary.⁷

When to use rhesus prophylaxis

Both ACOG and the RCOG issued guidelines about the use of anti-Rh (D) prophy-Rh-negative nonsensitized women.^{7,15,16} They agree that anti-D immune globulin should be administered to all nonsensitized RhD-negative women who have spontaneous complete or incomplete abortion after 12 gestational weeks.

Before 12 weeks, the amount of fetomaternal bleeding is thought to be minimal, and the risk for immunization negligible; administration of anti-D is controversial in these cases.

However, anti-D should be given after surgical or medical evacuation regardless of gestational age because uterine instrumentation is associated with significant fetomaternal hemorrhage.

CASE Patient selects medical management

In the opening case, the appearance of the intrauterine contents did not suggest molar pregnancy, so any of the 3 management modalities were appropriate. The patient was adamant about avoiding surgery, and was counseled only about medical and expectant management. She felt medical management would give her a stronger sense of control.

When prostaglandins are given, patients may be admitted for 2 days or until the products of conception are completely expelled, or be treated as outpatients, depending on the degree of bleeding anticipated, the reliability of the patient, and the ease of hospital access in the event of complications. All 3 factors were favorable in G.A.'s case, so 3 tablets (600 µg) of misoprostol were placed in the posterior fornix, and she was sent home with instructions to place 1 additional tablet before bedtime and take analgesics as needed. Because this patient was Rh-negative, 250 IU anti-D were administered.

Two days later, a repeat transvaginal scan showed complete evacuation of the uterus. She had started bleeding 13 hours after the first dose of misoprostol, and by the time she came to the hospital, the bleeding had diminished to spotting.

After 4 months, the patient became pregnant again. As of 13 weeks, she had a reassuring measurement of the nuchal translucency and was looking forward to the rest of her pregnancy and delivery.

REFERENCES

- 1. Ankum WM, Wieringa-De Waard M, Bindels PJ. Management of spontaneous miscarriage in the first trimester: an example of putting informed shared decision making into practice. BMJ. 2001;322:1343-1346.
- 2. Farguharson RG, Jauniaux E, Exalto N. Updated and revised nomenclature for description of early pregnancy events. Hum Reprod. 2005; Jul 8 [Epub ahead of print].
- 3. Forna F, Gulmezoglu AM. Surgical procedures to evacuate incomplete abortion. Cochrane Database Syst Rev. 2001:(1):CD001993.
- Bagratee JS, Khullar V, Regan L, Moodley J, Kagoro H. A randomized controlled trial comparing medical and expectant management of first trimester miscarriage. Hum Reprod. 2004;19:266-271.

CONTINUED

FAST TRACK

Offer medical and expectant management only if the patient has access to round-the-clock telephone advice and immediate hospitalization. if required

Women's Health Experience

Enhancing the patient/physician dialogue

Supporters include:























Now you can reach the most influential decision makers in healthcare — women and physicians — with one integrated program. For more information about how you can get involved in the Women's Health Experience contact David Small at 201-573-5556 or david.small@dowdenhealth.com

www.womenshealthexperience.com

Managing miscarriage:How the options stack up

- Ngai SW, Chan YM, Tang OS, Ho PC. Vaginal misoprostol as medical treatment for first trimester spontaneous miscarriage. Hum Reprod. 2001;16:1493-1496.
- Sotiriadis A, Makrydimas G, et al. Expectant, medical, or surgical management of first-trimester miscarriage: a meta-analysis. Obstet Gynecol. 2005;105(5 Pt 1):1104-1113
- Royal College of Obstetricians and Gynaecologists. Clinical Green Top Guidelines. The Management of Early Pregnancy Loss (25), Oct 2000. Available at: http://www.rcog.org.uk/index.asp?PageID=515 Accessed June 12. 2006.
- Centers for Disease Control. Clostridium sordellii toxic shock syndrome after medical abortion with mifepristone and intravaginal misoprostol-United States and Canada, 2001-2005. MMWR Morb Mortal Wkly Rep. 2005;54:724.
- Hurd WW, Whitfield RR, Randolph JF Jr, et al. Expectant management versus elective curettage for the treatment of spontaneous abortion. Fertil Steril. 1997;68:601-606.
- Royal College of Obstetricians and Gynaecologists. Clinical Green Top Guidelines. The Management of Gestational Trophoblastic Neoplasia (38), February 2004. Available at: http://www.rcog.org.uk/resources/Public/pdf/Gestational_ Troph_Neoplasia_No38.pdf Accessed June 12, 2006.
- Wieringa-De Waard M, Hartman EE, Ankum WM, Reitsma JB, Bindels PJ, Bonsel GJ. Expectant management versus surgical evacuation in first trimester miscarriage: healthrelated quality of life in randomized and non-randomized patients. Hum Reprod. 2002;17:1638-1642.
- Moodliar S, Bagratee JS, Moodley J. Medical vs. surgical evacuation of first-trimester spontaneous abortion. Int J Gynaecol Obstet. 2005;91:21-26.
- Wieringa-de Waard M, Bindels PJ, et al. Patient preferences for expectant management vs. surgical evacuation in firsttrimester uncomplicated miscarriage. J Clin Epidemiol. 2004;57:167-173.
- Nielsen S, Hahlin M, Moller A, Granberg S. Bereavement, grieving and psychological morbidity after first trimester spontaneous abortion: comparing expectant management with surgical evacuation. Hum Reprod. 1996;11:1767-1770.
- Royal College of Obstetricians and Gynaecologists. Use of anti-D immunoglobulin for Rh prophylaxis. London: RCOG; 2002 (number 22). Available at: http://www.rcog. org.uk/index.asp?PageID=512 Accessed June 12, 2006.
- American College of Obstetricians and Gynecologists. Practice bulletin #4: prevention of Rh D alloimmunization. May 1999. Clinical management guidelines for obstetrician-gynecologists. Int J Gynaecol Obstet 1999;66:63-70.
- Demetroulis C, Saridogan E, Kunde D, Naftalin AA. A prospective randomized control trial comparing medical and surgical treatment for early pregnancy failure. Hum Reprod. 2001;16:365-369.
- Wood SL, Brain PH. Medical management of missed abortion: a randomized clinical trial. Obstet Gynecol. 2002;99:563-566.
- Muffley PE, Stitely ML, Gherman RB. Early intrauterine pregnancy failure: a randomized trial of medical versus surgical treatment. Am J Obstet Gynecol. 2002;187:321-325
- Chung TK, Lee DT, Cheung LP, Haines CJ, Chang AM. Spontaneous abortion: a randomized, controlled trial comparing surgical evacuation with conservative management using misoprostol. Fertil Steril. 1999;71:1054-1059.
- Tang OS, Lau WN, Ng EH, et al. A prospective randomized study to compare the use of repeated doses of vaginal with sublingual misoprostol in the management of first trimester silent miscarriages. Hum Reprod. 2003;18:176-181.

The author has no financial relationships relevant to this article.