Cochrane for Clinicians

Putting Evidence into Practice

Management Options for Early Incomplete Miscarriage

QUYNH BUI, MD, MPH, *University of California, San Francisco, California*

The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Dr. Bui presents a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at http://www.cochrane.org/reviews/en/ab007223.html.

EB CME

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The series coordinator for *AFP* is Kenny Lin, MD, Department of Family Medicine, Georgetown University School of Medicine, Washington, DC.

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Clinical Scenario

Based on ultrasonography results, a 22-year-old patient is diagnosed with early incomplete miscarriage at nine weeks' gestation. At her follow-up visit, she asks for advice on treatment options.

Clinical Question

What are the safest and most effective management options in patients who have early incomplete miscarriage?

Evidence-Based Answer

For the management of incomplete miscarriage, limited-quality evidence shows that medical treatment with misoprostol (Cytotec), expectant care, and surgical evacuation have a completion of miscarriage success rate between 80 to 99 percent in pregnancies at less than 13 weeks' gestation.[1] Evidence comparing mortality, morbidity, and patient satisfaction also is limited, but suggests that all three methods are similar. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

An incomplete miscarriage occurs when the disruption or partial passage of the products of conception has occurred. It is diagnosed clinically by the finding of an open cervical os and is confirmed by ultrasonography when the gestational sac is found to be disrupted or if there is thickened endometrium with disorganized, residual products of conception present.[2] The differentiation of an incomplete miscarriage from a delayed miscarriage is important. A delayed miscarriage is characterized by the presence of a dead embryo or fetus, or by the absence of an embryo within the intact gestational sac (anembryonic pregnancy).[2] Because a delayed miscarriage contains viable, hormone-producing trophoblastic tissue, it is theoretically less responsive to uterotonic medications and more responsive to antihormone therapy than an incomplete miscarriage.[1] The success of different management options varies between incomplete and delayed miscarriage.[1,3,4] For this reason, this Cochrane review addresses only the management of incomplete miscarriage and excludes analysis of data from nonviable pregnancy and blighted ovum.

The options for management of an incomplete miscarriage have included surgical intervention (e.g., curettage, vacuum aspiration) to remove retained conception tissue, medical treatment with prostaglandin analogues (e.g., misoprostol), or expectant management.[2] Treatment with antiprogesterone medication or mifepristone (Mifeprex) has been used in delayed miscarriage in which placental hormones may still be present, as well as in incomplete miscarriage. Mifepristone may promote the expulsion of tissue after miscarriage, but it was not considered in depth in this Cochrane review because of scarcity of data.[1]

The reviewers performed a meta-analysis of data from a total of 2,750 women with diagnosed incomplete miscarriage before 13 weeks' gestation, which included 15 randomized controlled trials comparing misoprostol treatment with expectant or surgical management.[1] There was one trial of oral versus vaginal misoprostol, and one trial comparing two different doses of misoprostol. None of the included trials directly compared expectant management solely with surgical intervention.[1] The number and heterogeneity of the treatment comparisons in the included trials led to small sample sizes for some outcomes. The review makes note of the large confidence intervals of some of the risk estimates, which limit the strength of its recommendations.[1]

Cochrane Abstract

Background: Miscarriage occurs in 10 to 15 percent of pregnancies. The traditional treatment after miscarriage has been to perform surgery to remove any remaining pregnancy tissues in the uterus. However, it has been suggested that drug-based medical treatments or expectant care (no treatment) may also be effective, safe, and acceptable.

Objectives: To assess the effectiveness, safety, and acceptability of any medical treatment for early incomplete miscarriage (before 24 weeks' gestation).

Search Strategy: The authors searched the Cochrane Pregnancy and Childbirth Group's Trials Register (September 2009).

Selection Criteria: Randomized controlled trials comparing medical treatment with expectant care or surgery. Quasirandomized trials were excluded.

Data Collection and Analysis: Two authors independently assessed the studies for inclusion, assessed risk of bias, and carried out data extraction. Data entry was checked.

Main Results: Fifteen studies (n = 2,750) were included; there were no studies on women at more than 13 weeks' gestation. Studies addressed a number of comparisons, and data are therefore limited. Three trials compared misoprostol treatment (all vaginally administered) with expectant care. There was no significant difference in complete miscarriage (average risk ratio [RR] = 1.23; 95% confidence interval [CI], 0.72 to 2.10; two studies; n = 150), or in the need for surgical evacuation (average RR = 0.62; 95% CI, 0.17 to 2.26; two studies; n = 308). There were few data on deaths or serious complications.

Nine studies (n = 1,766) addressed the comparison of misoprostol (four oral, four vaginal, one combined vaginal and oral) with surgical evacuation. There was no statistically significant difference in complete miscarriage (average RR = 0.96; 95% CI, 0.92 to 1.00; eight studies; n = 1,377), with high success rates for both methods. Overall, there were fewer surgical evacuations with misoprostol (average RR = 0.07; 95% CI, 0.03 to 0.18; eight studies; n = 1,538), but more unplanned procedures (average RR = 6.32; 95% CI, 2.90 to 13.77; six studies; n = 1,158). There were few data on deaths or serious complications.

Limited evidence suggests that women generally seem satisfied with their care. Long-term follow-up from one included study identified no difference in subsequent fertility among the three approaches.

Authors' Conclusions: The available evidence suggests that medical treatment with misoprostol and expectant care are both acceptable alternatives to routine surgical evacuation, given the availability of health service resources to support all three approaches. Women experiencing miscarriage before 13 weeks' gestation should be offered an informed choice.

MEDICAL VS. EXPECTANT MANAGEMENT

Only three randomized controlled trials were identified, all of which compared vaginal misoprostol with expectant management. Results did not show any difference between the two treatments in the success of completed miscarriage. The success rate of expectant management ranged widely from 52 percent at follow-up after one week to 81 percent after two weeks. The success rate of misoprostol was about 80 percent.[1] In their comparison of misoprostol versus expectant management, the reviewers did not find any differences in mortality, serious complications, or the proportion of women requiring eventual surgical evacuation. There was also no difference in the development of pelvic infection, or the need for unplanned surgical intervention, blood transfusion, or pain relief. However, data on these outcomes are limited.[1]

MEDICAL VS. SURGICAL MANAGEMENT

A total of nine studies (n = 1,499 women) compared misoprostol treatment by various routes of administration (vaginal, oral, and combined vaginal and oral) with surgical management. These comparisons revealed no difference in successful completion of miscarriage, with a rate of 80 to 99 percent for misoprostol compared with 91 to 100 percent for surgical management.[1] There also were no differences in mortality or serious complications, anemia or need for blood transfusions, need for pain relief, or incidence of pelvic infection. Surgery did not result in more cervical damage. However, women treated with misoprostol experienced, on average, more days of bleeding (mean difference = 2.12; 95% confidence interval [CI], 1.18 to 3.07), nausea (risk ratio = 3.18; 95% CI, 1.78 to 5.70), and vomiting (risk ratio = 2.25; 95% CI, 1.14 to 4.43). They also had a higher risk of needing an unplanned surgical intervention than those already undergoing surgical management (risk ratio = 6.32; 95% CI, 2.90 to 13.77).[1] Surgical evacuation is predictable and highly successful, but invasive. It should be chosen when tissue is required for diagnosis, as in the case of recurrent pregnancy loss.[1,2]

Although data are limited, there were no differences in success of miscarriage by the route of misoprostol administration compared with surgery.[1,5] One trial directly comparing vaginal with oral misoprostol showed no difference in completion of miscarriage, or the need for surgical evacuation or unplanned surgical intervention, pain relief, or nausea.[5] Women experienced less diarrhea using vaginal rather than oral misoprostol.[5]

Overall, limited evidence suggests that the women were generally satisfied with any of the three miscarriage management options as long as they felt supported in their management decision. Convalescence and time off work were about eight to nine days overall, with few differences found among management options.[6-8] Participants often showed a strong preference for one method over the others, with up to 70 percent opting for expectant management.[2,6] Patient satisfaction ultimately was predicted by successful completion of the miscarriage and by the amount of support received for the preferred method, rather than by the type of management chosen.[2]

In counseling patients with early incomplete miscarriage, they should be informed that there are several reasonable and comparable options that all have advantages and disadvantages. Women asked about their treatment preferences appeared to value being informed of and offered choices.[9,10] In one small study of women who had experienced a miscarriage, 72 percent had opted for expectant management, but 55 percent stated they would alter their choice based on physician recommendation.[11]

Address correspondence to Quynh Bui, MD, MPH, at quynh.bui@ucsfmedctr.org. Reprints are not available from the author.

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Cochrane Briefs

Clozapine vs. Other Atypical Antipsychotics for Schizophrenia

Clinical Question

Compared with other atypical antipsychotic medications, what are the effects of clozapine (Clozaril) in patients with schizophrenia and schizophrenia-like psychoses?

Evidence-Based Answer

Although further trials are needed, there is some evidence that clozapine is slightly more effective than risperidone (Risperdal). Fewer participants taking clozapine dropped out of studies because of lack of effectiveness compared with those taking risperidone (number needed to treat = 11; 95% confidence interval [CI], 7 to 21). However, adverse effects led to a higher attrition rate in patients taking clozapine than those taking olanzapine (Zyprexa; number needed to harm = 25; 95% CI, 15 to 73) and risperidone (number needed to harm = 16; 95% CI, 9 to 59). Clozapine is associated with more sedation and hypersalivation than olanzapine, quetiapine (Seroquel), and risperidone; more seizures than olanzapine and risperidone; and more weight gain than risperidone. (Strength of Recommendation = B, based on inconsistent or limited-quality patient-oriented evidence)

Practice Pointers

Clozapine was developed as an alternative to chlorpromazine and haloperidol for the treatment of schizophrenia, in part because the older antipsychotics cause movement disorders. Although it is effective for refractory symptoms, clozapine is associated with fatal agranulocytosis, seizures, myocarditis, orthostatic hypotension, and respiratory and cardiac arrest. Blood counts must be carefully monitored during and after treatment. Other atypical antipsychotics have subsequently been developed, such as aripiprazole (Abilify), olanzapine, quetiapine, risperidone, and ziprasidone (Geodon).

In this Cochrane review, the authors compared single- and double-blind trials of clozapine versus other atypical antipsychotics; 27 studies with a total of 3,099 participants fulfilled their review criteria. Many of the studies included participants who had been unsuccessfully treated with other medications. Most of the studies compared clozapine with olanzapine, risperidone, and quetiapine.

Overall, the attrition rate in the studies was high (30.1 percent), requiring caution in the interpretation of the results. The attrition rate due to adverse effects was

higher for clozapine than for olanzapine or risperidone, but fewer patients taking clozapine left the study because of ineffectiveness versus those taking risperidone. Clozapine was not more effective at improving general mental state than olanzapine, quetiapine, risperidone, or ziprasidone. There was no difference in symptoms of schizophrenia, but there were fewer movement disorders with clozapine than with risperidone (number needed to treat = 7; 95% CI, 5 to 15). Patients taking clozapine had more blood dyscrasias, hypersalivation, seizures, and sedation than those taking olanzapine, risperidone, or quetiapine. Compared with those taking risperidone, the clozapine groups showed fewer extrapyramidal adverse effects but had an important weight gain not seen with risperidone.

The National Institute for Health and Clinical Excellence in the United Kingdom recommends clozapine for persons with schizophrenia who have not responded to two other antipsychotic medications, including another atypical antipsychotic.[1] The American Psychiatric Association has not issued a guideline on schizophrenia since April 2004.[2]

CLARISSA KRIPKE, MD

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