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REVIEW ARTICLE

Misoprostol to treat missed abortion in the first trimester

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Recommended Dosages
Vaginal misoprostol 800 μg
OR sublingual misoprostol 600 μg

KEYWORDS
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Abstract

Missed abortion in the first trimester is characterized by the arrest of embryonic or fetal development. The cervix is closed and there is no or only slight bleeding. Ultrasound examination shows an empty gestational sac or an embryo/fetus without cardiac activity. Based on a review of the published literature a single dose of 800 μg vaginal misoprostol may be offered as an effective, safe, and acceptable alternative to the traditional surgical treatment for this indication. Alternatively, 600 μg misoprostol can be administered sublingually. After administration of misoprostol, hospitalization is not necessary and the time to expulsion varies considerably. Bleeding may last for more than 14 days with additional days of light bleeding or spotting. The woman should be advised to contact a provider in case of heavy bleeding or signs of infection. A follow-up is recommended after 1 to 2 weeks.

1. Introduction

In some cases of first trimester pregnancy failure, arrest of embryonic or fetal development occurs some time before the expulsion (miscarriage). When this occurs, the cervix is closed and there is no or only slight bleeding. Ultrasound examination shows an empty gestational sac or an embryo/fetus without cardiac activity.

In the following article we will use the term missed abortion, but many other terms have been used to describe this event, including: silent or missed miscarriage, "anembryonic

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pregnancy", "blighted ovum", "early fetal demise", "nonviable pregnancy" and "embryonic/fetal death" (Table 1).

The usual treatment is suction curettage irrespective of the length of amenorrhea. However an increasing number of studies have shown that medical treatment may be effective, safe, and acceptable, as may be waiting for spontaneous expulsion (expectant management) (Table 1).

2. Rationale for regimen

2.1. Dosage and route

A Cochrane review including 19 randomized controlled trials (RCTs) on pregnancies less than 14 weeks concluded that vaginal misoprostol shortens the time to expulsion when compared with placebo [1]. In two RCTs, misoprostol reduced the need for uterine curettage (104 women, RR 0.40, 95% CI 0.26 to 0.60) with no significant increase in side effects like nausea or diarrhea [2,3] (Table 1). In these trials vaginal misoprostol was administered in doses of 400 μg, 600 μg, or 800 μg. Lower-dose regimens of vaginal misoprostol were tested in 2 RCTs and have shown to be less effective in inducing expulsion, but with a similar incidence of nausea [4,5].

A study compared 800 μg oral with the same dose of vaginal misoprostol with no difference in efficacy, but the mean time to expulsion was significantly longer in the oral group [6]. Sublingual misoprostol had equivalent efficacy compared with vaginal misoprostol in inducing complete miscarriage, but was associated with more frequent diarrhea [7].

2.2. Predictors of success

The success of the treatment seems to be higher for incomplete miscarriage and lower for an anembryonic pregnancy (empty gestation sac) compared to a pregnancy with an early embryonic death [8,9].

The diagnosis "spontaneous abortion" is often insufficiently defined and important details like cervical examination, bleeding or ultrasound findings are not reported. Thus many studies and reports on success rates are difficult to interpret or to compare. Efficacy rates vary widely from 13% to 93%, influenced by many factors such as diagnosis, sac size, whether follow-up is clinical or involves ultrasound, and maybe also the number of doses.

Other researchers have explored the efficacy of multiple misoprostol doses and timing of follow-up. Some investigators have found that vaginal or sublingual misoprostol used every 3 h for up to three doses is an effective treatment with acceptable side effects. Efficacy has been shown to be similar using a longer interval between doses or continued dosing for a week following the initial three doses [7,10,11].

The effectiveness of treatment with misoprostol also depends on the time interval to follow-up [12]. To avoid unnecessary intervention the assessment of success should be delayed for at least 7 to 10 days.

There seems no clear advantage to administering a 'wet' preparation of vaginal misoprostol, or adding methotrexate, or of using laminaria tents [13,14]. Two RCTs of pretreatment with mifepristone treatment generated conflicting results [15,16], and further studies are needed to evaluate whether the use of mifepristone increases efficacy.

Expectant management or medical treatment with misoprostol does not increase the risk of infection compared to surgery [17]. Furthermore there is no evidence that nonsurgical approaches will have a negative effect on future fertility, but further larger studies are needed to confirm this [18].

3. Contraindications

- Known allergy to misoprostol.
- Suspected ectopic pregnancy.
- Unstable hemodynamics and shock.
- Signs of pelvic infections and/or sepsis

4. Precautions

- Trophoblastic disease. There is no evidence for support of medical treatment. Surgery is recommended.
- Coagulation disorder/currently taking anticoagulants.

Table 1 RCTs comparing surgical and/or expectant and/or medical management

Placebo	Expectant	Vaginal misoprostol	Oral or sublingual misoprostol	Methotrexate	Mifepristone	Surgical evacuation	Notes	Trials
	•	•						[20]
•		•						[2,3,21,22]
		•				•		[23–25]
		•	•					[6,7,26]
		•					Comparing different dosages	[4,5]
		•		•			Methotrexate ± vaginal misoprostol	[13]
•					•			[15]
	•		•		•		Mifepristone + oral misoprostol versus expectant	[16]
	•	•				•		[17]

5. Regimen

A single dose of 800 μg vaginal misoprostol is recommended for this indication [4–6]. Alternatively, 600 μg misoprostol can be administered sublingually [7,11].

Treatment may be repeated twice with a 3 h interval but more studies are needed to evaluate the additional efficacy of repeated doses of misoprostol [7,10,11].

6. Course of treatment

The diagnosis of missed abortion is made by bimanual examination and ultrasound. If judged necessary serum β-HCG could be analyzed as well. A second ultrasound after 1–2 weeks may be needed to confirm the diagnosis.

All women should be given the choice between surgical, expectant or medical management.

There is no clinical reason to withhold misoprostol for the treatment of missed abortion in women with previous cesarean section.

After administration of misoprostol, hospitalization is not necessary as the time to expulsion varies considerably—it may occur in hours or over several weeks. Bleeding may last for more than 14 days with additional days of light bleeding or spotting. Uterine contractions usually start within a few hours following misoprostol. Routine antibiotic coverage is not necessary, but paracetamol or NSAIDs can be used for pain relief [19]. The woman should be advised to contact a provider in case of heavy bleeding or signs of infection.

The effectiveness of the treatment depends on the diagnosis and on the time until follow-up and evaluation.

Follow-up is best performed at 1 to 2 weeks after treatment where complete evacuation of the uterus is confirmed by history, clinical examination of the uterus, and with ultrasound if necessary.

A pregnancy test may also be needed. In the event of failure (or infection or heavy bleeding), a surgical evacuation may be needed. However, if the woman is clinically stable and willing to continue to wait for her uterus to empty, it is acceptable to give her another dose of misoprostol, 800 μg vaginally or 600 μg sublingually.

7. Effects and side effects

Prolonged or serious effects and side effects are rare.

7.1. Bleeding

After administration of misoprostol, bleeding typically lasts up to two weeks with additional days of spotting that can last for several weeks.

The woman should be instructed to contact a provider if she soaks more than two extra large sanitary pads an hour for more than two consecutive hours, or has bled continuously for more than two weeks and/or begins to feel dizzy or light-headed.

7.2. Cramping

Cramping usually starts within the first few hours but may begin within minutes after misoprostol administration. The pain may be stronger than that experienced during a regular period. Paracetamol or nonsteroidal anti-inflammatory drugs (NSAIDs) can be used for pain relief.

7.3. Fever and/or chills

Chills are a common side effect of misoprostol but are transient. Fever is less common and does not necessarily indicate infection. An antipyretic can be used for relief of fever, if needed. If fever or chills persist beyond 24 h after taking misoprostol, the woman may have an infection and should seek medical attention.

7.4. Nausea and vomiting

Nausea and vomiting may occur and will resolve 2 to 6 h after taking misoprostol. An anti-emetic can be used if needed.

7.5. Diarrhea

Diarrhea may also occur following administration of misoprostol but should be resolved within a day.

7.6. Skin rash

Occasionally skin rash occurs after administration of misoprostol.

The taste of the misoprostol tablets can be unpleasant when used sublingually, and some women may feel numbness in the tongue.

The woman should be informed where to seek help in case of heavy bleeding or signs of infection.

8. Additional information

Following vaginal administration of misoprostol undissolved tablets may be found in the vagina at an examination. This does not affect the absorption of misoprostol.

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Conflict of interest

The authors do not have any conflict of interest.

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