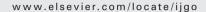


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## **REVIEW ARTICLE**

# Treatment of incomplete abortion and miscarriage with misoprostol

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## **Recommended Dosage**

Oral misoprostol 600  $\mu g$  as a single dose

## **KEYWORDS**

Misoprostol; Miscarriage; Incomplete abortion

#### Abstract

A literature review was conducted to determine whether misoprostol is an effective treatment for incomplete abortion and, if so, to recommend an appropriate regimen. All English language articles published before October 2007 using misoprostol in at least one of the study arms were reviewed to determine the efficacy of misoprostol when used to treat incomplete abortion in the first trimester. All available unpublished data previously presented at international scientific meetings were also reviewed. Sufficient evidence was found in support of misoprostol as a safe and effective means of non-surgical uterine evacuation. A single dose of misoprostol 600  $\mu g$  oral is recommended for treatment of incomplete abortion in women presenting with a uterine size equivalent to 12 weeks gestation.

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## 1. Introduction

Incomplete abortion continues to contribute disproportionately to maternal morbidity and mortality in much of the developing world. Incomplete abortions can be managed expectantly, surgically and with misoprostol. Surgical management has been the standard of care worldwide for many years,

and its safety and effectiveness is well proven in the context of high-quality medical care. Expectant management also works well; however, it is sometimes less desirable to women (and some providers), who may prefer immediate treatment.

Management of incomplete abortion using misoprostol is slowly gaining attention as an easy to use, feasible, and low cost means of uterine evacuation, and could revolutionize treatment for this indication.

This method promises to greatly improve access to services, by enabling women to seek appropriate, effective care at secondary and even primary healthcare facilities, with non-surgically trained, mid-level providers.

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At the same time, misoprostol for incomplete abortion and miscarriage could decrease the burden on tertiary health care facilities, and reduce costs to health care systems worldwide. It could limit the burden on skilled surgical providers, as well as reducing the need for surgical equipment and supplies, surgical wards, sterilization and anesthesia. Misoprostol treatment also has the additional benefit of being highly acceptable to women as it is less medicalized and less invasive than standard surgical treatment.

A review of studies of misoprostol for incomplete abortion/miscarriage shows varying efficacy rates with dosages ranging from 400  $\mu$ g to 1200  $\mu$ g [1–21]. Chung et al [1] studied 400  $\mu$ g misoprostol orally every four hours to a maximum dose of 1200  $\mu$ g and assessed efficacy on the same day of treatment. Overall success rates were low, with 50% of misoprostol users requiring additional surgical care. Another study compared oral and vaginal misoprostol with repeated 800  $\mu$ g doses and outcome assessment on the same day of treatment [2]. These 800  $\mu$ g regimens showed slightly higher success rates ( $\sim$ 60%) [2].

Studies in which efficacy was assessed later (3 to 15 days following initial treatment) have shown considerably higher success rates, ranging from 60%-95% [1-24]. For instance, Gronlund et al [4] compared 400 µg vaginal misoprostol to expectant management and achieved a 90% success rate in the misoprostol arm with assessment on days 8 and 14. Two studies comparing a single dose of oral misoprostol 600 µg versus 600 μg×2 doses (with a 4 hour interval) showed no difference in efficacy between the two regimens [19–20]. Weeks et al [20] compared 600 µg oral misoprostol to manual vacuum aspiration (MVA). In this study, the success rate with misoprostol was 96.3%, slightly better than MVA (91.5%) [4]. Three recent trials also documented efficacy rates above 90% for misoprostol when compared to MVA for treatement of incomplete abortion [21-23]. There has been concern that non-surgical management could lead to higher rates of infection. However, in a recent UK trial comparing medical vs. surgical vs. expectant treatment for incomplete abortion, the lowest rate of infection was in the expectant management arm [24].

If used for treatment of incomplete abortion, misoprostol promises to have an important public health impact. Women and health care systems worldwide could significantly benefit from this non-invasive treatment option. In low-resource countries, where infection, hemorrhage and uterine damage are far too commonly reported as consequences of (poor) surgical care, misoprostol treatment of incomplete abortion would be a tremendous step towards reducing morbidity and mortality due to abortion complications worldwide.

#### 2. Contraindications

- 1. Known allergy to misoprostol or other prostaglandins.
- 2. Suspected ectopic pregnancy.
- 3. Unstable hemodynamic status or shock.
- 4. Signs of pelvic infection and/or sepsis.

## 3. Precautions

- Women with an intrauterine device (IUD) in place should have the intrauterine device (IUD) removed before drug administration.
- 2. Coagulation disorders/ currently taking anticoagulants.

## 4. Regimen

A single dose of  $600~\mu g$  oral or  $400~\mu g$  sublingual misoprostol is indicated for treatment of incomplete abortion and miscarriage for women presenting with uterine size equivalent to a 12 week gestation.

600 μg oral misoprostol has been used to evacuate the uterus safely for thousands of women participating in clinical trials worldwide [18,20–23]. 400 μg sublingual misoprostol is being used in several ongoing trials and has been shown to be as safe and effective as the 600 μg oral dose [25]. At this time, however, there is less evidence supporting use of this lower dose regimen. The current evidence does not support the use of repeated doses [18,19].

## 5. Course of treatment

The course of treatment is brief and essentially involves two outpatient visits. At the first visit, the incomplete abortion status should be confirmed by history and clinical exam and eligibility for misoprostol assessed.

The crucial clinical findings are an open cervical os and a uterine size less than 12 weeks of gestation.

Where available, ultrasound may be used as an additional diagnostic tool if incomplete abortion status cannot be confirmed with history and clinical exam. Information about misoprostol management, possible side effects and success rate should be given to the woman. Given the small risk of retained uterine products following treatment, surgical intervention may be needed to empty the uterus for some women.

It is important to explain to women that the expulsion can occur over several hours to several weeks and that bleeding will most likely be heavy for about 3—4 days, followed by light bleeding or spotting for several weeks.

Routine antibiotic coverage is not necessary and local norms regarding antibiotic use should be followed. The provider may determine that the woman requires antibiotic coverage based on history or clinical exam.

Depending on the health care system and her wishes, the woman can take the misoprostol either at the health facility or at home. She should be given contact details and encouraged to consult the facility or the provider about any questions or concerns.

When used in studies, a single dose of  $600\,\mu g$  oral misoprostol successfully evacuated the uterus in nearly all women. Given that the method may fail in some women, it is recommended that all women have a follow-up visit in 7–14 days during which time clinical history and a bi-manual exam should enable the provider to determine the absence of symptoms and that the uterus is firm and well involuted. In cases of uncertainty, an ultrasound examination may be needed to confirm a complete expulsion.

Care should be taken not to over-diagnose "failed medical management"; for instance, a "thickened endometrium" is not a good predictor of the need for surgery. A decision for surgical completion should be based on the clinical condition of the woman and not on the ultrasound picture. Surgical intervention is not recommended prior to 7 days

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after treatment unless medically necessary (i.e. for hemostatic or infection control).

At the follow-up appointment, providers should give contraceptive counseling and a suitable contraceptive method if desired. Future research on at-home follow up may eliminate the need for the follow-up visit at the health facility. If the abortion is not complete at the follow-up visit and the woman is clinically stable and willing to continue to wait for her uterus to empty, it is acceptable practice to give her another dose of misoprostol.

The regimen recommended in this chapter applies to misoprostol use in incomplete abortion when the uterine size is not larger than expected in a 12 week pregnancy; however, the length of amenorrhea prior to starting treatment may be longer than 12 weeks.

Misoprostol can be used when the uterus is larger than a 12 weeks' gestation; however, the regimen is different. Typically, lower doses are needed for efficacy and safety when the uterus is larger [26]

## 6. Effects and side effects

Prolonged or serious side effects are rare

## 6.1. Bleeding

After administration of misoprostol, bleeding typically lasts up to two weeks with additional days of spotting that can continue until the next menstrual period. Women should be told to expect to bleed heavily for 3–4 days and instructed to contact a provider if any of the following occur: (1) if she soaks more than two extra large ("maxi") sanitary pads or local equivalent per hour for two consecutive hours, (2) if she suddenly experiences heavy bleeding after bleeding has slowed or stopped for several days, (3) if she has bled like a normal period, but continuously for weeks and begins to feel dizzy or light-headed.

## 6.2. Cramping

Cramping usually starts within the first few hours but may begin as early as 10 min after misoprostol administration. The pain may be stronger than that experienced during a regular period. Non-steroidal anti-inflammatory drugs (NSAIDs) or other analgesia can be used for pain relief without affecting the success of the method [27].

## 6.3. 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.

## 6.4. 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.

## 6.5. Diarrhea

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

#### 6.6. Skin rash

Occasionally skin rash occurs after administration of misoprostol and should resolve within several hours.

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#### Conflict of interest

The authors do not have any conflict of interest.

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