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REVIEW ARTICLE

Misoprostol for the termination of pregnancy with a live fetus at 13 to 26 weeks

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Recommended Dosage

13–22 weeks: vaginal
misoprostol 400 µg every
3 hours (max. 5 doses)

KEYWORDS

Misoprostol;
Termination of pregnancy;
Second trimester

Abstract

A combination of mifepristone and misoprostol is the regimen of choice for termination of pregnancy between 13 to 26 weeks. In many countries, mifepristone is still not available, and misoprostol has to be used alone. Many misoprostol-alone regimens have been reported in the literature with apparently good results. Most of the trials were conducted in pregnancies between 13 and 22 weeks. For this gestational period, we recommend the regimen of 400 µg of vaginal misoprostol every 3 h up to 5 doses, as it appears to be effective without excessive side effects or complications. There is inadequate data to recommend a regimen for the gestational period of 23 to 26 weeks but it is advisable to reduce the dose and frequency of administration of misoprostol. Common side effects of misoprostol-induced termination of pregnancy include gastrointestinal side effects, abdominal cramps, bleeding, fever and chills. Complications may include infection or rarely rupture of uterus.

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1. Introduction

Termination of pregnancy between 13 to 26 weeks constitutes about 10%–15% of all pregnancy terminations, but is

responsible for two-thirds of all major complications and 50% of all abortion-related maternal deaths [1]. The incidence of complications increases with the increase in gestational age. Termination of pregnancy between 13 and 26 weeks can be performed either by surgical or medical methods.

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The medical method recommended by the World Health Organization (WHO) [2] and the Royal College of Obstetricians and Gynaecologists (RCOG) [3] is the regimen of mifepristone followed by a prostaglandin analogue. When

this combined regimen is used, the induction to abortion interval (the interval between the first dose of prostaglandin to the expulsion of the products of conception) is significantly shorter than when prostaglandins are used alone.

Due to the limited access of mifepristone and greater costs of the combined method, medical abortions in the second trimester are most commonly performed by the administration of prostaglandin analogues, using a variety of doses by various routes [4]. Vaginal misoprostol has been shown to be associated with a shorter mean induction–abortion interval, compared with intra-amniotic PGF₂ α [5,6] or concentrated oxytocin infusions plus vaginal PGE₂ [7]. A recent meta-analysis of randomized trials comparing gemeprost with misoprostol (which included various dosage regimens of misoprostol) showed that vaginal misoprostol compared with gemeprost was associated with reduced need for narcotic analgesia and surgical evacuation of the uterus [8]. No other statistically significant differences were observed. Further, in a study comparing 400 μ g of vaginal misoprostol every 3 h with 1 mg of gemeprost every 3 h, the induction abortion interval was significantly shorter in the vaginal misoprostol group [9]

The laws governing termination of pregnancy differ widely among countries. In many countries, there is a limit on the gestational age beyond which termination of pregnancy is not allowed. Health care providers should be aware of the limits in their own countries.

It should also be noted that fetuses aborted after 20 weeks may show signs of life after abortion. For these terminations consideration may be given to inject intra-amniotic digoxin or potassium chloride into the fetal heart before initiation of medical abortion.

2. Contraindications

Allergy to misoprostol or hemodynamic instability.

3. Precautions

1. Presence of a uterine scar: Although there is no evidence that the presence of a previous cesarean section scar will increase the rate of complications [10–12], rupture of the uterus has been reported [13–15]. Therefore, misoprostol should be used with caution in these women – indeed it may be safer to start with a lower dose of misoprostol.
2. Signs of intrauterine infection or sepsis: Consideration may be given to the use of surgical evacuation under antibiotic cover. However, in centers where expertise for surgical evacuation in the second trimester is not available, a medical method may be used after starting antibiotic treatment.

4. Recommended regimens

4.1. 13–22 weeks

400 μ g of vaginal misoprostol every 3 h up to 5 doses [9,16]. Studies have shown that the additional use of mifepristone shortens the induction–abortion interval and reduces the

amount of prostaglandins required for the abortion [17,18]. A randomized trial showed that when the women were given mifepristone, and the first dose of misoprostol was given vaginally, the subsequent doses could be given orally without affecting the efficacy [19]. It has also been shown that 200 mg of mifepristone is as effective as 600 mg in termination of pregnancy in the second trimester [20]. Therefore, when mifepristone is available, 200 mg of mifepristone is given orally and 36–48 h later 800 μ g of misoprostol is administered vaginally followed by 400 μ g orally every 3 h up to 4 doses [3]. Further doses do not need to be given after complete expulsion of fetus and placenta.

4.1.1. Route

Randomized trials comparing oral and vaginal misoprostol showed that vaginal misoprostol is more effective than oral misoprostol in inducing abortion [21,22]. The incidence of side effects is also lower though more women prefer the oral route [21]. It is not yet known whether subsequent doses of misoprostol can be given orally without affecting its efficacy if a higher dose of vaginal misoprostol is given as the first dose. The sublingual administration of misoprostol has also been compared with vaginal misoprostol but it appeared to be less effective for this indication [23]. In summary, therefore, vaginal administration of misoprostol is more effective than other routes of administration and the incidence of side effects is lower.

4.1.2. Dose

A randomized trial compared three regimens of misoprostol-alone administration: (a) 400 μ g misoprostol 6-hourly (b) 200 μ g misoprostol 6-hourly and (c) 600 μ g misoprostol followed by 200 μ g misoprostol 6-hourly. Results showed that 6-hourly vaginal administration of 400 μ g misoprostol was the best regimen as it is more effective than 200 μ g regimen and the incidence of side effects is less than that of 600 μ g regimen [24].

4.1.3. Interval

Two randomized clinical trials showed that the induction–abortion interval with 3-hourly vaginal administration of 400 μ g of misoprostol is significantly shorter than 6-hourly administration without significant increase in side effects [16,25].

There are many regimens of misoprostol reported in the literature with apparently good results. The above regimens has been found to be effective without excessive side effects or complications. Lower doses of misoprostol or less frequent administration are also acceptable though the induction–abortion intervals may be longer.

4.2. 23–26 weeks

It should be noted that most of the studies for this indication were conducted at the gestational age of 13 to 22 weeks. There is inadequate data to make any recommendations on the dosage and regimen for termination of pregnancy between 23 to 26 weeks. Since the uterus becomes more sensitive to prostaglandins with increasing gestational age, it would be wise to reduce the dosage and frequency of administration.

5. Course of treatment

Because of the potential for heavy vaginal bleeding and serious complications, it is advisable to conduct second

trimester terminations of pregnancy in health care facilities where blood transfusion and access to emergency surgery (including laparotomy) are available.

At the initial evaluation, the woman should undergo a clinical assessment including history and clinical examination. The blood group including ABO and Rhesus typing should be checked. If the woman is Rhesus negative, 250–500 µg of anti-D immunoglobulin should be given intramuscularly [3]. Ultrasound examination is not necessary in the majority of women. It should be done when there is uncertainty about the diagnosis or gestational age.

Abortion may take place after any dose of misoprostol. With the regimen of a combination of oral mifepristone and vaginal misoprostol described above, the median induction–abortion interval is 5.9–6.6 h [22] and 97% of the women will abort within 24 h.

With the misoprostol alone regimen, the median induction abortion interval is 10–15 h and 80%–90% of the women will abort within 24 h [9,16,25].

Before each dose the woman should be examined to see if she has already aborted. If not, assess the frequency and strength of uterine contractions. The next dose may be deferred if there are strong and frequent uterine contractions (>3 contractions in 10 minutes).

After the fetus is aborted, the placenta is usually expelled within a short time. If the placenta is not delivered within 2 h, an infusion of 10 units oxytocin in 500 mL of normal saline at a rate of 20–30 drops/min may be given to help the expulsion of the placenta. After expulsion, the placenta should be examined to see whether it is complete. If the placenta is incomplete, evacuation of the uterus may be needed. If the placenta is not delivered after infusion of oxytocin, or the woman starts bleeding excessively, manual removal of the placenta may be required.

After abortion, the woman should be observed in the hospital for at least 4 h to monitor the vital signs and the amount of vaginal bleeding. If there is heavy vaginal bleeding, a careful speculum and pelvic examination should be performed to exclude the possibility of lacerations of the cervix. If there is no evidence of lacerations in the lower genital tract but the uterus is not contracting well, an oxytocin infusion may be given to stimulate the uterus to contract. If the bleeding persists despite the use of oxytocin infusion, the uterine cavity should be explored to see whether there are any retained products of conception.

During the recovery period in the hospital after the abortion, the woman should be provided with information on follow-up and contraception. All women should be followed up about two weeks after the abortion. The patient should be assessed for the amount of vaginal bleeding, and any signs of infection. The opportunity should be taken to discuss and advise on future methods of contraception. The contraceptive methods should be started as soon as possible.

If the woman fails to abort within 24 h after the first dose of misoprostol and there are no significant side effects, a second course of misoprostol can be given beginning at least 12 h after the last dose.

If the woman still fails to abort after the second course of misoprostol, other prostaglandins available in the center

may be tried to induce the abortion. Alternatively infusion of a high dose of oxytocin or dilatation and evacuation may be considered. Caution should be exercised in using a combination of prostaglandins and infusion of high doses of oxytocin as over stimulation of the uterus may lead to its rupture.

6. Side effects

6.1. Bleeding

The woman should be warned that bleeding and abortion might occur in the interval between the administration of mifepristone and misoprostol if mifepristone is used. They should come to the hospital if they develop significant vaginal bleeding or abdominal cramps. Most women however start bleeding after the administration of misoprostol and usually the amount of bleeding is not excessive. If heavy bleeding occurs, the patient should be assessed to exclude the possibility of retained products of conception, cervical tear or rupture of uterus. Heavy bleeding requiring transfusion was reported in less than 1% of women [26].

6.2. Abdominal cramps

Abdominal cramps usually develop after administration of misoprostol. They are due to uterine contractions, which are needed to abort the pregnancy. Appropriate selection of pain medications allows the woman to be awake and responsive, and minimizes her fear and discomfort. Non-steroidal anti-inflammatory drugs (NSAIDs) can be given every 4–8 h for pain relief without changing the effectiveness of the misoprostol [27]. Some women may require narcotic analgesics. Some centers may also use a paracervical block for pain relief. The analgesia requirement is significantly higher in younger women, those with more advanced pregnancies and those who require increased number of misoprostol doses, while women with previous live birth were significantly less likely to use analgesia [28].

6.3. Fever and chills

Fever and chills are fairly common after administration of misoprostol. With 400 µg every 3 h, fever more than 38 °C was reported in 30%–50% of women [9,16]. These do not indicate that the woman has an infection and antibiotics are not required unless there are other clinical signs of infection. The fever usually subsides 24 h after the last dose of misoprostol. Antipyretics may be given if necessary.

6.4. Nausea, vomiting and diarrhea

These are quite common side effects after administration of misoprostol. If there is significant vomiting, the women may be given anti-emetics. These usually resolve within 24 h of the last dose.

7. Complications

7.1. Rupture of uterus

This is a rare but serious complication in termination of pregnancy between 13 to 26 weeks using medical methods

[5–10], and it may occur even in women without a uterine scar. The woman may develop heavy vaginal bleeding and severe abdominal pain. Sometimes the woman may go into shock suddenly. Women with uterine rupture will require immediate surgical intervention.

7.2. Infection

Infection may occur with any induced abortions. About 3% of women required antibiotic treatment because of suspected infections in a large series of over 1000 women undergoing termination of pregnancy in the second trimester [26]. Symptoms and signs of infection may occur after abortion. The patient develops low abdominal pain associated with fever and chills. There may also be foul-smelling vaginal discharge or increased vaginal bleeding. There may also be cervical excitation pain and the uterus may be tender. The patient may be managed with the administration of antibiotics. If there is evidence that the abortion is incomplete, surgical evacuation of the uterus will be necessary.

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Conflict of interest

The authors do not have any conflict of interest.

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