

MARCH 2018



Clinical Updates in Reproductive Health

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Ipas works globally to improve access to safe abortion and contraception so that every woman and girl can determine her own future. Across Africa, Asia and Latin America, we work with partners to make safe abortion and contraception widely available, to connect women with vital information so they can access safe services, and to advocate for safe, legal abortion.

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MARCH 2018

Clinical Updates in Reproductive Health

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LIST OF ABBREVIATIONS

ACOG – American College of Obstetricians and Gynecologists

CI – confidence interval

D&E – dilatation and evacuation

FIGO – International Federation of Gynecology and Obstetrics

GRADE – Grading of Recommendations Assessment, Development and Evaluation

hCG – human chorionic gonadotropin

IM – intramuscular

IUD – intrauterine device

IV – intravenous

Kg – kilogram

LMP – last menstrual period

Mcg – microgram

Mg – milligram

mL – milliliter

MOOSE – Meta-analysis of Observational Studies in Epidemiology

MVA – manual vacuum aspirator

NSAID – nonsteroidal anti-inflammatory drug

PRISMA – Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RCOG – Royal College of Obstetricians and Gynaecologists

RR – relative risk

SC – subcutaneous

WHO – World Health Organization

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INTRODUCTION

Ipas's *Clinical Updates in Reproductive Health* contain up-to-date, evidence-based clinical recommendations on comprehensive abortion care, with new topics and resources added regularly. The *Clinical Updates in Reproductive Health* provide concise, easy-to-read information about abortion care, combining the latest evidence with lessons learned from health professionals globally to produce relevant clinical recommendations.

Who should use this resource

First published in 2013, the *Clinical Updates in Reproductive Health* were designed originally as an up-to-date, evidence-based clinical resource for Ipas staff. Over time, the publication has also been of use to:

- **clinicians** providing abortion care
- **clinical and public health professionals** working on patient care protocols in public health systems and the private sector
- **safe abortion advocates and policymakers** creating laws and policies that fulfill women's and girls' right to health

What's new in this revision

In this edition of the *Clinical Updates in Reproductive Health*, you will find updated, evidence-based recommendations on more than 40 abortion care topics. During the 2018 update we systematized our evidence review and revision process and improved transparency of our recommendation formation. For example:

- **We strengthened our evidence gathering and evaluation**, employing more robust standards to our systematic reviews of the literature and their documentation.
- **We built an ongoing data library** composed of evidence tables and annotated bibliographies. We will continue to build this library with future revisions of the Clinical Updates.
- **We introduced more oversight** by piloting a systematized peer review process, expanding the role of our regionally representative Clinical Advisory Group, and ensuring our recommendations are applicable in varied settings in which Ipas works.

We are launching an online version of the *Clinical Updates* in 2018 (www.ipas.org/clinicalupdates) that offers easy-to-use drop-down menus to help readers navigate quickly to the information they need. This online version as well as our print/PDF version will also be available in Spanish, French and Portuguese.

We have also updated a number of our clinical tools and job aids, which are drawn from the evidence and recommendations contained in the *Clinical Updates in Reproductive Health*, and these are also available online at www.ipas.org/clinicalupdates.

MAKING IPAS RECOMMENDATIONS

Ipas strives to integrate the best scientific evidence into our clinical programs. This section documents the methodology Ipas uses to make its clinical recommendations.

Using evidence to support recommendations

Clinical recommendations are based on relevant published, peer-reviewed evidence. For each clinical topic contained in the *Clinical Updates in Reproductive Health*, we conduct systematic reviews of the literature using a methodology drawn from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines (Moher, Liberati, Tetzlaff, Altman, & the PRISMA Group, 2009; Stroup, Berlin, & Morton, 2000).

Process for making recommendations

Ipas applies the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to its recommendation formation (Guyatt et al., 2008b). The GRADE system provides a framework to evaluate the quality of the available evidence, and to translate that evidence into a context-appropriate recommendation. For every recommendation in the *Clinical Updates*, both the quality of evidence and the strength of the recommendation based on that evidence are reported.

QUALITY OF EVIDENCE

Sources of clinical evidence range from well-designed large clinical studies that have minimized bias to uncontrolled clinical observations, case series or reports. When there is no available evidence, expert opinion may be used. In the GRADE system, the quality of evidence related to a specific clinical topic is defined as both the extent to which one can be confident that an estimate of effect is correct, and the extent to which the evidence relates to the specific context in which it is being applied (Guyatt et al., 2008a). When assessing the quality of evidence, the following criteria are considered (Guyatt et al., 2008a):

- study design
- study limitations and the risk of bias
- consistency of the results across available studies
- precision of the results (wide or narrow confidence intervals)
- applicability with respect to populations, interventions and settings where the proposed intervention may be used
- likelihood of publication bias

Quality of evidence determinations are reported as follows (Balslem et al., 2011):

- A **high** grade: we are very confident that the true effect lies close to the estimate of the effect.
- A **moderate** grade: we are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- A **low** grade: confidence in the effect estimate is limited. The true effect may be substantially different from the estimate.
- A **very low** grade: we have very little confidence in the estimate of the effect. The true effect is likely to be substantially different from the estimate.

For example, randomized trials are initially given a high grade, while observational studies are initially labeled as low quality.

STRENGTH OF RECOMMENDATION

Strength of recommendation is defined as the extent to which one can be confident that the desirable consequences of a recommendation outweigh its undesirable consequences (Andrews et al., 2013). Desirable effects include improved health outcomes, less burden for providers and health systems, and cost savings. Undesirable effects include harm to patients, inconvenience or hassle, and increased resource use.

- **Strong** recommendations are made when the desirable effects of a recommended intervention clearly outweigh the undesirable effects (Guyatt et al., 2008b). Most informed people would make the recommended choice for an intervention (Andrews et al., 2013).
- **Weak** recommendations are made when evidence suggests that desirable effects of a recommended intervention probably outweigh the undesirable effects, but there are

small benefits or benefits that may not be worth the costs (Guyatt et al., 2008b). While most informed people would choose the recommended course of action, a substantial number would not (Andrews et al., 2013).

Can you have a strong recommendation based on low-quality evidence?

Answer: Yes. There are many factors that influence the strength of a recommendation.

For example, although there is limited evidence about bimanual examination prior to uterine aspiration, several factors increase the strength of the recommendation that bimanual examination should be performed by the clinician who will perform the procedure: 1) the potential benefit to patients, 2) the low risk of harm associated with bimanual examination, and 3) its low cost as well as potential savings when complications are avoided. All or almost all providers and women, when informed of the balance between desirable and undesirable effects, would choose to include a bimanual examination before uterine procedures.

Maintaining the *Clinical Updates*

The *Clinical Updates* are revised annually. The “last reviewed” date for each topic indicates all relevant published literature up to that date has been considered and included where appropriate. New topics and proposed revisions to the document come from end-users, a regionally representative Clinical Updates Advisory Group, and observations made during routine quality monitoring of clinical services in Ipas-supported programs. The Lead Writer, Medical Editors and Medical Director review all proposed updates. New recommendations or substantially revised recommendations may undergo an internal peer review process. The revision process, including systematic review of literature, documentation of the body of evidence, generation and revision of recommendations, and resultant changes to the *Clinical Updates in Reproductive Health*, is documented and archived.

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SUMMARY OF RECOMMENDED MEDICAL ABORTION REGIMENS

1



Medical abortion with mifepristone and misoprostol

- **Before 10 weeks gestation (70 days since last menstrual period (LMP)):**
 - Mifepristone 200mg orally
 - Misoprostol 800mcg buccally, sublingually or vaginally 1-2 days after mifepristone
- **10-13 weeks gestation:**
 - Mifepristone 200mg orally
 - Misoprostol 800mcg vaginally 1-2 days after mifepristone, then misoprostol 400mcg vaginally or sublingually every 3 hours until expulsion
- **At or after 13 weeks gestation:**
 - Mifepristone 200mg orally
 - Misoprostol 400mcg buccally, sublingually or vaginally 1-2 days after mifepristone, then every 3 hours until fetal and placental expulsion

Medical abortion with misoprostol only

- **Before 13 weeks gestation:**
 - Misoprostol 800mcg sublingually or vaginally every 3 hours until expulsion
- **At or after 13 weeks gestation:**
 - Misoprostol 400mcg vaginally or sublingually every 3 hours until fetal and placental expulsion
 - Vaginal dosing is more effective than sublingual dosing for nulliparous women

Misoprostol for incomplete or missed abortion (postabortion care)

- **Less than 13 weeks uterine size:**
 - Incomplete abortion:
 - Misoprostol 600mcg orally in a single dose or 400mcg in a single dose sublingually or (in the absence of vaginal bleeding) vaginally
 - Missed abortion:
 - Misoprostol 800mcg vaginally or 600mcg sublingually every 3 hours until expulsion, for a maximum of 3 doses
- **13 weeks or larger uterine size:**
 - Misoprostol at least 200mcg buccally, sublingually or vaginally every 6 hours until expulsion
 - Pretreatment with mifepristone 200mg orally 1-2 days before misoprostol may decrease time from induction to expulsion
 - Misoprostol-only or mifepristone-misoprostol regimen for induced abortion at or after 13 weeks gestation can also be used

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2

UTERINE EVACUATION: REPLACE SHARP CURETTAGE WITH ASPIRATION OR MEDICATIONS

Recommendation

Vacuum aspiration or medical abortion should replace sharp curettage (also known as dilation and curettage (D&C)) for the treatment of abortion and postabortion care.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: October 31, 2017

The World Health Organization (WHO) and the International Federation of Gynecology and Obstetrics (FIGO) state that vacuum aspiration or medication regimens should replace sharp curettage (FIGO, 2011; WHO, 2012). In places where no uterine evacuation services exist, vacuum aspiration and medical abortion should be introduced.

A Cochrane review shows that vacuum aspiration is as effective as sharp curettage in treating incomplete abortion, and reduces procedure time, blood loss and pain (Tuncalp, Gulmezoglu, & Souza, 2010). In a retrospective case series of 80,437 women seeking induced abortion, vacuum aspiration was associated with less than half the rate of major and minor complications compared to sharp curettage (Grimes, Schulz, Cates Jr, & Tyler, 1976). A more recent series, including more than 100,000 abortion procedures, found that sharp curettage performed alone or in combination with vacuum aspiration was significantly more likely to be associated with complications, particularly incomplete abortion, than vacuum aspiration without curettage (Sekiguchi, Ikeda, Okamura, & Nakai, 2015).

Multiple studies on induced abortion and postabortion care have shown that because vacuum aspiration can be performed in an outpatient setting by physicians or midlevel providers without general anaesthesia, the costs to both the health system and women are significantly less (Benson, Okoh, KrennHrubec, Lazzarino, & Johnston, 2012; Choobun, Khanuengk-
itkong, & Pinjaroen, 2012; Farooq, Javed, Mumtaz, & Naveed, 2011; Johnston, Akhter, & Oliveras, 2012).

Although no trials exist comparing sharp curettage to medical management of induced, incomplete or missed abortion, the safety and tolerability of medical regimens for uterine evacuation are well documented and appear as effective as vacuum aspiration in the management of incomplete abortion (Kulier et al., 2011; Neilson, Gyte, Hickey, Vazquez, & Dou, 2013).

The use of sharp curettage to manage incomplete or missed abortion may be associated with Asherman's syndrome (intrauterine adhesions). A retrospective review from one ter-

tiary care center reported on 884 women who underwent sharp curettage, manual vacuum aspiration or misoprostol for early pregnancy failure (Gilman Barber, Rhone, & Fluker, 2014). In follow-up, 1.2% of women managed with sharp curettage were found to have Asherman's syndrome (6 out of 483 women), while no cases were found in the 401 women managed by manual vacuum aspiration or misoprostol.

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3

PROPHYLACTIC ANTIBIOTICS FOR VACUUM ASPIRATION AND DILATATION AND EVACUATION

Recommendation

- Administer prophylactic antibiotics prior to vacuum aspiration and dilatation and evacuation (D&E).
- Where antibiotics are unavailable, uterine evacuation procedures should still be offered.
- Administer treatment doses of antibiotics to those with signs or symptoms of sexually transmitted infection; partners of individuals with sexually transmitted infections also require treatment. Treatment should not delay uterine evacuation.

Strength of recommendation

Strong

Quality of evidence

- Vacuum aspiration: High
- D&E: Very low
- Incomplete or missed abortion: Very low

Last reviewed: November 16, 2017

Risk of infection

When objective measures are used to diagnose postabortion infection following vacuum aspiration performed before 13 weeks gestation, the infection rate ranges from 0.01-2.44% (Achilles & Reeves, 2011). In studies performed in the United States prior to routine use of antibiotic prophylaxis, reported rates of infection following D&E ranged from 0.8-1.6% (Achilles & Reeves, 2011).

Evidence for antibiotic prophylaxis

A Cochrane meta-analysis of 19 randomized controlled clinical trials showed that administration of prophylactic antibiotics at the time of vacuum aspiration for induced abortion before 13 weeks gestation significantly reduces the risk of infection (Low, Mueller, Van Vliet, & Kapp, 2012). Evidence to support use of prophylactic antibiotics before D&E is limited; however, because of the demonstrated benefit of prophylactic antibiotics before vacuum aspiration, the World Health Organization (WHO, 2014), Society of Family Planning (Achilles & Reeves, 2011), American College of Obstetricians and Gynecologists (ACOG, 2016) and Royal College of Obstetricians and Gynaecologists (RCOG, 2015) recommend prophylactic antibiotics for all women undergoing vacuum aspiration or D&E.

Four randomized trials have examined the use of prophylactic antibiotics before vacuum aspiration or curettage for incomplete or missed abortion (postabortion care) (Prieto, Eriksen, & Blanco, 1995; Ramin et al., 1995; Seeras, 1989; Titipant & Cherdchoogiet, 2012). None

of these studies found a statistically significant difference in postabortion infection rates between the groups that received antibiotic prophylaxis and those that received placebo or no treatment, however all studies suffered from serious methodologic flaws that limit the conclusions that can be drawn from them. Given the paucity of higher-quality evidence, and data indicating the benefit of routine prophylactic antibiotics before vacuum aspiration for induced abortion, it is prudent to administer prophylactic antibiotics for vacuum aspiration when used for postabortion care (Achilles & Reeves, 2011; RCOG, 2016).

Giving prophylactic antibiotics is more effective than screening all women and treating only those with evidence of infection (Levallois & Rioux, 1988). The inability to provide antibiotics should not limit access to abortion (WHO, 2014), as the overall risk of infection with abortion procedures is very low.

Regimen

Many antibiotic regimens for abortion prophylaxis have been studied, but the ideal antibiotic, dose and timing has not yet been established (Achilles & Reeves, 2011; Low et al., 2012). Tetracyclines (doxycycline) and nitroimidazoles (metronidazole and tinidazole) are commonly used because of their efficacy, oral availability, low cost and low risk of allergic reactions (Achilles & Reeves, 2011; O'Connell, Jones, Lichtenberg, & Paul, 2008). Although studies of abortion are limited (Caruso et al., 2008), evidence from the obstetrical (Costantine et al., 2008), gynecologic (Mittendorf et al., 1993) and general surgery (Classen et al., 1992) literature supports the practice of giving antibiotics before the procedure to decrease the risk of infection. Antibiotic regimens do not need to be continued after the abortion (Achilles & Reeves, 2011; Caruso, et al., 2008; Levallois & Rioux, 1988; Lichtenberg & Shott, 2003).

The following table lists regimens recommended by professional organizations based on clinical evidence and expert opinion.

COMMON REGIMENS	RECOMMENDER
Doxycycline 200mg orally before the procedure or Azithromycin 500mg orally before the procedure or Metronidazole 500mg orally before the procedure	Planned Parenthood Federation of America (PPFA, 2016)
Doxycycline 200mg orally no more than 2 hours before the procedure or Azithromycin 500mg orally no more than 2 hours before the procedure	Royal College of Obstetricians and Gynaecologists (RCOG, 2015)

Antibiotics with osmotic dilators

Although not well studied, cervical preparation with osmotic dilators does not appear to increase the risk of infection (Fox & Krajewski, 2014; Jonasson, Larsson, Bygdeman, & Forsum, 1989). Some providers start antibiotics at the time of osmotic dilator placement, but there are no studies evaluating the benefit of this practice (O'Connell et al., 2008).

Therapeutic antibiotics

Women at high risk should be screened for sexually transmitted infections in addition to receiving prophylactic antibiotics. Women who have signs and symptoms of sexually transmitted infection should be provided abortion services without delay and receive appropriate antibiotic treatment according to evidence-based regimens (WHO, 2014; WHO, 2005). Partners of women with sexually transmitted infections also require treatment (WHO, 2016).

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PROPHYLACTIC ANTIBIOTICS FOR MEDICAL ABORTION

Recommendation

- Routine use of antibiotics is not recommended for women undergoing medical abortion.
- Administer treatment doses of antibiotics to those with signs or symptoms of sexually transmitted infection. Partners of individuals with sexually transmitted infections also require treatment. Treatment should not delay medical abortion.

Strength of recommendation

Weak

Quality of evidence

Very low

Last reviewed: November 16, 2017

Risk of infection

The overall risk of infection found in prospective studies of medical abortion using mifepristone and a prostaglandin before 13 weeks gestation is approximately 0.01-0.5% (Achilles & Reeves, 2011; Chen & Creinin, 2015; Upadhyay et al., 2015). Serious infections requiring hospitalization are very uncommon, with rates in large retrospective studies from the United States ranging from 0.03% to 0.09% (Fjerstad, Trussel, Sivin, Lichtenberg, & Cullins, 2009; Henderson, Hwang, Harper, & Stewart, 2005). Infection rates for medical abortion at or after 13 weeks gestation are more difficult to determine, as fever is a common side effect of prostaglandin use. Available data report infection rates of 1-3% following medical abortion at or after 13 weeks gestation (Achilles & Reeves, 2011).

Infectious mortality

Nine cases of fatal *Clostridium* sepsis occurred in North America following mifepristone and misoprostol medical abortion before 13 weeks gestation (Cohen et al., 2007; Fischer et al., 2005; Meites, Zane, & Gould, 2010; Sinave, Le Templier, Blouin, Leveille, & Deland, 2002). One death from group A streptococcus has been reported in Australia and one death from *Clostridium sordelli* has been reported in Portugal (Reis et al., 2011) in women who used mifepristone and misoprostol. The overall mortality rate from infection related to medical abortion remains very low at 0.58 per 100,000 medical abortions (Meites et al., 2010).

Prophylactic antibiotics

There have been no randomized controlled trials examining the effect of antibiotic prophylaxis on medical abortion outcomes (Achilles & Reeves, 2011; Low, Mueller, Van Vliet, & Kapp, 2012). Given the large number of women who would need to take antibiotics to prevent a single infection, coupled with the expense and side effects of antibiotics, the American College of Obstetricians and Gynecologists (ACOG, 2014), the Society of Family Planning (Achilles & Reeves, 2011), the Royal College of Obstetricians and Gynaecologists

(RCOG, 2015) and the World Health Organization (WHO, 2014) do not recommend routine antibiotic use prior to medical abortion.

Therapeutic antibiotics

Women at high risk should be screened for sexually transmitted infections. Women who have signs and symptoms of sexually transmitted infection should be provided abortion services without delay and receive appropriate antibiotic treatment according to evidence-based regimens (WHO, 2014; WHO, 2005). Partners of women with sexually transmitted infections also require treatment (WHO, 2016).

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MEDICAL ABORTION CONTRAINDICATIONS AND PRECAUTIONS**Recommendation**

	MIFEPRISTONE AND MISOPROSTOL REGIMEN	MISOPROSTOL-ONLY REGIMEN
Contraindications	Previous allergic reaction to mifepristone or misoprostol Known or suspected ectopic pregnancy Inherited porphyria Chronic adrenal failure	Previous allergic reaction to misoprostol Known or suspected ectopic pregnancy
Precautions	Intrauterine device (IUD) in place Serious/unstable health problems, including but not limited to hemorrhagic disorders, heart disease and severe anemia Severe uncontrolled asthma or long-term corticosteroid therapy	IUD in place Serious/unstable health problems, including but not limited to hemorrhagic disorders, heart disease and severe anemia

Strength of recommendation

Weak

Quality of evidence

Graded for each specific contraindication or precaution below

Last reviewed: January 9, 2018**Definitions**

Contraindications: If a woman has any of these specific conditions, she should not be offered medical abortion with the specified regimen. Vacuum aspiration, dilatation and evacuation or treatment for ectopic pregnancy should be offered, as appropriate.

Precautions: If a woman has any of these specific conditions, medical abortion with the specified regimen may incur higher risks than normal. The risks, benefits and alternatives to medical abortion must be considered. Medical abortion provision to women with these conditions may require a higher degree of clinical judgment, skill and monitoring. Referral to a higher-level facility or alternative treatment may be appropriate.

Contraindications

Previous allergic reaction to one of the drugs involved: Allergic reactions have been reported after use of mifepristone and misoprostol (Bene et al., 2014; Cruz et al., 2009;

Hauseknecht, 2003; Sahraei, Mirabzadeh, & Eshraghi, 2016; Schoen, Campbell, Maratas, & Cheung, 2014). *Quality of evidence: High*

Known or suspected ectopic pregnancy: Mifepristone and misoprostol do not treat ectopic pregnancy, and use of the medications may delay diagnosis and treatment of this life-threatening condition. *Quality of evidence: High*

Inherited porphyria: Porphyrias are rare metabolic disorders in which genetic mutations alter the body's generation of heme. Theoretically, mifepristone could exacerbate the manifestation of porphyria (Ventura, Cappellini, & Rochi, 2009). *Quality of evidence: Low. No human studies exist, but animal models exhibit the effect of mifepristone* (Cable, Pepe, Donohue, Lambrecht, & Bonkovsky, 1994).

Chronic adrenal failure: Mifepristone is a glucocorticoid receptor antagonist (Spitz & Bardin, 1993). Mifepristone blocks negative feedback mechanisms that control cortisol secretion. In women with adrenal insufficiency on long-term corticosteroid therapy, mifepristone exposure may exacerbate the underlying condition (Sitruk-Ware & Spitz, 2003). *Quality of evidence: Very low. There are no data on mifepristone use in pregnant women with adrenal insufficiency, but there is experimental and animal data to support the recommendation.*

Precautions

IUD in place: A woman who is pregnant with an IUD is at significantly elevated risk of ectopic pregnancy (Barnhart, 2009) and must be evaluated for the presence of ectopic pregnancy. If the pregnancy is found to be intrauterine, the IUD should be removed before starting medical abortion due to the theoretical risk of uterine perforation from contractions during medical abortion and the potential risk of infection (Danco, 2016; Davey, 2006). *Quality of evidence: Very low. There are no studies to verify whether having an IUD in place poses actual risks during medical abortion.*

Serious medical problems: Medical abortion studies tend to exclude women with severe anemia or serious medical problems (Christin-Maitre, Bouchard, & Spitz, 2000; Sitruk-Ware & Spitz, 2003). One case report (Hou, 2016) documents successful medical abortion in a patient with mild hemophilia; this patient received specialized, additional medication to minimize bleeding risk. A second case report (Mazhar, Sultana, & Akram, 2018) documents a case of misoprostol-induced acute coronary syndrome which resolved completely after appropriate treatment and discontinuation of misoprostol. Whether to provide medical abortion to women with medical conditions will depend on clinical judgment, monitoring and options available for safe abortion care. *Quality of evidence: Very low*

Severe uncontrolled asthma or long-term corticosteroid therapy: Mifepristone is a glucocorticoid receptor antagonist (Spitz & Bardin, 1993). Mifepristone blocks negative endocrine feedback mechanisms that control cortisol secretion. In women on long-term corticosteroid therapy for severe or uncontrolled asthma, mifepristone may exacerbate the underlying condition (Sitruk-Ware & Spitz, 2003). There are no direct studies of medical abortion among women on corticosteroid treatment, but one review suggested that increasing the dose of the steroid medications can counteract the cortisol blunting effect of mifepristone (Davey, 2006).

Medical abortion in asthmatic women requiring systemic corticosteroids has not been studied as giving mifepristone to such women risks asthma exacerbation. One review suggests using a high level of caution when giving mifepristone to such women and only doing so if the asthma is well-controlled (Davey, 2006). The glucocorticoid dose should be increased for several days before and after mifepristone. Other experts recommend that women with

severe, poorly controlled asthma who are on long-term corticosteroids not take mifepristone due to the life-threatening nature of acute asthma exacerbation (Christin-Maitre et al., 2000; Creinin & Gemzell Danielsson, 2009; Sitruk-Ware, 2006).

Inhaled corticosteroids for asthma are not systemically absorbed and are not a contraindication to mifepristone. Some experts recommend that mifepristone and misoprostol should be available to women with asthma who are not on long-term systemic steroids (Creinin & Gemzell Danielsson, 2009). *Quality of evidence: Very low*

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MISOPROSTOL PRODUCT QUALITY

6



Recommendation

- Providers should track medical abortion success rates to ensure they are using an effective misoprostol product.
- If possible, purchase misoprostol in double-aluminum blister packs, keep the misoprostol in its original packaging and check the integrity of packaging before use.
- Store misoprostol in a cool, dry place.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: October 26, 2017

Manufacture of misoprostol

Good Manufacturing Practice is a system for ensuring medications are consistently produced according to quality standards (World Health Organization [WHO], 2014). There are at least 30-40 manufacturers of misoprostol worldwide, and some manufacturers subcontract production of the drug, which makes the enforcement of Good Manufacturing Practice and the assurance of quality across all brands difficult (Hall & Tagontong, 2016). Misoprostol brands approved by the European Union or the United States Food and Drug Administration conform to Good Manufacturing Practice and are high quality. Exposure to heat and humidity during manufacturing, packaging and storage may compromise the quality of misoprostol (Cayman Chemical, 2012). If misoprostol degrades, it may lead to decreased success rates with medical abortion and unsuccessful treatment of incomplete abortion and postpartum hemorrhage.

A 2016 study analyzed 215 misoprostol samples from countries all over the world (Hall & Tagontong, 2016). When samples were tested for content and purity, 5% contained more misoprostol than expected (110-121% of labeled content, to allow for degradation), 55% were within specification (90-100% of labeled content), and 40% were below specification (less than 90% of labeled content). Of the 85 samples that were below specification, 14 contained no misoprostol at all.

Three factors influence misoprostol integrity:

- impact of moisture at all stages
- manufacture and quality of the active pharmaceutical ingredient
- packaging

Clinic use and storage

Even misoprostol manufactured in high-quality conditions and packaged well can become inactive if it is shipped or stored in conditions that expose it to heat or humidity for prolonged periods of time. Misoprostol is stable when stored properly in room temperature conditions (25°C and 60% humidity). There have not been large field studies on the stability of misoprostol when stored in tropical climates, but laboratory studies have shown that misoprostol is less stable when exposed to moisture or heat (Chu, Wang, Pang, & Rogers, 2007; WHO, 2009).

Misoprostol packaged in double-aluminum blister packs (aluminum on top and bottom) retains the most active ingredient; after one year, 100% of pills packaged in plastic and single-aluminum blister packs will degrade, compared to 28% of misoprostol packaged in double-aluminum blister packs (Hall & Tagontong, 2016). The integrity of the double-aluminum blister packs must be preserved to maintain drug potency. If the packaging is inadvertently opened, even in normal room-temperature conditions, the tablets' potency degrades within 48 hours and continues to degrade over time (Berard et al., 2014).

Quality assurance

If providers notice a decrease in medical abortion success rates from expected baseline, they should discard the lot of misoprostol being used and start a new lot. Providers should consult with each other to determine which local misoprostol brands are most effective. Store misoprostol in dry conditions at temperatures at or below 25°C (77°F) (Pfizer, 2016).

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PAIN MANAGEMENT FOR MEDICAL ABORTION BEFORE 13 WEEKS GESTATION

7



Recommendation

- Always offer pain medication to women undergoing medical abortion.
- Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen are recommended and provide similar relief whether taken prophylactically or at the time cramping begins.
- Narcotic analgesics and non-pharmacologic pain management measures may be helpful.
- Paracetamol should not be used unless an allergy or contraindication to NSAIDs exists.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: October 25, 2017

Pain during medical abortion before 13 weeks gestation

Pain is the most commonly reported side effect of medical abortion (Fiala et al., 2014). In one study of 6,755 women using medical abortion up to 63 days gestation, 78.4% reported moderate or severe pain and cramping (Goldstone, Michelson, & Williamson, 2012). Similarly, a 2006 systematic review of five large British and American case series of analgesia use during medical abortion concluded that 75% of women experience pain requiring narcotic analgesia (Penney, 2006). Patient characteristics associated with more pain include increasing gestational age, younger patient age, nulliparity, no previous vaginal deliveries, and history of dysmenorrhea (Suhonen, Tikka, Kivinen, & Kauppila, 2011; Teal, Dempsey-Fanning, & Westhoff, 2007; Westhoff, Dasmahapatra, Winikoff, & Clarke, 2000).

There are few trials assessing effectiveness of pain management strategies during medical abortion before 13 weeks gestation. Neither pain nor its treatment are systematically reported in clinical trials of medical abortion; where these data are reported, multiple regimens and treatment protocols have been used, rendering them difficult to compare (Fiala et al., 2014; Jackson & Kapp, 2011).

Medications for pain management

Two small randomized controlled trials indicate that ibuprofen is more effective than placebo (Avraham, Gat, Duvdevani, Haas, & Frenkel, 2012) or acetaminophen (Livshits et al., 2009) in relieving medical abortion pain in women with pregnancies of less than seven weeks gestation. Pre-treatment with ibuprofen is no better for pain management than treatment once cramping starts (Raymond et al., 2013). Narcotic analgesics are another option for pain

control, although their effectiveness and the optimal drug, dose and timing is not known. One potential strategy is to provide women with NSAIDs and narcotic analgesics and advise them to take NSAIDs once cramping starts, continue to use NSAIDs as needed, and utilize narcotic analgesics as an adjunctive treatment.

Non-pharmacologic pain management

There are no comparative trials evaluating the benefit of non-pharmacologic pain management strategies for medical abortion before 13 weeks gestation. However, experts recommend adjunctive non-pharmacologic measures to improve women's comfort during a medical abortion, including thorough education about expected pain and bleeding (Teal, Dempsey-Fanning, & Westhoff, 2007), a supportive environment and application of a heating pad or hot water bottle to the lower abdomen (Akin, et al., 2001). These modalities are to be employed in addition to—not as substitutes for—pain medications.

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PAIN MANAGEMENT FOR MEDICAL ABORTION AT OR AFTER 13 WEEKS GESTATION

Recommendation:

- Always offer pain medication and nonpharmacologic pain management measures to women undergoing medical abortion.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended for all patients and should be initiated with misoprostol.
- Narcotic analgesics and anxiolytics should be offered in addition to NSAIDs.
- Regional anesthesia and patient-controlled anesthesia may be offered where available.

Strength of recommendation

Strong

Quality of evidence

Very Low

Last reviewed: October 25, 2017

Pain during medical abortion at or after 13 weeks gestation

In multiple cohort studies of medical abortion at or after 13 weeks gestation, most women required pain medication (Ashok, Templeton, Wagaarachchi, & Flett, 2004; Gemzell-Danielsson & Östlund, 2000; Hamoda, Ashok, Flett, & Templeton, 2004; Rose, Shand, & Simmons, 2006). Advanced gestational age, number of misoprostol doses and induction-to-abortion interval are associated with increased pain during medical abortion (Hamoda et al., 2004; Louie et al., 2017). Pain rarely starts after taking mifepristone but becomes more pronounced after misoprostol and typically peaks with expulsion (Mentula, Kalso, & Heikinheimo, 2014).

Medications for pain management

Little evidence exists regarding the optimal pain medication regimen for medical abortion at or after 13 weeks gestation (Jackson & Kapp, 2011). One randomized trial of 74 women at or after 13 weeks gestation undergoing abortion with mifepristone and misoprostol prophylactically treated patients with either an NSAID or with paracetamol plus codeine at the time of misoprostol administration. There was no difference in reported pain between the two groups, but NSAID pretreatment reduced the need for subsequent intravenous opiates (Fiala, Swahn, Stephansson, & Gemzell-Danielsson, 2005). Treatment with NSAIDs did not affect abortion outcome.

In the largest available cohort study, 1,002 women at or after 13 weeks gestation undergoing abortion with mifepristone and misoprostol were offered a combination of oral and parenteral narcotic analgesics and NSAIDs to manage pain (Ashok et al., 2004). Study authors

reported the proportion of women who used no analgesia (18%), and those who used paracetamol plus dihydrocodone (70%), parenteral morphine (7%) or NSAIDs (5%) for pain relief; women's pain or satisfaction with pain management was not reported. Ipas recommends a combination regimen involving prophylactic NSAIDs given at the time of misoprostol, plus oral and/or parenteral narcotic analgesics (Edelman & Mark, 2017). If the personnel, monitoring and equipment are available, regional (epidural) or patient-controlled anesthesia may be offered (Castro et al., 2003; Leoni Roberti Maggiore et al., 2016; Rosenblatt et al., 1991).

Two small studies examining use of paracervical block during medical abortion at or after 13 weeks gestation found no improvement in women's pain with this modality (Andersson, Benson, Christensson, & Gemzell-Danielsson, 2016; Winkler, Wolters, Funk, & Rath, 1997).

Non-pharmacologic pain management

There are no comparative trials evaluating the benefit of non-pharmacologic pain management strategies for medical abortion at or after 13 weeks gestation. However, experts recommend adjunctive non-pharmacologic measures to improve women's comfort during a medical abortion, including thorough education about expected pain and bleeding, a supportive environment and application of a heating pad or hot water bottle to the lower abdomen (Akin et al., 2001). These modalities are to be employed in addition to—not as substitutes for—pain medications.

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PAIN MANAGEMENT FOR VACUUM ASPIRATION

Recommendation

- Always offer pain medication to women undergoing vacuum aspiration.
- A combination of paracervical block and preprocedure non-steroidal anti-inflammatory drugs (NSAIDs) are recommended for all women.
- Narcotic analgesics and anxiolytics may be helpful.
- Intravenous sedation, where available, may be offered.
- Nonpharmacologic pain management measures may be helpful.
- Paracetamol is not effective for vacuum aspiration pain management.
- General anesthesia is not routinely recommended for vacuum aspiration pain management.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: October 25, 2017

Pain during vacuum aspiration

Most women undergoing vacuum aspiration will experience pain (Borgatta & Nickinovich, 1997). Pre-procedure depression or emotional distress is associated with more pain during uterine aspiration (Allen, Kumar, Fitzmaurice, Lifford, & Goldberg, 2006; Belanger, Melzack, & Lauzon, 1989), while prior vaginal deliveries is associated with less (Borgatta & Nickinovich, 1997). Clinicians consistently underestimate the amount of pain women experience during abortion (Singh et al., 2008).

Methods of pain management

For vacuum aspiration before 13 weeks gestation, a combination of pain medications, paracervical block with local anesthesia, and non-pharmacologic measures typically provides pain relief for most women (World Health Organization, 2014; Renner, Jensen, Nichols, & Edelman, 2010). Intravenous sedation may also be offered.

Local anesthesia

A paracervical block given before dilating the cervix has been shown to decrease pain with dilation and uterine aspiration (Acmaaz, Aksoy, Ozoglu, Aksoy, & Albayrak, 2013; Renner, Nichols, Jensen, Li, & Edelman, 2012; Renner et al., 2016). Paracervical block is a low-risk procedure that can be safely performed by physicians and midlevel providers (Warriner et

al., 2006). For further information, see “Pain Management: Paracervical block” on page 36.

Medications

Pre-procedure treatment with NSAIDs was found to decrease pain during and after the procedure in studies where women received paracervical block for pain relief (Renner et al., 2010; Romero, Turok, & Gilliam, 2008; Suprpto & Reed, 1984; Wiebe & Rawling, 1995); both oral and intramuscular NSAIDs are effective (Braaten, Hurwitz, Fortin & Goldberg, 2013). Two small studies examining use of oral NSAIDs alone for vacuum aspiration pain found no benefit (Acmaz et al., 2013; Li, Wong, Chan, & Ho, 2003). There are no studies assessing the additional benefit of NSAIDs when moderate sedation is used for pain relief; based on findings from three small randomized trials, it is unclear if NSAIDs provide additional benefit when deeper levels of sedation are used (Khazin et al., 2011; Lowenstein et al., 2006; Roche, Li, James, Fechner, & Tilak, 2012).

The benefit of narcotic analgesics in alleviating vacuum aspiration pain is unclear. In one randomized controlled trial, the addition of hydrocodone-acetaminophen to a pain management regimen of paracervical block, ibuprofen and lorazepam did not improve pain during uterine aspiration when compared to placebo (Micks et al., 2012). However, in a different randomized trial, the addition of fentanyl to the same regimen significantly improved procedural pain (Rawling & Weibe, 2001). In women who receive sedation, premedication with narcotic analgesics provides some pain relief, but may be less effective than NSAIDs (Khazin et al., 2011; Lowenstein et al., 2006; Romero et al., 2008).

Anxiolytics such as lorazepam or midazolam decrease anxiety related to the procedure and cause amnesia for some women, but do not affect pain (Allen, et al., 2006; Bayer et al., 2015; Wiebe, Podhradsky, & Dijak, 2003).

Only one study has assessed effectiveness of pretreatment with paracetamol on pain during uterine aspiration performed without paracervical block, finding no difference between the paracetamol group and control group (Acmaz et al., 2013). In two studies where women also received deep sedation or general anesthesia, paracetamol did not improve post-procedure pain (Cade & Ashley, 1993; Lowenstein et al., 2006).

Intravenous sedation

Intravenous sedation using a combination of narcotics and anxiolytics is an effective means of pain control and improves satisfaction with the abortion procedure (Allen, Fitzmaurice, Lifford, Lasic, & Goldberg, 2009; Allen, et al., 2006; Wells, 1992; Wong, Ng, Ngai, & Ho, 2002). Intravenous administration of narcotics and anxiolytics is more effective than oral administration for pain during uterine aspiration (Allen et al., 2009). In women who receive sedation for pain management, it is unclear if there is additional benefit in administering a paracervical block (Kan, Ng, & Ho, 2004; Renner et al., 2010; Wong et al., 2002). When delivered by trained staff and with appropriate monitoring, intravenous sedation is safe. A 2017 retrospective cohort study which included more than 20,000 normal weight, overweight and obese women who received intravenous sedation for vacuum aspiration found that the rate of any anesthesia-related adverse event was very low (0.2%) (Horwitz et al., 2018). However, providing intravenous sedation increases the expense, complexity and potential risks of an abortion procedure and requires a trained provider with equipment for patient monitoring. The increased monitoring necessary to deliver intravenous sedation safely requires facility investments in training and equipment.

General anesthesia

Although effective for pain control, general anesthesia increases the expense, complexity and potential risks associated with abortion and is not recommended for routine procedures (Atrash, Cheek, & Hogue, 1988; Bartlett et al., 2004; Royal College of Obstetricians and Gynaecologists, 2015). When general anesthesia is used, there is no additional benefit to using a paracervical block (Hall, Ekblom, Persson, & Irestedt, 1997; Renner et al., 2010).

Non-pharmacologic pain management

Medications and paracervical block should be supplemented with supportive techniques to decrease pain and anxiety. Some measures that may be helpful include respectful staff; a clean, secure and private setting; thorough education about what to expect during the procedure; verbal support; gentle and efficient technique; and application of a heating pad or hot water bottle to the lower abdomen in the recovery room (Akin et al., 2001). A 2016 systematic review of non-pharmacological adjunctive therapies to manage pain included studies of hypnosis, aromatherapy, music, relaxation and imagery exercises and use of dou-las. While the review found that no interventions showed a statistically significant reduction in pain or anxiety, women rated non-pharmacological interventions highly and recommend their use, particularly those that include dedicated support people (Tschann, Salcedo, & Kaneshiro, 2016; Wilson, Gurney, Sammel, & Schreiber, 2016).

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PAIN MANAGEMENT FOR DILATATION AND EVACUATION

10



Recommendation

- Women undergoing dilatation and evacuation (D&E) should receive pain medications and non-pharmacologic pain management measures.
- A combination of modalities including paracervical block, non-steroidal anti-inflammatory drugs (NSAIDs) and narcotic analgesics, with or without anxiolytics, is recommended.
- Intravenous sedation, where available, should be offered.
- The increased risks of general anesthesia must be weighed against the benefits.

Strength of recommendation

Strong

Quality of evidence

Very Low

Last reviewed: October 25, 2017

Pain during dilatation and evacuation

There is a lack of published evidence regarding the level of pain women experience during D&E, but experts generally agree that abortion procedures become more painful as a pregnancy advances. At later gestations, D&E requires more preoperative and operative cervical dilation, longer procedure times and deeper uterine manipulation.

Methods of pain management

Specific studies of pain control during D&E are lacking, and an optimal regimen for pain management has not been established. Studies focus instead on safety of pain management strategies during D&E, and most international consensus statements focus on the minimum amount of anesthesia at which a D&E can be performed to ensure access at lower-level facilities rather than on optimizing pain control (Royal College of Obstetricians and Gynaecologists, 2015; World Health Organization, 2014).

In studies reporting implementation of D&E programs, pain management usually consists of intravenous sedation with a combination of narcotics and anxiolytics, and a paracervical block (Altman, Stubblefield, Schlam, Loberfeld, & Osathanondh, 1985; Castleman, Oanh, Hyman, Thuy, & Blumenthal, 2006; Jacot et al., 1993). Ipas recommends a combination of paracervical block, NSAIDs and narcotic analgesics, with or without anxiolytics (Edelman & Kapp, 2017). Where available, paracervical block with intravenous sedation should be offered.

Local anesthesia

See “Pain Management: Paracervical block” on page 36.

Medications

No studies assess the effectiveness of oral, intramuscular or intravenous pain medications during D&E. However, studies of vacuum aspiration have found that pre-procedure administration of oral or intramuscular NSAIDs decreases women’s pain during and after the procedure (Braaten, Hurwitz, Fortin & Goldberg, 2013; Renner, Jensen, Nichols, & Edelman, 2010; Romero, Turok, & Gilliam, 2008; Suprpto & Reed, 1984; Wiebe & Rawling, 1995).

Intravenous sedation

No studies assess the effectiveness of intravenous sedation for pain control during D&E. Studies that have assessed safety of intravenous sedation with fentanyl and midazolam in combination with paracervical block have found rates of major procedure-related complications of less than 1% (Racek, Chen, & Creinin, 2010), and no additional anesthesia-related adverse events (Wilson, Chen, & Creinin, 2009; Wiebe, Byczko, Kaczorowski, & McLane, 2013). Intravenous deep sedation with propofol and without intubation is safe in the outpatient setting, with no reported aspirations and few complications (Dean, Jacobs, Goldstein, Gervitz & Paul, 2011; Mancuso et al., 2017).

Providing intravenous sedation increases the expense, complexity and potential risks of an abortion procedure, and requires a trained provider with equipment for patient monitoring. The increased monitoring necessary to deliver intravenous sedation safely requires facility investments in training and equipment.

General anesthesia

Although effective for pain control, general anesthesia increases the expense, complexity and potential risks associated with abortion and is not recommended for routine procedures (Atrash, Cheek, & Hogue, 1988; Bartlett et al., 2004; MacKay, Schulz, & Grimes, 1985; WHO, 2014).

Non-pharmacologic pain management

Medications and paracervical block should be supplemented with supportive techniques to decrease pain and anxiety. Some measures that may be helpful include respectful staff; a clean, secure and private setting; thorough education about what to expect during the procedure; verbal support; gentle and efficient technique; and application of a heating pad or hot water bottle to the lower abdomen in the recovery room (Akin et al., 2001).

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PARACERVICAL BLOCK**Recommendation**

- Paracervical block with local anesthetic is an effective method of pain management and should be a part of all vacuum aspiration, osmotic dilator placement and dilatation and evacuation (D&E) procedures.
- Midlevel providers can safely and effectively provide paracervical anesthesia.
- Paracervical block is not effective for managing pain associated with fetal expulsion during medical abortion at or after 13 weeks gestation.
- Twenty mL of 1% lidocaine, injected to a depth of 3cm at four paracervical points is recommended. If 1% lidocaine is unavailable, 10mL of 2% lidocaine may be substituted.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: October 31, 2017**Local anesthesia for pain management***VACUUM ASPIRATION*

A 2013 systematic review evaluating paracervical block for gynecologic procedures requiring cervical dilation, including aspiration abortion before 13 weeks, found that paracervical block reduced pain during cervical dilation and uterine interventions, although not post-procedure pain, when compared to placebo or no anesthesia (Tangsiriwatthana, Sangkomkamhang, Lumbiganon, & Laopaiboon, 2013). In a randomized controlled trial of 120 women undergoing aspiration abortion before 11 weeks gestation, women who received a paracervical block containing 20mL of 1% buffered lidocaine had less pain during dilation and aspiration compared to women who received a sham injection, where a capped needle was touched to the cervicovaginal junction to mimic administration of paracervical block (Renner, Nichols, Jensen, Li, & Edelman, 2012). In subsequent studies, the same authors found a four-point injection technique was superior to a two-point injection technique (Renner et al., 2016). Deeper injection (3cm) improves pain management compared to superficial (1.5cm) injection (Cetin, & Cetin, 1997; Renner, Jensen, Nichols, & Edelman, 2010). A waiting period between injection and cervical dilation is not necessary as it does not improve pain control (Phair, Jensen, & Nichols, 2002; Renner et al., 2016; Wiebe & Rawling, 1995).

In women who receive sedation for pain management, it is unclear if there is additional benefit to administering paracervical block (Kan, Ng, & Ho, 2004; Renner et al., 2010; Wells, 1992; Wong, Ng, Ngai, & Ho, 2002). When women receive general anesthesia, there is no additional benefit to administering paracervical block (Hall, Ekblom, Persson, & Irestedt,

1997; Renner et al., 2010).

DILATATION AND EVACUATION

No studies have evaluated paracervical block for pain management during D&E procedures without concomitant sedation or anesthesia. One randomized trial has examined paracervical block use during D&E when women also received deep sedation or general anesthesia; the addition of paracervical block did not improve postoperative pain (Lazenby, Fogelson, & Aeby, 2009). The recommendation to perform paracervical block for D&E has been extrapolated from data from vacuum aspiration studies and one randomized controlled trial of 41 women undergoing D&E which found significantly decreased pain during osmotic dilator placement when paracervical block was used (Soon, Tschann, Salcedo, Stevens, Ahn, & Kaneshiro, 2017).

MEDICAL ABORTION

No studies evaluate use of paracervical block for pain management during medical abortion before 13 weeks gestation. Two studies examining use of paracervical block during medical abortion at or after 13 weeks found no improvement in women's pain with this modality (Andersson, Benson, Christensson, & Gemzell-Danielsson, 2016; Winkler, Wolters, Funk, & Rath, 1997).

Midlevel providers

In an international, randomized multi-center study examining 2,894 procedures, midlevel providers had similar complication rates as physicians when performing vacuum aspiration with paracervical block (Warriner et al., 2006). The midlevel providers experienced no complications related to use of paracervical block.

Technique

More information on paracervical block technique can be found in Ipas's job aid, *Paracervical block technique*, which can be found online at www.ipas.org/clinicalupdates.

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ADOLESCENTS: SAFETY AND EFFECTIVENESS

12



Recommendation

- Vacuum aspiration and medical abortion are safe and effective for adolescents and should be offered as methods of induced abortion.
- Cervical preparation may be considered for adolescents prior to vacuum aspiration.
- Clinical services should promote timely access to safe abortion for adolescents.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: December 20, 2017

Adolescents and abortion

The World Health Organization (WHO) defines adolescents as individuals 10-19 years of age, and young women as 20-24 years of age. Adolescents face barriers to accessing safe abortion care and present for abortions at later gestational ages than adult women (Jatlaoui et al., 2017; Sowmini, 2013). Adolescents are at increased risk of complications of unsafe abortion due to delays in seeking and receiving care, seeking care from unskilled providers and not accessing services when complications arise (Olukoya, Kaya, Ferguson, & AbouZahr, 2001); WHO estimates that three million girls aged 15 to 19 undergo unsafe abortions annually (WHO, 2014a). Decreasing barriers to abortion services may particularly benefit adolescents and young women.

When adolescents receive safe abortion services, they experience fewer complications than do older women. In a large United States-based retrospective cohort study which captured all complications within six weeks of 54,911 surgical and medical abortions, adolescents experienced the lowest rate of abortion-related complications—1.5%—of any age group (Upadhyay et al., 2015). Results were not stratified by method of uterine evacuation, trimester or type of complication.

Vacuum aspiration

EFFECTIVENESS

Success rates for vacuum aspiration have not been disaggregated by age. In studies reporting data for adolescent and older women together, rates of incomplete and failed abortion were less than 1% (Upadhyay et al., 2015; Warriner et al., 2006; Weitz et al., 2013). A 2014 systematic review, which included 25 randomized and observational trials documenting abortion care for adolescent and young women concluded that abortion, including vacuum

aspiration, is safe and effective although specific effectiveness rates were not reported (Renner, de Guzman, & Brahmi, 2014).

SAFETY

A large, prospective, United States multi-center cohort study of 164,000 women undergoing legal abortion, 50,000 of whom were adolescents, found that mortality and major morbidity were lower in adolescents compared to older women (Cates Jr., Schulz, & Grimes, 1983). The mortality rate was 1.3 per 100,000 in women under 20 years old compared to 2.2 per 100,000 in women age 20 and older. Serious adverse events including major surgery, hemorrhage requiring transfusion, and uterine perforation were less common in those under age 20. However, age of 17 years or younger was associated with higher rates of cervical injury, even after controlling for nulliparity (5.5 per 1000 compared to 1.7 per 1000 in women aged 30 years and older, relative risk 1.9, 95% CI 1.2, 2.9) (Cates et al., 1983; Renner et al., 2014; Schulz, Grimes, & Cates, 1983). To reduce this risk, cervical preparation may be considered for young women prior to vacuum aspiration (Allen & Goldberg, 2016; WHO, 2014b).

ACCEPTABILITY

Age-stratified data on acceptability of vacuum aspiration among adolescents are lacking (Renner et al., 2014).

Medical abortion

EFFECTIVENESS

Clinical trials and cohort studies have shown that young women have similar (Haimov-Kochman et al., 2007; Heikinheimo, Leminen, & Suhonen, 2007) or increased (Niinimäki et al., 2011; Shannon et al., 2006) success rates when using mifepristone and misoprostol for medical abortion compared to older women. A large Finnish population-based retrospective cohort study that compared 3,024 adolescents to 24,006 adult women up to 20 weeks gestational age found the risk of surgical evacuation following medical abortion was significantly lower in adolescents (Niinimäki et al., 2011).

In a prospective cohort that included young women, the success rate of misoprostol-only medical abortion was the same for young and older women (Bugalho et al., 1996). Two prospective cohort studies of misoprostol-only abortion have enrolled only adolescents; efficacy in both studies was equivalent to that reported in trials of adult women (Carbonell et al., 2001; Velazco et al., 2000).

SAFETY

The Finnish population-based retrospective cohort study referenced above found that complication rates after medical abortion among adolescents were similar to or lower than those of older women, even when controlling for nulliparity. In this study, adolescents had a significantly lower incidence of hemorrhage, incomplete abortion, and need for surgical evacuation. Postabortion infection occurred at similar rates among adolescents and older women, despite adolescents' higher rates of chlamydia infection in the population (Niinimäki, et al., 2011). In studies of misoprostol-only medical abortion that include adolescents, adolescents do not experience higher rates of adverse outcomes than adult women (Carbonell et al., 2001; Velazco et al., 2000).

In one small, non-comparative study of 28 adolescents age 14-17 using mifepristone and misoprostol medical abortion, 96% found medical abortion acceptable and 79% reported satisfaction with the procedure by four weeks of follow-up (Phelps, Schaff, & Fielding, 2001).

Subsequent perinatal outcomes

Three studies have examined perinatal outcomes in pregnancies in adolescent and young women who have had a previous abortion—a United States-based retrospective cohort study comparing 654 nulliparous adolescent deliveries to 102 adolescent deliveries with a prior abortion (van Veen, Haeri, & Baker, 2015), a German retrospective cohort including 7,845 nulliparous adolescent deliveries and 211 adolescent deliveries with one prior induced abortion (Reime, Schucking, & Wenzlaff, 2008) and a Hong Kong case-control study comparing 118 adolescent deliveries with one or more prior abortions to 118 age- and parity-matched controls (Lao & Ho, 1998). The American and Hong Kong studies found no difference in adverse perinatal outcomes between study groups. After adjusting for confounding factors, the German study found an increased risk of very low birthweight infants among adolescents who had a previous abortion. Method of abortion and whether preoperative cervical preparation was undertaken was not specified in any of these studies.

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MIDLEVEL PROVIDERS: SAFETY AND EFFECTIVENESS

13



Key Information:

Many cadres of trained health workers can provide vacuum aspiration and medical abortion before 13 weeks gestation as safely and effectively as physicians.

Quality of evidence

High

Last reviewed: November 29, 2017

Who is a midlevel provider?

“Midlevel provider” is a general term used to describe multiple cadres of trained health-care providers such as nurses, nurse midwives, clinical officers, advanced practice clinicians and physician assistants. Expanding the abortion provider base to include midlevel providers increases access to safe abortion and postabortion care.

Vacuum aspiration

A 2015 systematic review compiled data from five studies, one randomized controlled trial and four cohort studies, that compared provision of aspiration abortion by midlevel providers to that by doctors (Barnard, Kim, Park, & Ngo, 2015). Included studies were from India, South Africa, the United States and Vietnam. Combined data found no difference in the overall risk of complications between physicians and non-physician providers (relative risk [RR] 1.36, 95% CI 0.86, 2.14). When examining risk of incomplete abortion separately, observational data (three studies including 13,715 women) indicated an increased risk of incomplete abortion when performed by midlevel providers (RR 2.25, 95% CI 1.38, 3.68) (Goldman, Occhuito, Peterson, Zapka, & Palmer, 2004; Jejeebhoy et al., 2011; Weitz et al., 2013); this increased risk was not observed in randomized controlled trial data (one study, 2789 women, RR 2.97, 95% CI 0.21, 41.82) (Warriner et al., 2006).

The World Health Organization (WHO) states that non-specialist doctors, associate and advanced associate clinicians, midwives and nurses can be trained to perform vacuum aspiration for induced abortion (WHO, 2015). In settings where there are established mechanisms to include auxiliary nurses and auxiliary nurse midwives in basic emergency obstetric care or postabortion care, these cadres can also perform vacuum aspiration. Where doctors of complementary medicine participate in other tasks related to maternal and reproductive health, they can also perform vacuum aspiration.

Medical abortion

A 2017 systematic review and meta-analysis comparing medical abortion provision by mid-level providers and doctors (Sjostrom, Dragoman, Fonhus, Ganatra, & Gemzell-Danielsson, 2017) included three randomized controlled trials, reporting outcomes for 3,670 women from Mexico, Nepal and Sweden. Midlevel providers in the included studies were nurses,

auxiliary nurse midwives, ayurvedic (traditional) physicians and midwives. The review found that effectiveness, measured as rate of complete pregnancy termination, was equivalent between the physician and non-physician groups (RR 1.0, 95% CI 0.99, 1.02). Across all included studies, only one serious adverse event—heavy bleeding requiring uterine aspiration—was recorded. Authors concluded that although the rarity of such events limits the ability to statistically analyze their likelihood based on provider type, the overall low rate was reassuring.

WHO states that, in addition to specialist and non-specialist doctors, associate and advanced associate clinicians, midwives, nurses, auxiliary nurses and auxiliary nurse midwives can be trained to provide medical abortion. Where doctors of complementary medicine participate in other tasks related to maternal and reproductive health, they can also provide medical abortion. WHO makes no recommendation regarding provision of medical abortion by pharmacists or lay health workers, based on lack of evidence (2015).

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GESTATIONAL DATING

Recommendation

- Gestational age should be calculated using a woman's last menstrual period (LMP) combined with bimanual examination.
- Routine use of ultrasound for gestational age determination is not necessary.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: November 10, 2017

Ultrasound

Although commonly used in some settings to determine pregnancy duration, ultrasound does not yield exact gestational age measurements due to variability between sonographers, machines and software (Callen, 2000). Additionally, ultrasound has an inherent margin of error of 3-5 days before 12 weeks gestation; this margin of error increases as the pregnancy advances (Hadlock, Shah, Kanon, & Lindsey, 1992). In studies conducted in low-resource settings with limited access to ultrasound, such as India, Nepal, Vietnam and Tunisia, lack of ultrasound has not had an impact on the success or safety of abortion (Coyaji et al., 2001; Mundle, Elul, Anand, Kalyanwala, & Ughade, 2007; Ngoc et al., 1999; Warriner et al., 2011). Ultrasound can be helpful to establish pregnancy duration when it is unclear, confirm an intrauterine pregnancy and identify uterine malformations (Clark, Gold, Grossman, & Winikoff, 2007; Kulier & Kapp, 2011). Dependence on routine ultrasound for gestational age determination can limit access to safe abortion services and is not necessary for accurate assessment of pregnancy duration (Kaneshiro, Edelman, Sneeringer, & Gómez Ponce de León, 2011; Royal College of Obstetricians and Gynaecologists [RCOG], 2015; World Health Organization [WHO], 2014).

LMP combined with bimanual examination

Provider assessment based on women's reported LMP combined with bimanual examination is an accurate means of determining gestational age prior to abortion (Bracken et al., 2011; Fielding, Schaff, & Nam, 2002; Kaneshiro et al., 2011). The two largest trials comparing use of LMP and bimanual examination to ultrasound prior to medical abortion found that fewer than 2% of the nearly 5,000 women included would have been inappropriately offered medical abortion beyond gestational age limits if LMP and bimanual examination were relied upon to determine pregnancy duration (Bracken et al., 2011; Fielding et al., 2002).

Two small cohort studies have examined accuracy of bimanual examination compared to ultrasound for gestational dating prior to vacuum aspiration (Kulier & Kapp, 2011). In one

study of 120 women, 81% of gestational age determinations made with provider assessment were concordant with ultrasound and an additional 13% were within two weeks of ultrasound estimates (Fakih, Barnea, Yarkoni, & DeCherney, 1986). A second study included 245 women, and found that experienced providers using bimanual examination only to assess gestational age were within two weeks of ultrasound estimates 92% of the time, while inexperienced providers were within two weeks only 75% of the time (Nichols, Morgan, & Jensen, 2002).

LMP alone

Most women recall their LMP reasonably well regardless of their education and whether they usually record their LMP dates (Harper, Ellertson & Winikoff, 2002; Wegienka & Baird, 2005). Several studies report the accuracy of LMP alone to determine gestational age compared to ultrasound prior to medical abortion (Blanchard et al., 2007; Bracken et al., 2011; Constant, Harries, Moodley, & Myer, 2017; Schonberg, Wang, Bennet, Gold, & Jackson, 2014). Two studies that included a combined total of 833 women, both found that 12% of women eligible for medical abortion based on their LMP were beyond gestational age limits as determined by ultrasound dating (Blanchard et al., 2007; Constant et al., 2017). However, in the largest available study only 3.3% of 4,257 women fell into this group when a 63-day cut off value for medical abortion eligibility was used; even fewer women (1.2%) determined to be eligible by LMP were beyond 70 days gestation (Bracken et al., 2011). This study also examined the accuracy of provider assessment of pregnancy duration using both LMP and bimanual examination (see above) and found that, when this method of gestational dating was used, the rate of women who were incorrectly determined to be eligible for medical abortion decreased from 3.3% to 1.6%.

Although generally able to recall their LMP, when asked to determine gestational age or medical abortion eligibility based on that LMP, a minority of women's assessments disagree with those of their providers. Three studies have compared gestational age determinations made using LMP to those determined by provider assessment (Andersen et al., 2017; Ellertson et al., 2000; Shellenberg, Antobam, Griffin, Edelman, & Voetagbe, 2017); all three studies also evaluated women's ability to self-determine their eligibility based on their LMP. In the earliest of these studies (Ellertson et al., 2000), 10% of the 173 women in India who used a worksheet and their LMP to determine gestational age believed they were eligible for medical abortion, while providers determined that their pregnancies were beyond the 56-day cut off. In Nepal, 13% of 3,091 women who used their LMP and a modified gestational dating wheel to determine their medical abortion eligibility, using a 63-day cut off, were incorrect when compared to providers' assessments (Andersen et al., 2017). Finally, in Ghana, 770 women used a modified gestational dating wheel and LMP to determine if their pregnancy was before or after 13 weeks gestation (Shellenberg et al., 2017); when compared to provider assessment, 3.6% of women incorrectly believed their pregnancies were less than 13 weeks. Of these women, one woman's pregnancy was 13 weeks (0.1% of 770), 15 were 14 weeks (1.9%), seven were 16 weeks (0.9%), two were 18 weeks and 22 weeks (0.3% each) and one was 28 weeks (0.1%).

Importance of gestational age assessment

Gestational age must be assessed prior to safe abortion care to determine appropriate method of uterine evacuation and medication regimen. If a provider is unable to assess gestational age through the combination of LMP, history and bimanual examination, a more experienced clinician should perform a bimanual examination or the patient should be referred for an ultrasound.

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SCREENING FOR ECTOPIC PREGNANCY

15



Recommendation

Ectopic pregnancy should be considered in women presenting for abortion who also have a concerning history or examination.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: October 17, 2017

Epidemiology

Data are scant from low resource settings regarding rates of ectopic pregnancy; in the United States, reported rates range from 1-2% of pregnancies (Stulberg, Cain, Dahlquist, & Lauderdale, 2013; Tao, Patel, & Hoover, 2016; Trabert, Holt, Yu, Van den Eeden, & Scholes, 2011). Ectopic pregnancy accounts for 2.7% of pregnancy-related deaths in the United States (Creanga, Syverson, Seed, & Callaghan, 2017). Ectopic pregnancy accounts for approximately 1% of pregnancy-related deaths in low resource settings where other causes of maternal death are more prevalent (Khan, Wojdyla, Say, Gulmezoglu, & Van Look, 2006).

Risk factors

Factors with the highest associated risk of ectopic pregnancy in pregnant women are:

RISK FACTOR	RISK OF ECTOPIC IN THE CURRENT PREGNANCY
Previous ectopic pregnancy	10-15% (Yao & Tulandi, 1997)
History of tubal surgery, including sterilization	25-50% (Barnhart, 2009)
Intrauterine device (IUD) in place	25-50% (Barnhart, 2009)

Other risk factors include a history of infertility and assisted reproductive technology, a history of pelvic infections, multiple partners, early age at first intercourse and smoking. (Barnhart, 2009).

Screening

Half of all ectopic pregnancies occur in women with no risk factors and with a benign clinical presentation (Stovall, Kellerman, Ling, & Buster, 1990). Providers should screen women for ectopic pregnancy risk factors during the history and physical examination including relevant history, such as previous ectopic pregnancy, tubal ligation, tubal surgery or an IUD in place.

Screening should also include signs of ectopic pregnancy that can be found during physical examination, such as an adnexal mass or pain on examination or vaginal bleeding.

Treatment for high-risk women

Ultrasound and serial hCG testing are often used to help assess pregnancy location (Fields & Hathaway, 2017). In some cases, the most expeditious way to confirm an intrauterine pregnancy is to perform vacuum aspiration; presence of products of conception in the uterine aspirate confirms an intrauterine pregnancy. A woman with suspicious signs and symptoms or a concerning physical exam should be diagnosed and treated as soon as possible or transferred immediately to a facility that can manage ectopic pregnancy. Early diagnosis and treatment of ectopic pregnancy can help preserve fertility and save women's lives.

Post-procedure screening

For women undergoing vacuum aspiration, the aspirate should be strained and examined to confirm the presence of products of conception (see "Examining products of conception," page 59). If products of conception are not seen, a diagnosis of ectopic pregnancy should be considered.

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SAFETY AND EFFECTIVENESS

16



Key information

- Vacuum aspiration is effective and safe, with success rates over 98% and major complication rates under 1%.
- Serious adverse events resulting from vacuum aspiration before 13 weeks are rare.

Quality of evidence

High

Last reviewed: January 8, 2018

Effectiveness

A successful vacuum aspiration requires no further intervention to evacuate the uterus. In a large United States-based observational study of 11,487 first-trimester aspiration abortions done by physicians, nurse practitioners, certified nurse midwives and physicians assistants, the need for repeat aspiration due to incomplete abortion was 0.28% and ongoing pregnancy was 0.16% (Weitz et al., 2013).

Safety

A 2015 systematic review analyzed 57 studies reporting data for 337,460 abortions performed before 14 weeks gestation in North America, Western Europe, Scandinavia and Australia/New Zealand (White, Carroll, & Grossman, 2015). Major complications requiring intervention (such as hemorrhage requiring transfusion or perforation necessitating repair) occurred in $\leq 0.1\%$ of procedures; hospitalization was necessary in $\leq 0.5\%$ of cases. Studies looking at different cadres of providers (physician assistants, nurses, nurse midwives, etc.) in other settings have had similar results (Hakim-Elahi, Tovell, & Burnhill, 1990; Jejeebhoy et al., 2011; Warriner et al., 2006; Weitz et al., 2013). In two studies that compared newly trained midlevel providers to experienced physician providers (Jejeebhoy et al., 2011; Weitz et al., 2013), there were no observed differences in abortion success or complication rates.

A retrospective cohort study conducted in the United States compared rates of procedural complications during outpatient aspiration abortion through 13 weeks and six days gestation in women with at least one medical comorbidity (diabetes, hypertension, obesity, HIV, epilepsy, asthma, thyroid disease and bleeding/clotting disorders) to women without comorbidities. The overall rate of complications—which included uterine perforation, blood loss greater than 100mL, cervical laceration and retained products of conception that required reaspiration—was 2.9%; there was no difference between the two groups (Guiahi, Schiller, Sheeder, & Teal, 2015). Two retrospective cohort studies, that together included 5,288 aspiration abortion procedures performed before 13 weeks gestation, found no differences in complication rates between obese, overweight and normal weight women (Benson, Micks, Ingalls, & Prager, 2016; Mark et al., 2017).

Mortality

In the United States, the mortality rate from legal induced abortion between 2008-2013 was 0.62 deaths per 100,000 reported abortions; mortality rates disaggregated by abortion type or length of pregnancy are not available (Jatlaoui et al., 2017). In comparison, during the period from 2011-2013 the mortality rate from live birth in the United States was 17 deaths per 100,000 live births (Creanga, Syverson, Seed & Callaghan, 2017). A secondary data analysis that compared mortality rates associated with live birth to those from legal induced abortion in the United States found that the risk of death from childbirth was 14-fold higher than the risk of death from abortion (Raymond & Grimes, 2012). In the 2015 systematic review about the safety of vacuum aspiration in multiple countries referenced above, no deaths were reported (White et al., 2015).

Complication rates by study

	UPADHYAY, 2015	WEITZ, 2013	JEJEEBHOY, 2011	WARRINER, 2006	HAKIM-ELAHI, 1990
Number of women included	34,744	11,487	897	2,789	170,000
Location	USA	USA	India	South Africa and Vietnam	USA
Provider type	Not specified	Experienced physicians and newly trained nurse practitioners, certified nurse midwives and physician assistants	Newly trained physicians and nurses	Experienced physicians, midwives and doctor-assistants	Experienced physicians
Time period	2009-2010	2007- 2011	2009-2010	2003-2004	1971-1987
Total minor complication rate	1.1%	1.3%	1% (all reported as incomplete abortion)	1%	0.85%
Incomplete abortion	0.33%	0.3%	1%	0.9%	Not reported (0.35% re-aspiration rate)
Ongoing pregnancy	0.04%	0.16%	Not reported	Not reported	0%
Minor infection	0.27%	0.12%	Not reported	0.1%	0.5%
Total major complication rate	0.16%	0.05% (6 complications: 2 perforations, 3 infections and 1 hemorrhage)	0.12% (1 complication: 1 high fever)	0%	0.07% (hospitalizations for perforation, ectopic pregnancy, hemorrhage, sepsis or incomplete abortion)
Death	0%	0%	0%	0%	0%

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CERVICAL PREPARATION

Recommendation

- Cervical preparation is recommended after 12-14 weeks gestation. Before 12-14 weeks gestation, cervical preparation may be considered, but should not be routinely used.
- Recommended methods for cervical preparation include:
 - Misoprostol 400mcg sublingually 1-3 hours before the procedure.
 - Misoprostol 400mcg vaginally or buccally 3 hours before the procedure.
 - Osmotic dilators placed in the cervix 6-24 hours before the procedure.
 - Mifepristone 200mg orally 1-2 days before the procedure.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: October 29, 2017

Benefits of cervical preparation

A meta-analysis of 51 randomized controlled clinical trials of cervical preparation through 13 weeks gestation found that procedure time was shorter with cervical preparation but there were no differences in serious complications, such as cervical laceration or uterine perforation, in women given cervical preparation compared to those given placebo (Kapp, Lohr, Ngo, & Hayes, 2010). In the largest multicenter randomized controlled trial, which included 4,972 women given either misoprostol 400mcg vaginally or placebo three hours before a vacuum aspiration, there was no difference in the rates of cervical laceration, perforation or infection between the two groups (Meirik, Huong, Piaggio, Bergel, & von Hertzen, 2012). However, a significant decrease in the risk of incomplete abortion was observed in those who received misoprostol for cervical preparation (<1%) compared to the placebo group (2%), but side effects were more frequent for women who were given misoprostol. For women at higher risk of complications during cervical dilation (young women, women with cervical abnormalities or prior cervical surgery) or for inexperienced providers, there may be a benefit from cervical preparation before 12-14 weeks gestation (Allen & Goldberg, 2016; Grimes, Schulz, & Cates, 1984; Kaunitz, Rovira, Grimes, & Schulz, 1985).

Side effects of cervical preparation

In the largest randomized controlled trial of misoprostol for cervical preparation, 55% of women who took misoprostol complained of pre-procedure abdominal pain and 37% had vaginal bleeding, compared to 22% and 7% in the placebo group (Meirik et al., 2012). In addition, cervical preparation adds cost, complexity and time to an abortion, as women must

visit the clinic a day before the procedure to have osmotic dilators placed or to receive mifepristone, or wait in the health center for misoprostol to take effect. Because abortion before 13 weeks gestation is very safe, the gestational age at which the benefit of cervical preparation outweighs the side-effects is not known (Kapp et al., 2010). Women's satisfaction with cervical preparation has not been systematically studied in randomized controlled trials but is an important consideration for quality of care and service delivery (Kapp et al., 2010).

Choice of methods

The choice of misoprostol, mifepristone or osmotic dilators for cervical preparation depends on availability, expense, convenience and preference. Sublingual misoprostol has superior effectiveness but more gastrointestinal side effects than vaginal misoprostol (Kapp et al., 2010; Saav, Kopp Kallner, Fiala, & Gemzell-Danielsson, 2015; Saxena, Sarda, Salhan, & Nanda, 2008). Mifepristone given 24 hours prior to the abortion is superior to misoprostol but adds time and expense to the abortion procedure (Ashok, Flett, & Templeton, 2000; Kapp et al., 2010). Misoprostol and osmotic dilators have similar effectiveness but dilator placement is associated with increased pain, increased time to procedure and reduced satisfaction for women (Bartz, et al., 2013; Burnett, Corbett, & Gertenstein, 2005; Maclsaac, Grossman, Balistreri, & Darney, 1999).

Young women

Adolescents may benefit from cervical preparation due to their increased risk of cervical injury during abortion (Allen & Goldberg, 2016; Schulz et al., 1983). This risk is independent of nulliparity (Meirik et al., 2014); adolescents have physiologically immature cervixes that may be more difficult to dilate regardless of obstetric history (Allen & Goldberg, 2016; Schulz et al., 1983). There are no clinical trials examining the use of cervical preparation in this patient population.

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BIMANUAL EXAMINATION

18



Recommendation

- Bimanual examination must be performed before any procedure in which instruments are being placed in the uterus, such as vacuum aspiration or intrauterine device insertion.
- The bimanual examination must be performed by the clinician doing the procedure.

Strength of recommendation

Strong

Quality of evidence

Very Low

Last reviewed: October 30, 2017

Importance of bimanual examination

Bimanual examination, a routine step before intrauterine procedures recommended by the World Health Organization (WHO, 2014), provides information about the client's comfort, pregnancy status, gestational age, presence of infection, anatomic abnormalities and uterine position, all of which affect management of intrauterine procedures. Ultrasound can be performed in addition but is not a replacement for bimanual examination before intrauterine procedures.

Determining uterine size

Bimanual examination, when paired with a woman's last menstrual period, enables accurate gestational age assessment (See "Recommendations for abortion before 13 weeks gestation: Gestational dating" on page 45). Medical regimens for abortion and postabortion care change based on the gestational age or uterine size. Techniques for vacuum aspiration and dilatation and evacuation, including instrument choice and need for cervical preparation, depend on accurate knowledge of uterine size.

Determining uterine position

The position of the uterus in the pelvis, orientation of the fundus to the cervix and firmness of the uterus are best determined with bimanual examination. Knowledge of uterine position assists providers in avoiding complications, particularly perforation, during procedures (Chen, Lai, Lee, & Leong, 1995; Mittal & Misra, 1985; Nathanson, 1972).

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EXAMINING PRODUCTS OF CONCEPTION

19



Recommendation

- Clinicians performing vacuum aspiration must inspect products of conception immediately after vacuum aspiration.
- Sending products of conception for routine histopathology evaluation is not recommended.

Strength of recommendation

Strong

Quality of evidence

Very Low

Last reviewed: November 16, 2017

Visual inspection of products of conception

Visual inspection of products of conception is a routine step in vacuum aspiration and is recommended by the World Health Organization (WHO, 2014), the Royal College of Obstetricians and Gynaecologists (RCOG, 2015), and the National Abortion Federation (NAF, 2017). Presence of products of conception on visual inspection confirms that the pregnancy was intrauterine and is consistent with successful abortion (Westfall, Sophocles, Burggraf, & Ellis, 1998). If products of conception are not seen, a woman should not leave the facility until plans are made for follow-up. Immediate examination of the products of conception can also expedite the diagnosis of ectopic pregnancy and decrease related morbidity and mortality (Goldstein, Danon, & Watson, 1994). If no pregnancy tissue is visualized and ectopic pregnancy is suspected, follow local guidelines to rule out ectopic pregnancy. In cases where abnormal pathology is suspected, such as molar pregnancy, histopathology may be used in addition to visual inspection.

Studies show that sending products of conception for routine histopathology exam does not affect clinical outcomes and increases the cost of abortion (Heath, Chadwick, Cooke, Manek, & MacKenzie, 2000; Paul, Lackie, Mitchell, Rogers, & Fox, 2002).

Instructions for visually inspecting products of conception are in Ipas's *Woman-Centered Comprehensive Abortion Care Reference Guide*, 2nd edition, page 177 (Ipas, 2013).

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PROCESSING IPAS MVA PLUS® AND IPAS SINGLE-VALVE ASPIRATORS



Recommendation

All Ipas multiple-use aspirators and adapters must be soaked, cleaned and high-level disinfected or sterilized between patients.

Last reviewed: October 30, 2017

Importance of correctly processing instruments

The manual vacuum aspirator (MVA) should not directly touch the patient's body. However, when it is used, the cylinder fills with blood. There is the potential risk that some contaminants from a previous patient could be introduced to another woman if the MVA is not fully processed (sterilized or high-level disinfected) between each use.

Steps

STEP 1: PRE-SOAK

Do not let the device dry. Until the instrument can be cleaned, soak it in water or a 0.5% chlorine solution.

STEP 2: CLEANING

Disassemble aspirator and adaptor (if used) and clean with warm water and detergent using a soft brush.

STEP 3: STERILIZATION OR HIGH-LEVEL DISINFECTION

All aspirators and adaptors must be sterilized or high-level disinfected after use.

STERILIZATION OPTIONS	HIGH-LEVEL DISINFECTION OPTIONS
Steam autoclave* instruments at 121°C (250°F) with a pressure of 106kPa (15lbs/in2) for 30 minutes	Boil* the instruments for 20 minutes
Glutaraldehyde** soak for the time recommended by the manufacturer—most recommend 10 hours***	Glutaraldehyde** soak for the time recommended by the manufacturer—recommendations range from 20-90 minutes***
Sporox II* solution soak for 6 hours***	Sporox II* solution soak for 30 minutes***
	0.5% chlorine solution soak for 20 minutes***

* IPAS SINGLE-VALVE ASPIRATOR CANNOT BE BOILED, AUTOCLAVED OR SOAKED IN SPOROX II.

** Because there are several glutaraldehyde products available with different recommendations for processing time, always follow the recommendations that come with your brand of glutaraldehyde.

*** If chemical agents were used in processing, aspirator parts and adaptors (if used) should be thoroughly rinsed in clean potable water (drinking water).

STEP 4: STORAGE

Aspirators and adapters may be dried, the O-ring lubricated and the device reassembled and stored in a clean dry area until use. The aspirator does not need to remain high-level disinfected or sterilized at the time of use and can be placed in a clean area or stored according to local standards.

Detailed information on MVA processing and other processing options are in Ipas's *Woman-centered comprehensive abortion care: Reference manual, 2nd edition*, page 150 (Ipas, 2013).

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SAFETY AND EFFECTIVENESS

Key information

- A combined regimen of mifepristone and misoprostol is effective and safe with success rates over 95%, continuing pregnancy rates of less than 2% and complication rates of less than 1% up to 10 weeks gestation.
- Between 10 and 13 weeks, the success rate of mifepristone combined with misoprostol is over 95%, with a continuing pregnancy rate of less than 2% and complication rate of 3%.
- A combined regimen of mifepristone and misoprostol is recommended for medical abortion; where mifepristone is not available, the misoprostol-only regimen may be used.
- A misoprostol-only regimen has lower success rates of about 85%, with continuing pregnancy rates of 3-10% and complication rates of 1-4% up to 13 weeks gestation.

Quality of evidence

High

Last reviewed: January 15, 2018

Background

A combined regimen of mifepristone and misoprostol is recommended for medical abortion as it is more effective than misoprostol only (Blum et al., 2012; Kulier et al., 2011; Ngoc et al., 2011). Where mifepristone is unavailable, the misoprostol-only regimen may be used.

Mifepristone and misoprostol

EFFECTIVENESS

Medical abortion success is defined as a complete abortion that needs no further intervention. A 2015 systematic review reported data from 20 studies that included a total of 33,846 women undergoing medical abortion with mifepristone and buccal misoprostol through 70 days gestation (Chen & Creinin, 2015). The overall success rate was 96.6% and the continuing pregnancy rate was 0.8%. Two prospective cohort studies have examined mifepristone combined with either 400mcg or 600mcg of sublingual misoprostol through 70 days gestation, finding success rates of 93-99% and ongoing pregnancy rates of less than 2% (Bracken et al., 2014; Platais, Tsereteli, Grebennikova, Lotarevich, & Winikoff, 2016). One prospective cohort study has examined mifepristone combined with vaginal misoprostol from 63-70 days gestation, finding a success rate of 95% (Gouk et al., 1999).

Between 10 and 13 weeks gestation only one available study, a retrospective cohort study of 1,076 women, has used the currently recommended regimen of 200mg mifepristone followed 36-48 hours later by misoprostol (800mcg vaginally or 600mcg sublingually), and then repeated doses of 400mcg misoprostol vaginally or sublingually every three hours for two additional doses (Hamoda, Ashok, Flett, & Templeton, 2005). The success rate for this

regimen was 95.8%, with an ongoing pregnancy rate of 1.5%. A smaller prospective cohort study which included 254 women used a similar regimen and reported a success rate of 91.7% and an ongoing pregnancy rate of less than 1% (Lokeland et al., 2010).

SAFETY

Three large cohort studies, including a total of 260,256 women, have reported complications observed during medical abortion with mifepristone and misoprostol up to nine weeks gestation (Cleland et al., 2013; Gatter, Cleland, & Nucatola, 2015; Goldstone, Walker, & Hawtin, 2017). These studies found rates of incomplete abortion requiring uterine aspiration of 2.3 to 4.8%; rates of all other outcomes, such as ongoing pregnancy, unrecognized ectopic pregnancy, and complications were less than 1%. Between 10 and 13 weeks, reported rates of uterine aspiration for any reason range from 4-8% (Hamoda et al., 2005; Lokeland et al., 2010) and complication rates are around 3% (Hamoda et al., 2005).

A large retrospective cohort study of 11,319 first-trimester medical abortions evaluated all complications from abortions provided in the state of California in the United States from 2009-2010 (Upadhyay et al., 2015). Researchers assessed complications arising at the time of the abortion, as well as complications diagnosed when patients sought additional care from sites other than the site where the abortion was provided, such as emergency departments. The overall rate of complications during the six weeks following medical abortion was 5.2%; only 0.3% were major complications—defined as requiring hospitalization, surgery or blood transfusion. Complications included incomplete abortion (0.87%), failed abortion (0.13%), hemorrhage (0.14%), infection (0.23%) and undetermined/other (3.82%).

COMPLICATIONS BY STUDY

	GOLDSTONE, 2017	CLELAND, 2013	GATTER, 2015
Number of women included	13,078	233,805	13,373
Gestational age	≤ 63 days	≤ 63 days	≤ 63 days
Location/organization	MSI Australia	Planned Parenthood USA	Planned Parenthood USA
Time period	2013-2015	2009-2010	2006-2011
Incomplete abortion requiring aspiration	4.84%	Not reported	2.3%
Unrecognized ectopic pregnancy	Not reported	0.007%	Not reported
Ongoing pregnancy	0.76%	0.5%	0.5%
Transfusion	0.13%	0.05%	0.03%
Infection	0.11%	0.02%	0.01%
Death	<0.01% (1 death from pneumonia, likely unrelated)	0.0004% (1 death from unrecognized ectopic pregnancy)	No deaths

Misoprostol only

Safety and effectiveness data for medical abortion with misoprostol only are more limited. Large retrospective case series documenting success and complication rates are not available. Disparate regimens, gestational age ranges, timeframes to measure abortion success and reporting of complications makes comparison of success and complication rates across studies of misoprostol-only medical abortion difficult.

EFFECTIVENESS

The largest randomized trial using the recommended misoprostol-only regimen, repeated doses of 800mcg of misoprostol by either the vaginal or sublingual route, included 2,046 women with gestations of seven weeks or less (von Hertzen et al., 2007). Success of misoprostol-only abortion was 84%. Smaller studies using similar regimens have reported success rates of 92% for gestations up to eight weeks (Fekih, 2010), 89-91% up to nine weeks (Salakos et al., 2005; Velazco et al., 2000), and from 84-87% from 9-13 weeks (Carbonell, Varela, Velazco, Tanda & Sanchez, 1999; Carbonell Esteve et al., 1998, Carbonell et al., 2001).

In general, higher rates of success with misoprostol-only regimens are associated with lower gestational ages (von Hertzen et al., 2007; Zikopoulos et al., 2002), higher number of repeat doses of misoprostol (Carbonell et al., 1999; Jain, Dutton, Harwood, Meckstroth, & Mishell, 2002) and a longer time period before provider follow-up to confirm abortion success (Bugalho, Mocumbi, Faundes, & David, 2000).

SAFETY

The most commonly reported complications with misoprostol-only medical abortion are incomplete and failed abortion requiring aspiration. In studies that used the recommended misoprostol-only regimen or similar regimens, the rate of aspiration for any reason ranges from 12-17%, with ongoing pregnancy rates of 3-10% (Carbonell et al., 1999; Carbonell et al., 2001; Velazco et al., 2000; von Hertzen et al., 2007). Other complications are infrequently reported: Bleeding requiring aspiration occurs in 1-4% of women (Velazco et al., 2000; Salakos et al., 2005; Carbonell et al., 1999; Carbonell Esteve et al., 1998), transfusion is required in less than 1% of women (von Hertzen, et al., 2007; Carbonell et al., 1999), and infection is reported in 1-4% of women (Velazco et al., 2000; Carbonell et al., 2001; von Hertzen et al., 2007; Carbonell et al., 1999).

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RISK OF FETAL MALFORMATIONS

22



Recommendation

Exposure to mifepristone alone has not been shown to cause fetal malformations. Exposure to misoprostol carries a small increased risk of malformations if the woman has an ongoing pregnancy and decides not to terminate. Women with an ongoing pregnancy after using misoprostol should be counseled about the risk if they choose to carry the pregnancy to term.

Strength of recommendation

Strong

Quality of evidence

- Mifepristone: Very low
- Misoprostol: Very low

Last reviewed: October 30, 2017

Background

The expected rate of fetal malformations in the general population is approximately 3% (Dolk, Loane, & Garne, 2010). Exposure to certain medications, infections, radiation or drugs of abuse during embryonic or fetal development may result in an increased risk of malformations if the pregnancy continues.

Mifepristone

Data on continuing pregnancy after mifepristone exposure without misoprostol are limited. The largest prospective study of 46 women continuing a pregnancy after mifepristone resulted in eight miscarriages and, in the pregnancies that continued, two major malformations (5.3%). Neither malformation was thought to be related to mifepristone exposure but may have been a result of other medical conditions (Bernard et al., 2013).

Misoprostol

Case reports, cohort studies (da Silva Dal Pizzol et al., 2005; Vauzelle, Beghin, Cournot, & Elephant, 2013) and case-control studies (da Silva Dal Pizzol, Knop, & Mengue, 2006) show that the incidence of malformations peaks if misoprostol is used between 5-8 weeks after a woman's last menstrual period (LMP) and is not associated with anomalies following exposure after 13 weeks following a woman's LMP (Philip, Shannon, & Winikoff, 2002). The most typical malformations associated with misoprostol use are Möbius sequence, a rare disorder of cranial nerve palsies associated with limb anomalies and craniofacial defects, and terminal transverse limb defects (da Silva Dal Pizzol, et al., 2006). Although not clearly established, the proposed mechanism is vascular disruption from uterine contractions leading to disordered fetal development (Gonzalez et al., 2005; Shepard, 1995).

A systematic review of four case-control studies with 4,899 cases of congenital anomalies and 5,742 controls showed an increased rate of misoprostol exposure in cases with anomalies (da Silva Dal Pizzol, et al., 2006). Misoprostol exposure was 25 times more likely in cases with Möbius sequence and 12 times more likely in cases with terminal transverse limb defects. In a cohort of 183 women exposed to misoprostol during the first 12 weeks of pregnancy, the major malformation rate was 5.5%; half of these were consistent with misoprostol malformation patterns (Auffret et al., 2016). However, a prospective follow-up study comparing women who used misoprostol before 12 weeks of pregnancy to women who used antihistamines did not find a statistically significant difference in the rate of fetal malformations, although three malformations (2%) in the misoprostol group were consistent with misoprostol-related anomalies (Vauzelle, et al., 2013).

Although the rate of misoprostol exposure is higher in children born with characteristic defects such as Möbius sequence, the anomalies are so rare that the overall risk is low that a woman who takes misoprostol before 13 weeks gestation and carries a pregnancy to term will have a child born with a malformation related to misoprostol exposure. The risk of fetal malformation related to misoprostol exposure is less than 10 per 1,000 exposures (Philip, et al., 2002).

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MIFEPRISTONE AND MISOPROSTOL: RECOMMENDED REGIMEN

23



Recommendation

- **Up to 10 weeks gestation (70 days since last menstrual period (LMP)):** Mifepristone 200mg orally followed 1-2 days later by misoprostol 800mcg buccally, sublingually or vaginally.
- **10-13 weeks gestation:** Mifepristone 200mg orally followed 1-2 days later by misoprostol 800mcg vaginally then 400mcg vaginally or sublingually every three hours until expulsion.

Strength of recommendation

Strong

Quality of evidence

- Up to 10 weeks gestation: High
- 10-13 weeks gestation: Low

Last reviewed: January 13, 2018

Up to nine weeks (63 days since LMP)

Multiple randomized controlled clinical trials have shown that the combination of mifepristone and misoprostol is an effective medical abortion regimen with success rates ranging from 95-98% up to nine weeks gestation (Chen & Creinin, 2015; Kapp, Baldwin, & Rodriguez, 2018; Kulier et al., 2011; Raymond, Shannon, Weaver, & Winikoff, 2012). Vaginal, buccal and sublingual misoprostol are more effective than oral misoprostol (Kulier et al., 2011). Buccal dosing (Middleton et al., 2005) and sublingual dosing (Tang, Chan, Ng, Lee, & Ho, 2003; von Hertzen et al., 2010) have higher rates of gastrointestinal side effects than vaginal dosing. Sublingual dosing is associated with more side effects than buccal dosing (Chai, Wong, & Ho, 2013). Decreasing the sublingual misoprostol dose to 400mcg to decrease rates of side effects, however, increases the rates of incomplete abortion and ongoing pregnancy (Bracken et al., 2014; Raghavan et al., 2013; von Hertzen et al., 2010); therefore, the recommended dose of sublingual misoprostol remains 800mcg.

In some settings, buccal or sublingual dosing may be preferred over vaginal dosing to accommodate women's preferences or legal restrictions.

9-10 weeks (64-70 days since LMP)

A 2015 review reports data from five comparative studies including 801 women with gestations between 64-70 days and 1,163 with gestations from 57-63 days (Abbas, Chong, & Raymond, 2015). In four studies, women received 200mg mifepristone followed by 800mcg buccal misoprostol (Boersma, Meyboom-de Jong, & Kleiverda, 2011; Pena et al., 2014; Sanhueza Smith et al., 2015; Winikoff et al., 2012) and in one study, women received mife-

pristone and 400mcg sublingual misoprostol (Bracken et al., 2014). There was no difference in success rates between the two gestational groups (93.9% at 57-63 days compared to 92.3% at 64-70 days). Further, there were no differences in serious adverse events, such as hospital admissions or transfers, between the groups (0.7% and 0.5% respectively). One observational study included in the review reported an abortion success rate of 94.5% from 9-10 weeks when women used a regimen of mifepristone followed by 800mcg of vaginal misoprostol (Gouk et al., 1999). An additional study published since this review used 200mg mifepristone followed by 600mcg of sublingual misoprostol with a reported abortion success rate of 99% for the gestational age range from 9-10 weeks (Platais, Tsereteli, Grebennikova, Lotarevich, & Winikoff, 2016).

10-13 weeks

A retrospective cohort study of 1,076 women showed that a combination of 200mg mifepristone followed 36-48 hours later by misoprostol (800mcg vaginally or 600mcg sublingually), and then repeated doses of 400mcg misoprostol vaginally or sublingually every three hours for two additional doses is safe and effective between 9-13 weeks (Hamoda, Ashok, Flett, & Templeton, 2005). All women took misoprostol in the health facility. The success rate for this regimen was high at 95.8%, with a low rate of serious adverse events. A smaller prospective cohort study (Lokeland et al., 2010) including 254 women reported an abortion success rate of 91.7% using a similar regimen. A small prospective cohort study examined effectiveness of mifepristone 200mg orally followed 36-48 hours later by misoprostol 800mcg vaginally as a single dose (Gouk et al., 1999), and found a success rate of 95% among 126 women with pregnancies between 70-83 days.

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MISOPROSTOL ONLY: RECOMMENDED REGIMEN

Recommended regimen before 13 weeks gestation

Misoprostol 800mcg vaginally or sublingually every three hours until expulsion.

Strength of recommendation

Strong

Quality of evidence

- Up to nine weeks gestation: Moderate
- 9-13 weeks gestation: Low

Last reviewed: January 15, 2018

Success of misoprostol-only medical abortion

The success rate of medical abortion with misoprostol only is around 85% (von Hertzen et al., 2007) and should be considered only when mifepristone is not available. In general, misoprostol-only regimens have higher rates of success at gestational ages less than 7 weeks (von Hertzen et al., 2007; Zikopoulos et al., 2002), with higher numbers of doses (Carbonell, Varela, Velazco, Tanda, & Sanchez, 1999) and with a longer time before provider follow-up to confirm abortion success (Bugalho, Mocumbi, Faundes, & David, 2000). However, women's satisfaction decreases the longer the abortion process lasts (Ngai, Tang, Chan, & Ho, 2000).

Misoprostol-only abortion up to 9 weeks

The only multicenter randomized controlled trial to compare different misoprostol-only dosing intervals showed that complete abortion rates are equivalent when misoprostol is given vaginally every 3-12 hours or sublingually every three hours for three doses. Sublingual dosing had a higher incidence of side effects than vaginal dosing (von Hertzen et al., 2007).

Misoprostol-only abortion between 9-13 weeks

There is scant evidence upon which to recommend an appropriate misoprostol-only regimen between 9-13 weeks. Findings from comparative trials indicate that vaginal and sublingual dosing have similar efficacy and are superior to oral dosing (Ganguly et al., 2010; Van Bogaert & Misra, 2010). Several small cohort studies confirm the effectiveness of the both the vaginal and sublingual routes, and also confirm increased success when multiple doses of misoprostol are used (Carbonell Esteve et al., 1998; Carbonell et al., 1999; Carbonell et al., 2001; Grapsas et al., 2008; Tang, Miao, Lee, & Ho, 2002). There is strong evidence in randomized controlled trials of misoprostol-only regimens that support using a vaginal dosing interval of every three hours for gestations over 13 weeks (von Hertzen et al., 2009). Extrapolating from the evidence supporting repeat doses of sublingual or vaginal misoprostol at gestations both below nine and above 13 weeks, the evidence-based regimen recommend-

ed for gestations below nine weeks may be used for gestations between 9-13 weeks.

Young women

Safety and efficacy of misoprostol-only abortion has been demonstrated in adolescents with pregnancies up to nine weeks gestation (Velazco et al., 2000) and between 9-12 weeks gestation (Carbonell et al., 2001). Success rates of misoprostol-only abortion in young women are similar to those seen in studies of older women.

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HOME USE OF MEDICATIONS UP TO 10 WEEKS GESTATION

Recommendation

- Women may take mifepristone in a facility or at home.
- Home use of misoprostol following mifepristone or in a misoprostol-only regimen may be offered up to 10 weeks gestation.

Strength of recommendation

Strong

Quality of evidence

- Up to 70 days gestation: Moderate
- Over 70 days gestation: Very low

Last reviewed: January 15, 2018

Mifepristone and misoprostol regimen

Traditionally, providers have given mifepristone to women to take in a facility to start the abortion process. Then 1-2 days later, women may take misoprostol in a health facility, their own home or another safe location. Because of women's individual preferences for privacy, support and timing, they should have options about the location of mifepristone and misoprostol use.

HOME USE OF MIFEPRISTONE

Two prospective, nonrandomized multicenter cohort studies conducted in the United States, which together included 701 women, showed that between a third and a half of women offered home or facility use of mifepristone chose home use (Chong et al., 2015; Swica et al., 2012). Women who used mifepristone at home were highly satisfied and had similar success rates and need for telephone or emergency room support as women who took mifepristone in the clinic. In similar studies conducted in Azerbaijan (Louie et al., 2014), Nepal (Conkling, Karki, Tuladhar, Bracken, & Winikoff, 2015) and Kazakhstan (Platais, Tsereteli, Grebennikova, Lotarevich, & Winikoff, 2016), 74%, 72% and 64% of women, respectively, chose home use. The most commonly cited reasons for the choice to take mifepristone at home were flexibility, ability to schedule abortion around duties, partner's presence and a more private experience. Abortion success rates were the same in the home use and clinic use groups. When a woman chooses home use of mifepristone, she should take it within one week of the clinic visit at which she received the prescription or medication, provided her pregnancy does not exceed 10 weeks at that time.

HOME USE OF MISOPROSTOL UP TO 70 DAYS

A systematic review of nine prospective comparative cohort studies including 4,522 women up to 56 days gestation showed that complete abortion rates and adverse event rates were

the same for home- and facility-based misoprostol use (Ngo, Park, Shakur, & Free, 2011) as part of a mifepristone-misoprostol regimen. Women found home use as acceptable as clinic use. A non-randomized comparative trial including 731 rural and urban Indian women up to 63 days gestation found no difference in abortion success or adverse events between home and facility administration of misoprostol (Iyengar et al., 2016). Large observational studies up to 59 days (Fjerstad et al., 2009) and 63 days (Gatter, Cleland, & Nucatola, 2015; Goldstone, Walker, & Hawtin, 2017; Lokeland, Iversen, Engeland, Okland, & Bjorge, 2014; Louie et al., 2014; Raghavan et al., 2013) also confirmed the safety and efficacy of home use of misoprostol. The World Health Organization (WHO, 2014) and Royal College of Obstetricians and Gynaecologists (RCOG, 2015) recommend home use of misoprostol up to 63 days gestation.

A multicenter study of 729 women in the United States comparing a single dose of buccal misoprostol 800mcg at home from 57-63 days and from 64-70 days as part of a mifepristone-misoprostol regimen showed no difference between the groups in success rates, ongoing pregnancy or adverse events (Winikoff et al., 2012). A prospective, open-label trial conducted in India, Georgia, Tunisia and Ukraine compared outcomes of 703 women who received mifepristone followed by 400mcg of sublingual misoprostol in the home for pregnancies of 57-63 days or 64-70 days gestation (Bracken et al., 2014). Success rates and ongoing pregnancy rates did not differ between groups, although women in the later gestational age group were more likely to receive an additional dose of misoprostol or require intervention for bleeding. Additional smaller studies have shown similar results (Boersma, Meyboom-de Jong, & Kleiverda, 2011; Platais et al., 2016). The American College of Obstetricians and Gynecologists (ACOG, 2014) and the National Abortion Federation (NAF, 2017) recommend offering home use of misoprostol up to 70 days gestation.

HOME USE OF MISOPROSTOL FROM 10-13 WEEKS

There are no data regarding home use of misoprostol as part of a combined regimen after 10 weeks gestation.

Misoprostol-only regimen

No studies have directly compared safety and effectiveness of home use of misoprostol in a misoprostol-only regimen to health facility use. However, several studies with misoprostol-only arms have allowed women to self-administer the medication at home up to nine weeks gestation without an effect on safety or medical abortion success (Blum et al., 2012; Ngoc et al., 2011). Additionally, three small prospective cohort studies of misoprostol-only abortion conducted in Cuba allowed home use of medication up to 9 (Carbonell, Valera, Velazco, Fernandez, & Sanchez, 1997; Velazco et al., 2000), or between 9-12 gestational weeks (Carbonell et al., 2001) without an effect on safety or success. Two studies that enrolled only adolescents (Carbonell et al., 2001; Velazco et al., 2000) found higher rates of nausea and vomiting than observed in studies with adult women.

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CONFIRMATION OF SUCCESS

Recommendation

- Most women undergoing abortion with a combined regimen of mifepristone and misoprostol can confirm success; routine follow-up is not required.
- Women using a misoprostol-only regimen for medical abortion need follow-up with a clinician to ensure the abortion was successful and to detect ongoing pregnancy.
- Providers may perform a clinical assessment to assist in the confirmation of successful abortion.
- Ultrasound or other testing is needed only in cases where the diagnosis is unclear.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: January 12, 2018

Medical abortion with mifepristone and misoprostol

The success rate of mifepristone followed by misoprostol for medical abortion up to 10 weeks gestation is over 95%, with ongoing pregnancy rates of less than 2% (Chen & Creinin, 2015; Kulier et al., 2011; Raymond, Shannon, Weaver, & Winikoff, 2012). The World Health Organization (WHO) has determined that routine follow-up after medical abortion with mifepristone and misoprostol is not required (2014). Multiple strategies have been examined to confirm a successful medical abortion and identify rare ongoing pregnancies when using the mifepristone and misoprostol regimen.

WOMEN'S ASSESSMENT OF SUCCESSFUL ABORTION

Evidence indicates that women can accurately determine when their mifepristone and misoprostol medical abortion is successful—that is, whether pregnancy expulsion has occurred. In studies comparing women's assessments of expulsion based on their symptoms to those made by clinicians (Cameron, Glasier, Johnstone, Dewart, & Campbell, 2015; Clark et al., 2010; Perriera et al., 2010; Rossi, Creinin, & Meyn, 2004) and by ultrasound (Rossi et al., 2004), women have repeatedly proven to be nearly as accurate as both.

CLINICAL ASSESSMENT

Providers may help confirm successful mifepristone and misoprostol abortion at a follow-up visit by reviewing a patient history and performing a bimanual exam if indicated. In studies comparing clinical assessment to ultrasound (Rossi et al., 2004; Pymar, Creinin, & Schwartz, 2001), clinicians determined pregnancy expulsion with high levels of accuracy.

ULTRASOUND

Ultrasound can be used to confirm successful abortion but is not necessary and can add to the cost and complexity of medical abortion, particularly where providers are inexperienced in reading post-medical abortion ultrasound (Kaneshiro, Edelman, Sneeringer, & Gómez Ponce de León, 2011). Ultrasound is helpful in cases where there is doubt about the presence of an ongoing pregnancy.

SERUM PREGNANCY TESTING

Serum pregnancy testing has been used as an alternative to ultrasound to diagnose an ongoing pregnancy following mifepristone and misoprostol and compares favorably to ultrasound in reducing interventions at the time of follow-up (Clark, Panton, Hann, & Gold, 2007; Dayananda, Maurer, Fortin, & Goldberg, 2013; Fiala, Safar, Bygdeman, & Gemzell-Danielsson, 2003). Serum pregnancy testing is only useful when a pre-treatment hCG has been obtained for comparison; hCG declines by more than 90% seven days after mifepristone is administered in the case of a successful medical abortion (Pocius et al., 2016). Serum pregnancy testing is useful only where laboratory testing is readily accessible.

URINE PREGNANCY TESTING

A negative urine pregnancy test is reassuring that an abortion has been successful. Rarely, however, a pregnancy test is negative but a woman is still pregnant (false negative). Both high-sensitivity and low-sensitivity urine pregnancy tests can have positive results even when the medical abortion has been successful (false positive) (Cameron, Glasier, Dewart, Johnstone, & Burnside, 2012; Clark et al., 2010; Godfrey, Anderson, Fielding, Meyn, & Creinin, 2007; Perriera et al., 2010). A number of studies have examined use of low-sensitivity (Cameron et al., 2012, Cameron et al., 2015; Constant, Harries, Daskilewicz, Myer, & Gemzell-Danielsson, 2017; Iyengar et al., 2015; Michie & Cameron, 2014) and semi-quantitative or multi-level (Oppegaard et al., 2015; Raymond et al., 2017a; Raymond et al., 2017b) urine pregnancy tests, often in combination with a symptom checklist, to confirm a successful abortion or identify an ongoing pregnancy without returning for follow-up. A 2017 meta-analysis, which included seven studies that examined use of multi-level pregnancy tests to confirm abortion success when using the combined regimen up to 9 weeks gestation, found that the tests identified all continuing pregnancies (21 out of 1,599 participants, 1.3%) and that most women can successfully perform the tests themselves at home (Raymond et al., 2017a).

Medical abortion with misoprostol only

Due to the lower success rate (85%) and higher rate of ongoing pregnancy following misoprostol-only medical abortion before 13 weeks gestation (von Hertzen et al., 2007), WHO recommends routine clinic follow-up for all women undergoing medical abortion with misoprostol only to ensure success of the abortion (WHO, 2014).

FOLLOW-UP ASSESSMENT

There are no studies examining different strategies to determine abortion success when using the misoprostol-only regimen. Possible follow-up strategies, extrapolated from studies about the combined regimen (detailed above) and programmatic data, include a history and physical examination, bimanual examination, ultrasound and/or a serum or urine pregnancy testing to rule out an ongoing pregnancy.

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ULTRASOUND FINDINGS AT FOLLOW-UP

Recommendation

If clinicians choose to use ultrasound for medical abortion follow-up, the only ultrasound finding that requires intervention is an ongoing viable pregnancy.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: October 31, 2017

Background

Ultrasound is not necessary to provide abortion care (World Health Organization (WHO), 2014) but may be common in some settings. Ultrasound for follow-up after medical abortion has diagnostic limitations. Except for the rare case of an ongoing viable pregnancy, intervention after a medical abortion should be based on clinical symptoms and not ultrasound findings.

Ultrasound findings at follow-up

Endometrial thickening: After a successful medical abortion, endometrial thickness varies and can be associated with a complex or heterogeneous appearance.



Endometrial thickening

Courtesy of Mary Fjerstad

Multiple retrospective and prospective cohort studies have shown that endometrial thickness has a wide range in women after medical abortion, with significant overlap between women with successful and failed medical abortion (Cowett, Cohen, Lichtenberg, & Stika, 2004; Markovitch, Tepper, Klein, Fishman, & Aviram, 2006; Parashar, Iversen, Midbøe, Myking, & Bjørge, 2007; Rørbye, Nørgaard, & Nilas, 2004; Tzeng, Hwang, Au, & Chien, 2013).

In a pooled analysis of 2,208 women one week after medical abortion, after women with a persistent gestational sac were excluded, the average endometrial thickness was 10.9mm in women who did not require more intervention and 14.5mm in 30 women who did require intervention (Reeves, Fox, Lohr, & Creinin, 2009). Although the average endometrial thickness in women who require intervention tends to be higher, because of the range and overlap between successful and unsuccessful abortion, no study has found that there is a thickness above which a diagnosis of unsuccessful medical abortion can be made. The decision to intervene should be made on clinical signs and symptoms, such as ongoing or heavy bleeding, rather than on ultrasound findings.

Persistent gestational sac: A persistent gestational sac, in which the sac is present but there is no viable embryonic tissue, occurs in less than 1% of medical abortions with the recommended mifepristone and misoprostol regimen (Creinin et al., 2004; Creinin et al., 2007; Winikoff et al., 2008). A persistent gestational sac is not a viable pregnancy and may be managed with aspiration, a second dose of misoprostol or expectant management according to a woman's preference. In a study of women with a persistent gestational sac within 11 days of medical abortion, a second dose of misoprostol was found to lead to expulsion of a nonviable sac in 69% of women (Reeves, Kudva, & Creinin, 2008).



Persistent gestational sac

Courtesy of Mary Fjerstad

Ongoing viable pregnancy: An ongoing pregnancy, in which a growing sac and/or embryo with cardiac activity are present, occurs in less than 1% of medical abortions with the recommended mifepristone and misoprostol regimen (Von Hertzen et al., 2009; Winikoff et al., 2008). Some women will be able to identify this outcome without ultrasound due to lack of bleeding or continued pregnancy symptoms. A woman with an ongoing pregnancy should be offered uterine evacuation as soon as possible with either vacuum aspiration or a second dose of misoprostol, depending on gestational age and local context. The success rate of misoprostol after failed medical abortion is 36% (Reeves et al., 2008; WHO, 2014). If a woman chooses a second dose of misoprostol, she must be followed to see if it is successful.

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WHO HAS ABORTIONS AT 13 WEEKS OR LATER?

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Key information

Women who present for abortion at 13 weeks of pregnancy or later are more likely than those who present at earlier gestations to be young or a victim of violence, have detected their pregnancy later, feel ambivalent about the abortion decision, and/or have financial and logistical barriers to care. Additionally, medical or fetal indications for an abortion may not be apparent until after 13 weeks. Reasons for presenting at or after 13 weeks gestation appear similar across countries and cultures and disproportionately affect underserved women.

Quality of evidence

High

Last reviewed: December 11, 2017

Epidemiology of abortion at 13 weeks and later

While abortions at or after 13 weeks gestation comprise a minority (around 10-15%) of the total abortions worldwide, they are responsible for the majority of serious abortion-related complications (Harris & Grossman, 2011; Jatlaoui et al., 2017; Loeber & Wijssen, 2008). In more restrictive settings, or where safe abortion access is limited, presentation at or after 13 weeks gestation for postabortion care is more common. In Cambodia 17%, in Ethiopia 38%, and in Kenya 41% of women needing postabortion care present at or after 13 weeks gestation. (African Population and Health Research Center, Ministry of Health Kenya, Ipas Kenya, & Guttmacher Institute, 2013; Feters, Vonthanak, Picardo, & Rathavy, 2008; Gebreselassie et al., 2010).

Why do women need abortions at 13 weeks and later?

Young age: Young women are disproportionately likely to seek abortion at or after 13 weeks. In the United States, 22.6% of girls younger than age 15 and 12.5% of adolescents ages 15-19 seeking abortion care do so after 13 weeks gestation (Jatlaoui et al., 2017). Smaller case-control and cohort studies in Ethiopia, India, Nepal, Singapore and the United States have found young age to be a risk factor for later presentation (Bonnen, Tuijje, & Rasch, 2014; Foster & Kimport, 2013; Lim, Wong, Yong, & Singh, 2012; Sowmini, 2013).

Late detection of pregnancy: A common risk factor in all studies for presenting for abortion at or after 13 weeks is late recognition of pregnancy. Absence of pregnancy signs and symptoms, menstrual irregularity, contraceptive use, or amenorrhea after recent pregnancy can mask physical signs of pregnancy and delay pregnancy diagnosis (Drey et al., 2006; Foster & Kimport, 2013; Gallo & Nghia, 2007; Harries, Orner, Gabriel, & Mitchell, 2007; Ingham, Lee, Clements, & Stone, 2008; Jones & Jerman, 2017; Purcell et al., 2014). In one case-control study in the United States, women who sought abortion after 20 weeks were much more likely to have been eight weeks pregnant or more at the time they discovered they were pregnant (68%), compared to women who had abortions before 13 weeks gestation (12%) (Foster & Kimport, 2013).

Ambivalence and/or difficulty with abortion decision: Women's decisionmaking may be delayed due to social pressures, fears, religious attitudes and changes in relationship status. Changes in circumstance (such as abandonment by partner) cause some women to seek an abortion after initially planning to continue the pregnancy (Foster & Kimport, 2013; Gallo & Nghia, 2007; Harries et al., 2007). Discouraging family and friends may also delay a woman seeking care (Waddington, Hahn, & Reid, 2015).

Financial and logistical barriers: Unemployment and lack of insurance are risk factors for presentation at 13 weeks or later, according to studies conducted in the United States, as are poverty (Usta, Mitchell, Gebreselassie, Brookman-Amisshah, & Kwizera, 2008), being an immigrant (Gonzalez-Rabago, Rodriguez-Alvarez, Borrell, & Martin, 2017; Loeber & Wijssen, 2008) and rural residence (Bonnen et al., 2014). Delays may be related to raising enough money to cover the cost of the procedure, particularly as procedures later in gestation are more expensive (Foster & Kimport, 2013; Kiley, Yee, Niemi, Feinglass, & Simon, 2010). Abortions at or after 13 weeks gestation are provided at a limited number of facilities and travel logistics present difficulties for many. In one case-control study of women presenting for abortion at over 20 weeks gestation, women were much more likely than those at earlier gestations to have travelled over three hours to access care (Foster & Kimport, 2013). Clients at 13 weeks gestation or later may be referred by other providers or have trouble finding a provider before finally accessing care (Drey et al., 2006; Harries et al., 2007). Women may also need to travel out of their own country to access legal abortion after 13 weeks (Cameron et al., 2016; Loeber & Wijssen, 2008).

Fetal indications: Diagnosis of fetal anomalies typically occurs after the first 12 weeks of pregnancy, and women may make the decision to terminate pregnancy based on the diagnosis (Lyus, Robson, Parsons, Fisher, & Cameron, 2013).

Maternal indications: A woman may have a medical condition that worsens through the course of pregnancy or a new condition may arise in pregnancy that endangers her life or health. Severe preeclampsia or preterm premature rupture of membranes may require termination of pregnancy to save a woman's life (American College of Obstetricians and Gynecologists, 2015).

Victims of violence: Victims of violence have a higher risk of late presentation (Colarossi & Dean, 2014; Perry et al., 2015).

Failed abortion: Although failures are rare, women who experience an ongoing pregnancy after an abortion before 13 weeks may not discover they are still pregnant until after 13 weeks gestation (Gallo & Nghia, 2007).

Cultural beliefs: In rare cases there are local beliefs that having an abortion at 13 weeks or later is safer than the first 12 weeks of pregnancy, thus causing women to delay care (Marlow et al., 2014).

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COMPARING METHODS

Key information

- Dilatation and evacuation (D&E) and medical abortion with mifepristone and misoprostol or misoprostol only are safe and effective methods of abortion.
- Women should be offered a choice of methods when both D&E and medical abortion are available.
- Medical abortion has a higher rate of retained products of conception, failed abortion and minor adverse events.
- D&E requires a trained, experienced provider and specialized equipment.

Quality of evidence

Moderate

Last reviewed: December 11, 2017

Comparison of methods

In retrospective cohort studies, women with gestations 13-24 weeks who had medical abortions had an increased rate of failed abortion and retained products of conception with a need for further intervention compared to women who had D&E (Autry, Hayes, Jacobson, & Kirby, 2002; Bryant, Grimes, Garrett, & Stuart, 2011; Sonalkar, Ogden, Tran, & Chen, 2017). However, the rate of major adverse events including infection, transfusion, hysterectomy and death does not differ between the two methods.

The largest trial comparing methods randomized 122 women with gestations between 13-20 weeks to D&E or medical abortion with mifepristone and misoprostol (Kelly, Suddes, Howel, Hewison, & Robson, 2010). Overall rates of complications were similar in the two groups, although the types of complications differed. Five women in the medical arm required uterine evacuation for retained products of conception and one suffered bleeding requiring transfusion; only one woman in the surgical arm required repeat uterine evacuation, one suffered a cervical laceration, and five had hemorrhage that did not require transfusion. A statistically significant proportion of women randomized to medical abortion had more bleeding and pain and found abortion less acceptable than women who had D&E. A pilot randomized trial of 18 women with gestations between 14-19 weeks comparing D&E and medical abortion with mifepristone and misoprostol found a higher rate of adverse events, specifically retained placenta and fever, in women undergoing medical abortion, although none were serious (Grimes, Smith, & Witham, 2004).

In published studies of medical abortion compared to D&E, rates of intervention for medical abortion may be artificially high because failure was defined as no delivery within 24 hours (Bryant et al., 2011) and retained placenta was diagnosed after two hours (Grimes et al., 2004). In practice, more time may be allowed for successful medical abortion to occur.

The importance of choice

In settings where both D&E and medical abortion are available, if a woman is a candidate for either procedure, she should be offered a choice. Both randomized trials referenced above (Kelly et al., 2010; Grimes, et al., 2004) had difficulty with recruitment due to women's strong preferences for one type of abortion over the other. Choice of methods is very individual—some women prefer the speed and predictability of D&E, while others prefer a more “labor-like” process with an intact fetus (Kelly et al., 2010; Kerns et al., 2012). Some women may want to see or hold an intact fetus, and an intact fetus may allow for a more comprehensive fetal autopsy where it is needed.

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GESTATIONAL DATING

Recommendation

- Gestational age should be calculated using a woman's last menstrual period (LMP) combined with physical examination.
- Routine use of ultrasound for gestational age determination is not necessary.

Strength of recommendation

Strong

Quality of evidence

Very low

Last reviewed: January 23, 2018

Importance of accurate gestational dating

Errors in gestational dating can increase the risks associated with abortion. If gestational age is underestimated prior to dilatation and evacuation (D&E), providers may not have the experience and equipment to complete the procedure safely. Accurate assessment of gestational age enables providers to determine whether the facility is equipped to provide the requested service, and refer to another facility if necessary.

Dating

Gestational dating using bimanual examination and women's LMP is well established during prenatal care, as is the use of ultrasound. No trials have compared the accuracy of different methods of gestational dating prior to abortion at or after 13 weeks, and a 2011 systematic review aimed at determining if preabortion ultrasound affected the safety or efficacy of abortion procedures both before and after 13 weeks found no relevant studies (Kulier & Kapp, 2011). In the United States, 99% of providers use ultrasound for gestational dating after 12 weeks gestation, but data are lacking from other country contexts (O'Connell, Jones, Lichtenberg, & Paul, 2008).

Prior to medical abortion, gestational age can be estimated using the first day of a woman's LMP and a physical examination that includes bimanual and abdominal examination (Nautiyal, Mukherjee, Perhar, & Banerjee, 2015; Ngoc et al., 2011; Royal College of Obstetricians and Gynaecologists [RCOG], 2015; World Health Organization [WHO], 2014). Measuring fundal height, as in routine obstetric care, can provide additional information. Ultrasound can be used to confirm gestational age if the LMP and clinical examination are discordant or if there is uncertainty about gestational age, but is not required prior to medical abortion.

In published studies of D&E, including reports of implementation of D&E programs (Castleman, Oanh, Hyman, Thuy, & Blumenthal, 2006; Jacot et al., 1993), ultrasound has been routinely used to establish or confirm gestational age prior to D&E. However, one published

report (Altman, Stubblefield, Schlam, Loberfeld, & Osathanondh, 1985), unpublished programmatic data (A. Edelman, personal communication, January 12, 2018) and expert opinion support use of LMP and physical examination for gestational dating, with use of ultrasound as needed (RCOG, 2015; WHO, 2014). If ultrasound is used, biparietal diameter is a simple and accurate method to confirm gestational age (Goldstein & Reeves, 2009). A femur length measurement can be used to confirm the biparietal diameter or used if there are technical difficulties in obtaining a biparietal measurement.

Women who present with fetal demise, incomplete abortion or for postabortion care may have discordant LMP dates and uterine size; they should be treated according to uterine size (RCOG, 2016).

After the abortion, clinicians can confirm gestational age by comparing actual fetal measurements (fetal foot length) to the expected gestational age (Drey, Kang, McFarland, & Darney, 2005). This comparison provides feedback regarding the accuracy of pre-procedure dating estimates. Pregnancy dating tools, such as fetal measurements, are included in Ipas's Dilation & Evacuation (D&E) Reference Guide: Induced Abortion and Postabortion Care at or After 13 Weeks Gestation, page 38 (2017), and Medical Abortion Reference Guide: Induced Abortion and Postabortion Care at or After 13 Weeks Gestation, page 30 (2017).

Identification of fetal sex with ultrasound

After 14 weeks gestation ultrasonographic visualization of the male penis or female labial folds can be used to determine fetal sex in approximately 90% of gestations (Gelaw & Bistrat, 2011; Meagher & Davidson, 1996; Watson, 1999; Whitlow, Lazanakis & Economides, 1999).

Before 14 weeks, male and female genitals are similar in size and appearance on ultrasound (Feldman & Smith, 1975) and sex determination must instead be made by identification and evaluation of the genital tubercle (a protuberance on the lower ventral wall of the embryo that eventually becomes the penis or clitoris), (Efrat, Akinfewa, & Nicolaides, 1999). A 2013 review of studies determining fetal sex through ultrasonographic evaluation of the genital tubercle (Colmant, Morin-Surroca, Fuchs, Fernandez, & Senat, 2013) found that sex determination via this method was unreliable below 12 weeks gestation. Findings published since the review have been similar (Gonzalez Ballano, Saviron Cornudella, Puertas, & Luis, 2015; Lubusky, Studnickova, Skrivanek, Vomackova, & Prochazka, 2012; Manzanares, Benitez, Naveiro-Fuentes, Lopez-Criado & Sanchez-Gila, 2016).

Regardless of the method employed to determine fetal sex, accuracy improves with increasing gestational age (Elejalde, Elejalde, & Heitman, 1985; Colmant et al., 2013) and skill of the ultrasonographer (Lubusky et al., 2012). Unfavorable fetal position and a woman's body habitus may limit the ability to determine fetal sex regardless of gestational age or ultrasonographer skill (Behrendt, Foy, Center, & Durnwald, 2012; Efrat, Perri, Ramati, Tugendreich, & Meizner, 2006; Elejalde et al., 1985).

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INDUCED FETAL DEMISE

Recommendation

Induced fetal demise prior to medical abortion or dilatation and evacuation (D&E) at or after 13 weeks gestation does not increase the safety of abortion and is not recommended for medical indications. There may be legal or other indications for inducing fetal demise.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: October 31, 2017

Background

Some providers induce fetal demise prior to medical abortion or D&E at or after 13 weeks gestation. Practices and techniques used vary (Denny, Baron, Lederle, Drey, & Kerns, 2015). In some cases, patients, providers or staff may prefer that fetal demise occurs before an abortion procedure (Jackson, Teplin, Drey, Thomas, & Darney, 2001). Before medical abortion, induced fetal demise is one way to prevent transient fetal survival.

Safety and efficacy of inducing fetal demise

A randomized, controlled trial of induced fetal demise with intra-amniotic digoxin prior to D&E, which compared digoxin to saline injection, showed no benefit to digoxin and an increased rate of vomiting (Jackson et al., 2001). A retrospective cohort study comparing women with digoxin injection prior to D&E with historical controls who did not receive digoxin showed an increase in complications, including more hospital admissions, extramural deliveries and infections in women who received digoxin (Dean et al., 2012). One case series, which included nearly 5,000 D&E abortions performed between 18 and 24 weeks after digoxin injection found rates of extramural deliveries (0.3%) and infection (0.04%) that authors concluded were acceptably low (Steward, Melamed, Kim, Nucatola, & Gatter, 2012). There are no trials to evaluate the safety and efficacy of induced fetal demise before medical abortion with the currently recommended regimens for use at or after 13 weeks. There is no evidence that shows a medical benefit for the practice.

Technique

Fetal demise can be achieved prior to abortion at or after 13 weeks by injecting potassium chloride directly into the fetal heart or digoxin into the fetus or amniotic fluid.

Potassium chloride: Potassium chloride injection requires skill in ultrasound guidance techniques and has more potential risk due to the possibility of maternal intravascular injection

which can cause cardiac arrest (Borgatta & Kapp, 2011; Coke, Baschat, Mighty, & Malinow, 2004). It is not recommended in a low-resource setting.

Digoxin: In a pharmacokinetic study of eight women between 19-23 weeks who had intra-amniotic injection of digoxin 1mg prior to D&E, maternal serum digoxin levels were in the low therapeutic range and were not associated with cardiac changes (Drey, Thomas, Benowitz, Goldschlager, & Darney, 2000). A pilot randomized trial of intra-amniotic or intra-fetal digoxin at doses of 1mg or 1.5mg showed an overall rate of fetal demise of 87% with no difference in effectiveness based on the dose or route of administration (Nucatola, Roth, & Gatter, 2010). To be effective, digoxin intra-amniotic injection should be performed 1-2 days before the planned abortion procedure. Digoxin may be given transabdominally or transvaginally (Tocce, Sheeder, Edwards, & Teal, 2013).

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FOLLOW-UP

Recommendation

- Routine follow-up care is not necessary unless desired by the woman or necessary for her chosen contraceptive method.
- At the time of the abortion, clients should receive adequate information regarding post-abortion care and warning signs.

Strength of recommendation

Weak

Quality of evidence

Very low

Last reviewed: October 16, 2017

Follow-up

There is no scientific data to demonstrate that routine follow-up is beneficial after abortion at or after 13 weeks. In addition, there is no evidence to suggest that a pelvic examination is beneficial in an asymptomatic woman if she does return for a routine follow-up visit.

Quality of evidence

Very low. The recommendation is based on expert opinion (World Health Organization [WHO], 2014).

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CERVICAL PREPARATION**Recommendation**

- Routine preoperative cervical preparation is recommended before dilatation and evacuation (D&E).
- Osmotic dilators, misoprostol and mifepristone are options for cervical preparation. The choice depends on availability, expense, gestational age and timing of the procedure.

Strength of recommendation

Strong

Quality of evidence

High

Last reviewed: November 13, 2017**Background**

Cervical preparation prior to D&E reduces the risk of procedure related complications (Fox & Krajewski, 2014; Peterson, Berry, Grace, & Gulbranson, 1983). There is limited data to suggest the best method of cervical preparation before D&E because the trials that exist have heterogeneous comparisons, small enrollment numbers, and include few women with pregnancies over 20 weeks. Available trials typically show differences in cervical dilation or procedure times, however they do not include enough participants to show differences in rare but more serious outcomes such as cervical or uterine injuries or inability to complete the procedure (Newmann et al., 2010). Choice of method of cervical preparation is often limited by supply availability, especially in low-resource settings.

Possible cervical preparation methods include:

METHOD	DOSING	NOTE
Osmotic dilators (laminaria or synthetic osmotic dilators)	6-24 hours prior to procedure	Synthetic osmotic dilators may be used the day of the D&E
Misoprostol	400mcg buccally or vaginally 3 hours prior to procedure	May be used as a single agent up to 18 weeks, only very limited data to support use as a single agent over 18-20 weeks May be combined with osmotic dilators or mifepristone May be repeated as needed

METHOD	DOSING	NOTE
Mifepristone	200mg orally 24-48 hours prior to procedure	No data to support use as a single agent over 16 weeks Often used prior to misoprostol

Osmotic dilators

Numerous cohort studies have demonstrated that osmotic dilators are safe, effective and do not increase infectious morbidity (Bryman, Granberg, & Norström, 1988; Fox & Krajewski, 2014; Jonasson, Larsson, Bygdeman, & Forsum, 1989; Peterson et al., 1983). A Cochrane meta-analysis of cervical preparation before D&E between 14-24 weeks gestation showed that overnight osmotic dilators provide better cervical dilation when compared to prostaglandins, and decreased procedure time between 13-16 weeks gestation (Newmann et al., 2010). In one randomized controlled trial, synthetic dilators and laminaria worked equally well (Newmann et al., 2014). Decisions about the number and timing of dilators to place should be individualized and take into consideration the type of dilator and its size, the gestational age of the pregnancy, parity and cervical compliance, and the provider's experience (Fox & Krajewski, 2014; Newmann, Dalve-Endres, & Drey, 2008). Administration of paracervical block prior to dilator insertion eases the discomfort of dilator placement for women (Soon et al., 2017).

Misoprostol

Misoprostol is inexpensive, safe (Nucatola, Roth, Saulsberry, & Gatter, 2008), and more readily available than osmotic dilators in many low-resource settings. Misoprostol may be used alone for cervical preparation prior to D&E up to 18 weeks gestation (Fox & Krajewski, 2014; O'Connell, Jones, Lichtenberg, & Paul, 2008); there is limited data to support use of misoprostol as a single agent after 18 weeks (Maurer, Jacobson, & Turok, 2013). In studies comparing osmotic dilators to misoprostol, dilators provided more cervical dilation (Goldberg et al., 2005; Sagiv et al., 2015). However, women who received misoprostol for cervical preparation were able to have their procedures safely completed on the same day (Bartz et al., 2013; Goldberg et al., 2005; Sagiv et al., 2015), and women often preferred misoprostol to dilators (Goldberg et al., 2005). Misoprostol may be given to women with a prior cesarean delivery, as uterine rupture is rare (Fox & Krajewski, 2014).

Misoprostol plus osmotic dilators

Three randomized controlled trials have shown that misoprostol added to overnight laminaria improves cervical dilation between 16-19 weeks gestation (Goldberg et al., 2015), and improves cervical dilation and decreases operating time between 19-21 weeks gestation (Drey et al., 2013; Edelman, Buckmaster, Goetsch, Nichols, & Jensen, 2006) when compared to dilators alone. In all studies, side effects were greater among women using misoprostol.

One small prospective randomized trial has examined adding misoprostol to dilators for same-day D&E (Borras et al., 2016). Investigators ended this study early due to an unexpectedly high rate of complications—specifically serious cervical lacerations—in women over 19 weeks gestation who received dilators alone for cervical preparation.

Mifepristone

One randomized trial of 50 women between 14-16 weeks gestation compared mifepristone as a single agent to dilators, both administered the day prior to the abortion procedure (Borgatta et al., 2012). Women who had cervical preparation with osmotic dilators had a slightly

shorter procedure time and greater dilation compared to women given mifepristone, but women had less pain with mifepristone and strongly preferred it.

In studies examining the use of mifepristone in combination with misoprostol, same-day administration of mifepristone plus misoprostol is no better than misoprostol alone (Casey, Ye, Perritt, Moreno-Ruiz, & Reeves, 2016), and while administration of mifepristone 2 days prior to misoprostol resulted in improved cervical dilation in one study, the rate of preprocedure fetal expulsions was also increased (Carbonell et al., 2007). When compared to overnight dilators plus misoprostol, mifepristone administered the day prior to the abortion plus same-day misoprostol is less effective (Shaw et al., 2017).

Mifepristone plus osmotic dilators

Two randomized trials have assessed the addition of mifepristone when women received overnight osmotic dilators plus misoprostol for cervical preparation; neither study showed additional benefit with mifepristone (Shaw et al., 2017; Shaw et al., 2015). A third randomized trial compared overnight dilators alone, overnight dilators plus misoprostol, and overnight dilators plus mifepristone (Goldberg et al., 2015), and found that procedure times were no different between the three groups, although providers reported that procedures between 19-24 weeks gestation were easier in the dilators plus mifepristone group.

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SAFETY AND EFFECTIVENESS**Key information**

- A combined regimen with mifepristone and misoprostol is recommended over a misoprostol-only regimen for medical abortion at or after 13 weeks gestation.
- The combined regimen is safe and effective, with fetal expulsion rates of over 90% at 24 hours, median induction-to-abortion time of 6-10 hours and major complication rates of less than 1%.
- Where mifepristone is not available, misoprostol-only medical abortion is safe and effective, with fetal expulsion rates of 72-91% at 24 hours, average induction-to-abortion time of around 10-15 hours and major complication rates of less than 1%.

Quality of evidence

High

Last reviewed: January 5, 2018**Combined regimen with mifepristone and misoprostol***EXPULSION RATES*

Studies using the recommended regimen of mifepristone and misoprostol show fetal expulsion rates of 94% at 24 hours and 97% at 48 hours (Abbas et al., 2016), and fetal and placental expulsion rates of 88% at 24 hours and 92% at 48 hours (Dabash et al., 2015). When women continue misoprostol until expulsion with no cut off time, 99% of women eventually have a successful abortion (Ashok, Templeton, Wagaarachchi, & Flett, 2004; Louie et al., 2017).

INDUCTION-TO-ABORTION INTERVAL

In studies using the recommended mifepristone and misoprostol regimen, the median times to fetal expulsion were from 6-10 hours, with a wide range of times until complete expulsion (Abbas et al., 2016; Dabash et al., 2015; Louie et al., 2017; Ngoc et al., 2011; Shaw, Topp, Shaw, & Blumenthal, 2013). The induction-to-abortion interval is longer in nulliparous women, older women and women with pregnancies at a later gestational age (Abbas et al., 2016; Ashok et al., 2004; Dabash et al., 2015; Louie et al., 2017). The addition of mifepristone to a misoprostol medical abortion regimen consistently reduces the induction-to-abortion interval (Constant et al., 2016; Dabash et al., 2015; Kapp, Borgatta, Stubblefield, Vragovic, & Moreno, 2007; Ngoc et al., 2011).

COMPLICATION RATES

The rate of major complications from mifepristone and misoprostol medical abortion at or after 13 weeks gestation is low, although minor complications—such as needing a procedure for bleeding or retained products of conception—are more frequent than for dilatation and evacuation (Autry, Hayes, Jacobson, & Kirby, 2002). The largest related cohort study of medical abortion with mifepristone and misoprostol included 1,002 women between 13-21

weeks gestation. Eighty-one women (8.1%) needed a uterine evacuation procedure, the majority of which were needed for retained placenta; only two women needed an evacuation to terminate the pregnancy (Ashok et al., 2004). In this study, serious complications such as hemorrhage, blood transfusion or unanticipated surgery occurred in eight women (less than 1%). In a 2017 cohort study in which 120 women between 13-22 weeks gestation received mifepristone followed by unlimited dosing of misoprostol until fetal and placental expulsion, 99% of women evacuated the uterus without any additional intervention (Louie et al., 2017). No serious adverse events were reported in this study and only one woman failed to abort with the combined regimen.

In a meta-analysis of data from medical abortion studies at or after 13 weeks gestation using either the combined regimen or a misoprostol-only regimen, the overall rate of uterine rupture was 0.08%, with a rate of 0.28% in women with a previous cesarean section (Goyal, 2009).

SUBSEQUENT PERINATAL OUTCOMES

A Finnish register-based study of women who had a medical abortion up to 12 weeks gestation (3,427 women) or between 12-20 weeks gestation (416 women) compared incidence of several outcomes in subsequent pregnancies—preterm birth, low birth weight, small-for-gestational-age infants and placental complications (Mannisto et al., 2014). No differences were observed between the two groups, suggesting medical abortion at or after 13 weeks does not increase risk of these outcomes in subsequent pregnancies compared to earlier medical abortion.

Misoprostol-only regimen

EXPULSION RATES

The largest international randomized controlled trial of medical abortion at or after 13 weeks gestation with the recommended vaginal or sublingual misoprostol-only regimen included 681 women between 13-20 weeks gestation (von Hertzen et al., 2009). The fetal expulsion rate was 84.8% at 24 hours and 94.3% at 48 hours. Smaller randomized trials using vaginal or sublingual misoprostol every three hours showed fetal expulsion rates of 72-91% at 24 hours and 91-95% at 48 hours (Bhattacharjee, Saha, Ghoshroy, Bhowmik, & Barui, 2008; Tang, Lau, Chan, & Ho, 2004), and fetal and placental expulsion rates of 62-64% at 24 hours and 79-82% at 48 hours (Bhattacharjee et al., 2008). In nulliparous women, vaginal misoprostol has higher expulsion rates than sublingual misoprostol (von Hertzen et al., 2009).

INDUCTION-TO-ABORTION INTERVAL

In the von Hertzen trial cited above, the median time to fetal expulsion was 12 hours (range 4.1-61.8 hours), with parous women having faster induction-to-abortion times than nulliparous women (von Hertzen et al., 2009). In smaller randomized trials, time to expulsion ranges from 10-15 hours (Bhattacharjee et al., 2008; Tang et al., 2004). Lengthening the dosing interval of misoprostol from every three to every six hours increases the induction-to-abortion time (Wong, Ngai, Yeo, Tang, & Ho, 2000).

COMPLICATION RATES

The rate of major complications from misoprostol-only abortion at or after 13 weeks is low. In the trial cited above, 12 adverse events (0.02%) were reported; 10 women required blood transfusions (von Hertzen et al., 2009).

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MIFEPRISTONE AND MISOPROSTOL: RECOMMENDED REGIMEN

Recommended regimen for 13-24 weeks gestation

Mifepristone 200mg by mouth, followed 1-2 days later by misoprostol 400mcg vaginally, sublingually or buccally every three hours until fetal and placental expulsion.

Strength of recommendation

Strong

Quality of evidence

- Up to 20 weeks gestation: Moderate
- 21-24 weeks gestation: Low

Last reviewed: January 5, 2018

Background

Mifepristone combined with misoprostol is the preferred regimen for medical abortion at or after 13 weeks gestation, as it is highly efficacious, resulting in a short induction-to-abortion interval with an excellent safety profile (Borgatta & Kapp, 2011; Wildschut et al., 2011; World Health Organization [WHO], 2014). Mifepristone combined with misoprostol has a consistently shorter induction-to-abortion interval and higher expulsion rate at 15 (Ngoc et al., 2011), 24 (Constant et al., 2016) and 48 hours when compared to misoprostol alone (Dabash et al., 2015).

Mifepristone timing

A 2013 systematic review evaluating the effect of dosing interval between mifepristone and misoprostol on induction-to-abortion interval included 20 randomized controlled trials and nine observational studies (Shaw, Topp, Shaw, & Blumenthal, 2013). Based on the results of three randomized controlled trials, the review found that when mifepristone was given 12-24 hours before misoprostol, the induction-to-abortion interval was slightly longer (median 7.3 hours, range 7 to 8.5) than when mifepristone was administered 36 to 48 hours before misoprostol initiation (6.8 hours, range 6.3 to 7.2), but the abortion rate at 12 and 24 hours was the same (Shaw et al., 2013). In studies examining simultaneous administration of mifepristone and misoprostol, median expulsion times in the simultaneous group ranged from 10 to 13 hours, compared to 5 to 8 hours in women who waited 24 to 36 hours between mifepristone and misoprostol; however, rates of expulsion at 48 hours were equivalent in the two groups (Abbas et al., 2016; Chai et al., 2009).

Misoprostol loading dose

Although an early, large case series used an initial loading dose of vaginal misoprostol (Ashok, Templeton, Wagaarachchi & Flett, 2004), a more recent small, randomized controlled trial assigned 77 women to receive a loading dose of misoprostol vaginally (600mcg,

followed by 400mcg every six hours) and 80 women to receive a no-loading dose regimen (400mcg every six hours) (Pongsatha & Tongsong, 2014). Median induction-to-abortion intervals and rates of complete abortion at 24 and 48 hours did not differ between groups, but the loading dose group suffered significantly more misoprostol-related side effects. Recent clinical trials that did not use loading doses of misoprostol showed average induction-to-abortion intervals of 8-10 hours and similar or better success rates as studies with loading doses (Abbas et al., 2016; Dabash et al., 2015; Louie et al., 2017; Ngoc et al., 2011). Therefore, a high initial dose of misoprostol appears to confer no benefit on expulsion times.

Misoprostol dosing

Route: In clinical trials of medical abortion at or after 13 weeks, misoprostol 400mcg vaginally or sublingually has higher success and shorter induction-to-abortion intervals than oral dosing (Dickinson, Jennings & Doherty, 2014; Tang, Chang, Kan & Ho, 2005). Buccal misoprostol has not been directly compared to other routes in a combined regimen for medical abortion at or after 13 weeks, but has similar efficacy as other routes of administration in abortion before 13 weeks (Kulier et al., 2011; Raymond, Shannon, Weaver, & Winikoff, 2013). Studies that use buccal misoprostol as part of a combined mifepristone-misoprostol regimen show an average induction-to-abortion interval of 8-10 hours (Abbas et al., 2016; Dabash, 2015; Louie et al., 2017; Ngoc et al., 2011).

Dose: Misoprostol 400mcg has higher expulsion rates, shorter induction-to-abortion intervals and similar side effects compared to 200mcg, regardless of route of administration (Brouns, van Wely, Burger, & van Wijngaarden, 2010; Shaw et al., 2013).

Timing: In one randomized trial examining two regimens of misoprostol-only medical abortion at or after 13 weeks gestation, the induction-to-abortion interval was shorter and the expulsion rate at 24 hours was higher when misoprostol was given every three hours compared to every six hours; rates of adverse events were similar (Wong, Ngai, Yeo, Tang, & Ho, 2000).

Number of doses: A prospective cohort study of 120 women between 13 and 22 weeks gestation who received mifepristone followed 24 hours later by misoprostol 400mcg buccally every 3 hours until fetal and placental expulsion reported a complete abortion rate of 99% without additional intervention (Louie et al., 2017). The median number of misoprostol doses necessary was four (range 2 to 6) and no adverse events were reported.

Quality of evidence: The recommendation is based on multiple randomized clinical trials and a Cochrane meta-analysis comparing different mifepristone and misoprostol doses, dosing intervals and routes of administration in the second trimester (Wildschut et al., 2011). Most randomized controlled trials of medical abortion at or after 13 weeks do not include women with pregnancies greater than 21 weeks gestation.

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MISOPROSTOL ONLY: RECOMMENDED REGIMEN

Recommended regimen for 13-24 weeks gestation

Misoprostol 400mcg vaginally or sublingually every three hours until fetal and placental expulsion. Vaginal dosing is more effective than sublingual dosing for nulliparous women.

Strength of recommendation

Strong

Quality of evidence

- Up to 20 weeks gestation: Moderate
- 20-24 weeks gestation: Low

Last reviewed: January 9, 2018

Background

A combination regimen with mifepristone and misoprostol has shorter induction-to-abortion intervals and higher success rates than misoprostol only for medical abortion at or after 13 weeks gestation (Wildschut et al., 2011). If mifepristone is not available, a misoprostol-only regimen with dosing every three hours is an acceptable alternative (Wildschut et al., 2011; World Health Organization (WHO), 2014).

Vaginal route

In randomized controlled clinical trials, misoprostol 400mcg vaginally every three hours is associated with a median induction-to-abortion interval of 10-15 hours and a 48-hour successful abortion rate of 90-95% (Bhattacharjee, Saha, Ghoshroy, Bhowmik, & Barui, 2008; Koh et al., 2017; Tang, Lau, Chan, & Ho, 2004; von Hertzen et al., 2009). A 400mcg dose vaginally is more effective than a 200mcg dose (Koh et al., 2017).

Sublingual route

In a meta-analysis of 1,178 women from three randomized controlled trials, misoprostol 400mcg sublingually is similar (Bhattacharjee et al., 2008) or slightly inferior to vaginal dosing when given every three hours (Tang et al., 2004; von Hertzen et al., 2009; Wildschut et al., 2011). In the trials that showed reduced efficacy, the difference was driven by an inferior response to sublingual misoprostol in nulliparous women only. Of note: all of these studies found that women prefer the sublingual route to vaginal administration by health care workers.

Other routes

Buccal route: One trial randomized 130 women to misoprostol 400mcg every three hours either vaginally or buccally. Women in the vaginal group had a shorter mean induction-to-fe-

tal expulsion interval (25 compared to 40 hours, $p=0.001$) and higher rates of fetal expulsion at both 24 hours (63% compared to 42%, $p=0.014$) and 48 hours (91% compared to 68%, $p=0.001$) (Al & Yapca, 2015). A smaller trial of 64 women showed buccal misoprostol was as effective as vaginal; however, all of the women received an initial loading dose of misoprostol 400mcg vaginally and were randomized to 200mcg buccally or vaginally every six hours thereafter (Ellis, Kapp, Vragovic, & Borgatta, 2010). Finally, a trial including a cohort of 60 women who received misoprostol 400mcg buccally every three hours until fetal and placental expulsion found a complete abortion rate of 71% at 48 hours (Dabash et al., 2015). Based on these studies, vaginal and sublingual administration appear to be superior to buccal misoprostol dosing in this gestational age range.

Oral route: In multiple randomized clinical trials, oral dosing has been shown to be less effective with longer time-to-abortion intervals than vaginal or sublingual dosing (Akoury et al., 2004; Bebbington et al., 2002; Behrashi & Mahdian, 2008; Nautiyal, Mukherjee, Perhar, & Banerjee, 2015).

Dosing interval

In one randomized trial that examined two different regimens of vaginal misoprostol, lengthening the dosing interval from every three to every six hours decreases the efficacy of medical abortion (Wong, Ngai, Yeo, Tang, & Ho, 2000).

Quality of evidence

The recommendation is based on multiple randomized clinical trials and a Cochrane meta-analysis comparing different misoprostol doses, dosing intervals and routes of administration at or after 13 weeks gestation (Wildschut et al., 2011). This body of evidence is limited by the fact that most randomized controlled trials of medical abortion do not include women with pregnancies over 20 weeks gestation.

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PRESENCE OF UTERINE SCAR: RECOMMENDED REGIMEN

Recommendation

- **Less than 22-24 weeks gestation with one uterine scar:** No changes to recommended regimens necessary.
- **More than 22-24 weeks gestation with one uterine scar or 13-24 weeks gestation with more than one uterine scar:** Consider decreasing the misoprostol dose with or without lengthening the misoprostol dosing interval. There is insufficient evidence to know if this impacts the risk of uterine rupture in these women.

Strength of recommendation

Weak

Quality of evidence

Very Low

Last reviewed: November 21, 2017

Risk of uterine rupture with medical abortion

Uterine rupture has been reported during medical abortion at or after 13 weeks gestation in women both with and without a uterine scar. The risk of uterine rupture for any woman undergoing a medical abortion at or after 13 weeks gestation is very rare, occurring in fewer than 1 in 1,000 women (Goyal, 2009). In a meta-analysis of 16 studies of 3,556 women undergoing medical abortion at or after 13 weeks gestation with combined or misoprostol-only regimens, three women suffered uterine rupture resulting in a rate of 0.28% with a previous cesarean section and 0.04% without (Goyal, 2009).

One single-center retrospective review of 279 women undergoing abortion between 14-26 weeks included 60 women with one and 26 women with more than one uterine scar (Küçük-göz Güleç et al., 2013). Women received misoprostol 200mcg vaginally every four hours; three had a uterine rupture. In another retrospective review of 263 women between 12-24 weeks undergoing misoprostol-only abortion, 48 had one and 29 had more than one scar; one rupture was observed in a woman with three prior cesarean sections who received a misoprostol regimen of 200mcg sublingually every three hours (Cetin et al., 2016). A third retrospective review included 231 women with one and 37 women with two prior cesarean deliveries, and used a regimen of 800mcg of misoprostol as a loading dose followed by 200mcg every two hours for three doses; no women experienced rupture (Torriente, Steinberg, & Joubert, 2017).

Regimen for women with a uterine scar

Due to the rarity of uterine rupture in women with a previous scar, no clear guidance can be obtained from the published literature (Borgatta & Kapp, 2011; Daponte, Nzewenga, Dimopoulos, & Guidozzi, 2006; Daskalakis et al., 2004; Dickinson, 2005; Morris et al., 2017).

Expert opinion supports:

- No change in medical abortion regimen for women with one uterine scar whose gestation is less than 22-24 weeks.
- After 22-24 weeks gestation with a single uterine scar or 13-24 weeks gestation with more than one uterine scar:
 - Consider decreasing the dose of misoprostol with or without lengthening the dosing interval (Ho et al., 2007; Küçükgöz Güleç et al., 2013).

There is insufficient evidence to know if changing the dosing regimen will decrease the risk of uterine rupture.

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RECOMMENDED MISOPROSTOL REGIMEN FOR TREATMENT OF INCOMPLETE AND MISSED ABORTION FOR LESS THAN 13 WEEKS UTERINE SIZE

Recommendation

- **Incomplete abortion:** Misoprostol 600mcg orally in a single dose or 400mcg in a single dose sublingually or (in the absence of vaginal bleeding) vaginally.
- **Missed abortion:** Misoprostol 800mcg vaginally or 600mcg sublingually every three hours until pregnancy expulsion, for a maximum of three doses.

Strength of recommendation

Strong

Quality of evidence

Moderate

Last reviewed: December 13, 2017

Definitions

Incomplete abortion: An abortion—whether spontaneous or induced—in which some pregnancy tissue passes out of the uterus but some remains.

Missed abortion: A type of spontaneous abortion where the pregnancy stops developing normally but remains in the uterus and the woman has no symptoms.

Incomplete abortion

In a Cochrane review of 24 studies which included 5,577 women presenting with incomplete abortion under 13 weeks, management with misoprostol was as effective as expectant care to complete the abortion (relative risk [RR] 1.23, 95% confidence interval [CI] 0.72, 2.10), and was less effective than surgical treatment (RR 0.96, 95% CI 0.94, 0.98); success rates were high for all management strategies (Kim et al., 2017). Completion rates were 52-85% for expectant management, 80-99% for treatment with misoprostol, and 91-100% for surgical treatment (Kim et al., 2017). In the analysis, oral, sublingual and vaginal misoprostol showed similar efficacy and side effect profiles; lengthening the time to follow-up assessment increased the success of misoprostol treatment.

Missed abortion

A 2017 systematic review and network meta-analysis of misoprostol management of missed abortion, which included 18 studies reporting on 1,802 women, concluded that misoprostol 800mcg vaginally or 600mcg sublingually are the most effective treatments (Wu, Marwah, Wang, Wang, & Chen, 2017). A single dose of misoprostol 800mcg vaginally results in suc-

successful uterine evacuation in 76 to 93% of women (Fernlund, Jokubkiene, Sladkevicius, & Valentin, 2017; Mizrachi et al., 2017; Ngoc, Blum, Westheimer, Quan, & Winikoff, 2004). In one study, when women were managed expectantly over seven days after a single dose of misoprostol, their complete abortion rates increased over time (Ngoc et al., 2004). Although a number of studies have reported an increase in complete abortion rates when an additional dose of misoprostol is administered 24 (Barcelo et al., 2012; Graziosi, Mol, Ankum, & Bruinse, 2004; Muffley, Stitely, & Gherman, 2002), 48 (Lyra, Cavaco-Gomes, Moucho, & Montenegro, 2017) or 72 hours after the initial dose (Gilles et al., 2004; Zhang et al., 2005), it has been unclear whether this is due to the additional medication or the increased time to evaluation. A 2017 trial which randomized women to receive a single dose of misoprostol 800mcg vaginally, or to receive an additional dose of misoprostol after four days, found that both groups had nearly identical completion rates after seven days-77 and 76% respectively (Mizrachi et al., 2017).

Misoprostol 600mcg sublingually repeated every three hours following the initial dose for a maximum of two more doses achieves complete abortion rates of 88-92% (Tang, Lau, Ng, Lee, & Ho, 2003; Tang et al., 2006). No studies have evaluated single doses of sublingual misoprostol.

A 2015 systematic review assessed if complete abortion rates could be improved by adding mifepristone to misoprostol for treatment of missed abortion (van den Berg, Gordon, Snijders, Vandenbussche, & Coppus, 2015). Authors concluded that existing evidence is insufficient to draw conclusions about the value of adding mifepristone to misoprostol alone for missed abortion.

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RECOMMENDED MISOPROSTOL REGIMEN FOR TREATMENT OF INCOMPLETE AND MISSED ABORTION FOR 13 WEEKS OR LARGER UTERINE SIZE

Recommendation

- Misoprostol in a dose of at least 200mcg buccally, sublingually or vaginally every six hours until expulsion.
- Pretreatment with mifepristone 200mg orally 1-2 days before misoprostol may decrease the time from induction to fetal expulsion.
- The misoprostol-only or mifepristone-misoprostol regimens for induced abortion at or after 13 weeks gestation may also be used.
- Where skilled providers and supportive facilities exist, dilatation and evacuation (D&E) may be offered.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: December 13, 2017

Background

The majority of postabortion care research and programs focus on women with uterine size less than 13 weeks (Ipas, 2013). However, where unsafe abortion is prevalent, as many as 40% of women needing postabortion care present at or after 13 weeks gestation (Ministry of Health of Kenya, Ipas, & Guttmacher Institute, 2013). Women may present with incomplete abortion, retained placenta, fetal demise or ruptured membranes, all of which require uterine evacuation.

Medical regimens

Evidence is limited to suggest the optimal medical regimen for postabortion care at or after 13 weeks uterine size, but a systematic review of the literature suggests that at least 200mcg vaginally, sublingually or buccally given every six hours is effective (Bracken et al., 2014; Mark, Borgatta, & Edelman, 2015). Pretreatment with mifepristone 1-2 days prior to misoprostol may reduce the time to fetal expulsion (Niinimäki et al., 2017; Stibbe & de Weerd, 2012). Guidelines by the International Federation of Gynecology and Obstetrics (FIGO) based on available evidence and expert opinion regarding the use of misoprostol alone in gynecology and obstetrics supports using medical abortion regimens at or after 13 weeks (Morris et al., 2017).

D&E

No studies have compared medical management versus vacuum aspiration or D&E for postabortion care at or after 13 weeks. D&E can be offered to women for postabortion care where skilled providers and supportive facilities exist (World Health Organization, 2014).

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POSTABORTION CONTRACEPTION: WHEN AND WHAT TYPE

Recommendation

- Following vacuum aspiration or dilatation and evacuation (D&E), hormonal and non-hormonal contraception, including intrauterine device (IUD) placement and female sterilization, may be initiated immediately.
- Hormonal methods, including pills, patches, rings, injectables and implants may be started on the day of the first pill of medical abortion. IUD placement and female sterilization should be performed when it is reasonably certain the woman is no longer pregnant.
- Male sterilization (vasectomy) is safe and effective and can be performed at any time.
- Long-acting contraceptive methods have higher continuation rates and lower pregnancy rates compared to short-acting methods.
- People, including adolescents, should be able to choose whether to use a contraceptive method, and to select their preferred method, based on accurate contraceptive information and their personal needs and preferences.

Strength of recommendation

Strong

Quality of evidence

- IUDs and combined oral contraceptives: High
- Implants: Moderate
- Other methods: Low to Moderate

Last reviewed: November 18, 2016

Fertility return

Following induced abortion at less than 13 weeks gestation, women will typically ovulate within three to four weeks, however women can ovulate in as little as eight days (Boyd & Holmstrom, 1972; Lahteenmaki & Luukkainen, 1978; Schreiber, Sober, Ratcliffe, & Creinin, 2010; Stoddard & Eisenberg, 2011). At least 85% of women will ovulate before their first menses (Boyd & Holmstrom, 1972; Lahteenmaki & Luukkainen, 1978; Cameron & Baird, 1988). There is no difference in time to ovulation following medical abortion compared to vacuum aspiration (Cameron & Baird, 1988).

Data for return to fertility after abortion performed at or after 13 weeks gestation are limited. One study with only nine participants found that 66% ovulated within 21 days (Marrs, Kletzky, Howard, & Mishell, 1979). Given the rapid return to fertility, all women who wish to begin contraception should receive their preferred method at the time of their abortion. If a woman's preferred method is not available, she should be provided a referral and, if desired, an interim method (World Health Organization [WHO], 2014b).

Safety and acceptability of postabortion contraception

For adult women, WHO's 2015 *Medical Eligibility Criteria for Contraceptive Use* classifies all contraceptive methods as category one, or safe for immediate use, following first-trimester uncomplicated abortion; recommendations do not differ based on the type of abortion. Female sterilization is classified as acceptable after an uncomplicated abortion.

Similarly, the *Medical Eligibility Criteria for Contraceptive Use* (WHO, 2015) classifies all contraceptive methods as category one, or safe for immediate use, following uncomplicated second-trimester abortion—except IUDs. Due to an increased risk of expulsion when used after abortion at or after 13 weeks gestation, IUDs are classified as category two, meaning the advantages of using the method generally outweigh the risks. Female sterilization is classified as acceptable after an uncomplicated abortion at or after 13 weeks gestation.

Two of these recommendations differ for adolescent women: Depot medroxyprogesterone acetate (DMPA) injection is classified by WHO as a category two for women under 18 years of age, due to theoretical concerns about bone mineral density. Sterilization may be performed on young women, but special precautions may need to be taken due to the increased risk of regret (WHO, 2015).

In comparison to short-acting methods, long-acting methods of contraception such as implants and IUDs have higher continuation rates and lower pregnancy and abortion rates (Blumenthal, Wilson, Remsburg, Cullins & Huggins, 1994; Cameron et al., 2012; Kilander et al., 2016; Korjamo, Mentula, & Heikinheimo, 2017; Langston, Joslin-Rohr, & Westhoff, 2014; Peipert, Madden, Allsworth, & Secura, 2012; Pohjoranta, Mentula, Gissler, Suhonen, & Heikinheimo, 2015; Roberts, Silva, & Xu, 2010; Rose, Garrett, & Stanley, 2015). Uptake of long-acting methods is higher after surgical abortion as compared to medical abortion (Laursen, Stumbras, Lewnar, & Haider, 2017).

Contraceptive start

Following vacuum aspiration, D&E or medical abortion where pregnancy expulsion occurs in a facility, all hormonal and nonhormonal contraceptive methods, including IUD insertion and female sterilization, may be initiated immediately (WHO, 2015). Fertility awareness-based methods may be initiated once a woman has had at least one postabortion menses. Male sterilization (vasectomy) may be performed at any time.

For medical abortion where pregnancy expulsion is expected to occur at home, most forms of contraception (including pills, injectables and implants) may be started with the first pill of the medical abortion if there are no medical contraindications (WHO, 2015). IUDs may be inserted and sterilization performed as soon as it is reasonably certain that a woman is no longer pregnant (WHO, 2014a).

Evidence related to specific contraceptive methods

IUDs: see "Postabortion IUD use: Safety and timing," p 123.

Progestin-only subdermal implants: Two randomized non-inferiority trials conducted in women undergoing medical abortion before 13 weeks gestation (Hognert et al., 2016; Raymond et al., 2016b) have demonstrated that abortion success rates are the same in women receiving a contraceptive implant on the day they receive mifepristone compared to delayed placement. In both studies, insertion rates were higher for women receiving their implant on the day they received mifepristone. One study (Hognert et al., 2016) reported a significantly

higher pregnancy rate in the delayed insertion group at follow-up six months after the abortion (3.8% compared to 0.8%).

Progestin-only injection: A study of 132 women using DMPA immediately after aspiration abortion reported no serious adverse events but low method continuation rates (22%) at one year and high repeat pregnancy rates (Goldberg, Cardenas, Hubbard, & Darney, 2002). One randomized, controlled non-inferiority trial (Raymond et al., 2016a) comparing 220 women undergoing medical abortion up to 75 days gestation who received DMPA on the day of mifepristone to 226 women who did not found similar rates of surgical intervention for any reason after medical abortion (6.4% and 5.3%, respectively) and pregnancy rates at six months after the intervention (2.3% and 3.2% respectively). However, ongoing pregnancy as a reason for medical abortion failure in the DMPA injection group was significantly higher (3.6% vs 0.9%). Smaller retrospective cohort studies have found no differences in medical abortion success rates or ongoing pregnancy rates in women who start progestin-only injections on the same day as mifepristone administration (Douthwaite et al., 2016; Park, Robinson, Wessels, Turner, & Geller, 2016). Women report high satisfaction with same-day administration of progestin-only contraceptives (Raymond et al., 2016a)

Combined oral contraceptives (COCs): A review of seven studies including 1,739 women demonstrated no serious adverse events using COCs immediately after aspiration or medical abortion before 13 weeks gestation (Gaffield, Kapp, & Ravi, 2009). Additionally, women who used COCs immediately demonstrate similar bleeding patterns to women using no contraception, and less bleeding than copper IUD users. Two randomized controlled trials of COCs compared to placebo started immediately after medical abortion up to 49 or 63 days gestation showed that pills do not have a significant effect on the efficacy of medical abortion or the quantity or duration of blood loss (Tang, Gao, Cheng, Lee, & Ho, 1999; Tang, Xu, Cheng, Lee, & Ho, 2002).

Combined vaginal ring: A cohort study of 81 women who placed a vaginal ring one week after aspiration or medical abortion before 13 weeks gestation showed no serious adverse events or infections (Fine, Tryggestad, Meyers, & Sangi-Haghpeykar, 2007).

Combined contraceptive patch: A trial of 298 women randomized to either immediate post-abortion start or delayed start the Sunday after an abortion showed no difference in continuation rates at two and six months. In the 53% of women who could be contacted at six months, half had stopped using the contraceptive patch (Steinauer et al., 2014).

Quality of evidence

Because of the demonstrated safety of contraception after vacuum aspiration and medical abortion before 13 weeks, the *2015 Medical Eligibility Criteria for Contraceptive Use* categorizes the immediate initiation of hormonal injections, implants, combined hormonal contraception (pills, patches and rings) and progestin-only pills as category one, or safe for use (WHO, 2015).

With the exception of IUD use following D&E, the immediate use of most methods of contraception have not been adequately studied following D&E or medical abortion at or after 13 weeks gestation. The *2015 Medical Eligibility Criteria for Contraceptive Use* recommendations do not differ based on type of abortion performed, whether medical or D&E. A woman's immediate need for reliable contraception after abortion, coupled with the reduced uptake of contraception when provision is delayed, strongly supports the recommendation to start contraceptive methods immediately.

Informed decision making

WHO recommends that sexual and reproductive health services, including contraceptive services, be delivered in a way that ensures fully informed decision-making, respects dignity, autonomy, privacy and confidentiality, and is sensitive to individuals' needs and perspectives (WHO, 2014b). People should be able to choose or refuse contraception based on their personal needs and preferences. Evidence-based, comprehensive contraceptive information, non-directive contraceptive counseling and support should be accessible for all people, including adolescents, so that patients are able to make an informed decision. Ideally a range of contraceptive methods should be available, appropriate referrals for methods not available on site should be offered, and these services should be integrated with abortion and postabortion care (WHO, 2014b).

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POSTABORTION IUD USE: SAFETY AND TIMING

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Recommendation

- When a woman chooses an intrauterine contraceptive device (IUD), it should be placed immediately following a successful, uncomplicated vacuum aspiration or dilatation and evacuation (D&E) abortion.
- When a woman chooses an IUD following medical abortion, it should be placed when it is reasonably certain she is no longer pregnant.

Strength of recommendation

Strong

Quality of evidence

High

Last reviewed: November 18, 2017

IUD placement after abortion before 13 weeks gestation

The World Health Organization's (WHO) 2015 *Medical Eligibility Criteria for Contraceptive Use* classifies IUDs as category one, or safe for immediate use, following first-trimester abortion; recommendations do not differ based on type of abortion.

In comparison to short-acting methods, long-acting reversible methods of contraception such as implants and IUDs have higher continuation rates and lower pregnancy and abortion rates (Blumenthal, Wilson, Remsburg, Cullins, & Huggins, 1994; Cameron et al., 2012; Korjamo, Mentula & Heikinheimo, 2017b; Langston, Joslin-Rohr, & Westhoff, 2014; Peipert, Madden, Allsworth, & Secura, 2012; Pohjoranta, Mentula, Gissler, Suhonen, & Heikinheimo, 2015; Roberts, Silva, & Xu, 2010). A 2014 Cochrane review of 12 trials including 7,119 women concluded that IUD insertion following vacuum aspiration and D&E is safe and practical (Okusanya, Oduwale, & Effa, 2014). The review found no differences in serious adverse events, such as infection or perforation, between immediate and delayed insertion. A 2011 trial randomized 575 women to immediate or delayed IUD insertion after uterine aspiration before 12 weeks (Bednarek et al., 2011). Although rates of IUD expulsion were slightly higher following immediate postabortion insertion (5% compared to 2.7%), women assigned to the delayed insertion group were significantly less likely to receive an IUD (75% compared to 100% in the immediate group) and more likely to have a subsequent pregnancy (5 women compared to none). A historical cohort study compared immediate postprocedure IUD insertion performed by midlevel providers to physicians, and found no difference in adverse outcomes between the two groups (Patil et al., 2016).

Following a medical abortion before 13 weeks gestation, IUDs may be placed as soon as it is reasonably certain that a woman is no longer pregnant (WHO, 2014). IUDs placed within 5-10 days of a successful medical abortion have low rates of expulsion, high continuation rates (Betstadt, Turok, Kapp, Feng, & Borgatta, 2011; Sääv, Stephansson, & Gemzell-Daniels-

son, 2012) and lower pregnancy rates than delayed insertion (Pohjoranta, Suhonen, Mentula, & Heikinheimo, 2017; Saav et al., 2012; Shimoni, Davis, Ramos, Rosario, & Westhoff, 2011).

IUD placement after abortion at or after 13 weeks gestation

The WHO *Medical Eligibility Criteria for Contraceptive Use* (2015) classifies IUD use following uncomplicated second-trimester abortion as category two, meaning the advantages of using the method outweigh risks, due to an increased risk of IUD expulsion. The Cochrane review of immediate postabortion insertion of IUDs following an abortion procedure referenced above concluded that although expulsion rates may be higher with immediate placement, continuation is higher with no increase in complications (Okusanya et al., 2014). In two randomized controlled trials of immediate versus delayed IUD placement after D&E, rates of IUD use were significantly higher with immediate insertion, without an increase in infection or complication rates (Cremer et al., 2011; Hohmann et al., 2012). Expulsion rates for women who had immediate insertion in both studies were low (3.1% and 6.8%) and were not different from delayed insertion. Notably, in both studies, about half of women randomized to delayed insertion did not return to have the IUD inserted. Requiring a follow-up visit for IUD insertion is a significant barrier to obtaining the IUD (Stanek, Bednarek, Nichols, Jensen, & Edelman, 2009).

The only available study of IUD placement immediately following medical abortion at or after 13 weeks gestation found that insertion is feasible and safe, however the study was underpowered to assess rate of expulsions (Korjamo, Mentula, & Heikinheimo, 2017a; Korjamo et al., 2017b). The WHO *Medical Eligibility Criteria for Contraceptive Use* (2015) recommendations for IUD use after second-trimester abortion do not differ based on the type of abortion performed, whether medical or surgical. Although not directly translatable, the evidence from post-partum IUD insertion is reassuring (Lopez, Bernholc, Hubacher, Stuart, & Van Vliet, 2015). An IUD may be placed following fetal and placental expulsion.

Young women

The IUD for women under the age of 20 is classified by WHO as category two, in which the benefits generally outweigh the risks (WHO, 2015). A large, United States-based, prospective cohort study which examined pregnancy, birth and abortion rates in women provided all birth control methods at no cost included 1,056 women under the age of 20 and found that 62% of young women chose a long acting reversible contraceptive method—either the IUD (22%) or implant (40%)—compared to 71% of older women (Mestad et al., 2011). Continuation rates at 12 and 24 months were the same among older and younger women (Birgisson, Zhao, Secura, Madden & Peipert, 2015). Pregnancy, birth and induced abortion rates among the young women in the study were reduced by 75% compared to national averages (Secura et al., 2014).

A large 2017 systematic review and meta-analysis exploring risk factors for repeat pregnancies among teens, which included 26 studies reporting on more than 160,000 adolescent women, found that use of long acting reversible contraceptives exerted a significant protective effect, along with improved educational attainment and school continuation (Maravilla, Betts, Couto e Cruz, & Alati, 2017).

A 2017 systematic review examining risk of adverse outcomes in young women using the IUD found no differences in rates of perforation, contraceptive failure, pelvic inflammatory disease, or heavy bleeding in women younger than 25 compared to older women; rates of IUD expulsion were slightly higher in young women (Jatlaoui, Riley, & Curtis, 2017). IUDs do not increase young women's risk of infertility (Grimes, 2000), and women's fertility returns to baseline rates rapidly following IUD removal (Hov, Skjeldestad, & Hilstad, 2007).

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MANAGING POSTABORTION HEMORRHAGE

Recommendation

Hemorrhage caused by atony may be treated with uterine massage, uterotonic medications, re-aspiration, tamponade or surgery. Women need to be closely monitored for symptoms of shock.

Strength of recommendation

Strong

Quality of evidence

Low

Last reviewed: November 16, 2017

Epidemiology

Definitions of postabortion hemorrhage vary, making comparisons of incidence, risk factors and treatments across studies difficult. A definition proposed by the Society for Family Planning is: excessive bleeding that requires a clinical response such as transfusion or hospital admission, and/or bleeding in excess of 500mL (Kerns & Steinauer, 2013). Hemorrhage after induced abortion is rare, occurring in 0-3 per 1,000 cases following medical abortion up to 9 weeks gestation or vacuum aspiration before 13 weeks gestation, and 0.9-10 per 1,000 cases following uterine evacuation at or after 13 weeks gestation (Kerns & Steinauer, 2013; Upadhyay et al., 2014). Causes of bleeding include placenta previa or accreta, uterine atony, retained products of conception, cervical or vaginal laceration, uterine injury, and coagulopathy (Kerns & Steinauer, 2013; Perriera, Arslan, & Masch, 2017).

Diagnosis

When postabortion hemorrhage is suspected, clinicians should take a rapid, systematic approach to assessing and treating women. Initial assessment includes inspection of the cervix for laceration, bimanual examination to assess for uterine atony and tenderness, and uterine aspiration or ultrasound examination to evaluate for retained products of conception or blood.

Management

Cervical lacerations may be treated with direct pressure with gauze or ring forceps, application of topical clotting agents (silver nitrate or ferric subsulfate solution), or by placing absorbable sutures.

Uterine atony requires a rapid, sequential response starting with uterine massage, followed by uterotonics, re-aspiration, uterine tamponade and finally surgical measures. Clinicians should move quickly to the next step if bleeding is not controlled. When uterotonic medica-

tions are used, additional or repeat doses may be used if bleeding does not improve after the first dose.

Uterotonic medications and dosages:*

MEDICATION	DOSAGE
Methylergonovine	0.2mg intramuscularly or intracervically; can be repeated every 2-4 hours. Avoid in women with hypertension.
Misoprostol	800mcg sublingually or rectally
Oxytocin	10-40 units per 500-1000mL fluid intravenously or 10 units intramuscularly
Intrauterine tamponade	Sterile gauze, 30-75mL Foley catheter balloon, condom catheter or obstetric balloon placed in uterus

*Extrapolated from postpartum data (American College of Obstetricians and Gynecologists, 2017; Kerns & Steinauer, 2013; Mavrides et al., 2016; Morris et al., 2017; Prata & Weidert, 2016; World Health Organization, 2012).

If tamponade is used to stop bleeding, the Foley balloon, obstetric balloon, gauze or inflated condom catheter should be left in place for several hours while the patient is observed. If the woman remains stable after the balloon or gauze is removed, she may be discharged.

When bleeding continues after assurance of complete uterine evacuation and no visible lacerations, providers must consider other complications, such as perforation, coagulopathy or placenta accreta (National Abortion Federation, 2017). If coagulopathy, such as disseminated intravascular coagulation, is present, blood products may be required. Surgical measures including hysterectomy, uterine compression sutures, uterine artery ligation or uterine artery embolization can be performed for severe bleeding that cannot be controlled by other measures. Providers at health centers without available operating theaters or expertise should have clear protocols for resuscitation and transfer to a higher level of care. Women at risk of shock require intravenous line placement, supplemental oxygen, fluid resuscitation and replacement of blood products as indicated.

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APPENDIX: PAIN MEDICATION TABLE

The medications listed in the table below are commonly used for pain management during vacuum aspiration and dilatation and evacuation. Many other options exist. This table does not cover general anesthetic agents.

Both anxiolytics and narcotics may cause respiratory depression, especially when they are used together. Accordingly, lower doses should be used when they are together than when they are used separately. When medications are given intravenously immediately before a procedure they should be given slowly and intermittently by a specially trained provider. Problematic side effects can be avoided by repeated small intravenous doses that are titrated to a woman's level of pain and sedation. The peak analgesic effect should occur during the procedure to avoid excessive postprocedure sedation.

Even clinicians using lighter sedation analgesia must be able to manage respiratory arrest, in the unlikely event that an unintentional overdose should occur. Providers should be trained in airway management and cardiopulmonary resuscitation. Resuscitative equipment and appropriate antagonist drugs (naloxone and flumazenil) should be available.

Disclaimer: This resource is designed to be a supplemental resource for clinicians and is NOT intended to serve as a replacement for drug label information or clinical judgment that accounts for patients' and facilities' unique circumstances.

Last reviewed: February 10, 2018

DRUG TYPE	GENERIC DRUG NAME	DOSE AND TIMING	HALF-LIFE	SIDE EFFECTS	COMMENTS
Local anesthetic <i>See "Pain management: Paracervical block," p.36</i>	Lidocaine	20ml of 1% solution or 10mL of 2% solution in a paracervical block not to exceed 4.5mg/kg	60-90 minutes	ringing in ears; dizziness; numbness in lips, mouth and tongue; metallic taste Extremely rare: Seizures	<ul style="list-style-type: none">• Pull back plunger before injecting to avoid intravascular injection• Allergic reaction is very rare. Reactions that do occur may be due to preservatives in multi-dose vials. Preservative-free lidocaine allergy is extremely rare.

DRUG TYPE	GENERIC DRUG NAME	DOSE AND TIMING	HALF-LIFE	SIDE EFFECTS	COMMENTS
Nonsteroidal anti-inflammatory drug (NSAID)	Ibuprofen	Oral: 400-800mg 1 hour before the procedure	2 hours	Possible gastrointestinal upset	Do not use in women with active peptic ulcer disease or renal failure
	Naproxen	Oral: 500mg 1 hour before the procedure	12-17 hours	Possible gastrointestinal upset	Do not use in women with active peptic ulcer disease or renal failure
	Ketorolac	Oral: 20mg 1 hour before procedure IV: 30mg over at least 15 seconds 30-60 minutes before procedure IM: 60mg 30-60 minutes before procedure For women less than 50kg, all doses should be halved	4-6 hours		<ul style="list-style-type: none"> Single dose IM ketorolac prior to surgery may reduce opioid use and postoperative pain (de Oliveira, 2012; Roche, 2011) Do not use in women with active peptic ulcer disease, renal failure, breastfeeding or sensitivity to other NSAIDs Breakthrough pain should be managed with narcotics rather than increasing ketorolac beyond the recommended doses
Analgesic	Acetaminophen	Oral: 500-1,000mg 30-60 minutes before procedure	2-4 hours		<ul style="list-style-type: none"> Not a first-line pain medication for vacuum aspiration or medical abortion. May be used as an antipyretic. Liver toxicity from overdose (maximum dose=4,000mg/day) is a risk
Narcotic/analgesic combination	Acetaminophen 300mg + codeine 30mg	Oral: 1-2 tablets 1 hour before procedure	2-4 hours	Drowsiness; light-headedness; nausea and vomiting	Be aware of combining with other acetaminophen-containing products. Liver toxicity from overdose of acetaminophen (maximum dose=4,000 mg/day) is a risk.
	Acetaminophen 500mg + hydrocodone 5mg	Oral: 1-2 tablets 1 hour before procedure	4-6 hours	Drowsiness; light-headedness; nausea and vomiting	Be aware of combining with other acetaminophen-containing products. Liver toxicity from overdose of acetaminophen (maximum dose=4,000 mg/day) is a risk.

DRUG TYPE	GENERIC DRUG NAME	DOSE AND TIMING	HALF-LIFE	SIDE EFFECTS	COMMENTS
Narcotic	Meperidine	Oral: 100-150mg 30-60 minutes before procedure IV: 25-50mg 5-15 minutes prior to procedure IM/SC: 50-100mg 30-90 minutes prior to procedure	2-4 hours	Drowsiness; light-headedness; nausea and vomiting; decreased breathing rate; loss of consciousness; hypotension; seizures	<ul style="list-style-type: none"> • IM or SC administration preferred over IV • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with naloxone (see end of chart) • More rapid onset and shorter duration of action than morphine • Meperidine 300mg PO=Meperidine 75mg IV=morphine 10mg IV
	Fentanyl	IV: 50-100mcg immediately before procedure (may repeat every 5-10 minutes, not to exceed 250mcg) IM: 50-100mcg 30-60 minutes before procedure	4 hours	Drowsiness; light-headedness; weakness; bradycardia; decreased breathing rate; loss of consciousness; hypotension; seizures	<ul style="list-style-type: none"> • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with naloxone (see end of chart) • More rapid onset and shorter duration of action than meperidine • Fentanyl 100mcg IV=morphine 10mg IV • Onset of action is 2-7 minutes when given IV
	Tramadol	IV/IM: 50-100mg 15-30 minutes before the procedure Oral/suppository: 50-100mg 60-90 minutes prior to the procedure	6-8 hours	Drowsiness; light-headedness; sweating; weakness; fatigue; seizures	<ul style="list-style-type: none"> • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with naloxone (see end of chart) • If using IV, inject slowly over 2-3 minutes • Less respiratory depression than morphine or meperidine

DRUG TYPE	GENERIC DRUG NAME	DOSE AND TIMING	HALF-LIFE	SIDE EFFECTS	COMMENTS
Anxiolytic (Benzodiazepine)	Diazepam	Oral: 5-10mg 1 hour before procedure IV: 2-5mg 20 minutes before procedure	30-60 hours	Blurred vision; dizziness; disorientation; pain and redness on injection; decreased breathing rate; loss of consciousness	<ul style="list-style-type: none"> • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with flumazenil (see end of chart) • Has a mild amnestic effect • Onset of action is 1-22 minutes when given IV
	Midazolam	IV: 1-2mg immediately before the procedure, then 0.5-1mg IV every 5 minutes as needed, not to exceed 5mg IM: 0.07-0.08mg/kg or about 5mg up to 1 hour before procedure	2.5 hours	Blurred vision; dizziness; disorientation; CNS and respiratory depression	<ul style="list-style-type: none"> • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with flumazenil (see end of chart) • Midazolam 2.5mg=diazepam 10mg • Stronger amnestic effect than diazepam • Onset of action is 1-5 minutes when given IV and 15-30 minutes when given IM
	Lorazepam	Oral: 1-2mg 30-60 minutes before procedure IV: 2mg given over 1 minute 15-20 minutes before the procedure IM: 0.05mg/kg up to a maximum of 4mg within 2 hours before the procedure	14 hours	Blurred vision; dizziness; disorientation; decreased breathing rate; loss of consciousness	<ul style="list-style-type: none"> • If respiration is compromised, assist with breathing (airway management, oxygen and ambu bag) and reverse with flumazenil (see end of chart) • Amnestic effect

DRUG TYPE	GENERIC DRUG NAME	DOSE AND TIMING	HALF-LIFE	SIDE EFFECTS	COMMENTS
Reversal agent for narcotic	Naloxone	IV/IM/SC: 0.4mg every 2 minutes until reversal is seen	1-1.5 hours		<ul style="list-style-type: none"> Naloxone's duration of action is 1 hour and may wear off before the narcotic. Therefore, patients treated with naloxone must be monitored closely for several hours. Maintain airway and respirations while giving naloxone
Reversal agent for benzodiazepine	Flumazenil	IV: 0.2mg every minute until respirations return. Do not exceed 1mg	1 hour		<ul style="list-style-type: none"> Flumazenil's duration of action is 1 hour and may wear off before the benzodiazepine. Therefore, patients treated with flumazenil must be monitored closely for several hours. In the event of overdose with narcotic and benzodiazepine, reverse the narcotic first with naloxone and use flumazenil subsequently if needed. Maintain airway and respirations while giving flumazenil
Treatment for hypersensitivity reaction/anaphylaxis	Epinephrine	IM/SC: 0.2-0.5mg every 5 to 15 minutes IV: 0.1mg diluted with 10mL of saline administered over 5 to 10 minutes	1 minute	Tachycardia; palpitations; nausea; diaphoresis; dizziness; anxiety	<ul style="list-style-type: none"> There are no contraindications to epinephrine in the setting of anaphylaxis IM administration preferred Consider giving methylprednisolone 125mg IV Support respiration. If wheezing is present, inhaler may be helpful Immediate intubation if evidence of impending airway obstruction

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