Clinical Guidelines

First-trimester abortion in women with medical conditions

Release date October 2012
SFP Guideline #20122

Abstract

Most women undergoing first-trimester abortion are healthy. However, abortion providers also encounter women with a wide variety of medical conditions, some of which are serious and complex. When such a condition exists, consultation with the woman's physician or a specialist can facilitate decision making regarding hospital referral and additional preparations that may be required. Medical conditions may determine the approach to abortion. Surgical abortion is preferred when mifepristone or methotrexate is contraindicated. Medication abortion may be preferred when lithotomy position is not possible or in patients with extreme obesity. Limited data suggest that women treated with anticoagulation therapy bleed more than other women during surgical abortion, although this additional bleeding may be clinically unimportant. The decision to temporarily discontinue anticoagulation therapy will depend on the agent used and the underlying risk of thrombosis. According to the American Heart Association, additional antibiotics are not recommended to prevent endocarditis in women with cardiac lesions during surgical abortion. We review specific recommendations for women with common medical conditions. In some women, highly effective postabortion contraception is essential to prevent pregnancy-related morbidity. The *U.S. Medical Eligibility Criteria for Contraceptive Use*, *2010*, provides guidance for method selection for women with medical problems.
© 2012 Elsevier Inc. All rights reserved.

Keywords: Abortion; Medical conditions; Guidelines; Contraindications

Background

Induced abortion is common, safe and most often performed in the first-trimester. In 2005–2008, approximately 1.2 million abortions were performed annually in the United States [1]. In 1998–2005, the mortality rate related to induced abortion was 0.6 deaths per 100,000 abortions, compared with the pregnancy-associated mortality rate of 8.8 deaths per 100,000 live births during the same period [2]. These data reflect the safety of first-trimester abortion, particularly in comparison with childbirth, and the general good health of the patient population [3]. More than 60% of abortions are performed at ≤ 8 weeks and more than 90% at ≤ 13 weeks gestation [4], when abortion is safest.

Women with a wide variety of medical conditions seek abortion services. The goal of these guidelines is to make recommendations for the care of women with medical conditions undergoing first-trimester abortion. In the United States, chronic conditions such as diabetes mellitus, obesity and hypertension are increasing among young women [5]. Women with more serious medical problems also seek abortion services. Such women face an increased risk of adverse health events during pregnancy [6–8]. For example, women with such preexisting cardiovascular diseases as cardiomyopathy face a higher risk of pregnancy-related morbidity and mortality than their healthy peers, and the number of pregnancy-related deaths associated with cardiovascular conditions is increasing [5,7,8]. When chronically ill women decide to end their pregnancies, prompt abortion care coupled with highly effective postabortion contraception reduces pregnancy-associated morbidity and mortality. The *U.S. Medical Eligibility Criteria for Contraceptive Use*, *2010*, provides guidance for selection of postabortion contraceptive methods for women with medical conditions [6].

Little published research addresses the frequency or safety of abortion in women with medical problems. The number of women obtaining abortions who have such problems is not known. In one large survey, 12% of women reported a problem with their health as a reason for abortion [9]. The leading reasons for abortion-related mortality in the first trimester are infection, anesthesia complications, hemorrhage and embolism [3], which may or may not be more likely to occur in women with chronic medical problems. Other causes, such as cardiac events, accounted for 17% of first-trimester abortion-related deaths [3]; however, no information is available as to whether these women had preexisting medical conditions.

Women presenting for abortion care may report discontinuation or reduction of needed medications during pregnancy, thereby exacerbating their underlying conditions. Many pregnant women with chronic medical conditions discontinue or reduce their usual medications for fear of teratogenicity [7,10,11], on the advice of their physician [10] or, paradoxically, out of concern for their own safety (personal observation). A study of 37 women who were taking an antidepressant or benzodiazepine found that 34 abruptly discontinued their medication for fear of harming the fetus and 11 subsequently reported suicidal ideation [10]. We observe this even among women seeking abortion. In some cases, healthcare providers unfamiliar with the care of pregnant women may recommend discontinuation of medication without providing an alternative.

For all women seeking abortion, delays should be minimized because the safety of abortion is strongly related to gestational age, even in the first trimester [3]. The mortality rate for women obtaining an abortion at ≤ 8 weeks was 0.1 per 100,000 legal induced abortions, compared with 0.4 per 100,000 legal induced abortions at ≤ 12 weeks [3]. For women with medical problems, avoiding delays is particularly important because their condition may deteriorate with advancing pregnancy. For example, pregnancy-related physiological changes such as increased maternal blood volume and cardiac output begin in the middle of the first trimester of pregnancy, with associated cardiac risks that peak by the end of the second trimester [7]. Further, effective postabortion contraception is essential for preventing morbidity from future pregnancies.

For healthy women, early abortion is safe with surgery or medications. For women with medical conditions, absolute and relative contraindications to medication abortion drugs preclude their use in certain patients (Section Ib-c). Current labeling precautions related to the safety of medication abortion regimens for women with chronic medical conditions reflect the lack of available data; such patients have been excluded from clinical trials. Some of the contraindications listed (chronic adrenal failure, inherited porphyria, long-term corticosteroid therapy) relate to pharmacologic properties of medication abortion drugs and associated known or theoretical implications [12].

Most medication abortion regimens include a prostaglandin. Prostaglandins are vasoactive. Depending on the target organ's receptors, prostaglandins lead to vasodilation or vasoconstriction [13]. Misoprostol is a synthetic prostaglandin E1 that is currently marketed in the United States for prevention of peptic ulcer disease [13]. Limited data exist regarding the cardiovascular effects of misoprostol. Ramsey et al. [13] assessed cardiovascular effects of 600 mcg of misoprostol vaginally administered to nine healthy women undergoing midtrimester pregnancy interruption and found no differences before and after treatment in maternal cardiac function as measured by transthoracic electrical bioimpedance.

Use of misoprostol in women with cardiac disease has received little study. One retrospective analysis of a group of women with heterogeneous cardiac disorders undergoing induced abortion showed no adverse effects related to administration of mifepristone and misoprostol in the first or second trimester. Only 65 patients were examined in this study; results should be interpreted cautiously [14]. This small case series [14] and a prior case report [15] demonstrated no adverse effects following misoprostol use for induced abortion in women with cardiac diseases including congenital heart disease, cardiomyopathy and rheumatic valvular disease.

Prostaglandins inhibit platelet aggregation, which, when combined with a vasodilatation effect, is considered beneficial in the setting of ischemic stroke [16] and potentially protective against cerebral ischemia [17]. However, one case report described a previously healthy woman who presented with right hemiparesis and aphasia consistent with an acute ischemia infarct after receiving a one-time dose of 1,800 mcg intravaginal misoprostol for an elective abortion earlier in the day [18]. This isolated outcome is likely related to the unusual dosage used or the pregnancy itself.

Clinical questions and recommendations

1. What are potential indications for referral to a hospital-based provider?

Stable, controlled chronic medical conditions such as hypertension, diabetes, or asthma are common and can be safely managed in outpatient settings (freestanding clinics, other clinics and doctors' offices), where 96% of abortions occur [1]. Statistics on the morbidity and mortality related to abortion reflect the safety of caring for such women in nonhospital settings.

Occasionally, preexisting medical conditions necessitate referral to a hospital setting for abortion care [19]. Table 1 lists conditions for which referral to a hospital setting may be appropriate. Direct communication with the patient's personal physician or an appropriate specialist is often helpful in deciding if the hospital referral is necessary, and if so, what special preparations should be anticipated. The specialist may overestimate abortion-related risk. Communication between the clinicians caring for the patient to clarify details of the planned surgical procedure and options for analgesia may prevent an unnecessary referral. Any provider considering referral to a hospital setting must assess obstacles such as higher cost for inpatient care [20], distance to travel and whether a competent and caring hospital-based provider is available. Most women seeking abortion services experience delays related to nonmedical issues [21], and additional delays may occur when preexisting medical conditions exist.

Hospital-based providers may choose an office setting or an operating room environment. The operating room may increase the ease and safety of the procedure with improved lighting, instruments for retraction to improve visualization, a variety of patient positioning options, monitoring equipment,

Table 1
Indications for referral to hospital-based provider (with permission [19])

Central Nervous System
- Vascular–untreated aneurysm
- Space occupying lesions

Renal Disease
- Impaired renal function (serum creatinine >2.5 mg/dL)

Hypertension
- Uncontrolled BP (systolic blood pressure >160 or diastolic blood pressure >105)

Endocrine
- Uncontrolled hyperthyroidism, uncontrolled diabetes, pheochromocytoma

Cardiac
- Congenital (cyanotic disease, right or left ventricular dilation, uncontrolled tachyarrhythmia)
- Coronary disease — (history of myocardial infarction, treatment angina)
- Cardiomyopathy — (dilated, hypertrophic, history of peripartum cardiomyopathy)
- Valvular disease — (AS peak gradient ≥60 mmHg, MS valve area <1.5 cm2, MR or AR with LV dilation)

Pulmonary
- Uncontrolled asthma
- Restrictive lung disease
- Pulmonary hypertension

Rheumatological
- Lupus flare
- Lupus inhibitor requiring anticoagulation

GI
- Hepatic disease elevated PT
- Esophageal varices with history of bleeding
- Uncontrolled inflammatory bowel disease

Hematological
- Severe anemia
- Sickle cell disease with a history of crisis
- Idiopathic thrombocytopenia purpura with active thrombocytopenia
- Thrombophilia requiring anticoagulation

Oncology
- Counseling regarding treatment options and timing of abortion
- Gynecologic cancers restricting access to the uterus

Transplant
- Significantly impaired renal function (creatinine >2.5 mg/dL)
- History of recent rejection
- Poorly functioning transplanted organ

Psychiatric
- Inability to obtain informed consent
- Inability to tolerate an outpatient procedure
- History of suicide attempt

rapid access to medications and blood products, support staff to assist with complicated procedures and a range of anesthesia services. For example, one case report described a patient with Eisenmenger syndrome who benefited from a procedure with local anesthesia performed in the operating room with continuous monitoring [22].

2. When is surgical management preferred over medication abortion?

General considerations

Surgical abortion allows for a wide range of anesthetic options that can be tailored to the medical needs of the patient and administered in a setting with continuous monitoring. Sedation during surgical abortion may be important when anxiety- and pain-related physiological changes such as tachycardia compromise maternal status. In some cases, local or regional anesthesia may be preferred (e.g., with poorly controlled asthma). Patients with chronic conditions who are sensitive to pain (e.g., fibromyalgia) may prefer sedation.

Critically ill pregnant women with time-sensitive medical needs, such as an upcoming transplant surgery, benefit from efficient surgical management. The surgical approach provides immediate confirmation of complete abortion in the vast majority of cases. Surgical abortion can be performed at the same time as another procedure (i.e., cholecystectomy), shortening anesthesia exposure and inpatient length of stay. Medication abortion in critically ill, intubated women is possible with intramuscular methotrexate and misoprostol, by administration of mifepristone and/or misoprostol through the endotracheal tube (i.e., for women who are unable to be placed in lithotomy position), or with the use of vaginal misoprostol alone. Medication abortion in such settings relies on available staff familiar with what to expect.

Surgical abortion is preferred when mifepristone is contraindicated

Mifepristone is an orally active synthetic steroid with potent antiprogesterone and antiglucocorticoid activities [12,23]. In healthy subjects, the pituitary and adrenal glands respond with increased secretion of adrenocorticotrophic hormone (ACTH) and cortisol after mifepristone intake [23]. Patients with primary (Addison's disease), secondary (ACTH deficiency) or tertiary (i.e., chronic high-dose glucocorticoid therapy) chronic adrenal insufficiency may lack the compensatory increase in ACTH and cortisol resulting in a deficit of cortisol [12,23]. Mifepristone's antiglucocorticoid activity, while potent, may not be relevant to patients undergoing medication abortions who ingest a single dose of 200 mg of mifepristone. In humans, mifepristone's antiglucocorticoid activity is dose-dependent and expressed at a dose of 400 mg and above (single administration) or 200 mg/day for several consecutive days [23]. No clinical or laboratory signs of adrenal failure have been observed during chronic administration of mifepristone among volunteers with normal adrenal function [23].

In most cases of chronic corticosteroid therapy, the glucocorticoid dose can be empirically increased for a few days following mifepristone administration in consultation with the prescribing physician [12,23]. Readjustment of corticosteroids for patients with severe uncontrolled asthma should be undertaken with caution because severe asthma attacks can be life-threatening [12,23].

Hemorrhagic disorders and concurrent anticoagulation therapy are listed as contraindications on the product labeling for Mifeprex® (Danco, New York, NY, USA) although not for Mifegyne® (Exelgyn, France) [12]. There is no evidence that mifepristone or misoprostol affects hemostasis. The known complication of hemorrhage following a medication

abortion, however, could be exacerbated by a bleeding disorder or when a patient is on anticoagulation medication. Preexisting anemia may increase the likelihood that a blood transfusion is necessary should hemorrhage occur. For women with a bleeding diathesis, surgical management offers direct observation and immediate uterine evacuation and less often leads to a delayed hemorrhage [24].

Inherited porphyria is also listed as a contraindication to mifepristone [25]. In an animal model, mifepristone caused a series of metabolic effects leading to significant accumulations of protoporphyrin [25]. These results indicate that mifepristone may pose a risk in patients with known porphyria by precipitating or exacerbating attacks [25].

Mifepristone undergoes hepatic and renal metabolism; therefore, it is logical to avoid administration in patients with severe hepatic impairment or renal failure, given the concern for drug accumulation [23]. Specific drug interactions with mifepristone remain unstudied. Mifepristone is metabolized by the cytochrome p450 system. Ketoconazole, itraconazole, erythromycin and certain antiretroviral drugs (ARVs) may inhibit the P450 enzyme system and mifepristone's metabolism, potentially increasing serum levels of mifepristone [23,26]. In contrast, rifampicin, St. John's Wort, certain antiepileptic drugs (phenytoin, phenobarbital, carbamazepine, oxcarbazepine) and certain ARVs [6] may induce the p450 system, thereby increasing mifepristone metabolism and lowering serum levels [23,26]. The clinical significance of decreased or increased mifepristone levels is unlikely to be clinically meaningful; doses as low as 100 mg are effective and Food and Drug Administration studies have demonstrated the effectiveness of 600-mg doses. When mifepristone is contraindicated, a multidose regimen of misoprostol alone is an alternative. The substantially lower efficacy rate and side effects, however, make multidose misoprostol less acceptable than surgical management for most women.

Surgical abortion is preferred when methotrexate is contraindicated

Methotrexate is a folic acid antagonist [27]. Folic acid is reduced to tetrahydrofolate by the enzyme dihydrofolate reductase (DHFR), a step in the synthesis of DNA and RNA precursors. Methotrexate inhibits DHFR, causing depletion of cofactors required for DNA and RNA synthesis. Based on its pharmacological action, methotrexate should not be administered in patients with evidence of immunodeficiency, moderate to severe anemia, leukopenia or thrombocytopenia, active pulmonary disease, active peptic ulcer disease, clinically important hepatic dysfunction or clinically important renal dysfunction [27].

3. When is medication abortion preferred over surgical abortion?

Patients at risk of surgical and anesthetic complications may benefit from medical management, sometimes in the inpatient setting [15]. Medication abortion may provide a

safer alternative for patients with extreme obesity, pelvic tumors that interfere with access to the cervix or a known history of serious reactions to anesthetic agents. Medication abortion, which does not require lithotomy positioning, may be preferred in the context of orthopedic (e.g., hip disease) or neurologic conditions (e.g., cerebral palsy). In some cases, hospitalized patients with psychiatric disorders can choose medication abortion if staff is willing to administer medications and assist patients as needed.

4. What are special issues related to use of routine abortion medications?

The use of ergot alkaloids is contraindicated for patients taking potent inhibitors of CYP3A4 (which include protease inhibitors, azole antifungals and some macrolide antibiotics) and/or with hypertension [28]. Most providers do not routinely administer uterotonics for the management of first-trimester abortions [29]. Carboprost tromethamine is contraindicated in patients with active cardiac, pulmonary, renal, or hepatic disease [30]. In general, lidocaine is an antiarrhythmic that can be used safely for patients with cardiac disease. Nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided in patients with thrombocytopenia or other preexisting platelet defects (e.g., von Willebrand disease), patients at risk of acute renal failure or gastrointestinal bleeding or patients with significant preexisting cardiovascular disease [31].

5. What considerations are important for common chronic conditions?

Diabetes

Women with type I diabetes are more prone to hypoglycemia in the first trimester. In type I diabetes, an initial increase in insulin requirements for the first trimester is followed by a clinically meaningful reduction in insulin requirement between 7 and 12 weeks of gestation [32]. Hyperemesis may also complicate oral intake for diabetic pregnant women, further disrupting glycemic control.

Management of diabetic women having surgical abortions depends in part on pain management plans. A regular diet and usual medication can be continued before and after abortion under local anesthesia. Deep sedation requires preprocedure fasting and a common approach is to administer half of the patient's usual long-acting insulin dose the evening before and omit the morning dose of short-acting insulin [33]. Ideally, a woman with diabetes is scheduled first or as an early case in the day, so that she can eat and take her usual dose of morning insulin after the procedure [19].

When advising women regarding medications and diet, providers should keep in mind that modest hyperglycemia poses no acute risk to women undergoing an abortion. For example, a transient blood glucose level of 180–200 mg/dL during an abortion is not worrisome, whereas a blood glucose of 30 mg/dL is a concern. Hence, providers should

have food, intravenous glucose solutions, or glucagon available. After the procedure, the patient's medication requirements may decrease substantially. Coordination of care with her medical provider is recommended, especially during this transitional time [19].

Women with diabetes desiring postabortion contraception can, in general, be offered all options. The use of combined hormonal contraception, however, is usually contraindicated for women with evidence of vascular disease or end-organ damage [6].

Hypertension

Hypertension is not uncommon among young women [34] and is often clinically silent and undertreated. Outpatient procedures are appropriate for women with mild to moderate hypertension. Poorly controlled hypertension [systolic blood pressure (BP) > 160 mmHg; diastolic BP > 105 mmHg] warrants treatment or management of the abortion in the hospital setting. Ergot drugs should be avoided in women with hypertension; oxytocin and misoprostol are acceptable uterotonic agents for such patients [19]. The *U.S. Medical Eligibility Criteria for Contraceptive Use* provide guidelines for contraceptive choice in hypertensive women seeking postabortion contraception [6].

Obesity

Surgical abortion for obese women may be associated with increased technical difficulty [35] and, for second-trimester procedures, with adverse outcomes such as increased blood loss [35,36]; prompt care is therefore important. Ventilation difficulties with deep sedation may be more common with obese patients. Consultation with an anesthesiologist may be helpful. Stafford et al. [37] demonstrated that rates of undesired outcomes following medication abortion, such as surgical interventions, were similar across all BMI categories, suggesting that medication abortion may be the better option for obese women. Obese women can benefit from almost all postabortion contraceptive options [38].

HIV

The advent of highly active antiretroviral therapy (HAART) has reduced the abortion rate among HIV-infected women because more women continue their pregnancies [39,40]. Nevertheless, underuse of highly effective contraceptives leaves many infected women at risk of unintended pregnancy [41]. Little is known about potential interactions between HIV infection and abortion. One small cohort study found no higher risk of infectious morbidity after curettage abortion among HIV-infected women than in uninfected women. The overall complication rate was higher among women with HIV, but these events included retained placenta and anesthesia problems unlikely to be related to HIV [42]. No published studies examine outcomes after medication abortion in the context of HIV infection. Women taking ARVs should continue them without interruption. Those with profound immunosuppression or AIDS may need

their abortion care to be coordinated with the patient's usual treating physician [19].

Discussion of postabortion contraception for patients taking ARVs should take into consideration potential drug interactions between many ARV drugs (particularly some non-nucleoside reverse transcriptase inhibitors and ritonavir-boosted protease inhibitors) and hormonal contraceptives [6]. These interactions might alter the safety and effectiveness of both the hormonal contraceptive and the ARV drug [6].

Epilepsy

Women with well-controlled epilepsy may receive outpatient abortion care; those with recent onset or uncontrolled seizures may benefit from hospital-based care. The dose of mifepristone may be increased in patients who take antiepileptic drugs that augment the hepatic p450 system that metabolizes mifepristone (i.e., phenytoin, phenobarbital, carbamazepine, and oxcarbazepine) [19,23,26]. No research data guide the choice of mifepristone dose. A mifepristone dose of up to 600 mg is approved as safe and effective for abortion care.

For a woman with epilepsy, a seizure may occur at any time. If a seizure occurs during abortion in an awake patient, appropriate measures include maintaining patient safety (safe positioning with support) and interrupting the abortion procedure if possible until the seizure resolves. Most seizures resolve spontaneously and do not require intravenous anticonvulsants. Status epilepticus is rare. Intravenous benzodiazepines, such as midazolam, will control prolonged or repetitive tonic-clonic seizures quickly and prevent seizure-related neurological and systemic injury [43]. Ancillary measures include airway maintenance, oxygen administration, administration of intravenous fluids, monitoring of vital signs and prompt hospitalization [19]. For postabortion contraception, consideration should be given to the interaction of certain anticonvulsants with combined hormonal contraception, which may reduce the effectiveness of such contraceptive methods or cause breakthrough seizures [6]. There are no data to guide dosing of DMPA in the context of antiepileptic drug therapy. In the context of drug interactions, intrauterine contraception may be ideal.

Asthma

Asthma is more likely to worsen in the second trimester, third trimester or postpartum than in the first trimester [44]. Women with a history of asthma without current symptoms may undergo usual care. Women with current well-controlled asthma should be encouraged to use usual medications and to bring an inhaler with them for their abortion visit. Even if their lungs are clear on auscultation, prophylactic use of an inhaler with nebulized albuterol or metaproterenol before the procedure may be prudent. The facility must be equipped to manage the rare acute asthma exacerbations. Concurrent respiratory infection or inadequately controlled asthma may require delaying the abortion until treatment achieves better control. Carboprost tromethamine (PGF 2α) is not

recommended for women with asthma, since it may cause bronchoconstriction; misoprostol is not contraindicated [19].

The use of inhaled corticosteroids does not require "stress dose" steroids at the time of surgery. However, if the woman has received repeated oral glucocorticoid therapy for asthma control (doses equivalent to at least 20 mg a day of prednisone for 5 or more days) [33,45], stress dose(s) of hydrocortisone may be used to prevent acute adrenal insufficiency. The dose should be individualized. Mifepristone medication abortion should be avoided in women with poorly controlled asthma on systemic glucocorticoid therapy [19].

Severe asthma with bronchospasm constitutes a medical emergency requiring intensive medical intervention. Indeed, the asthma mortality rate for women is 45% higher than that for men [46]. Women with recent emergency room visits for asthma or intubation may benefit from abortion provided in a hospital. Management may include premedication with steroids and the availability of pulmonary specialists. Local or regional anesthesia may be preferable if severe, uncontrolled asthma is present in order to avoid broncho-spasm during deep sedation or intubation [19]. Postabortion contraception for asthmatic patients is unrestricted [6].

Thyroid disease

Hyperthyroidism in pregnancy may present with tachy-cardia, vomiting, tremulousness, and wide pulse pressure. In addition, some women with hydatidiform mole present with clinical hyperthyroidism related to high human chorionic gonadotropin production [47]. Women with mild hyperthy-roidism may undergo usual abortion care; however, uncontrolled hyperthyroidism can lead to thyroid storm. Hence, treatment should begin promptly and the abortion should proceed after the disease is stabilized by medication. For advanced gestational ages, hospital care may be needed to manage a thyroid storm while performing an abortion expeditiously. Consultation with an anesthesiologist is advisable if the patient is to receive deep sedation or general anesthesia [19]. Postabortion contraception for patients with thyroid disease is generally unrestricted [6].

von Willebrand disease

von Willebrand disease (VWD) is the most common inherited bleeding disorder. VWD results from a deficiency or defect in von Willebrand factor (VWF), which mediates platelet adhesion and is a carrier protein for factor VIII (FVIII). The severity of VWD is classified using clinical laboratory tests and type of genetic mutations (Type 3 is considered severe) [48,49]. In healthy pregnant women, FVIII and VWF levels increase beginning in the second trimester, peak at term and return to baseline postpartum [48]. Some women are at risk of bleeding in early pregnancy [48]. FVIII and VWF levels also increase in most women with VWD, which may explain the frequent improvement in minor bleeding manifestations and the masking of the disease during pregnancy [48]. The hemostatic response to pregnancy depends on both the type and the severity of disease. Hemorrhage requiring transfusion is uncommon but has been reported weeks after a suction aspiration abortion [48]. When replacement therapy is indicated for hemorrhage prophylaxis, surgical abortion is preferred because the onset and peak of bleeding is more predictable than during medication abortion. Women with moderate or severe disease are best served with abortion care at a center with an obstetrician, hematologist and anesthesiologist experienced in managing coagulation disorders [49]. NSAIDs [31] and oxytocin [50] should be avoided with these patients.

6. How does anticoagulation affect management?

When patients requiring anticoagulation medication(s) seek abortion, providers are faced with the clinical decision of whether to interrupt or modify therapy. Reversal of anticoagulation may decrease bleeding, but increase the risk of thromboembolism, particularly during pregnancy [51] and especially with certain high-risk conditions (e.g., patients with cardiac valve replacement). Further, it may take several days to reverse anticoagulation, thereby delaying abortion. Women with a high risk of thrombosis maintained on warfarin may be transitioned to heparin, which can be held for surgery, and then warfarin may be restarted. This approach is time-consuming and complex.

Whether specific anticoagulation therapies increase blood loss at the time of a first-trimester abortion is unknown. Kaneshiro et al. [52] compared blood loss following suction aspiration up to 12 weeks gestation among women receiving anticoagulation therapy ($n=4$) versus healthy controls ($n=6$). Anticoagulation therapies included heparin, low-molecular-weight heparin and warfarin. The median procedural blood loss was higher among anticoagulated women than in controls, 70 mL versus 22.5 mL, respectively, but changes in hemoglobin before and after the procedure were clinically unimportant in both groups and no transfusions occurred. A larger study would provide additional information but may not be feasible. Medication abortion is not recommended for women who are anticoagulated.

For patients on antiplatelet therapies such as aspirin and clopidogrel, the risk of bleeding must be carefully weighed against the risk of coronary artery ischemic events. No recent study has examined the risk of bleeding for either therapy in women undergoing abortion. In general, low-dose aspirin therapy does not increase the severity of bleeding compli-cations or perioperative mortality [53]. Compared to monotherapy, patients on combination antiplatelet therapy (i.e., clopidogrel and aspirin) face an increased risk of systemic bleeding [54]. Clopidogrel should not be discon-tinued in the first 12 months after a drug eluting stent has been placed [33]. In general, the optimal period for discontinuation of antiplatelet therapy prior to any surgery is five days [33]. Such cases warrant consultation with a cardiologist or neurologist to determine if and when discontinuation of such medications is warranted.

7. Should additional antibiotics be administered at the time of abortion for patients to prevent infective endocarditis?

The Society of Family Planning recommends antibiotic prophylaxis to reduce infectious morbidity in all patients undergoing surgical or medication abortion in the first trimester [55]. For patients at risk of infective endocarditis, the American Heart Association (AHA) does not recommend antibiotic prophylaxis before or during genitourinary procedures [56]. The revised AHA guidelines emphasize that susceptible individuals with high-risk cardiac conditions are more likely to develop endocarditis from bacteremia associated with daily activities such as tooth brushing than from surgical procedures [56]. Based on these recommendations, no additional antibiotic coverage is warranted for patients with high-risk cardiac conditions undergoing surgical or medication abortion.

Conclusions and recommendations

Some serious, complex medical problems pose a dramatically increased risk for adverse health events during pregnancy. Early abortion care and effective postabortion care for women with such medical problems will reduce pregnancy-associated morbidity and mortality. To date, no level A evidence supports clinical recommendations for care of women with medical conditions who are undergoing abortion. We offer guidance in this paper on the basis of clinical experience combined with known features of coexisting conditions and abortion care.

On the basis of the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A: Recommendations are based primarily on good and consistent scientific evidence.

- There is no level A evidence to support our practice recommendations.

Level B: Recommendations are based primarily on limited or inconsistent scientific evidence.

- The dose of mifepristone should be increased above 200 mg when medical abortion is undertaken for women who are also being given inducers of the hepatic cytochrome p450 system.
- In steroid-dependent conditions, mifepristone's anti-glucocorticoid properties necessitate an increase in usual steroid doses.

Level C: Recommendations are based primarily on consensus and expert opinion.

- Women with stable, controlled hypertension, diabetes, or asthma can be safely managed in an outpatient setting.
- Hospital-based abortion is recommended for women with certain medical conditions (see Table 1).

- Patients with high-risk cardiac conditions do not require additional antibiotics for the prevention of infective endocarditis.
- Surgical abortion is preferred for women who have a bleeding disorder or who are anticoagulated in the first trimester.

4. Important questions to be answered

1. Do first-trimester abortion outcomes differ between women with preexisting conditions and their healthy peers?
2. Is the efficacy of mifepristone, which is metabolized by the hepatic p450 system, affected by co-administration of medications that induce p450 enzymes?
3. Should women on anticoagulant therapy continue, modify or discontinue such therapy when undergoing surgical abortion?

References

[1] Jones RK, Kooistra K. Abortion incidence and access to services in the United States, 2008. Perspect Sex Reprod Health 2011;43(1):41–50 [Evidence Grade: III].

[2] Raymond EG, Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012;119(2 Pt 1):215–9 [Evidence Grade: II].

[3] Bartlett LA, Berg CJ, Shulman HB, et al. Risk factors for legal induced abortion-related mortality in the United States. Obstet Gynecol 2004;103(4):729–37 [Evidence Grade: II-2].

[4] Pazol K, Zane S, Parker WY, et al. Abortion surveillance — United States, 2007. MMWR Surveill Summ 2011;60(1):1–2 [Evidence Grade: III].

[5] Berg CJ, Callaghan WM, Syverson C, Henderson Z. Pregnancy-related mortality in the United States, 1998 to 2005. Obstet Gynecol 2010;116(6):1302–9 [Evidence Grade: III].

[6] U.S. Medical Eligibility Criteria for Contraceptive Use, 2010. MMWR Recomm Rep 2010;59(RR-4):1–6 [Evidence Grade: III].

[7] Newstead-Angel J, Gibson PS. Cardiac drug use in pregnancy: safety, effectiveness and obstetric implications. Expert Rev Cardiovasc Ther 2009;7(12):1569–80 [Evidence Grade: III].

[8] Chang J, Elam-Evans LD, Berg CJ, et al. Pregnancy-related mortality surveillance — United States, 1991 — 1999. MMWR Surveill Summ 2003;52(2):1–8 [Evidence Grade: III].

[9] Finer LB, Frohwirth LF, Dauphinee LA, Singh S, Moore AM. Reasons U.S. women have abortions: quantitative and qualitative perspectives. Perspect Sex Reprod Health 2005;37(3):110–8 [Evidence Grade: III].

[10] Einarson A, Selby P, Koren G. Abrupt discontinuation of psychotropic drugs during pregnancy: fear of teratogenic risk and impact of counselling. J Psychiatry Neurosci 2001;26(1):44–8 [Evidence Grade: III].

[11] Williams J, Myson V, Steward S, et al. Self-discontinuation of antiepileptic medication in pregnancy: detection by hair analysis. Epilepsia 2002;43(8):824–31 [Evidence Grade: III].

[12] Davey A. Mifepristone and prostaglandin for termination of pregnancy: contraindications for use, reasons and rationale. Contraception Jul 2006;74(1):16–20 [Evidence Grade: III].

[13] Ramsey PS, Hogg BB, Savage KG, Winkler DD, Owen J. Cardiovascular effects of intravaginal misoprostol in the mid trimester of pregnancy. Am J Obstet Gynecol 2000;183(5):1100–2 [Evidence Grade: III].

[14] Bagga R, Choudhary N, Suri V, et al. First and second trimester induced abortions in women with cardiac disorders: a 12-year analysis from a developing country. J Obstet Gynaecol 2008;28(7):732–7 [Evidence Grade: III].

[15] Hackney DN, Creinin MD, Simhan H. Medical management of early pregnancy failure in a patient with coronary artery disease. Fertil Steril 2007;88(1):212e211–3 [Evidence Grade: III].

[16] Komaba Y, Kitamura S, Terashi A. Effect of prostaglandin E1 on cerebral blood flow in patients with chronic cerebral infarction. Intern Med 1998;37(10):841–6 [Evidence Grade: III].

[17] Li J, Liang X, Wang Q, Breyer RM, McCullough L, Andreasson K. Misoprostol, an anti-ulcer agent and PGE2 receptor agonist, protects against cerebral ischemia. Neurosci Lett 2008;438(2):210–5 [Evidence Grade: III].

[18] Patel N, Shatzmiller R, Sanossian N, Sahai-Srivastava S. Cryptogenic stroke in the setting of intravaginal prostaglandin therapy for elective abortion. Clin Neurol Neurosurg 2008;110(5):529–31 [Evidence Grade: III].

[19] Davis A, Easterling T. Medical evaluation and management. In: Paul M, Lichtenberg ES, Borgatta L, Grimes DA, Stubblefield P, & Creinin MD, editors. Management of unintended and abnormal pregnancy: Comprehensive abortion care. Wiley-Blackwell, ed. Oxford: Blackwell Publishing Ltd; 2009, pp. 78–89. [Evidence grade III].

[20] Blumenthal PD, Remsburg RE. A time and cost analysis of the management of incomplete abortion with manual vacuum aspiration. Int J Gynaecol Obstet 1994;45(3):261–7 [Evidence Grade III].

[21] Finer LB, Frohwirth LF, Dauphinee LA, Singh S, Moore AM. Timing of steps and reasons for delays in obtaining abortions in the United States. Contraception 2006;74(4):334–44 [Evidence Grade: III].

[22] Tsutsumi Y, Mizuno J, Takada S, Morita S. [Paracervical block for dilatation and curettage in a parturient with Eisenmenger's syndrome]. Masui. 59(3):379–382. [Evidence Grade: III]

[23] Sitruk-Ware, R. Mifepristone and misoprostol sequential regimen side effects, complications and safety. Contraception. 2006. 74(1): p. 48–55. 24. [Evidence Grade: III]

[24] Allen RH, Westhoff C, De Nonno L, Fielding SL, Schaff EA. Curettage after mifepristone-induced abortion: frequency, timing, and indications. Obstet Gynecol 2001;98(1):101–6 [Evidence Grade: II-2].

[25] Cable EE, Pepe JA, Donohue SE, Lambrecht RW, Bonkovsky HL. Effects of mifepristone (RU-486) on heme metabolism and cytochromes P-450 in cultured chick embryo liver cells, possible implications for acute porphyria. Eur J Biochem 1994;225(2):651–7 [Evidence Grade: III].

[26] DeHart RM, Morehead MS. Mifepristone. Ann Pharmacother 2001;35(6):707–19 [Evidence Grade: III].

[27] Barnhart K, Coutifaris C, Esposito M. The pharmacology of methotrexate. Expert Opin Pharmacother 2001;2(3):409–17 [Evidence Grade: III].

[28] Methylergonovine: drug information, UpToDate.

[29] Lichtenberg ES, Paul M, Jones H. First trimester surgical abortion practices: a survey of National Abortion Federation members. Contraception 2001;64(6):345–52 [Evidence Grade: III].

[30] Carboprost tromethamine: Drug information, in UpToDate.

[31] Solomon, D., Nonselective NSAIDs: Overview of adverse effects, UpToDate.

[32] Jovanovic L, Knopp RH, Brown Z, et al. Declining insulin requirement in the late first trimester of diabetic pregnancy. Diabetes Care 2001;24(7):1130–6 [Evidence Grade: II-2].

[33] Johnson BE, Porter J. Preoperative evaluation of the gynecologic patient: considerations for improved outcomes. Obstet Gynecol May 2008;111(5):1183–94 [Evidence Grade: III].

[34] Geronimus AT, Bound J, Keene D, Hicken M. Black-white differences in age trajectories of hypertension prevalence among adult women and men, 1999–2002. Ethn Dis Winter 2007;17(1):40–8 [Evidence Grade: II-3].

[35] Grimes DA, Shields WC. Family planning for obese women: challenges and opportunities. Contraception Jul 2005;72(1):1–4 [Evidence Grade: III].

[36] Marchiano DA, Thomas AG, Lapinski R, Balwan K, Patel J. Intraoperative blood loss and gestational age at pregnancy termination. Prim Care Update Ob Gyns 1998;5(4):204–5 [Evidence Grade: II-2].

[37] Strafford MA, Mottl-Santiago J, Savla A, Soodoo N, Borgatta L. Relationship of obesity to outcome of medical abortion. Am J Obstet Gynecol 2009;200(5):e34–6 [Evidence Grade: II-2].

[38] Higginbotham S. Contraceptive considerations in obese women: release date 1 September 2009, SFP Guideline 20091. Contraception 2009;80(6):583–90 [Evidence Grade: III].

[39] Massad LS, Springer G, Jacobson L, et al. Pregnancy rates and predictors of conception, miscarriage and abortion in US women with HIV. AIDS 2004;18(2):281–6 [Evidence Grade: II-2].

[40] Sharma A, Feldman JG, Golub ET, et al. Live birth patterns among human immunodeficiency virus-infected women before and after the availability of highly active antiretroviral therapy. Am J Obstet Gynecol 2007;196(6):541e541–6 [Evidence Grade: II-3].

[41] Massad LS, Evans CT, Wilson TE, et al. Contraceptive use among U.S. women with HIV. J Womens Health (Larchmt) 2007;16(5):657–66 [Evidence Grade: III].

[42] Stuart GS, Sheffield JS, Hill JB, McIntire DD, McElwee B, Wendel GD. Morbidity that is associated with curettage for the management of spontaneous and induced abortion in women who are infected with HIV. Am J Obstet Gynecol 2004;191(3):993–7 [Evidence Grade: III].

[43] Sirven JI, Waterhouse E. Management of status epilepticus. Am Fam Physician 2003;68(3):469–76 [Evidence Grade: III].

[44] Kwon HL, Belanger K, Bracken MB. Effect of pregnancy and stage of pregnancy on asthma severity: a systematic review. Am J Obstet Gynecol 2004;190(5):1201–10 [Evidence Grade: III].

[45] Axelrod L. Perioperative management of patients treated with glucocorticoids. Endocrinol Metab Clin North Am 2003;32(2):367–83 [Evidence Grade: III].

[46] Akinbami LJ, Moorman JE, Liu X. Asthma prevalence, health care use, and mortality: United States, 2005–2009. Natl Health Stat Report 2012;32:1–4 [Evidence Grade: II-2].

[47] Erturk E, Bostan H, Geze S, Saracoglu S, Erciyes N, Eroglu A. Total intravenous anesthesia for evacuation of a hydatidiform mole and termination of pregnancy in a patient with thyrotoxicosis. Int J Obstet Anesth 2007;16(4):363–6 [Evidence Grade: III].

[48] Kujovich JL. von Willebrand disease and pregnancy. J Thromb Haemost 2005;3(2):246–53 [Evidence Grade: III].

[49] Lipe BC, Dumas MA, Ornstein DL. Von Willebrand disease in pregnancy. Hematol Oncol Clin North Am 2011;25(2):335–58 [Evidence Grade: III].

[50] James AH, Manco-Johnson MJ, Yawn BP, Dietrich JE, Nichols WL. Von Willebrand disease: key points from the 2008 National Heart, Lung, and Blood Institute guidelines. Obstet Gynecol 2009;114(3):674–8 [Evidence Grade: III].

[51] Blickstein I. Thrombophilia and women's health: an overview. Obstet Gynecol Clin North Am 2006;33(3):347–56 [Evidence Grade: III].

[52] Kaneshiro B, Bednarek P, Isley M, Jensen J, Nichols M, Edelman A. Blood loss at the time of first-trimester surgical abortion in anticoagulated women. Contraception 2011;83(5):431–5 [Evidence Grade: II-2].

[53] Burger W, Chemnitius JM, Kneissl GD, Rucker G. Low-dose aspirin for secondary cardiovascular prevention - cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation - review and meta-analysis. J Intern Med 2005;257(5):399–414 [Evidence Grade: III].

[54] Squizzato A, Keller T, Romualdi E, Middeldorp S. Clopidogrel plus aspirin versus aspirin alone for preventing cardiovascular disease. Cochrane Database Syst Rev 2007;3:CD005158 [Evidence Grade: I].

[55] Achilles SL, Reeves MF. Prevention of infection after induced abortion: release date October 2010: SFP guideline 20102. Contraception 2011;83(4):295–309 [Evidence Grade: III].

[56] Wilson W, Taubert KA, Gewitz M, et al. Prevention of infective endocarditis: guidelines from the American Heart Association: a guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. Circulation 2007;116(15):1736–54 [Evidence Grade: III].

Sources

We used the PUBMED database to identify publications related to first-trimester abortion and coexisting medical conditions. We also identified articles related to medical problems in the context of general health, perioperative guidelines and pregnancy. In addition, the references of publications found through these databases were reviewed to capture any additional articles that may have been missed.

Authorship

These guidelines were prepared by Maryam Guiahi, M.D., M.S., and Anne Davis, M.D., M.P.H., and reviewed and approved by the Board of Directors of the Society of Family Planning.

Conflict of interest

Maryam Guiahi, M.D., M.S., and Anne Davis, M.D., M.P.H., report no significant relationships with industries relative to these guidelines. The Society of Family Planning receives no direct support from pharmaceutical companies or other industries.

Intended audience

This guideline is for Society of Family Planning fellows and any other health care professionals involved in the provision of first-trimester abortion care. This guideline may be of interest to other professional groups that set practice standards for family planning services. The purpose of this document is to review the medical literature evaluating common approaches of providing first-trimester abortion care to women with coexisting medical conditions. This evidence-based review should guide clinicians, although it is not intended to dictate clinical care.