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Clinical Guidelines

Cervical dilation before first-trimester surgical abortion (<14 weeks' gestation)

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Abstract

First-trimester surgical abortion is a common, safe procedure with a major complication rate of less than 1%. Cervical dilation before suction aspiration is usually accomplished using tapered mechanical dilators. Risk factors for major complications in the first trimester are increasing gestational age and provider inexperience. Use of laminaria for cervical priming reduces the risk of cervical laceration and, to a lesser extent, uterine perforation. While pharmacological priming agents may potentially have the same effects, no published studies to date have been large enough to assess these outcomes. Given an experienced provider, the risk of these injuries during suction aspiration is very small.

Cervical priming can be achieved with osmotic dilators or pharmacological agents. The advantages of osmotic dilators such as laminaria, Dilapan-S™ and Lamicel® are their ability to produce wide cervical dilation, and for the synthetic types, their advantages include predictable effects and rapid onset of action. A disadvantage of osmotic dilators is that they require a speculum examination and a trained clinician to perform the insertion. When cervical priming is performed, misoprostol is the prostaglandin analogue most commonly used worldwide. Compared to laminaria, vaginal misoprostol requires a shorter period of time to achieve the same dilatation, is associated with less discomfort and is preferred by women. The sublingual route appears as effective as vaginal administration and requires less time for priming (2 h), but it is associated with more side effects. Oral administration can produce equivalent dilation to vaginal or sublingual administration, but higher doses and longer treatment periods (8 to 12 h) are required. Buccal administration of misoprostol appears to have a pharmacokinetic and physiologic profile similar to vaginal administration; however, there are no published studies of buccal misoprostol prior to first-trimester suction abortion.

While extensive data demonstrate that a variety of agents are safe and effective at causing cervical softening and dilation preoperatively, there are not enough data to conclude that routine cervical priming is necessary to reduce complications of first-trimester surgical abortion. Cervical priming increases preoperative cervical dilation, making the procedure easier and quicker for the physician. However, in order to preoperatively dilate the cervix, the woman must receive the agent at least 3 to 4 h prior to her procedure. Besides the additional waiting, the woman might experience bleeding and cramping prior to the procedure. There are insufficient data evaluating how cervical priming affects women's quality of life in relation to abortion. Based on existing evidence, the Society of Family Planning does not recommend routine cervical priming for suction aspiration procedures. The Society of Family Planning further recommends that providers consider cervical priming only for women who may be at increased risk of complications from cervical dilation, including those late in the first trimester, adolescents and women in whom cervical dilation is expected to be difficult due to either patient factors or provider experience.

Keywords: Surgical abortion; Cervical dilation; Laminaria; Misoprostol

Background

Induced abortion is one of the most common surgical procedures in the United States. In 2002, 1.3 million pregnancies were terminated, approximately 90% at less than 14 weeks' gestation [1]. First-trimester surgical abortion is a safe procedure with a mortality rate of 0.7 per 100,000 procedures performed under 13 weeks' gestation and a major complication rate of less than 1% [2,3]. The rate of recognized uterine perforation during first-trimester surgical abortion ranges from 0.1 to 4 per 1000 procedures [3–15]. The rate of cervical injury ranges from 0.1 to 10 per 1000 procedures, with higher rates in adolescents [3–10,12,16,17]. The rate of immediate complications depends on provider experience and gestational age. Within the complication ranges reported above, the higher complication rates come from studies with a large proportion of physicians-in-training performing abortion procedures in a hospital setting. Experienced providers in high-volume outpatient clinics can anticipate lower complication rates [8].

Cervical dilation before suction aspiration can be the most difficult part of the abortion procedure for both the patient

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and the provider. The cervical dilatation needed can be achieved mechanically with tapered Pratt or Denniston dilators at the time of the procedure. Blunt Hern and Hegar dilators are not generally recommended because they require more force [18,19]. In early gestations, cervical dilation can sometimes be avoided by using the smallest diameter cannula that fits through the internal os of the cervix.

Shortly after the legalization of induced abortion in the United States, studies demonstrated that the use of laminaria, an osmotic dilator, reduced the risk of cervical laceration and, to a lesser extent, uterine perforation [11,16,20]. These risk reductions were observed primarily in settings with a high baseline complication rate. There were also reports of the utility of laminaria in reducing the pain associated with rigid dilation, allowing procedures to be performed using local anesthesia; however, these studies lacked a control group [21–23]. Other studies hypothesized that passive dilation of the cervix with prostaglandins or similar agents might also avert uterine perforation and cervical laceration through a reduction in the force required for cervical dilation [24,25]. No published studies to date, however, have been large enough to assess the role of preoperative misoprostol in preventing complications. Given an experienced provider, the risk of these injuries during first-trimester suction aspiration is very small.

Older medical literature reflected a concern that forceful cervical dilation could cause permanent damage to the cervical tissue, leading to poor reproductive outcomes [18,21,26–30]. For this reason, use of cervical preparatory agents was advocated to prevent long-term complications such as spontaneous abortion, incompetent cervix and preterm delivery. Because published studies disagree about whether surgical abortion is truly associated with subsequent spontaneous abortion and preterm delivery [31–46], evidence about whether preoperative cervical preparation influences these risks is lacking.

This guideline provides recommendations for cervical dilation before first-trimester surgical abortion. The goals of the guideline are to identify the techniques that are most effective, safe and acceptable to women. Risk factors for immediate complications from cervical dilation will be discussed, and the guideline will explore the evidence for the use of cervical priming agents in the first trimester, with a focus on whether cervical preparation is necessary or beneficial in all cases or only in certain circumstances. Rigid dilation, osmotic dilators and prostaglandin analogues, with a focus on misoprostol, will be discussed.

Risk factors for immediate complications

Immediate complications from suction abortion include uterine perforation, hemorrhage, cervical laceration and incomplete abortion. The same factors that predispose to uterine and cervical injury will also make incomplete abortion more likely: provider inexperience, increasing gestational age and an abnormal uterine cavity [47]. From 1975 to 1978, the Joint Program for the Study of Abortion III (JPSA III) of the Centers for Disease Control and Prevention (CDC) collected data on the immediate complications of both first- and second-trimester legally induced abortions at 13 institutions. Some of these institutions were large academic medical centers with a high proportion of physicians in training and access to general anesthesia. The overall rate of uterine perforation in JPSA III was 0.9 per 1000. Less experienced providers had higher uterine perforation rates, and the osmotic dilator, laminaria, had a strong protective effect [11]. In one setting where both residents and attending physicians performed procedures, the relative risk for uterine perforation was 3.6 for residents compared to attending physicians. In a related study of procedures under 12 weeks, Schulz et al. [16] found that the overall rate of cervical injury was 10 in 1000 procedures. Significant protective factors were the use of laminaria and an attending physician performing the procedure. These early studies highlighted the benefit of cervical preparation with laminaria in reducing immediate complications, especially when physicians in training were involved. However, the absolute rate of complications reported in these studies was generally higher than that reported contemporaneously by high-volume outpatient clinics with experienced providers [8,12,13,48]. None of these studies specified whether previous deliveries were vaginal or cesarean.

Many studies of surgical abortion have demonstrated that treatment by trainees is a significant risk factor for complications [5,9,11,12,16,24,47,49,50]. One study comparing manual and electric vacuum aspiration in the first trimester did not find a difference in complication rates between trainees and experienced providers [51]. This might be because the trainees were third-year gynecology residents in a clinical training program with a high volume of surgical terminations or because the study had insufficient power to detect a difference in complication rates. The literature also demonstrates that increasing gestational age is an important risk factor for major complications but is inconsistent on the role of parity, history of previous abortion or the age of the woman [5–9,11,12,16,49,52,53]. Risk factors for major complications differ based on the specific complication. For example, JPSA III found that increasing parity was a risk factor for uterine perforation but not cervical injury. This finding may be due to differential changes in the myometrium and cervical stroma after delivery [11,16]. Adolescents are at higher risk for cervical laceration, even controlling for parity [6]. These studies seem to indicate that young age is not a proxy for nulliparity. Rather, adolescents have small, physiologically immature cervices that are perhaps more difficult to dilate regardless of obstetric history [16].

Other reports contemporary to JPSA III reported similar or lower rates of immediate complications in ambulatory abortion clinics, none of which routinely employed cervical priming. One of the earliest descriptions of abortion-related complications in the United States reported a major complication rate of 22 per 1000 with 36 uterine perforations out of 26,000 procedures (1.4 per 1000) [48]. A prospective

study of 10,453 abortions under 12 weeks performed by experienced providers at a single outpatient clinic using local anesthesia reported a major complication rate of 1.4%, with only 10 recognized uterine perforations (1 per 1000) and no cervical lacerations [13]. This clinic promoted the use of the "soft" technique, in which flexible cannulae were used under 8 weeks, and the cervix was minimally and gently dilated with Pratt dilators. Bozorgi [12] reported on 10,890 abortions performed at less than 14 weeks with a major complication rate of 0.7%. Specifically, he noted only 2 uterine perforations (0.2 per 1000) and 20 cervical lacerations (2 per 1000). The technique described included local anesthesia, mechanical dilation with half-size Hegar dilators and use of a rigid, plastic suction curette. This study documented that increasing gestational age and providers who performed fewer procedures were both directly related to the rate of complications [12]. The largest series published, an analysis of 170,000 first-trimester abortions performed by experienced providers without cervical priming, found that complications requiring hospitalization occurred in only 1 out of every 1405 procedures (0.07%), and the uterine perforation rate was 0.1 per 1000 [8].

In sum, the only clear risk factors for major complications in the first trimester are increasing gestational age and provider inexperience. Adolescents and nulliparous women may also have an increased risk of complications; however, data are conflicting. There are not enough data in the literature to support any comment on the risk of complications specifically in women with prior cervical conization, cesarean delivery and cervical stenosis or in women whose uterus is acutely anteflexed or retroflexed [8,53]. The results of a recently completed World Health Organization (WHO) randomized, placebo-controlled trial of more than 4700 women evaluating misoprostol for cervical priming in the first trimester may provide these missing data.

Rigid dilation

Cervical dilation might not always be required for suction aspiration, for example, in multiparous women. However, if dilatation is needed, most providers in North America employ rigid dilation alone with steel Pratt dilators or its plastic equivalent, the Denniston dilator [54]. The Pratt dilator is characterized by a gradual taper at the end of the instrument and comes in sizes ranging from 9 to 79 F. For most pregnant women, dilation can easily be initiated with a 17-F dilator. Each French unit is equivalent to 0.33 mm in diameter. By comparison, Hegar dilators have a blunt end and come in sizes ranging from 1 to 26 mm in diameter. Hegar dilators increase in size more rapidly than tapered dilators, potentially reducing the time necessary for dilation. With Hegar dilators, it is easier to sense the loss of resistance of the internal os than with Pratt dilators [54]. There are no trials comparing the safety and efficacy of Pratt and Hegar dilators. Nevertheless, Hegar dilators are generally not recommended because they require more force [18,19]. Only a minority of providers currently report using the Hegar dilator [55].

Cervical priming agents

Cervical priming can be accomplished mechanically with osmotic dilators that absorb water from the cervix and slowly expand to dilate the cervical os or biochemically with prostaglandin analogues or progesterone antagonists. As of 1997, only a small percentage of North American providers (2%) routinely prepare the cervix with osmotic dilators or misoprostol prior to first-trimester abortion, although this percentage increases markedly (25%) after 12 weeks' gestation [55]. The commercially available options for cervical priming include osmotic dilators, laminaria, Dilapan-S™ and Lamicel®, as well as pharmacological agents such as misoprostol (PGE_1), gemeprost (PGE_1), dinoprostone (PGE_2) and mifepristone. Other agents for cervical priming have been described, including danazol and nitric oxide donors; use of such agents is considered investigational.

Osmotic dilators

There are three types of osmotic dilators available in the United States: laminaria (*Laminaria digitata*, *Laminaria japonicum*), Dilapan-S™ (GelMed International, Czech Republic) and Lamicel® (Medtronic, Mystic, CT). All osmotic dilators require a trained medical provider and a speculum exam for insertion.

Laminaria tents are dried compressed stalks of hygroscopic seaweed that absorb water from the cervical stroma, swelling to three or four times their dry diameter. Laminaria tents are available in multiple dry diameters. Laminaria apply radial force to the walls of the cervical canal and also induce the local production of prostaglandins to promote dilation [56,57]. Since bacterial spores can remain despite treatment of the laminaria with ethylene oxide or irradiation for sterilization, clinicians have worried about the risk of infection with laminaria use. There have been case reports of bacteremia following laminaria placement in the second trimester [58,59]. Researchers theorize that laminaria insertion can facilitate the transfer of cervical or vaginal flora into the uterine cavity and cause an ascending infection [60]. However, a randomized trial comparing laminaria and rigid dilation in first-trimester abortion found no significant difference in rates of postabortal infection [61]. In the first trimester, it is general practice to remove all osmotic devices no later than 24 h after insertion to reduce the possibility of infection. Because they are made of a natural material, laminaria have been associated with hypersensitivity reactions (urticaria, angioedema, respiratory distress) and anaphylaxis in women with previous exposure to laminaria, albeit rarely [62–64]. Investigators believe that the mechanism for this allergic reaction is IgE mediated, but the true incidence of this reaction is unknown [63]. Finally, many providers do not use laminaria tents before first-trimester surgical abortion because they act slowly and often require an extra visit.

Dilapan-S™ and Lamicel® were developed to overcome these issues; these synthetic dilators are completely sterile and swell more rapidly than laminaria. Additional advantages of synthetic dilators are the consistency of length and shape and, therefore, more predictable results. Since laminaria come from the stem of a type of seaweed, they cannot be manufactured to specification.

Dilapan-S™ is a rod-shaped hydrophilic dilator made from polyacrylate-based hydrogel (Hypan) available in the following dimensions: 3×55, 4×55 and 4×65 mm. Dilapan-S™ absorbs water from the cervical tissue; in 4 h, the 3-mm diameter swells to an average of 8 to 9 mm and the 4-mm diameter swells to an average of 10 to 11 mm, according to the manufacturer. In the United States, the Dilapan-S™ product label limits its use to one device placed up to 4 h prior to suction abortion in gestations less than 16 weeks. In other countries, Dilapan-S™ is not subject to these limitations on number of devices, indication or duration of use. The original version of Dilapan™ that debuted in 1986 tended to break when subjected to high mechanical stress such as a difficult removal [65]. The reformulated version released in 1998 internationally and in 2002 in the United States was designed not to fracture. The reformulated Dilapan™, named Dilapan-S™, has not generated any reports of breakage [66]. The advantage of Dilapan-S™ is its rapid swelling, making it ideal for same-day procedures.

Lamicel® is a polyvinyl alcohol polymer sponge impregnated with 450 mg magnesium sulfate and compressed to form a thin cylindrical tent. When placed in the cervical canal, Lamicel® absorbs water from the cervical stroma and swells to four times its original size, transforming into a soft sponge [27,67]. Lamicel's mechanism of action is biochemical rather than mechanical, exerting no outward pressure on the cervical canal [30]. Lamicel® reduces the amount of force needed to dilate the cervix [27,30] and is approved for cervical priming for gestations less than 16 weeks. Lamicel® is significantly easier to remove than laminaria or Dilapan-S™. Although Lamicel® is the most expensive osmotic dilator, it often takes multiple laminaria to achieve the same priming effect that one Lamicel® can produce in 4 h. Lamicel® is 75 mm long and is available in either 3 or 5 mm dry diameters internationally.

Pharmacological agents

Pharmacological agents such as prostaglandin analogues and progesterone antagonists can also be used for cervical priming in the first trimester. Studies examining the efficacy of these agents have measured baseline cervical dilatation, subjective ease of dilation, force required for dilation, procedure time, ability to complete the procedure and blood loss. When evaluating cervical priming agents, important clinical outcomes are whether adequate cervical dilatation can be achieved to complete the procedure as planned and whether complications are reduced [68]. The side effects of cervical priming agents and their acceptability to women, including quality of life, are equally vital clinical outcomes. While prostaglandin analogues and progesterone antagonists have been shown to be equivalent to osmotic dilators in reducing the amount of force needed for cervical dilation [26], there is inadequate published evidence to demonstrate that they also reduce major immediate complications such as uterine perforation and cervical laceration. It requires an extremely large sample size to prove such a reduction because complications in first-trimester surgical abortion are rare. However, one multicenter randomized trial of 1001 women showed that routine cervical priming with 15-methyl-$PGF_{2\alpha}$ vaginal suppositories (Carboprost) reduced the risk of complications (infection and recurettage) in women terminating pregnancies between 8 and 12 weeks' gestation [69]. There were no differences in cervical laceration rates, and no uterine perforations were reported.

Misoprostol is now the medication most commonly used for cervical priming [70]. Misoprostol is a PGE_1 synthetic analogue marketed as an oral preparation to prevent and treat gastroduodenal damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs). E-series prostaglandins are preferred over F-series prostaglandins because they stimulate uterine smooth muscle more than intestinal or vascular smooth muscle and do not cause bronchoconstriction [71]. Misoprostol's advantages are its low cost (US$0.89–1.47 per 200-μg tablet [72]), long shelf life and lack of need for refrigeration. Other prostaglandins such as gemeprost and dinoprostone are not used for cervical priming before surgical dilation in North America because they are more expensive but no better than misoprostol at cervical priming [73–76] and require refrigeration for transport and storage [77]. Mifepristone is a progesterone antagonist that withdraws hormonal support of the pregnancy [78–81], causing cervical softening [82]. Mifepristone, while effective at cervical priming, is not often used because of its high cost and limited availability in many clinical settings.

Investigators have examined different routes of misoprostol administration. The ideal route must take into account not only efficacy but also patient and staff acceptance and convenience. Misoprostol can be administered orally, vaginally, sublingually, buccally or rectally. Pharmacokinetic studies (Fig. 1) comparing oral and vaginal administration have shown that vaginal misoprostol is associated with slower absorption, lower peak plasma levels and slower clearance, similar to an extended-release preparation [83–85]. Vaginal misoprostol is also associated with a greater overall exposure to the drug, greater area under the curve (AUC) and greater effects on the cervix and uterus [84]. There is no clinically significant difference between vaginal misoprostol that is administered dry and vaginal misoprostol moistened with water, saline or acetic acid [86–89]. The rectal route of administration shows a similar pattern to vaginal administration but a lower AUC, including a significantly lower maximum peak concentration [85]. The sublingual route of administration has an AUC similar to vaginal administration but more rapid absorption and higher peak levels than either vaginal or oral administration [90].

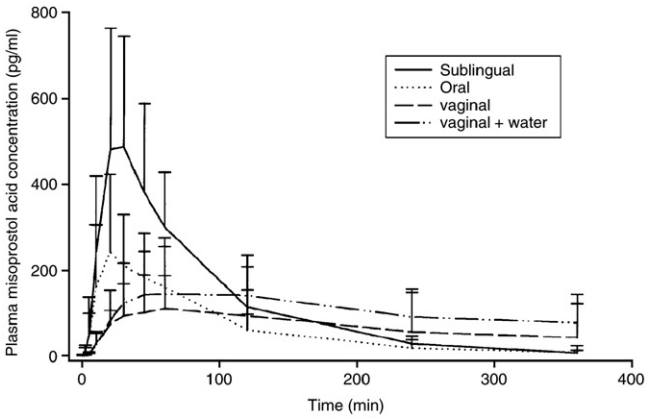

Fig. 1. Mean plasma concentrations of misoprostol acid over time (error bars=1 SD). Reprinted from Ref. [86]. Copyright© 2002 with permission from Oxford University Press.

These properties result in higher rates of gastrointestinal side effects. The sublingual route also causes uterine contractions at a rate equivalent to vaginal administration [90]. The buccal route of administration has recently been studied and shows a lower AUC, a lower peak concentration and fewer side effects than sublingual administration [91]. The buccal route has a pattern of absorption similar to the vaginal route but produces lower serum levels overall. Nevertheless, the buccal route of administration produces similar uterine tone and activity as compared to vaginal administration. The buccal route of administration is also felt to be the least variable in terms of drug exposure and peak levels [92]. The administration of NSAIDs for pain relief does not alter the efficacy of misoprostol for cervical priming [93].

Most providers in North America continue to use rigid dilators for cervical dilation without preoperative priming [8,9,55]. This practice occurs because the risk of uterine perforation or cervical laceration with first-trimester suction aspiration, given an experienced provider, is very small and each method of cervical priming is associated with its own profile of side effects and additional inconvenience for the patient. Previous guidelines for cervical priming have been published internationally, including recommendations from the WHO and the Royal College of Obstetricians and Gynaecologists (RCOG). The WHO recommends cervical priming for all women younger than 18 years old, nulliparous women over 9 weeks' gestation and all women over 12 weeks' gestation [94]. The RCOG guidelines state that cervical priming should be routine in women under 18 years of age or women at more than 10 weeks' gestation [95]. In North America, the National Abortion Federation recommends that the "cervix be dilated gently and gradually" and that under 14 weeks' gestation, adequate dilatation may be achieved by osmotic dilators or misoprostol [96]. The Planned Parenthood Federation of America states that, in first-trimester abortions, the use of osmotic dilators or misoprostol is optional [97].

Guideline questions

1. How much rigid dilation is needed to perform a suction abortion?

There is no consensus among providers regarding the desired width of dilation. Frequently, in early first-trimester procedures (<8 weeks), no dilation is required to insert the desired cannula, especially in multiparous women. In the past, when half-size Hegar dilators were preferred, providers dilated the cervix 0.5 to 2 mm less than the gestational age in weeks [12]. According to a recent survey of North American providers, approximately half report dilating the cervix to a diameter in millimeters equal to the gestational age in weeks. An additional one third of providers dilate to 1 to 2 mm greater than the number of gestational weeks. The remainder dilate to 1 to 3 mm less than the gestational age, using a smaller cannula to evacuate the pregnancy [55]. Most providers dilate the cervix incrementally, but some skip dilator sizes if the internal os is compliant [54].

In Marie Stopes outpatient centers in the United Kingdom, no rigid dilation or cervical priming is used for first-trimester surgical abortion [98]. These providers employ atraumatic tenaculums, flexible cannulae and 1% lidocaine gel for local anesthesia. The smallest cannula size possible for a given gestation is used to evacuate the uterine contents (<6 weeks: 4 mm cannula, 6 to 7 weeks: 5 mm cannula, 8 to 9 weeks: 6 mm cannula and 10 to 12 weeks: 7 mm cannula). If any dilation is necessary, cannulae of the appropriate size are employed as dilators. Rarely, os finders are needed to ascertain the path of the cervical canal. This method has not been compared to other techniques in any clinical trials.

2. How should the efficacy of cervical priming agents be defined?

There are several factors to consider when defining the efficacy of cervical priming agents. Most studies have evaluated some combination of baseline cervical dilatation, need for further mechanical dilation, duration of the procedure, subjective assessment of ease of dilation, force required for dilation measured by cervical tonometer, intraoperative blood loss, premature passage of fetal or chorionic tissue, side effects (preoperative bleeding, fever, pain, nausea, vomiting and diarrhea), acceptability and complication rates [26,75,76,99–125]. Primary outcomes, on which sample sizes are calculated, however, tend to be baseline cervical dilatation or force required to reach a certain diameter of dilatation. These primary outcomes illustrate only whether cervical priming works to soften and dilate the cervix.

Another important measure in terms of patient acceptability is the rate of side effects and time spent waiting for the abortion procedure. It is rare that the side effects of cervical priming and its acceptability to women are the primary objectives of a study. Women generally prefer 1-day

procedures to 2-day procedures and prefer misoprostol to laminaria for cervical priming [113,126]. Most women find both the oral and vaginal routes of misoprostol acceptable [101,105,113]. The benefit of passive dilation of the cervix prior to the surgical procedure in terms of decreased operative time and improved ease of procedure must be balanced against the patient's individual circumstances such as type of anesthesia available and side effects experienced while waiting [103]. The frequency of side effects has varied in cervical priming trials. Often, those showing no difference lack the power to detect an effect. Those that do have significant results find that the placebo arm experiences significantly fewer side effects than the misoprostol arm. Medication abortion trials have demonstrated that self-administration of vaginal misoprostol at home and in the clinic is acceptable to women [127–130]. One study has similarly documented the feasibility of home administration of misoprostol prior to surgical evacuation [131]. This method might avoid the waiting period required in the clinic and allow for more rapid patient turnover. However, home use in this manner would require additional counseling in the event the patient develops heavy bleeding or even expels the pregnancy at home. Additionally, in the event that a woman does not return, a continuing pregnancy exposed to misoprostol might be at risk for congenital anomalies [132–134].

Ideally, the efficacy of cervical priming should be defined by its impact on complication rates. Whether or not cervical priming is worth the added inconvenience and side effects depends on its ability to make the procedure safer and the underlying absolute risk of complications in the population. Women might more readily accept the intervention if they could be told that the complication rate would decrease in a clinically significant way. Given the rarity of immediate complications, however, only a few studies have had sufficient power to evaluate a decrease in complication rates due to cervical priming. The majority of these studies show that complications are so rare, given an experienced provider, that cervical priming might not be worth the added inconvenience to women [8,13].

3. Are there certain patients who are more likely to benefit from cervical priming in the first trimester?

Adolescents and women late in the first trimester are more likely to benefit from cervical priming. In addition, women with uterine anomalies or known cervical stenosis might also benefit [47]. Existing data support an increased risk of immediate complications as gestational age increases, even in the first trimester [2,11,12,16,49,52]. Because studies differed in their reference groups, categories of gestational age and whether or not second-trimester procedures were included, there is no clear evidence to dictate when cervical priming should begin. Taken together, however, the risk of complications tends to increase after 9 weeks and even more in the 12th and 13th week of gestation.

Data addressing the role of parity in complication risk are inconsistent. Some studies show that parity is not a significant factor [6,9,12,16,49]; some indicate that multiparity increases the risk of complications [11,47,52], and one study demonstrates that nulliparity increases the risk of complications [5,10]. None of these studies report on whether prior deliveries were vaginal or cesarean, and few also include data on prior induced abortion. The role of prior induced abortion is protective for cervical injury in one study and a risk factor for uterine perforation in another study [16,53]. There is no evidence that prior cesarean delivery, whether single or multiple, increases the risk of complications in first-trimester curettage [53]. Intuitively, nulliparity should be related specifically to the risk of cervical injury; however, this association has not been adequately demonstrated [16]. The evidence for increased complication rates in adolescents is more compelling [6,10,16]. Controlling for parity, adolescents have a higher risk of cervical injury, especially over 12 weeks, than adult women [6,16].

4. Are osmotic dilators safe and effective for cervical priming in the first trimester and which type is preferred?

The insertion of one medium laminaria is effective in dilating the cervix to at least 9 mm in more than 75% of women, reducing the need for rigid dilation [20–23,135,136]. The dilatation achieved with laminaria tents has been shown to increase with the number of tents used and gestational age [111,137]. Laminaria show some effect after 4 h, but more time is necessary for them to induce prostaglandin release and reach their maximum diameter [135,138]. The diameter of each laminaria increases by 25% if left in place for 4 h and by 90% if left in place overnight [135,139]. The use of laminaria prior to first-trimester surgical abortion has also been shown to decrease the incidence of cervical lacerations in certain clinical settings and, to a lesser extent, uterine perforations [6,11,16,20].

Bokstrom and Wiqvist [140] studied the use of Dilapan™ for cervical priming in women in their 10th to 12th week of gestation. They found that a 3-mm Dilapan™ achieved 8 mm of dilatation after 3 to 4 h and 10 mm of dilation after 16 to 20 h, while a 4-mm Dilapan™ reached 8.5 and 11.3 mm of dilatation, respectively. Although 16 to 20 h of treatment with Dilapan™ provided significantly more dilation than 3 to 4 h of treatment, the additional dilation gained with longer durations of use might not be clinically significant in the first trimester.

Lamicel® similarly swells rapidly, and its administration 4 h preoperatively has been shown to be as effective as 16 h for increasing baseline cervical dilatation [67]. In fact, studies indicate that the total force required for dilation drops rapidly after 2 h of Lamicel® placement and then plateaus [141]. One randomized trial of 629 women showed that Lamicel® achieved a higher mean dilation compared to placebo (8.2 mm vs. 5.8 mm, $p<.001$). The study failed to show that priming with Lamicel® significantly reduced uterine perforations, infection or recurettage. However, the perforation rate in the Lamicel® group was 0.4% versus

1.7% in the control group (p<.25), and the study may have had insufficient power to detect a difference in complication rates [141].

There are advantages and disadvantages to all types of osmotic dilators. Investigators have conducted a number of comparative trials testing their efficacy for cervical priming before first-trimester surgical abortion. No published trials have evaluated the new formulation of Dilapan™, Dilapan-S™. Randomized trials have demonstrated that one Dilapan™ device outperforms a laminaria with a similar diameter with 4 h of use, but the two are equivalent at 6 h [111,142]. There is a trend toward more cramping and difficult removals with Dilapan™ and laminaria than with Lamicel®. Some surgeons report anecdotally that combining Dilapan™ with laminaria makes removal easier [54]; however, there is no evidence in the literature to support this recommendation. Finally, case reports of entrapment and displacement into the uterine cavity have involved both Dilapan™ and laminaria but not Lamicel® [143–145]. Since the release of the reformulated version, however, Dilapan-S™ has not been associated with breakage or entrapment [66].

The ideal osmotic dilator depends not only on effectiveness but also on convenience and side effects. The evidence supports that Dilapan-S™ is superior to laminaria for short treatment periods (4 h), but laminaria would achieve the same dilatation if allowed more time (at least 6 h). It also appears that Dilapan-S™ and multiple laminaria are superior to Lamicel® for any duration of time in causing wider initial dilatation [68,146]. However, the ability to subsequently achieve the desired dilation easily with rigid dilators is comparable with all three methods. Therefore, a same-day procedure could more easily be accomplished with Dilapan-S™ or Lamicel® than with laminaria. In terms of price, one Lamicel® is approximately twice the cost of one Dilapan-S™ and, in turn, one Dilapan-S™ is twice the cost of one laminaria [66]. However, multiple laminaria are often required to achieve the same dilation as one Lamicel® or one Dilapan-S™ [68]. No published studies to date have been large enough to detect a difference in complication rates comparing Dilapan-S™ or Lamicel® and placebo.

5. Is misoprostol safe and effective for cervical priming in the first trimester?

Several randomized trials have compared misoprostol and placebo or no therapy for cervical priming before first-trimester surgical abortion. These studies analyzed vaginal doses of 100 to 750 μg [76,102,106,107,112,114,116,147], oral doses of 400 to 600 μg [114,115,148] and a sublingual dose of 400 μg [118,124]. Almost all of these studies demonstrated an increased baseline cervical dilatation with misoprostol, and some also found a greater subjective ease of dilation [106,115,148], lower measured cumulative force with dilation [76,114], shorter procedure time [102,106,107,115,118,124] or lower estimated blood loss [114,115,118,124]. The majority of studies measured baseline cervical dilation with Hegar dilators, but a few used a cervical tonometer to measure the force required for cervical dilation. Many of these studies reported more cramping (although mild) with misoprostol compared to placebo [106,107,114,118,148]. In general, differences between misoprostol and placebo in terms of operative time and blood loss are statistically, but not clinically, significant. The WHO has recently completed the largest trial to date, a multicenter randomized placebo-controlled trial of more than 4700 women given 400 μg of vaginal misoprostol 3 h prior to surgical abortion under 12 weeks' gestation [149]. The full data analysis of this trial has not been completed.

It is important to note that if misoprostol is used for cervical priming and the woman is unable to undergo surgical abortion as planned, she is at some risk for expelling the pregnancy. Therefore, before receiving misoprostol, all women should give informed consent for the abortion procedure and be adequately screened by appropriately trained personnel. Although studies suggest that misoprostol is superior to placebo for cervical priming at different dosages and routes of administration, the clinical appropriateness of routine use of misoprostol is still not understood.

6. What is the optimal misoprostol regimen?

Table 1 reviews studies performed to evaluate the optimal dose, route and timing of administration of misoprostol for effectiveness, minimizing side effects and acceptability to women.

Vaginal administration

For vaginal dosing, randomized trials have found that 200 μg misoprostol is inferior to 400 μg in terms of baseline cervical dilatation as measured by the largest Hegar dilator that could be passed through the cervical os without resistance [108,122,150,151]. Studies that increased the dose of misoprostol to 600 or 800 μg demonstrate higher rates of side effects such as abdominal pain, bleeding and fever [122,151] with minimal gain in cervical dilatation. Other studies have decreased the time interval from 3 h using 400 μg of vaginal misoprostol to 2 h using 600 and 800 μg to determine whether higher doses of vaginal misoprostol could dilate the cervix more rapidly. Subjects experienced more vaginal bleeding (25% vs. 17%), abdominal pain (50% vs. 13%) and fever (12% vs. 0%) as well as less cervical dilatation with the 600-μg dose given for 2 h than with the 400-μg dose given 3 h before the procedure [150,151]. This effect was even more pronounced with the 800-μg dose. Other studies of 400 μg vaginal misoprostol have shown that no effect is seen after 1 h of use and that the peak effect is achieved between 3 and 4 h of use [121,150,151]. No additional dilation is gained from administering vaginal misoprostol for more than 4 h preoperatively [113,152]. Time intervals beyond 4 h only increase the frequency of bleeding and passage of products of conception prior to scheduled curettage [152]. Thus, 400 μg of vaginal misoprostol given 3 to 4 h before the procedure appears to be the optimal dose and time for achieving adequate dilation.

Table 1
Cervical priming: studies evaluating different doses of misoprostol and routes of administration (mean±SD for cervical dilation diameters unless otherwise stated)

Study	*n*	Gestational age (weeks)	Intervention	Results	Vaginal bleeding	Pain	Fever	Nausea/ Vomiting
Vaginal administration								
Singh et al. [122]	120	<14	RCT	Mean dilation by Hegar dilator				Not reported
			Misoprostol 3–4 h preop					
			200 μg PV	6.4±1.3 mm	43.3%	6.7%	0%	
			400 μg PV	8.2±0.8 mm	63.3%	36.7%	0%	
			600 μg PV	8.5±0.7 mm	80%	73.3%	6.6%	
			800 μg PV	9.9±0.8 mm	100%	100%	43.3%	
				No difference between 400-, 600- and 800-μg groups but all superior to 200 μg	For all side effects, 800-μg vs. 600-μg and 600-μg vs. 400-μg dose significantly different			
Singh et al. [150]	60	<12	RCT	Mean dilation by Hegar dilator				Not reported
			Misoprostol PV					
			400 μg 3 h preop	8.1±0.1 mm (SEM)	20%	10%	0%	
			600 μg 2 h preop	6.6±0.2 mm (SEM)	26.7%	53.5%	10%	
				p=.001	p=.76	p=.001	p=.24	
Singh et al. [151]	180	<12	RCT	Mean dilation by Hegar dilator				Not reported
			Misoprostol PV					
			400 μg 3 h preop	8.1±0.1 mm (SEM)	10%	13.3%	0%	
			600 μg 2 h preop	6.7±0.1 mm (SEM)	25%	50%	11.7%	
			800 μg 2 h preop	6.8±0.1 mm (SEM)	31.7%	80%	25%	
				p=.001 for 800 and 600 μg vs. 400 μg	NS	p=.001 for 800 and 600 μg vs. 400 μg	p=.01 for 800 and 600 μg vs. 400 μg	
Fong et al. [108]	60	<14	RCT	Mean dilation by Hegar dilator			Not reported	Not reported
			Misoprostol 3–4 h preop					
			200 μg PV	8.2±0.8 mm (SEM)	63.3%	36.7%		
			400 μg PV	6.4±1.3 mm (SEM)	43.3%	6.2%		
				p=.001	p=.20	p=.01		
Oral administration								
Oppegaard et al. [117]	551	<13	RCT	Mean dilation by Hegar dilator			Not reported	Not reported
			Misoprostol 10–16 h preop					
			200 μg PO	5.4±1.5 mm	37%	8%		
			400 μg PO	5.9±1.7 mm	15%	3%		
				p=.004	p=.001	p=.002		
Sublingual administration								
Vimala et al. [153]	120	<12	RCT	Mean dilation by Hegar dilator	2- and 3-h groups combined			
			Misoprostol either 2 or 3 h preop					
			200 μg SL	6.0±1.2 mm	60%	46.6%	1.6%	13.3%
			400 μg SL	8.2±2.0 mm	71.3%	61.6%	3.3%	16%
				p=.001	p=.01	p=.009	p=.761	p=.237

				In the 400-μg group, no difference between 2 and 3 h. In the 200-μg group, 3 h time resulted in more women achieving cervical dilation of ≥ 8 mm (40%) than 2 h time (26%)				
Comparisons								
Lawrie et al. [99]	60	<13	RCT Misoprostol	Mean dilatation and mean cumulative force required to dilate the cervix to 9 mm by cervical tonometer	Mean bleeding score (0–5)	Mean pain score (0–5)	Not reported	Not reported
			400 μg PO 12 h preop	6.91 mm 44.05 N	0.37	0.78		
			800 μg PV 2–4 h preop	6.99 mm 39.73 N	0.19	0.46		
				NS	p value not reported	p value not reported		
Ngai et al. [114]	204	<13	RCT Misoprostol 3 h preop	Mean dilation by cervical tonometer			Not reported	
			200 μg PO	6.6±0.9 mm	4.7%	7%		0%
			400 μg PO	7.2±1.0 mm, p=.05	12.5%	20%		5%
			200 μg PV	6.8±1.2 mm	15%	17.5%		2.5%
			400 μg PV	6.8±1.3 mm, NS	13.5%	21.6%		0%
				Misoprostol oral vs. vaginal cumulative force, NS	Misoprostol oral vs. vaginal, NS for all side effects			
Carbonell et al. [105]	900	<9	RCT Misoprostol	Mean dilation by Hegar dilator			Not reported	
			400 μg PO 8 h preop	8.1±1.6 mm	29.5%	55.1%		17%/7.8%
			400 μg PV 4 h preop	8.5±1.5 mm	30.2%	46%		1.8%/1.3%
				p=.0001	p=.86	p=.008		p=.005
Inal et al. [154]	120	<14	RCT Misoprostol 10 h preop	Dilation ≥7 mm (measure not described)	Not reported		Not reported	
			200 μg PO	43.3%		33.3%		26.7%
			Placebo PO	13.3%				
			200 μg PV	46.7%		53.3%		23.3%
			Placebo PV	3.3%		p value not reported		p value not reported
				Misoprostol oral vs. vaginal NS				
Ashok et al. [101]	64	<13	RCT Misoprostol 2–4 h preop	Mean dilation and mean cumulative force required to dilate cervix to 9 mm by cervical tonometer			Not reported	
			400 μg PO	7 mm 37.5 N	25%	69%		56%/6%
			400 μg PV	7 mm 39 N	34%	62%		25%/6%
				NS	NS	NS		Nausea significantly different, vomiting NS

(continued on next page)

Table 1 (*continued*)

Study	*n*	Gestational age (weeks)	Intervention	Results	Vaginal bleeding	Pain	Fever	Nausea/ Vomiting
Sharma et al. [121]	90	<11	RCT Misoprostol 1 h preop	Mean cumulative force required to dilate the cervix by cervical tonometer			Not reported	
			400 μg PO	47.2 N	1.1%	1.1%		1.1%
			800 μg PV	50.6 N	0%	1.1%		0%
			No treatment	70.1 N	0%	0%		0%
				Ratios of mean adjusted for parity NS	p value not reported	p value not reported		p value not reported
Cakir et al. [103]	160	<11	RCT Misoprostol 3 h preop	Mean dilation by Hegar dilator				
			400 μg PO	6.6±1.5 mm	52.5%	70%	5%	57.5%/10%
			Placebo PO	3.4±2.0 mm p=.001				
			400 μg PV	7.2±0.8 mm	57.5%	75%	0%	47.5%/5%
			Placebo PV	3.6±1.9 mm, p=.001	NS	NS	NS	NS
Oppegaard et al. [131]	338	<13	RCT Misoprostol	Median dilation by Hegar dilator		Median pain score	Not reported	Not reported
			400 μg PO at 10:00 p.m. the night before procedure	6.2 mm (0–11)	43%	2.9 (0–10)		
			400 μg PV at 6:00 a.m. the morning of procedure	6.5 mm (0–11)	6.7%	1.2 (0–10)		
				p=.30	p=.001	p=.001		
Aronsson et al. [100]	32	<13	RCT Misoprostol 3 h preop	Mean dilation and mean cumulative force required to dilate the cervix to 9 mm by cervical tonometer		Use of analgesics	Not reported	
			400 μg SL	7.5±1.2 mm 36.5 N	47%	29%		6%
			400 μg PO	7.0±1.8 mm 45.6 N	33%	67%		40%
				NS	NS	p=.01		p=.01
Saxena et al. [119]	100	<13	Sequential allocation Misoprostol 3 h preop	Median dilation by Hegar dilator	"Within normal limits" for both groups	Not reported		
			400 μg SL	10 mm			6%	2%
			400 μg PO	8 mm p=.001			4% p value not reported	4% p value not reported

Hamoda et al. [110]	74	<12	RCT Misoprostol 2–4 h preop	Median dilation and median cumulative force required to dilate the cervix by cervical tonometer	Not reported		Not reported	
			400 μg SL	8 N, 35 N		71%		63%/29%
			400 μg PV	7.5 N, 33 N		64%		31%/6%
				NS		NS		Nausea p=.008, vomiting NS
Tang et al. [123]	80	<12	RCT Misoprostol 3 h preop	Mean dilation and median cumulative, required to dilate the cervix by cervical tonometer			Not reported	
			400 μg SL	7.6±1.3 mm 5.5 N	37.5%	85%		20%/2.5%
			400 μg PV	7.7±0.73 mm 5.0 N	22.5%	77.5%		35%/7.5%
				NS	p value not reported	p value not reported		p value not reported
Vimala et al. [125]	100	<13	RCT Misoprostol 2 h preop	Mean dilation by Hegar dilator				
			400 μg SL	8.61±4.0 mm	68%	86%	8%	26%
			400 μg PV	6.8±2.6 mm	36%	82%	12%	18%
				p=.05	p=.05	NS	NS	NS
Carbonell et al. [104]	1424	<12	RCT Misoprostol 1–3 h preop	Mean dilation by Hegar dilator	Not reported	Not reported		
			400 μg SL	6.8±0.8 mm			19%	12.4%/ 10.1%
			400 μg PV	6.7±0.9 mm			18.2%	2.5%/3.8%
				p=.76			p=.18	p=.001
Saxena et al. [120]	100	<13	Sequential allocation Misoprostol 3 h preop	Mean dilation by Hegar dilator			Not reported	
			400 μg SL	9.84±2.2 mm	44%	24%		2%
			400 μg PV	7.84±2.9 mm	22%	14%		2%
				p=.0002	p value not reported	p value not reported		p value not reported

NS, not significant; RCT, randomized controlled trial; SEM, standard error of the mean; N, newtons.

Oral administration

In the case of oral administration, results of studies examining different doses of misoprostol are inconsistent, likely because of the variable methods used to define success. One trial that compared 200 and 400 μg misoprostol the night before the procedure showed that the 400-μg dose resulted in statistically greater baseline cervical dilation than the 200-μg dose as measured by Hegar dilator; however, the difference was not felt to be clinically significant [117]. Another trial compared 200 and 400 μg misoprostol 3 h prior to the procedure and found that the higher dose resulted in greater baseline cervical dilation, as measured by cervical tonometer, but no difference in cumulative force required to dilate the cervix to 8 mm [114]. Studies show that oral misoprostol is effective compared to placebo when given at least 3 to 20 h prior to the procedure [78,103,114,115]. One study determined that 600 μg misoprostol resulted in equivalent baseline dilation as measured by Hegar dilator at 10 and 17 h prior to procedure, but there were fewer side effects with the 10-h dosing schedule [75]. Cervical priming with oral misoprostol most likely requires a 400- to 600-μg dose and a longer treatment period than is needed with vaginal administration for maximum effectiveness.

Sublingual administration

For sublingual dosing, one randomized trial has shown that 400 μg is superior to 200 μg at both 2 and 3 h prior to procedure when evaluating efficacy as measured by cervical dilation using Hegar dilators [153]. However, the women using the 400-μg dose experienced more side effects. With the 400-μg dose, increasing the time interval from 2 to 3 h did not offer any advantages [153].

Comparisons

Clinical trials comparing different routes of misoprostol administration have shown mixed results. Oral administration and vaginal administration have been widely compared. Studies favoring vaginal administration have shown that 400 μg produced baseline dilatation superior to the same dose given orally (measures included Hegar and Pratt dilators) [105, 113]. Vaginal administration resulted in less severe side effects than oral administration, including abdominal pain (46% vs. 55%), nausea (1.8% vs. 17%) and vomiting (1.3% vs. 7.8%) [105]. Additionally, vaginal administration was found to be more effective than oral administration later in the first trimester and in multiparous women [113, 131]. However, other studies have shown no difference between vaginal and oral administration [101,103,114,154]. Such studies have shown that 400 μg of oral misoprostol produced equivalent dilatation at 3 h to 400 μg vaginal dosing, all with similar side effects. A randomized controlled trial from Scotland in 64 women showed that 400 μg of oral misoprostol was equivalent to 400 μg of vaginal misoprostol for cervical priming taken 2 to 4 h preoperatively [101]. The study was powered to detect a 0.75-N difference in cumulative force required to dilate the cervix. However, subjects were exposed to the vaginal misoprostol for a significantly shorter period of time than the oral misoprostol (2.3 h vs. 3.5 h) because of clinic logistics.

Two studies have shown that 400 μg of sublingual misoprostol is more effective than 400 μg of oral misoprostol given 3 h prior to procedure in terms of baseline cervical dilatation and the force required for cervical dilation over 7 mm [100,119]. Sublingual administration has been shown to be either equivalent to or better than vaginal administration when 400 μg is given 1 to 4 h preprocedure [104,110,120,123,125]; however, sublingual administration is associated with significantly more nausea (12.4% vs. 2.5%), vomiting (10.1% vs. 3.8%) and diarrhea (26.4% vs. 7.6%) [104,110,125]. Nonetheless, sublingual administration is associated with high patient and staff acceptability [104,120,123]. There are data to indicate that some women prefer to take misoprostol tablets by mouth to avoid a vaginal examination or vaginal self-administration of misoprostol [155]. Buccal administration, with a pharmacokinetic and physiologic profile similar to vaginal administration, might offer the effectiveness and decreased side effects of vaginal administration combined with high acceptability for both patient and staff [92,156]. Buccal misoprostol has not yet been investigated for cervical priming before first-trimester abortion.

In sum, compared with the oral route, vaginal administration of misoprostol is equally or more effective and is associated with fewer side effects. Self-administration of vaginal misoprostol is acceptable to most women, as shown previously in medication abortion trials [113]. However, staff responsible for the vaginal placement of misoprostol tend to prefer the oral or the sublingual route of administration [101]. The sublingual route is more effective than oral administration and is equivalent to or better than vaginal administration but is associated with more side effects than either oral or vaginal administration.

7. How does misoprostol compare to osmotic dilators for cervical priming?

There are no trials comparing misoprostol to Dilapan-S™ or Lamicel®. There have been two randomized controlled trials comparing misoprostol to laminaria for cervical priming before first-trimester surgical abortion. One trial compared 400 μg of oral or vaginal misoprostol to one medium laminaria for 4 h prior to suction aspiration [113]. Vaginal misoprostol significantly outperformed oral misoprostol in mean cervical dilatation (28.0±7.3 mm vs. 24.2±4.8 mm). The mean cervical dilation in women treated with laminaria (25.9±5.8 mm) was less than with vaginal misoprostol but more than with oral misoprostol. Still, neither comparison reached significance, primarily because the laminaria group, with only 14 subjects, was underpowered to detect significant differences. There were no differences between the groups in the proportion of subjects requiring additional dilation, the difficulty of additional dilation, blood loss or the duration of the procedure. The women who received laminaria experienced significantly

more discomfort with insertion than those using oral or vaginal misoprostol. Groups were equivalent in level of pain during the waiting period and requests for pain medication. Overall acceptability of the method of dilation was greater than 90% in each group and was not significantly different among groups. The study authors concluded that vaginal misoprostol was preferable because of its efficacy, ease of use and lack of major side effects.

The second trial compared one 3-mm laminaria tent to 200 μg of vaginal misoprostol, both administered the day prior to the procedure (19 to 26 h) [152]. This Canadian study found that laminaria achieved greater baseline cervical dilatation compared to vaginal misoprostol (35 mm vs. 28 mm, $p<.001$). There was no difference in operative times or ease of dilation between the two groups. The women who received laminaria reported significantly more pain with insertion, but the women using misoprostol had significantly more bleeding in the hours between the insertion and the procedure. Two subjects who received misoprostol passed pregnancy tissue before their scheduled curettage. Nevertheless, significantly more women preferred to use misoprostol than laminaria in the future.

In summary, vaginal misoprostol requires less time to achieve the same dilatation as overnight laminaria, is associated with less discomfort and is preferred by women. The ideal comparison to misoprostol, however, would be Dilapan™ or Lamicel®—agents that also are effective in 4 h.

8. Does cervical priming reduce pain during first-trimester surgical abortion?

The goal of cervical priming is to make suction aspiration safer and easier for the patient. If cervical priming reduces pain in women undergoing surgical abortion without general anesthesia, then it should be routinely considered. While studies evaluating cervical priming agents often collected data on pain before, during and after the procedure, no study examined pain as a primary outcome. Discomfort with the placement of the cervical ripening agent occurs more often in women treated with laminaria than in those treated with misoprostol [113,152]. Preoperative cramping and abdominal pain occur more frequently in women exposed to both osmotic dilators and misoprostol versus placebo [75,103,106,113,157]. In clinical studies, this level of pain is usually described as mild without the need for analgesic agents [103,106,107,114,118]. One study, however, showed that cervical priming with prostaglandin analogues increased both preoperative and postoperative pain and the use of analgesics [157]. Another study showed that cervical priming with both vaginal and oral misoprostol did not reduce intraoperative pain levels compared to placebo [103]. The higher the dose and the longer the interval of use for any cervical priming agent, the more women will experience preoperative discomfort, which might include bleeding from incomplete abortion and the distress of passing products of conception [75,122,151,152]. While most trials show that cervical priming shortens operative time by reducing the need for mechanical dilation, this does not always translate into a pain reduction perceived by the patient [103]. In conclusion, the overall impact of cervical priming on pain is unclear. Studies examining preoperative, intraoperative and postoperative pain level as primary outcomes are needed.

9. Is cervical priming before first-trimester surgical abortion acceptable to women?

Investigators have not focused on women's quality of life surrounding cervical priming as compared to mechanical dilation before first-trimester suction aspiration. There is a lack of evidence to describe women's preferences for or against cervical priming. It has been documented that women prefer misoprostol to laminaria, but no studies have compared misoprostol with Dilapan-S™ or Lamicel® [113]. Very few placebo-controlled trials of misoprostol for cervical ripening explicitly analyzed patient acceptability. The amount of time a woman is willing to wait for cervical priming to produce its proposed benefits (reduced intraoperative pain, shorter procedure time and decreased occurrence of rare complications) is not known. Nor is it known whether some women would choose to tolerate slightly more intraoperative pain, for a brief duration, to avoid waiting and an increased risk of unpleasant side effects preoperatively, like bleeding, cramping, nausea and vomiting. Women's preferences regarding the route of administration and method of application (self-administration vs. administration by a provider) also need to be studied further. Similar to studies undertaken to analyze women's preferences for medication abortion or surgical abortion, the family planning field needs evaluations of whether or not women would choose preoperative cervical priming to prevent rare adverse outcomes. Cervical priming cannot yet be declared the standard of care for all women without stronger evidence that complications are decreased by cervical priming in exchange for the added inconvenience and side effects.

10. Is routine cervical priming necessary before first-trimester surgical abortion?

There are not enough data to conclude that routine cervical priming is necessary to reduce complications before first-trimester surgical abortion. Despite the evidence from the frequently cited studies by CDC investigators that laminaria reduce cervical laceration and, to a lesser extent, uterine perforation rates, the rarity of these events given an experienced provider makes routine cervical priming with any agent debatable [8,11,16]. The final results of the WHO randomized trial will be instrumental in making recommendations [149]. Clinical groups have attempted to create guidelines that capture the nuances of the evidence, specifying cervical priming only for women under 18 years of age and for women with more advanced gestations, some taking into account parity [94,95]. In terms of advancing gestational age, there is likely some benefit with cervical priming late in the first trimester; however, there is no clear evidence to dictate when cervical priming should begin.

Surprisingly, other clinical groups make no mention of provider inexperience, although that was the strongest risk factor for complications in all studies. There are insufficient data evaluating how cervical priming affects women's quality of life surrounding the abortion procedure. Therefore, the Society of Family Planning does not recommend routine cervical priming for suction aspiration procedures. Based on existing evidence, the Society of Family Planning recommends that providers consider cervical priming for women late in the first trimester, adolescents and women in whom cervical dilation is expected to be difficult due to either patient factors or provider experience.

Conclusions

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

- Advancing gestational age and provider inexperience are risk factors for immediate complications during first-trimester surgical abortion.
- Adolescents are at higher risk for cervical injury than adult women.
- Cervical priming may protect against complications such as cervical injury and uterine perforation; however, the absolute risk of these complications, given an experienced provider, is quite low.
- Effective methods of cervical priming include osmotic dilators and misoprostol; the shortest time for efficacy (3 to 4 h) occurs with the use of Dilapan-S™, Lamicel® and misoprostol. When misoprostol is used prior to suction abortion, the optimal dose and timing are 400 μg vaginally 3–4 h, orally 8–12 h or sublingually 2–4 h before the procedure.

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

- Women find vaginal administration as acceptable as the oral and sublingual routes of misoprostol administration. The oral and sublingual routes cause more side effects than vaginal administration.
- Osmotic dilators do not increase the postabortal infection rate in the first trimester.

Level C: recommendations are based primarily on consensus and expert opinion

- The amount of cervical dilation required for suction aspiration is provider dependent.
- Cervical priming should be considered for all adolescents and is strongly recommended for adolescents at 12 to 14 weeks' gestation.
- Cervical priming is recommended for all women at 12 to 14 weeks' gestation and for any woman in whom an initial attempt at rigid dilation is difficult.
- The use of cervical priming to reduce pain during first-trimester abortion should be individualized to the patient and clinic setting because data are lacking on its efficacy.

Important questions to be answered

Further studies should evaluate whether routine cervical priming with misoprostol reduces the frequency of immediate complications during first-trimester suction aspiration. Given the rarity of such events and the dependency of these events on various factors (adolescence, parity, gestational age, prior cervical surgery and provider experience), an extremely large sample size would be required to detect a difference between misoprostol and placebo. The recently completed WHO trial [149] must take these factors into consideration before the results can be placed in the appropriate context for clinical practice. It is especially important to examine the effect of misoprostol on preoperative, intraoperative and postoperative pain, compared to placebo.

Published studies comparing misoprostol and osmotic dilators have used overnight laminaria, an inappropriate comparator. Studies are needed, particularly in women late in the first trimester, to compare misoprostol to Dilapan™ or Lamicel®—agents that also are effective in 4 h.

More studies are necessary to evaluate the quality of life surrounding cervical preparation and women's preferences for any type of cervical priming compared to rigid dilation alone. In addition, studies should be conducted comparing misoprostol and osmotic dilators designed to work in a similar time interval (Dilapan-S™ or Lamicel®).

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Sources

Included articles were obtained from a PubMed literature search from 1966 to 2006 including the following MeSH terms and text words: induced abortion, surgical abortion, first-trimester, misoprostol, cervical priming, cervical ripening, cervical dilation, laminaria, Dilapan-S™ and Lamicel®. The "related articles" search in PubMed was utilized frequently to identify any similar studies omitted on the initial search. The Cochrane Library was searched to identify systematic reviews, meta-analyses and controlled clinical trials. Reference lists of nonsystematic review articles and studies obtained from the initial search were hand searched to identify articles not yet indexed. Non-English articles were excluded.

Authorship

These guidelines were prepared by Rebecca H. Allen, MD, MPH, and Alisa B. Goldberg, MD, MPH, and were reviewed and approved by the Board of the Society of Family Planning.

Conflict of interest

Rebecca H. Allen, MD, MPH, and Alisa B. Goldberg, MD, MPH, report no significant relationships with industry. The Society of Family Planning receives no direct support from pharmaceutical companies or other industries.

Intended audience

This guideline has been developed under the auspices of the Society of Family Planning for its members and for any physicians or advanced-practice clinicians who provide first-trimester surgical abortion services. This guideline will also be of interest to other professional groups who care for women undergoing abortion, including but not limited to the American College of Obstetricians and Gynecologists, the American Academy of Family Physicians, the Association of Reproductive Health Professionals, the National Abortion Federation and the Planned Parenthood Federation of America.