Contraception

Clinical guidelines

Cervical dilation before first-trimester surgical abortion (<14 weeks' gestation)[☆,☆☆,★,★★]

Rebecca H. Allen[a,*], Alisa B. Goldberg[b]

[a]Women's and Infants' Hospital/Brown University, 101 Dudley Street, Providence, Rhode Island 02905-2401
[b]Harvard Medical School, Planned Parenthood League of Massachusetts, 1055 Commonwealth Ave., Boston, Massachusetts 02215-1001

Abstract

First-trimester surgical abortion is a common, safe procedure with a major complication rate of less than 1%. Cervical dilation before suction abortion is usually accomplished using tapered mechanical dilators. Risk factors for major complications in the first trimester include increasing gestational age and provider inexperience. Cervical priming before first-trimester surgical abortion has been studied using osmotic dilators and pharmacologic agents, most commonly misoprostol. Extensive data demonstrate that a variety of agents are safe and effective at causing preoperative cervical softening and dilation; however, given the small absolute risk of complications, the benefit of routine use of misoprostol or osmotic dilators in first-trimester surgical abortion is unclear. Although cervical priming results in reduced abortion time and improved provider ease, it requires a delay of at least 1 to 3 h and may confer side effects. The Society of Family Planning does not recommend routine cervical priming for first-trimester suction abortion but recommends limiting consideration of cervical priming for women 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 challenging.
© 2016 Elsevier Inc. All rights reserved.

Keywords: Surgical abortion; Cervical dilation; Laminaria; Misoprostol; Dilapan; Pain

1. Background

Induced abortion is one of the most common surgical procedures in the United States. In 2011, 1.06 million pregnancies were terminated, approximately 88% of them at less than 14 weeks of gestation [1]. First-trimester surgical abortion is safe, with a mortality rate of 0.7 per 100,000 procedures performed at less than 13 weeks of gestation and a major complication rate of less than 1% [2–5]. The rate of recognized uterine perforation during first-trimester surgical abortion ranges from 0.1 to 4.0 per 1000 procedures [6–19]. The rate of all types of cervical injury ranges from 0.1 to 10.0 per 1000 procedures, with higher rates in adolescents (age ≤17) [6–13,15,19–21]. 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 trainee physicians. Lower complication rates are associated with experienced providers in high-volume outpatient clinics [11]. Accumulated evidence also shows comparable safety when first-trimester abortions are performed by advanced practice clinicians or physicians [22].

Shortly after the legalization of induced abortion in the United States, studies demonstrated that the use of laminaria, an osmotic dilator, was associated with a reduced risk of cervical laceration and, to a lesser extent, uterine perforation [14,20,23]. These reduced risks were observed primarily in settings with a high baseline complication rate. Reports also demonstrated the usefulness of laminaria in reducing pain associated with rigid dilation, allowing the use of local anesthesia alone, although these studies lacked a control group [24–26]. Other studies hypothesized that passive dilation of the cervix with prostaglandins or similar agents might avert uterine perforation and cervical laceration through a reduction in the force required for dilation [27,28]. In addition, older medical literature reflects a concern that forceful cervical dilation may cause permanent damage to the cervical tissue, leading to poor reproductive outcomes [24,29–34]. Cervical priming was therefore recommended to prevent such long-term complications as spontaneous abortion, cervical insufficiency and preterm delivery. However, subsequent large population-based prospective studies have shown no association between induced abortion and subsequent adverse pregnancy outcomes [35–39]. Cervical priming prior to first-trimester abortion fell out of favor until the emergence of misoprostol, an agent easier to administer than osmotic dilators.

This guideline:

1. Discusses the methods of cervical dilation before first-trimester surgical abortion.
2. Discusses risk factors for immediate complications from cervical dilation.
3. Explores the evidence for and against the use of cervical priming agents in the first trimester based on safety, efficacy and acceptability.
4. Discusses mechanical dilation, osmotic dilators, prostaglandin analogues and progesterone antagonists.
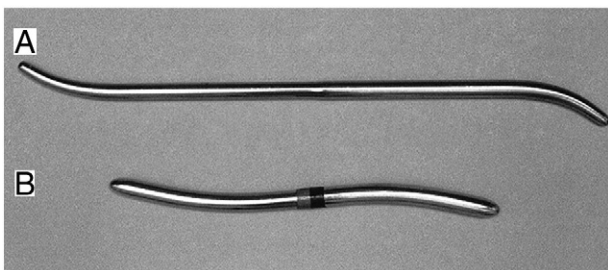

Fig. 1. Reproduced with permission from: Stovall DW. Dilation and curettage. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on 8/11/2015.) Copyright © 2015 UpToDate, Inc. For more information visit www.uptodate.com.

1.1. Rigid dilation

When cervical dilation is needed, most North American providers employ rigid dilation alone with steel Pratt dilators (Fig. 1a) or the plastic equivalent, Denniston dilators [40]. 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 be initiated easily with a 17-F dilator. Each French unit refers to the circumference of the dilator in millimeters. To obtain the diameter of the dilator in millimeters, the French unit is divided by Pi (approximately 3). By comparison, Hegar dilators (Fig. 1b) 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 but also requiring more force [33,41]. It is easier to sense the loss of resistance of the internal os with Hegar dilators than with Pratt dilators [40]. No trials have compared the safety and efficacy of Pratt and Hegar dilators. A minority of providers report using the Hegar dilator [42].

1.2. Cervical priming agents

Cervical priming can be accomplished mechanically with osmotic dilators that absorb moisture from the cervix and slowly expand to dilate the cervical os or biochemically with prostaglandin analogues or progesterone antagonists. The commercially available options for cervical priming include osmotic dilators, laminaria and Dilapan-S, as well as pharmacological agents such as misoprostol (PGE1), gemeprost (PGE1), dinoprostone (PGE2) and mifepristone. Other agents for cervical priming include nitric oxide donors (e.g., isosorbide mononitrate, glyceryl trinitrate?), which are currently under study. As of 2002, 18% of North American providers routinely used misoprostol for cervical ripening prior to 11 weeks' gestation, and 16% used it for multiparous women. Beginning at 11 to 12 weeks of gestation, 25% used misoprostol for nulliparous women and 20% for multiparous women [43].

1.3. Osmotic dilators

Two types of osmotic dilators are available in the United States: laminaria tents made of seaweed and synthetic dilators. All osmotic dilators require a trained provider and a speculum examination for insertion.

Laminaria tents are dried compressed stalks of hygroscopic seaweed (*Laminaria digitata, Laminaria japonicum*) that absorb water from the cervical stroma, swelling to three or four times their dry diameter overnight. 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 [44,45].

Laminaria are safe; adverse events following their use occur infrequently. 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. Case reports have described bacteremia following laminaria placement in the second trimester [46,47]. Researchers theorize that laminaria insertion can facilitate the transfer of cervical or vaginal flora into the uterine cavity and cause an ascending infection [48]. However, a randomized trial comparing laminaria and rigid dilation in first-trimester abortion found no significant difference in rates of postabortion infection [49]. In the first trimester, all osmotic devices are generally removed no later than 24 h after insertion to reduce the possibility of infection. Because laminarias derive from a natural material, their use rarely results in hypersensitivity reactions (urticaria, angioedema, respiratory distress) and anaphylaxis in women with previous exposure [50–52]. The true incidence of this reaction is unknown. Investigators believe that the mechanism for this allergic reaction is IgE-mediated [51].

Use of laminaria before first-trimester surgical abortion may pose an access barrier: laminaria acts slowly and often require an extra visit. To address the limitations of laminaria, investigators created two synthetic dilators, Dilapan-S (GelMed International, Czech Republic) and Lamicel® (Medtronic, Mystic, CT, USA), which are sterile and swell more rapidly than laminaria. An additional advantage of synthetic dilators is the consistency of length and shape, which leads to more predictable results.

Dilapan-S is a rod-shaped hydrophilic dilator made from polyacrylate-based hydrogel (Hypan) available in the following dimensions: 3 mm×55 mm, 4 mm×55 mm and 4 mm×65 mm. Dilapan-S absorbs moisture 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 recommends one device placed up to 4 h prior to suction abortion in gestations of less than 16 weeks. In other countries, Dilapan-S is not subject to limitations on number of devices, indication or duration of use. Therefore, US providers commonly use Dilapan-S in an off-label fashion. Problems from breakage due to entrapment with the original version of Dilapan were resolved with release of a new formulation in 1998 internationally and in 2002 in the United States [53]. The reformulated Dilapan, named *Dilapan-S*, has not generated any reports of breakage [54]. Advantages of Dilapan-S are its significant radial force and rapid swelling, making it ideal for same-day procedures.

Lamicel, a polyvinyl alcohol polymer sponge impregnated with 450-mg magnesium sulfate and compressed to form a thin cylindrical tent, is no longer available in the United States. When placed in the cervical canal, Lamicel absorbs water from the cervical stroma and swells to four times its original size, transforming itself into a soft sponge [30,55]. Lamicel's mechanism of action is biochemical rather than mechanical, exerting no outward pressure on the cervical canal [34]. Lamicel reduces the amount of force needed to dilate the cervix [30,34] and is approved by the Food and

Drug Administration for cervical priming for gestations of 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-mm or 5-mm dry diameters internationally.

1.4. Pharmacologic agents

Pharmacologic agents, such as prostaglandin analogues and progesterone antagonists, can be used for cervical priming in the first trimester. Misoprostol is the medication most commonly used for cervical priming [56]. Misoprostol is a PGE1 synthetic analogue marketed as an oral preparation to prevent and treat gastroduodenal damage induced by nonsteroidal antiinflammatory 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 [57]. Misoprostol's advantages are its low cost, 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 [58–61]; in addition, they require refrigeration for transport and storage [62].

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. Pharmacokinetics studies comparing oral and vaginal administration (Fig. 2) have shown that vaginal misoprostol is associated with slower absorption, lower peak plasma levels and slower clearance, similar to an oral extended-release preparation [63–65]. Vaginal misoprostol is also associated with a greater overall exposure to the drug, area under the curve (AUC) and greater effects on the cervix and uterus [64]. There is no clinically significant difference between vaginal misoprostol that is administered dry and vaginal misoprostol moistened with water, saline or acetic acid [66–69]. The rectal route of administration shows a pattern similar to vaginal administration but a lower AUC, including a significantly lower maximum peak concentration [65]. 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 [70]. This translates into higher rates of gastrointestinal side effects. The sublingual route also causes uterine contractions at a rate equivalent to vaginal administration [70]. The buccal route of administration shows a lower AUC, a lower peak concentration, and fewer side effects than sublingual administration [71]. The buccal route has a pattern of absorption similar to the vaginal route but produces lower serum levels overall. Nevertheless, the
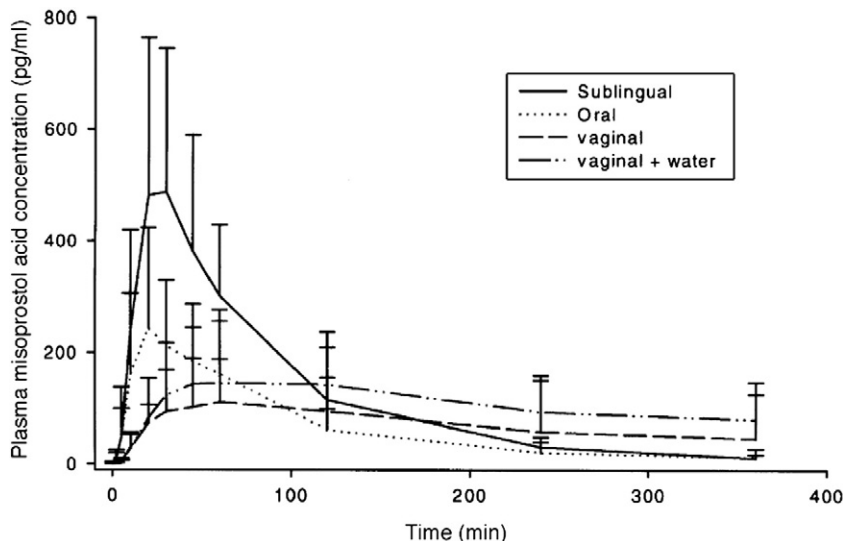
Fig. 2. Reprinted from Tang OS, Schweer H, Seyberth HW, Lee W, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. Hum Reprod 2002;17:332-6. Copyright © 2002 with permission from Oxford University Press. Mean plasma concentrations of misoprostol acid over time (arrow bars = 1 SD).

buccal route of administration produces uterine tone and activity similar to that resulting from vaginal administration. The buccal route of administration is also felt to be the least variable in terms of drug exposure and peak levels [72]. The administration of NSAIDs for pain relief does not alter the efficacy of misoprostol for cervical priming [73].

The adverse effects caused by misoprostol have prompted research into other agents that can dilate the cervix effectively without causing abdominal pain, nausea, vomiting and diarrhea. Mifepristone is a progesterone antagonist that withdraws hormonal support of the pregnancy [74–77], causing cervical softening [78]. One randomized trial suggests that mifepristone is as effective at cervical priming as misoprostol and better tolerated [79]. Nevertheless, mifepristone, while effective at cervical priming, is not often utilized because of its high cost and limited availability in many clinical settings. In addition, mifepristone is typically administered 24 h prior to a procedure, where misoprostol is administered 2–3 h prior. Both misoprostol and mifepristone are believed to exert their effects on the cervix via nitric oxide [80,81]. Because nitric oxide inhibits contractions in the uterus but still induces cervical softening, nitric oxide donors have been investigated as potential cervical priming agents [82]. While nitric oxide donors (e.g., isosorbide mononitrate) are more effective than placebo or no treatment in dilating the cervix, a systematic review found that prostaglandins were superior to nitric oxide donors [83]. Furthermore, nitric oxide donors were associated with their own side effect profile of headache, palpitations and dizziness.

Most providers in North America continue to use rigid dilators for cervical dilation without preoperative priming [11,12,42]. They do so because the risk of uterine perforation or cervical laceration with first-trimester suction aspiration is very small, and each method of cervical priming is associated with side effects and additional inconvenience

for the patient. Previous international guidelines for cervical priming have been published, including recommendations from the World Health Organization (WHO) and the Royal College of Obstetricians and Gynaecologists (RCOG). WHO recommends cervical preparation prior to surgical abortion for all pregnancies of 12 to 14 weeks' gestation. The guidelines note that cervical preparation may be considered for women at any gestational age, in particular those at high risk for cervical injury or uterine perforation, such as adolescents and women with cervical anomalies or previous cervical surgery [84]. The RCOG guidelines state that cervical priming should be considered for all women in the first trimester, recommending that misoprostol 400 mcg be administered vaginally 3 h prior to surgery or sublingually 2 to 3 h prior to surgery. They note that cervical preparation is likely "particularly beneficial where risk factors for cervical injury or uterine perforation exist, such as [in] adolescents aged less than 17 years, advanced gestational age (particularly among parous women), cervical anomalies or previous surgery, or when a less experienced surgeon is operating" [85].

2. Clinical questions

2.1. 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. According to a 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 37% of providers dilate to 1 to 2 mm greater than the number of gestational weeks. The remainder dilates to 1 to 3 mm less

than the gestational age, using a smaller cannula to evacuate the pregnancy [43]. Most providers dilate the cervix incrementally, but some skip dilator sizes if the internal os is compliant [40].

The Marie Stopes Procedure performed in some parts of the United Kingdom differs markedly from North American practices. In Marie Stopes outpatient centers, no rigid dilation or cervical priming is used for first-trimester surgical abortion [86]. Marie Stopes providers employ atraumatic tenaculums, flexible cannulas and 1% lidocaine gel for local anesthesia. They use the smallest cannula size possible for a given gestation 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, cannulas of the appropriate size are employed as dilators. In rare cases, 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.

2.2. What outcome measures should be used in research evaluating the advantages and disadvantages of cervical priming in first-trimester abortion?

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 [87]. 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 [29,60,61,88–114]. 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 or not cervical priming works to soften and dilate the cervix.

Another important outcome measure is patient-centered, the frequency of side effects and time spent waiting for the abortion procedure. Rarely are the side effects of cervical priming, and their acceptability to women is the primary objective of a study. Women generally prefer 1-day procedures to 2-day procedures and prefer misoprostol to laminaria for cervical priming [102,115]. Most women find both the oral and vaginal routes of misoprostol acceptable [90,94,102]. 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 side effects experienced while waiting [92]. 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 show 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, or in the clinic, is acceptable to women [116–119].

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 whether it makes the procedure safer. Given the rarity of complications with first-trimester abortion, however, only a few studies have had sufficient power to evaluate a difference in complication rates using cervical priming [11,16,19,120].

2.3. Are certain women more likely to benefit from cervical priming in the first trimester?

Immediate complications from suction abortion include uterine perforation, hemorrhage, cervical laceration (deep or superficial) and incomplete abortion. Risk factors for major complications differ according to the specific complication. For example, increasing parity is a risk factor for uterine perforation but not for cervical injury. This finding may reflect differential changes in the myometrium and cervical stroma after delivery [14,20]. The increased risk of perforation observed with higher parity may also be related to the frequency of prior cesarean deliveries, but past studies do not always specify delivery mode. A recent large WHO multicenter trial of misoprostol versus placebo in first-trimester abortion did not find that parity was associated with the rate of acute or delayed complications, although the two deep cervical tears from dilation and four uterine perforations all occurred in the parous group [19]. Evidence for higher complication rates in adolescents is more compelling [9,13,20]. When the effect of parity is controlled for, adolescents have a higher risk of cervical injury, especially at gestations of more than 12 weeks, than do adult women [9,20]. It appears that young age is not a proxy for nulliparity. Rather, adolescents (age ≤17) have small, physiologically immature cervices that may be more difficult to dilate than those of adult women, regardless of obstetric history [20]. The WHO trial cited above did not include enough adolescents to evaluate differing complication rates.

Existing data provide evidence of an increasing risk of immediate complications as gestational age increases, even in the first trimester [2,14,15,20,121,122]. Because studies differed in their reference groups, categories of gestational age and whether or not second-trimester procedures were included, they provide no clear evidence to guide decisions about when cervical priming should begin [123]. Taken together, however, these studies suggest that the risk of complications increases after 9 weeks, accelerating at 12 and 13 weeks' gestation. Published data are insufficient to support any comment on the risk of complications specifically in women with prior cervical conization, cesarean section or cervical stenosis or in women who are

obese or have acutely anteflexed or retroflexed uteri [11,124].

In sum, women late in the first trimester and adolescents are more likely to benefit from cervical priming. Women with uterine anomalies or known cervical stenosis might also benefit [125].

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

The insertion of one medium laminaria effectively dilates the cervix to at least 9 mm in more than 75% of women, reducing the need for rigid dilation [23–26,126,127]. The dilatation achieved with laminaria tents increases with the number of tents used and with gestational age [100,128]. Laminaria show some effect after 4 h, but more time is necessary for them to induce prostaglandin release and reach their maximum diameter [126,129]. The diameter of each laminaria tent increases by 25% if left in place for 4 h and by 90% if left in place overnight [126,130]. The use of laminaria prior to first-trimester surgical abortion, in certain clinical settings, decreases the incidence of cervical lacerations and, to a lesser extent, uterine perforations [9,14,20,23].

Bokstrom and Wiqvist [131] studied the use of Dilapan for cervical priming in women from weeks 10 to 12 of gestation. They found that a 3-mm Dilapan achieved 8 mm of dilatation at 3 to 4 h and 10 mm of dilatation at 16 to 20 h, while a 4-mm Dilapan reached 8.5 mm and 11.3 mm of dilatation, respectively. The additional dilation gained with the longer duration of retention might not be clinically significant in the first trimester.

Lamicel similarly swells rapidly, and its administration 4 h preoperatively is as effective as 16 h at increasing baseline cervical dilatation [55]. In fact, studies indicate that the total force required for dilation drops rapidly after 2 h of Lamicel placement and then plateaus [132]. One randomized trial of 629 women showed that Lamicel achieved a higher mean dilation than placebo (8.2 mm vs. 5.8 mm, p<0.001). However, the study failed to show that priming with Lamicel significantly reduced the rates of uterine perforation, infection or recurettage. However, the perforation rate in the Lamicel group was 0.4% versus 1.7% in the control group (nonsignificant), and the study may not have had sufficient power to detect a difference in complication rates [132].

All types of osmotic dilators have advantages and disadvantages. Investigators have conducted a number of comparative trials testing their efficacy for cervical priming before first-trimester surgical abortion. Randomized trials have demonstrated that one Dilapan™ device outperforms a similar diameter laminaria with 4 h of use, but the two are equivalent at 6 h [100,133]. A recent trial of Dilapan-S compared with 400 mcg of buccal misoprostol 3 to 4 h prior to surgical abortion at 12 to 15 weeks showed similar baseline cervical dilation (10.8 mm vs. 10.2 mm, p=0.065) [134]. 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 [40]; however, no evidence is available in the literature to support this practice. Finally, case reports of breakage, entrapment and displacement into the uterine cavity have involved both Dilapan and laminaria but not Lamicel [135–137]. Since the release of the reformulated version, however, Dilapan-S has not been associated with these adverse events [54].

Important characteristics of osmotic dilators include convenience and side effects as well as effectiveness. The evidence indicates that Dilapan-S is superior to laminaria for short treatment periods (4 h) but that 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 given duration of time in causing wider initial dilatation [87,138]. 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. One Lamicel is approximately twice the cost of one Dilapan-S, and in turn, one Dilapan-S is twice the cost of one laminaria [54]. However, multiple laminaria are often required to achieve the same dilation as one Lamicel or one Dilapan-S [87]. To date, no published studies comparing Dilapan-S or Lamicel with a placebo have been large enough to detect a difference in complication rates.

2.5. 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 and found that misoprostol increases baseline dilation and facilitates further dilation. These studies analyzed vaginal doses of 100 to 750 mcg [19,61,91,95,96,101,103,105,139,140], oral doses of 400 to 600 mcg [103,104,141] and a sublingual dose of 400 mcg [107,113,142]. Almost all of these studies demonstrated an increased baseline cervical dilatation with misoprostol, and some also found a greater subjective ease of dilation [19,95,104,140–142], lower measured cumulative force with dilation [61,103], shorter procedure time [19,91,95,96,104,107,113] or lower estimated blood loss [103,104,107,113]. 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 than with placebo [19,95,96,103,107,141]. In general, differences between misoprostol and placebo in terms of operative time and blood loss are statistically, but not clinically, significant. The effectiveness of misoprostol is not influenced by whether manual vacuum aspiration or electric suction is used [140].

In the largest trial to date, the WHO randomized 4972 women in 14 countries to either 400 mcg of misoprostol or placebo vaginally 3 h prior to surgical abortion up to 12 0/7 weeks of pregnancy [19]. In the misoprostol arm, there was a reduced risk of superficial damage to the cervix due to tenaculum tears [3 vs. 12, relative risk (RR): 0.25, 95% confidence interval (CI): 0.07–0.89]. Only 2 of 14 study sites reported this complication, which suggests that it may be related to provider experience or technique. There was no difference in the risk of deeper cervical tears due to dilation or uterine perforation between the two groups [19]. The risk of the delayed complication of incomplete abortion with or without the need for recurettage was lower in the misoprostol arm than in the placebo arm (19/2427 vs. 55/2431, RR: 0.35 95% CI: 0.21–0.58) [19]. The investigators attributed this difference to (a) the ability of providers to use larger cannula sizes for procedures in the misoprostol arm, thus facilitating evacuation of the uterus and (b) a larger cervical diameter postprocedure, which eased emptying of the cavity of any retained products of conception. However, it is also possible that the reduction in incomplete abortion observed with misoprostol was due to its uterotonic effects, assisting with postprocedure expulsion of any retained tissue. Of interest, this difference was more pronounced in multiparous women.

If misoprostol is used for cervical priming and the woman is unable to undergo surgical abortion as planned, then she is at some risk for expelling the pregnancy and theoretically a risk of congenital anomalies should she continue the pregnancy. Therefore, before receiving misoprostol, all women should give informed consent for the abortion procedure and be adequately screened by appropriately trained personnel.

2.6. What is the optimal misoprostol regimen?

2.6.1. Vaginal administration

For vaginal dosing, randomized trials have found that 200 mcg is inferior to 400 mcg in terms of baseline cervical dilatation [97,111,143,144]. Studies that increased the dose to 600 or 800 mcg demonstrated increased rates of such side effects as abdominal pain, bleeding and fever [111,144], with minimal gain in cervical dilatation. Other studies have changed the regimen from an interval of 3 h and a dose of 400 mcg of vaginal misoprostol to an interval of 2 h and a dose of 600 mcg or 800 mcg 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%), fever (12% vs. 0%) and less cervical dilatation with the 600-mcg dose given 2 h before the procedure than with the 400-mcg dose given 3 h before the procedure [143,144]. This effect was even more pronounced with the 800-mcg dose. Other studies of 400-mcg vaginal misoprostol have shown that no effect is seen 1 h after use and that the peak effect is achieved between 3 and 4 h after use [110,143,144]. No additional dilation is gained from administering vaginal misoprostol

more than 4 h preoperatively [102,145]. Intervals of more than 4 h only increase the frequency of bleeding and passage of products of conception prior to scheduled curettage [145]. Thus, 400 mcg of vaginal misoprostol given 3 to 4 h before the procedure appears to be the optimal regimen for achieving adequate dilation.

2.6.2. Oral administration

In the case of oral administration, results of studies examining different doses of misoprostol are inconsistent, likely because of the varied methods used to define success. One trial that compared 200 mcg and 400 mcg of oral misoprostol the night before the procedure showed that the 400-mcg dose resulted in statistically greater baseline cervical dilatation than the 200-mcg dose; however, the difference was not felt to be clinically significant [106]. Another trial comparing 200 mcg and 400 mcg of oral misoprostol 3 h prior to the procedure found that the higher dose resulted in greater baseline cervical dilatation, as measured by cervical tonometer but no difference in the cumulative force required to dilate the cervix to 8 mm [103]. The optimal time between oral misoprostol administration and the procedure is unclear. Studies show that oral misoprostol is more effective than placebo when given at least 3 to 20 h prior to the procedure [74,92,103,104]. One study determined that 600 mcg of misoprostol resulted in equivalent baseline dilation at 10 and 17 h prior to procedure, but administration 10 h before the procedure was associated with fewer side effects [60]. Cervical priming with oral misoprostol most likely requires a dose of 400 to 600 mcg and a longer preoperative interval than is needed with vaginal administration for maximum effectiveness.

2.6.3. Sublingual administration

For sublingual dosing, one randomized trial has shown that 400 mcg is superior to 200 mcg at both 2 and 3 h prior to procedure when efficacy is measured by cervical dilation [146]. However, women using the 400-mcg dose experienced more side effects. With the 400-mcg dose, increasing the time interval from 2 h to 3 h did not offer any advantages [146]. Similarly, a randomized controlled trial evaluated 200 mcg, 400 mcg and 600 mcg of sublingual misoprostol prior to first-trimester suction curettage in 90 nulliparous women. The primary outcome was the ease of the procedure as reported by the provider. The 600-mcg dose of misoprostol was the most effective, with 23.3% of the cases rated as extremely easy, compared with 10% in the 400-mcg arm and 0% in the 200-mcg arm. However, among the 27 women with an embryonic or fetal demise, 33.3% in the 400-mcg group and 77.7% in the 600-mcg group delivered prior to surgery. In addition, the incidence of each side effect examined — abdominal pain, vaginal bleeding, nausea, vomiting, chills, shivering, fatigue, dizziness, headache and diarrhea— was higher in the women administered 600 mcg. This study concluded that 400 mcg was the dose that balanced efficacy and side effects. In sum, a 400-mcg dose 2

to 3 h preoperatively appears to be the optimal sublingual dosing strategy.

2.6.4. Buccal

The first study to evaluate buccal misoprostol for cervical priming prior to first-trimester abortion was a retrospective cohort study from Chicago [147]. Researchers examined the records of 685 women undergoing surgical abortion between 6 and 13 6/7 weeks who received 400 mcg of misoprostol 1 to 2 h before the procedure. Adequate dilation was measured by the provider's ability to perform the abortion without the need for further mechanical dilation with a cannula size that equaled the gestational age (e.g., 9 mm for 9 weeks). Adequate dilation was achieved in 44.2% of patients overall. Adequacy was higher in earlier gestational ages with 58.2% adequate among women 6 to 7 weeks and 22.4% among women 12 to 13 weeks. In addition, multiparous women were more likely to have adequate dilation than nulliparous women.

2.6.5. Comparisons

Clinical trials comparing different routes of misoprostol administration have shown mixed results. Oral and vaginal administration have been widely compared. Studies favoring vaginal administration have shown that 400 mcg produced baseline dilatation superior to the same dose given orally [94,102]. Vaginal administration also 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%) [94]. In addition, vaginal administration was found to be more effective than oral administration later in the first trimester and in multiparous women [102,148]. However, other studies have shown no difference between vaginal and oral administration [90,92,103,149]. Such studies have shown that 400 mcg of oral misoprostol produced equivalent dilatation at 3 h to 400-mcg vaginal dosing, all with similar side effects. A randomized controlled trial from Scotland involving 64 women showed that 400 mcg of oral misoprostol was equivalent for cervical priming to 400 mcg of vaginal misoprostol when taken 2 to 4 h before surgery [90]. The study was powered to detect a 0.75 Newton difference in the 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. A Cochrane meta-analysis of two studies demonstrated that, compared to oral administration, the vaginal route was associated with significantly greater initial cervical dilation [92,103,123].

Three studies have shown that 400 mcg of sublingual misoprostol is more effective than 400 mcg of oral misoprostol given 3 h prior to procedure in terms of baseline cervical dilatation and the force required for cervical dilation greater than 7 mm [89,108,150]. Sublingual administration has been shown to be either equivalent to or better than vaginal administration when 400 mcg is given 1 to 4 h preprocedure [93,99,109,112,114,150–152]; however, it is associated with

significantly more nausea (12.4% vs. 2.5%), vomiting (10.1% vs. 3.8%) and diarrhea (26.4% vs. 7.6%) [93,99,114]. Nonetheless, sublingual administration is associated with high patient and staff acceptability [93,109,112,150]. One study showed that 200 mcg of sublingual misoprostol given 2 h preoperatively was equivalent to 400 mcg of vaginal misoprostol given 3 h preoperatively in terms of cervical dilation [153]. A Cochrane meta-analysis comparing sublingual to vaginal misoprostol favored the sublingual route, which was associated with less need for further dilation (RR: 1.41, 95% CI: 1.15–1.73) [93,99,112,114,123]. However, the sublingual route was associated with a higher occurrence of nausea [123]. Routes other than vaginal administration of misoprostol have been favored because of concern about the uniformity of vaginal absorption of misoprostol. In addition, data indicate that some women prefer to take misoprostol tablets by mouth to avoid a vaginal examination or vaginal self-administration of misoprostol [150,154]. 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 [72,155].

In sum, compared with the oral route, vaginal administration 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 [102]. However, staff responsible for the vaginal placement of misoprostol in the clinic tend to prefer the oral or sublingual routes of administration [90]. The sublingual route is more effective than oral administration, works faster than vaginal administration, but is associated with more side effects than either oral or vaginal administration.

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

Two randomized controlled trials have compared misoprostol to laminaria for cervical priming before surgical abortion at 7 to 14 weeks. One trial compared 400 mcg of oral or vaginal misoprostol to one medium laminaria for 4 h prior to the suction aspiration [102]. Vaginal misoprostol significantly outperformed oral misoprostol in mean cervical dilatation (28.0 mm ± 7.3 vs. 24.2 mm ± 4.8). The mean cervical dilatation with laminaria (25.9 mm ± 5.8) was less than with vaginal misoprostol but greater than with oral misoprostol. Still, neither comparison reached significance, primarily because of inadequate statistical power. The groups did not differ in the proportion of subjects requiring additional dilation, the difficulty of additional dilation, amount of blood loss or the duration of the procedure. The women who received laminaria experienced significantly more discomfort with insertion than did 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 mcg of vaginal misoprostol, both administered the day prior to the procedure (19 to 26 h) [145]. This Canadian study found that laminaria achieved greater baseline cervical dilatation than vaginal misoprostol (35 mm vs. 28 mm, p<0.001). 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 said they would prefer misoprostol for cervical dilation if they had an abortion in the future.

A third study compared 400 mcg of buccal misoprostol with a single 4-mm Dilapan-S 3 to 4 h prior to surgical abortion between 12 0/7 and 15 0/7 weeks [134]. A total of 125 women were randomized, with a mean gestational age of 13 3/7 weeks. The study procedures required a sham dilator placement for the misoprostol arm. There was a slight difference between the treatment arms in preoperative cervical dilation (Dilapan-S, 10.8-mm diameter, vs. miso-prostol, 10.2-mm diameter, p=0.065), and 95% of women in each group required further mechanical dilation. Mechanical dilation was rated as more difficult by the provider in the misoprostol arm. However, the two groups did not differ in procedure time, estimated blood loss, recovery time or acute complications. More women in the misoprostol arm than in the Dilapan-S arm experienced preoperative cramping, but the frequency of bleeding, nausea, vomiting or diarrhea did not differ. The authors concluded that both cervical priming methods were reasonable options.

In summary, same-day vaginal misoprostol requires less time to achieve the same dilatation as overnight laminaria, is associated with less discomfort with insertion and is preferred by women. Buccal misoprostol is comparable to Dilapan-S in providing adequate dilation for same-day late first-trimester and early second-trimester abortion.

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

The goal of cervical priming is to make suction aspiration safer and less uncomfortable for the patient. 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 [102,145]. Preoperative cramping and abdominal pain occur more frequently in women exposed to both osmotic dilators or misoprostol versus placebo

[19,60,92,95,102,156]. In clinical studies, this level of pain is usually described as mild, without the need for analgesic agents [92,95,96,103,107]. One study, however, found that cervical priming with prostaglandin analogues increased both preoperative and postoperative pain and the use of analgesics [156]. Another study showed that intraoperative pain levels were not lower with cervical priming using either vaginal or oral misoprostol than with placebo [92]. The higher the dose and the longer the interval of use for any cervical priming agent, the more women experienced preoperative discomfort, which might include bleeding from incomplete abortion and the distress of passing products of conception [60,111,144,145]. While most trials show that cervical priming shortens operative time by reducing the need for mechanical dilation, this does not always translate into a reduction in pain as perceived by the patient [92].

To directly evaluate the pain experienced with misoprostol for cervical priming, one prospective cohort study followed 102 women undergoing surgical abortion between 7 and 14 weeks gestation who chose (in collaboration with their physician) either overnight laminaria or same-day misoprostol (400 mcg vaginally 3 to 4 h prior to the procedure) [157]. The study was limited by its lack of randomization, and by the greater percentage of women in the misoprostol group than in the laminaria group who were at less than 10 weeks of gestation (92% vs. 58%). Pain scores (0 to 10) at insertion were higher in the laminaria group, 4.26, than in the misoprostol group, 0.74 (p<.001). As seen in other studies, significantly more women in the misoprostol group than in the laminaria group experienced fever, chills and diarrhea, but they found the method easier to use. Right before the procedure, the pain score in the misoprostol group was 2.44, compared with 1.10 in the laminaria group (p= .002). After multivariable analysis, this effect was blunted. Although the pain control used during the procedure was not controlled and could have induced a paracervical block, nitrous oxide, fentanyl and/or midazolam, the average pain score 1 h after the procedure was 2.24 in the misoprostol group and 0.78 in the laminaria group (p<.001). This difference held after multivariable analysis with moderate to severe pain occurring postoperatively in 24% of the misoprostol group and 4.5% in the laminaria group. The authors speculate that continuing uterine contractions caused by the misoprostol contributed to the postoperative pain levels. In sum, cervical priming does not reduce pain before, during or after surgical abortion.

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

Investigators have not focused on the acceptability to women of cervical priming as compared to mechanical dilation before first-trimester suction aspiration. Evidence indicating whether women prefer cervical priming is lacking. Studies have documented that women prefer same-day

misoprostol to overnight laminaria [102]. One randomized controlled trial found no difference in satisfaction when comparing misoprostol to same-day Dilapan-S; however, both arms underwent a speculum exam to provide adequate blinding [134]. 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 (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 preoperative side effects, like bleeding, cramping, nausea and vomiting. The largest placebo-controlled trial to date reported that 1355 (55%) women randomized to 400-mcg vaginal misoprostol 3 h before their procedure experienced abdominal pain, compared with 545 (22%) of women randomized to the placebo arm [19]. Furthermore, 909 (37%) of women in the misoprostol arm, compared with 167 (7%) of those in the placebo arm, experienced vaginal bleeding before the procedure.

One study explored whether or not routine use of misoprostol influences certain outcomes. A retrospective cohort study of 4000 women who had had a first-trimester surgical abortion at the Pregnancy Advisory Centre of South Australia was published in 2009 [158]. The authors examined four historical cohorts: (a) those with no cervical priming; (b) those with cervical priming with 200 mcg of oral misoprostol 30 min before their procedure; (c) those with cervical priming with 200 mcg of sublingual misoprostol 30 min before their procedure; and (d) those who received 200 mcg of oral misoprostol 3 h before their procedure and 200 mcg of vaginal misoprostol at the end of the procedure. The vaginal misoprostol at the end of the procedure was added to act as a uterotonic. The proportion of procedures in which cervical dilation was rated as "not difficult" by the provider (compared to moderately, very or extremely difficult) was 74% in the first group, 86% in the second group, 84% in the third group and 95.4% in the fourth group. This difference likely was due to the longer exposure to misoprostol in the fourth group. According to the authors' records, the percentage of women who made postoperative phone calls and clinic visits for pain and bleeding was higher in the first group (6.1%) than in the fourth group (1.8%). Complications were low overall (0.54%), but the authors did not perform any statistical comparisons on the complication rates in the four groups. This finding would have to be confirmed in a prospective randomized trial.

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

The information available to date shows that the routine use of misoprostol reduces the rate of incomplete abortion from 2.3% to 0.8%, and the rate of superficial cervical lacerations due to the tenaculum from 0.50% to 0.12% in pregnancies of less than 12 0/7 weeks [19]. On the basis of these data, 72 women would need to be treated with misoprostol to prevent one uterine reevacuation. However, treatment with misoprostol is associated with significantly more preoperative pain and bleeding than rigid dilation alone and requires that the patient spend additional hours waiting for the priming agent to take effect. The rarity of acute complications and the apparent lack of effectiveness in preventing major complications (cervical lacerations and uterine perforation), combined with the additional time needed and the adverse effects associated with cervical priming, makes the usefulness of routine cervical priming with any agent debatable [11,14,19,20]. Patient perspectives on whether this trade-off is worthwhile are lacking. Clinical groups have attempted to create guidelines that capture the nuances of the evidence, specifying cervical priming only for women younger than 18 and those with more advanced gestations, some taking into account parity [84,85]. In terms of advancing gestational age, cervical priming likely confers some benefit late in the first trimester; however, no clear evidence dictates when cervical priming should begin [123]. Therefore, the Society of Family Planning does not recommend routine cervical priming for first-trimester suction aspiration procedures. The Society of Family Planning recommends that providers consider cervical priming for women late in the first trimester, for adolescents, and for women in whom cervical dilation is expected to be challenging.

3. Recommendations

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

- Cervical priming in the first trimester with either osmotic dilators or misoprostol may protect against complications such as cervical injury and uterine perforation. The absolute risk of these complications is extremely low.
- Cervical priming with misoprostol may reduce the incidence of incomplete abortion.
- Effective methods of cervical priming include osmotic dilators and misoprostol; the shortest time for efficacy (2 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 mcg vaginally 3 to 4 h, orally 8 to 12 h, buccal 3 to 4 h or sublingually 2 to 4 h before the procedure.
- Routine first-trimester cervical priming is not advised because it delays the procedure, is associated with side effects and does not confer proven benefit.

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

- If used, vaginal, oral, buccal and sublingual administration are all acceptable to women. 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.

- Providers vary in the amount of cervical dilation they attempt to achieve for suction curettage.
- 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.

4. Important questions for future research

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, patient perspectives on whether cervical priming to reduce the likelihood of incomplete abortion is worthwhile would be important to include. In any study, it is especially important to examine the effect of misoprostol on preoperative, intraoperative and postoperative pain, compared to placebo. Finally, studies are needed to determine the gestational age at which cervical preparation appears to significantly decrease adverse events.

References

[1] Jones RK, Jerman J. Abortion incidence and service availability in the United States, 2011. Perspect Sex Reprod Health 2014;46:3–4 [Evidence Grade: II-2].
[2] Bartlett LA, Berg CJ, Shulman HB, Zane SB, Green CA, Whitehead S, et al. Risk factors for legal induced abortion-related mortality in the United States. Obstet Gynecol 2004;103:729–37 [Evidence Grade: II-2].
[3] Upadhyay UD, Desai S, Zlidar V, Weitz TA, Grossman D, Anderson P, et al. Incidence of emergency department visits and complications after abortion. Obstet Gynecol 2015;125:175–83 [Evidence Grade: II-2].
[4] Pazol K, Creanga AA, Burley KD, Jamieson DJ. Abortion surveillance - United States, 2011. MMWR CDC Surveill Summ 2014;63:1–1 [Evidence Grade: II-2].
[5] Raymond EG, Grimes DA. The comparative safety of legal induced abortion and childbirth in the United States. Obstet Gynecol 2012;119:215–9 [Evidence Grade: II-2].
[6] Royal College of General Practitioners, Royal College of Obstetricians and Gynaecologists. Induced abortion operations and their early sequelae. J R Coll Gen Pract 1985;35:175–80 [Evidence Grade: II-3].
[7] Andolsek L, Cheng M, Hren M, Ogrinc-Oven M, Ng A, Ratnam S, et al. The safety of local anesthesia and outpatient treatment: a controlled study of induced abortion by vacuum aspiration. Stud Fam Plan 1977;8:118–24 [Evidence Grade: II-2].
[8] Nesheim BI. Induced abortion by the suction method. An analysis of complication rates. Acta Obstet Gynecol Scand 1984;63:591–5 [Evidence Grade: II-2].
[9] Cates Jr W, Schulz KF, Grimes DA. The risks associated with teenage abortion. N Engl J Med 1983;309:621–4 [Evidence Grade: II-2].
[10] Heisterberg L, Kringelbach M. Early complications after induced first-trimester abortion. Acta Obstet Gynecol Scand 1987;66:201–4 [Evidence Grade: II-2].
[11] Hakim-Elahi E, Tovell HM, Burnhill MS. Complications of first-trimester abortion: a report of 170,000 cases. Obstet Gynecol 1990;76:129–35 [Evidence Grade: II-2].
[12] Ferris LE, McMain-Klein M, Colodny N, Fellows GF, Lamont J. Factors associated with immediate abortion complications. Can Med Assoc J 1996;154:1677–85 [Evidence Grade: II-2].
[13] Zhou W, Nielsen GL, Moller M, Olsen J. Short-term complications after surgically induced abortions: a register-based study of 56 117 abortions. Acta Obstet Gynecol Scand 2002;81:331–6.
[14] Grimes DA, Schulz KF, Cates Jr WJ. Prevention of uterine perforation during curettage abortion. JAMA 1984;251:2108–11 [Evidence Grade: II-2].
[15] Bozorgi N. Statistical analysis of first-trimester pregnancy terminations in an ambulatory surgical center. Am J Obstet Gynecol 1977;127:763–8 [Evidence Grade: II-2].
[16] Hodgson JE, Portmann KC. Complications of 10,453 consecutive first-trimester abortions: a prospective study. Am J Obstet Gynecol 1974;120:802–7 [Evidence Grade: II-2].
[17] Lindell G, Flam F. Management of uterine perforations in connection with legal abortions. Acta Obstet Gynecol Scand 1995;74:373–5 [Evidence Grade: II-2].
[18] King TM, Atienza MF, Burkman RT. The incidence of abdominal surgical procedures in a population undergoing abortion. Am J Obstet Gynecol 1980;137:530–3 [Evidence Grade: II-2].
[19] Meirik O, My Huong NT, Piaggio G, Bergel E, von Hertzen H, Regulation WHORGoPMoF. Complications of first-trimester abortion by vacuum aspiration after cervical preparation with and without misoprostol: a multicentre randomised trial. Lancet 2012;379:1817–24 [Evidence Grade: I].
[20] Schulz KF, Grimes DA, Cates Jr W. Measures to prevent cervical injury during suction curettage abortion. Lancet 1983;1:1182–5 [Evidence Grade: II-2].
[21] Jacot FR, Poulin C, Bilodeau AP, Morin M, Moreau S, Gendron F, et al. A five-year experience with second-trimester induced abortions: no increase in complication rate as compared to the first trimester. Am J Obstet Gynecol 1993;168:633–7 [Evidence Grade: II-2].
[22] Weitz TA, Taylor D, Desai S, Upadhyay UD, Waldman J, Battistelli MF, et al. Safety of aspiration abortion performed by nurse practitioners, certified nurse midwives, and physician assistants under a California legal waiver. Am J Public Health 2013;103:454–61 [Evidence Grade: II-2].
[23] Hale RW, Pion RJ. Laminaria: an underutilized clinical adjunct. Clin Obstet Gynecol 1972;15:829–50 [Evidence Grade: II-2].
[24] Golditch IM, Glasser MH. The use of laminaria tents for cervical dilatation prior to vacuum aspiration abortion. Am J Obstet Gynecol 1974;119:481–5 [Evidence Grade: II-3].
[25] Niswander KR. Laminaria tents as an aid in suction abortion. Calif Med 1973;119:11–4 [Evidence Grade: II-3].
[26] Hern WM. Laminaria in abortion. Use in 1368 patients in first trimester. Rocky Mt Med J 1975;72:390–5 [Evidence Grade: II-3].
[27] Moberg P. Uterine perforation in connection with vacuum aspiration. Int J Gynaecol Obstet 1976;14:77–80 [Evidence Grade: II-3].
[28] Borell U, Bygdeman M, Leader A, Lundstrom V, Martin Jr JN. Successful first trimester abortion with 15(S) 15-methyl-prostaglandin F2alpha-methyl ester vaginal suppositories. Contraception 1976;13:87–94 [Evidence Grade: II-2].
[29] Gupta JK, Johnson N. Should we use prostaglandins, tents or progesterone antagonists for cervical ripening before first trimester abortion? Contraception 1992;46:489–97 [Evidence Grade: II-1].
[30] Nicolaides KH, Welch CC, MacPherson MB, Johnson IR, Filshie GM. Lamicel: a new technique for cervical dilatation before first trimester abortion. Br J Obstet Gynaecol 1983;90:475–9 [Evidence Grade: I].

[31] Morris ND, McCallum GI, Hammond L. Preoperative cervical dilatation: a trial of laminaria tents and prostaglandin F2 alpha gel. Aust N Z J Obstet Gynaecol 1986;26:36–9 [Evidence Grade: I].

[32] Sema S, Hingorani V, Kumar S, Kinra G. Three methods for gradual cervical dilatation prior to vacuum aspiration in late first trimester pregnancy. Contraception 1983;28:223–31 [Evidence Grade: II-3].

[33] Hulka JF, Lefler Jr HT, Anglone A, Lachenbruch PA. A new electronic force monitor to measure factors influencing cervical dilation for vacuum curettage. Am J Obstet Gynecol 1974;120:166–73 [Evidence Grade: II-3].

[34] Wheeler RG, Schneider K. Properties and safety of cervical dilators. Am J Obstet Gynecol 1983;146:597–601 [Evidence Grade: II-3].

[35] Zhou W, Olsen J. Are complications after an induced abortion associated with reproductive failures in a subsequent pregnancy? Acta Obstet Gynecol Scand 2003;82:177–81 [Evidence Grade: II-2].

[36] Zhou W, Olsen J, Nielsen GL, Sabroe S. Risk of spontaneous abortion following induced abortion is only increased with short interpregnancy interval. J Obstet Gynaecol 2000;20:49–54 [Evidence Grade: II-2].

[37] Zhou W, Sorensen HT, Olsen J. Induced abortion and low birthweight in the following pregnancy. Int J Epidemiol 2000;29:100–6 [Evidence Grade: II-2].

[38] Hogue CJ, Boardman LA, Stotland N. Answering questions about long-term outcomes. In: Paul M, Lichtenberg ES, Borgatta L, Grimes DA, Stubblefield PG, & Creinin MD, editors. Management of unintended and abnormal pregnancy. West Sussex, UK: Wiley-Blackwell; 2009.

[39] Raatikainen K, Heiskanen N, Heinonen S. Induced abortion: not an independent risk factor for pregnancy outcome, but a challenge for health counseling. Ann Epidemiol 2006;16:587–92 [Evidence Grade: II-2].

[40] Meckstroth K, Paul M. First-trimester aspiration abortion. In: Paul M, Lichtenberg ES, Borgatta L, Grimes DA, Stubblefield PG, & Creinin MD, editors. Management of unintended and abnormal pregnancy. West Sussex, UK: Wiley-Blackwell; 2009.

[41] Novak F, Andolsek L. Comparison of the medical effects of induced abortion by two methods, curettage and vacuum aspiration. In: & Andolsek L, editor. The Ljubljana Abortion Study, 1971-1973. Bethesda: National Institutes of Health, Center for Population Research; 1974.

[42] Lichtenberg ES, Paul M, Jones H. First trimester surgical abortion practices: a survey of National Abortion Federation members. Contraception 2001;64:345–52 [Evidence Grade: II-3].

[43] O'Connell K, Jones HE, Simon M, Saporta V, Paul M, Lichtenberg ES. First-trimester surgical abortion practices: a survey of National Abortion Federation members. Contraception 2009;79:385–92 [Evidence Grade: II-2].

[44] Olund A, Jonasson A, Kindahl H, Fianu S, Larsson B. The effect of cervical dilatation by laminaria on the plasma levels of 15-keto-13,14-dihydro-PGF2 alpha. Contraception 1984;30:23–7 [Evidence Grade: II-3].

[45] Jonasson A, Larsson B. Contractile activity in the human uterine cervix and corpus during cervical dilatation by laminaria tent in first trimester legal abortions. Acta Obstet Gynecol Scand 1989;68:401–4 [Evidence Grade: II-2].

[46] Sutkin G, Capelle SD, Schlievert PM, Creinin MD. Toxic shock syndrome after laminaria insertion. Obstet Gynecol 2001;98:959–61 [Evidence Grade: III].

[47] Acharya PS, Gluckman SJ. Bacteremia following placement of intracervical laminaria tents. Clin Infect Dis 1999;29:695–7 [Evidence Grade: III].

[48] Evaldson GR, Fianu S, Jonasson A, Larsson B, Nord CE, Olund AR. Does the hygroscopic property of the laminaria tent imply a risk for ascending infection in legal abortions? A microbiological study. Acta Obstet Gynecol Scand 1986;65:257–61 [Evidence Grade: II-1].

[49] Jonasson A, Larsson B, Bygdeman S, Forsum U. The influence of cervical dilatation by laminaria tent and with Hegar dilators on the intrauterine microflora and the rate of postabortal pelvic inflammatory disease. Acta Obstet Gynecol Scand 1989;68:405–10 [Evidence Grade: I].

[50] Kim SH, Chang YH, Kim WK, Kim YK, Cho SH, Kim YY, et al. Two cases of anaphylaxis after laminaria insertion. J Korean Med Sci 2003;18:886–8 [Evidence Grade: III].

[51] Chanda M, Mackenzie P, Day JH. Hypersensitivity reactions following laminaria placement. Contraception 2000;62:105–6 [Evidence Grade: III].

[52] Nguyen MT, Hoffman DR. Anaphylaxis to laminaria. J Allergy Clin Immunol 1995;95:138–9 [Evidence Grade: III].

[53] Usta IM, Khalil A. Long-term complications and ultrasound findings in retained Dilapan fragments. Int J Gynaecol Obstet 1999;65:311–2 [Evidence Grade: III].

[54] Canvin J. Personal communication. F.E.M.A. International U.S. Headquarters: J.C.E.C. Company Inc; 2006 [Evidence Grade: III].

[55] Nicolaides KH, Welch CC, Koullapis EN, Filshie GM. Cervical dilatation by Lamicel–studies on the mechanism of action. Br J Obstet Gynaecol 1983;90:1060–4 [Evidence Grade: II-3].

[56] Meckstroth KR, Darney PD. Prostaglandins for first-trimester termination. Best Pract Res Clin Obstet Gynaecol 2003;17:745–63 [Evidence Grade: III].

[57] O'Brien WF. The role of prostaglandins in labor and delivery. Clin Perinatol 1995;22:973–84 [Evidence Grade: III].

[58] Eckerhovd E, Radulovic N, Norstrom A. Gemeprost versus misoprostol for cervical priming before first-trimester abortion: a randomized controlled trial. Obstet Gynecol 2003;101:722–5 [Evidence Grade: I].

[59] Henry AM, Haukkamaa M. Comparison of vaginal misoprostol and gemeprost as pre-treatment in first trimester pregnancy interruption. Br J Obstet Gynaecol 1999;106:540–3 [Evidence Grade: I].

[60] Platz-Christensen JJ, Nielsen S, Hamberger L. Is misoprostol the drug of choice for induced cervical ripening in early pregnancy termination? Acta Obstet Gynecol Scand 1995;74:809–12 [Evidence Grade: I].

[61] el-Refaey H, Calder L, Wheatley DN, Templeton A. Cervical priming with prostaglandin E1 analogues, misoprostol and gemeprost. Lancet 1994;343:1207–9 [Evidence Grade: I].

[62] Sparrow MJ, Tait JD, Stone PR. Vaginal dinoprostone versus oral misoprostol for predilatation of the cervix in first trimester surgical abortion. Aust N Z J Obstet Gynaecol 1998;38:64–8 [Evidence Grade: I].

[63] Zieman M, Fong SK, Benowitz NL, Banskter D, Darney PD. Absorption kinetics of misoprostol with oral or vaginal administration. Obstet Gynecol 1997;90:88–92 [Evidence Grade: I].

[64] Danielsson KG, Marions L, Rodriguez A, Spur BW, Wong PY, Bygdeman M. Comparison between oral and vaginal administration of misoprostol on uterine contractility. Obstet Gynecol 1999;93:275–80 [Evidence Grade: I].

[65] Khan RU, El-Refaey H, Sharma S, Sooranna D, Stafford M. Oral, rectal, and vaginal pharmacokinetics of misoprostol. Obstet Gynecol 2004;103:866–70 [Evidence Grade: I].

[66] Tang OS, Schweer H, Seyberth HW, Lee SW, Ho PC. Pharmacokinetics of different routes of administration of misoprostol. Hum Reprod 2002;17:332–6 [Evidence Grade: I].

[67] Singh K, Fong YF, Prasad RN, Dong F. Does an acidic medium enhance the efficacy of vaginal misoprostol for pre-abortion cervical priming? Hum Reprod 1999;14:1635–7 [Evidence Grade: I].

[68] Creinin MD, Carbonell JL, Schwartz JL, Varela L, Tanda R. A randomized trial of the effect of moistening misoprostol before vaginal administration when used with methotrexate for abortion. Contraception 1999;59:11–6 [Evidence Grade: I].

[69] Ngai SW, Tang OS, Chan YM, Ho PC. Vaginal misoprostol alone for medical abortion up to 9 weeks of gestation: efficacy and acceptability. Hum Reprod 2000;15:1159–62 [Evidence Grade: I].

[70] Aronsson A, Bygdeman M, Gemzell-Danielsson K. Effects of misoprostol on uterine contractility following different routes of administration. Hum Reprod 2004;19:81–4 [Evidence Grade: II-1].

[71] Schaff EA, DiCenzo R, Fielding SL. Comparison of misoprostol plasma concentrations following buccal and sublingual administration. Contraception 2005;71:22–5 [Evidence Grade: I].

[72] Meckstroth KR, Whitaker AK, Bertisch S, Goldberg AB, Darney PD. Misoprostol administered by epithelial routes: drug absorption and uterine response. Obstet Gynecol 2006;108:582–90 [Evidence Grade: I].

[73] Li CFI, Wong CYG, Chan CPB, Ho PC. A study of co-treatment of nonsteroidal anti-inflammatory drugs (NSAIDs) with misoprostol for cervical priming before suction termination of first trimester pregnancy. Contraception 2003;67:101–5 [Evidence Grade: I].

[74] Bokstrom H, Atterfelt P, Alexandersson M, Brannstrom M, Norstrom A. Preoperative cervical softening before first trimester legal abortion by mifepristone and misoprostol: a double-blind, randomized, clinical, biochemical, and immunohistochemical study. Contraception 1998;58:157–63 [Evidence Grade: I].

[75] Johnson N, Bryce FC. Could antiprogesterones be used as alternative cervical ripening agents? Am J Obstet Gynecol 1990;162:688–90 [Evidence Grade: II-3].

[76] Durlot F, Dubois C, Brunerie J, Frydman R. Efficacy of progesterone antagonist RU486 (mifepristone) for pre-operative cervical dilatation during first trimester abortion. Hum Reprod 1988;3:583–4 [Evidence Grade: I].

[77] Radestad A, Christensen NJ, Stromberg L. Induced cervical ripening with mifepristone in first trimester abortion. A double-blind randomized biomechanical study. Contraception 1988;38:301–12 [Evidence Grade: I].

[78] Swahn ML, Bygdeman M. The effect of the antiprogestin RU 486 on uterine contractility and sensitivity to prostaglandin and oxytocin. Br J Obstet Gynaecol 1988;95:126–34 [Evidence Grade: II-2].

[79] Ashok PW, Flett GM, Templeton A. Mifepristone versus vaginally administered misoprostol for cervical priming before first-trimester termination of pregnancy: a randomized, controlled study. Am J Obstet Gynecol 2000;183:998–002 [Evidence Grade: I].

[80] Vaisanen-Tommiska M, Butzow R, Ylikorkala O, Mikkola TS. Mifepristone-induced nitric oxide release and expression of nitric oxide synthases in the human cervix during early pregnancy. Hum Reprod 2006;21:2180–4 [Evidence Grade: II-1].

[81] Vaisanen-Tommiska M, Mikkola TS, Ylikorkala O. Misoprostol induces cervical nitric oxide release in pregnant, but not in nonpregnant, women. Am J Obstet Gynecol 2005;193:790–6 [Evidence Grade: II-1].

[82] Chwalisz K, Garfield RE. Role of nitric oxide in the uterus and cervix: implications for the management of labor. J Perinat Med 1998;26:448–57 [Evidence Grade: III].

[83] Promsonthi P, Preechapornprasert D, Chanrachakul B. Nitric oxide donors for cervical ripening in first-trimester surgical abortion. Cochrane Database Syst Rev 2011:CD007444 [Evidence Grade: I].

[84] World Health Organization. Safe Abortion: Technical and Policy Guidance for Health Systems. Geneva: WHO; 2012.

[85] Royal College of Obstetricians & Gynaecologists. The care of women requesting induced abortion. London: RCOG Press; 2011.

[86] Baldock S. Personal communication: Marie Stopes Procedure. Marie Stopes International; 2006 [Evidence Grade: III].

[87] Grimes DA, Ray IG, Middleton CJ. Lamicel versus laminaria for cervical dilation before early second-trimester abortion: a randomized clinical trial. Obstet Gynecol 1987;69:887–90 [Evidence Grade: I].

[88] Lawrie A, Penney G, Templeton A. A randomised comparison of oral and vaginal misoprostol for cervical priming before suction termination of pregnancy. Br J Obstet Gynaecol 1996;103:1117–9 [Evidence Grade: I].

[89] Aronsson A, Helstrom L, Gemzell-Danielsson K. Sublingual compared with oral misoprostol for cervical dilatation prior to vacuum aspiration: a randomized comparison. Contraception 2004;69:165–9 [Evidence Grade: I].

[90] Ashok PW, Hamoda H, Nathani F, Flett GM, Templeton A. Randomised controlled study comparing oral and vaginal misoprostol

[91] for cervical priming prior to surgical termination of pregnancy. BJOG 2003;110:1057–61 [Evidence Grade: I].

[91] Bugalho A, Bique C, Almeida L, Bergstrom S. Application of vaginal misoprostol before cervical dilatation to facilitate first-trimester pregnancy interruption. Obstet Gynecol 1994;83:729–31 [Evidence Grade: I].

[92] Cakir L, Dilbaz B, Caliskan E, Dede FS Dilbaz S, Haberal A. Comparison of oral and vaginal misoprostol for cervical ripening before manual vacuum aspiration of first trimester pregnancy under local anesthesia: a randomized placebo-controlled study. Contraception 2005;71:337–42 [Evidence Grade: I].

[93] Carbonell JL, Mari J, Valero F, Llorente M, Salvador I, Varela L, et al. Sublingual versus vaginal misoprostol (400 ug) for cervical priming in first-trimester abortion: a randomized trial. Contraception 2006;74:328–33 [Evidence Grade: I].

[94] Carbonell JL, Velazco A, Rodriguez Y, Tanda R, Sánchez C, Barambio S, et al. Oral versus vaginal misoprostol for cervical priming in first-trimester abortion: a randomized trial. Eur J Contracept Reprod Health Care 2001;6:134–40 [Evidence Grade: I].

[95] de Jonge ET, Jewkes R, Levin J, Rees H. Randomised controlled trial of the efficacy of misoprostol used as a cervical ripening agent prior to termination of pregnancy in the first trimester. S Afr Med J 2000;90:256–62 [Evidence Grade: I].

[96] Ficicioglu C, Tasdemir M, Tasdemir S. Effect of vaginal misoprostol application for cervical softening in pregnancy interruption before ten weeks of gestation. Acta Obstet Gynecol Scand 1996;75:54–6 [Evidence Grade: I].

[97] Fong YF, Singh K, Prasad RN. A comparative study using two dose regimens (200 microg or 400 microg) of vaginal misoprostol for pre-operative cervical dilatation in first trimester nulliparae. Br J Obstet Gynaecol 1998;105:413–7 [Evidence Grade: I].

[98] Golland IM, Vaughan-Williams CA, Elstein M. A comparison of osmotic dilators, Lamicel and Dilapan, and a prostaglandin E1 analogue, gemeprost, for ripening the cervix before legal abortion. J Obstet Gynaecol 1989;9:210–2 [Evidence Grade: I].

[99] Hamoda H, Ashok PW, Flett GM, Templeton A. A randomized controlled comparison of sublingual and vaginal administration of misoprostol for cervical priming before first-trimester surgical abortion. Am J Obstet Gynecol 2004;190:55–9 [Evidence Grade: I].

[100] Kline SB, Meng H, Munsick RA. Cervical dilation from laminaria tents and synthetic osmotic dilators used for 6 hours before abortion. Obstet Gynecol 1995;86:931–5 [Evidence Grade: I].

[101] Limongelli MD, Belletti F, Cecere AT, Oliva L, Carlomagno G. Vaginal misoprostol as a cervical ripening agent prior to suction curettage for first-trimester termination of pregnancy. Ital J Gynaecol Obstet 2004;16:32–4 [Evidence Grade: II-1].

[102] MacIsaac L, Grossman D, Balistreri E, Darney P. A randomized controlled trial of laminaria, oral misoprostol, and vaginal misoprostol before abortion. Obstet Gynecol 1999;93:766–70 [Evidence Grade: I].

[103] Ngai SW, Chan YM, Tang OS, Ho PC. The use of misoprostol for pre-operative cervical dilatation prior to vacuum aspiration: a randomized trial. Hum Reprod 1999;14:2139–42 [Evidence Grade: I].

[104] Ngai SW, Tang OS, Lao T, Ho PC, Ma HK. Oral misoprostol versus placebo for cervical dilatation before vacuum aspiration in first trimester pregnancy. Hum Reprod 1995;10:1220–2 [Evidence Grade: I].

[105] Okanlomo KA, Ngotho D, Moodley J. Effect of misoprostol for cervical ripening prior to pregnancy interruption before twelve weeks of gestation. East Afr Med J 1999;76:552–5 [Evidence Grade: I].

[106] Oppegaard KS, Abdelnoor M, Nesheim BI, Jerve F, Eskild A. The use of oral misoprostol for pre-abortion cervical priming: a randomised controlled trial of 400 versus 200 microg in first trimester pregnancies. BJOG 2004;111:154–9 [Evidence Grade: I].

[107] Saxena P, Salhan S, Sarda N. Role of sublingual misoprostol for cervical ripening prior to vacuum aspiration in first trimester interruption of pregnancy. Contraception 2003;67:213–7 [Evidence Grade: I].

[108] Saxena P, Salhan S, Sarda N. Comparison between the sublingual and oral route of misoprostol for pre-abortion cervical priming in first

trimester abortions. Hum Reprod 2004;19:77–80 [Evidence Grade: II-1].

[109] Saxena P, Salhan S, Sarda N. Sublingual versus vaginal route of misoprostol for cervical ripening prior to surgical termination of first trimester abortions. Eur J Obstet Gynecol Reprod Biol 2006;125:109–13 [Evidence Grade: II-1].

[110] Sharma S, Refaey H, Stafford M, Purkayastha S, Parry M, Axby H. Oral versus vaginal misoprostol administered one hour before surgical termination of pregnancy: a randomised controlled trial. BJOG 2005;112:456–60 [Evidence Grade: I].

[111] Singh K, Fong YF, Prasad RN, Dong F. Randomized trial to determine optimal dose of vaginal misoprostol for preabortion cervical priming. Obstet Gynecol 1998;92:795–8 [Evidence Grade: I].

[112] Tang OS, Mok KH, Ho PC. A randomized study comparing the use of sublingual to vaginal misoprostol for pre-operative cervical priming prior to surgical termination of pregnancy in the first trimester. Hum Reprod 2004;19:1101–4 [Evidence Grade: I].

[113] Vimala N, Mittal S, Kumar S. Sublingual misoprostol for preabortion cervical ripening in first-trimester pregnancy termination. Contraception 2003;67:295–7 [Evidence Grade: I].

[114] Vimala N, Mittal S, Kumar S, Dadhwal V, Sharma Y. A randomized comparison of sublingual and vaginal misoprostol for cervical priming before suction termination of first-trimester pregnancy. Contraception 2004;70:117–20 [Evidence Grade: I].

[115] Goldberg AB, Drey EA, Whitaker AK, Kang MS, Meckstroth KR, Darney PD. Misoprostol compared with laminaria before early second-trimester surgical abortion: a randomized trial. Obstet Gynecol 2005;106:234–41 [Evidence Grade: I].

[116] Kiran U, Amin P, Penketh RJ. Self-administration of vaginal misoprostol after mifepristone for termination of pregnancy: Patient acceptability. J Obstet Gynaecol 2006;26:679–81 [Evidence Grade: II-3].

[117] Kiran U, Amin P, Penketh RJ. Self-administration of misoprostol for termination of pregnancy: safety and efficacy. J Obstet Gynaecol 2004;24:155–6 [Evidence Grade: II-3].

[118] Schaff EA, Fielding SL, Westhoff C, Ellertson C, Eisinger SH, Stadalius LS, et al. Vaginal misoprostol administered 1, 2, or 3 days after mifepristone for early medical abortion: A randomized trial. JAMA 2000;284:1948–53 [Evidence Grade: I].

[119] Schaff EA, Fielding SL, Westhoff C. Randomized trial of oral versus vaginal misoprostol 2 days after mifepristone 200 mg for abortion up to 63 days of pregnancy. Contraception 2002;66:247–50 [Evidence Grade: I].

[120] World Health Organization's Task Force on Prostaglandins for Fertility Regulation. Vaginal administration of 15-methyl-PGF2 alpha methyl ester for preoperative cervical dilatation. Contraception 1981;23:251–9 [Evidence Grade: I].

[121] Child TJ, Thomas J, Rees M, MacKenzie IZ. Morbidity of first trimester aspiration termination and the seniority of the surgeon. Hum Reprod 2001;16:875–8 [Evidence Grade: II-2].

[122] Buehler JW, Schulz KF, Grimes DA, Hogue CJ. The risk of serious complications from induced abortion: do personal characteristics make a difference? Am J Obstet Gynecol 1985;153:14–20 [Evidence Grade: II-2].

[123] Kapp N, Lohr PA, Ngo TD, Hayes JL. Cervical preparation for first trimester surgical abortion. The Cochrane database of systematic reviews; 2010CD007207 [Evidence Grade: I].

[124] Pridmore BR, Chambers DG. Uterine perforation during surgical abortion: a review of diagnosis, management, and prevention. Aust N Z J Obstet Gynaecol 1999;39:349–53 [Evidence Grade: III].

[125] Kaunitz AM, Rovira EZ, Grimes DA, Schulz KF. Abortions that fail. Obstet Gynecol 1985;66:533–7 [Evidence Grade: II-2].

[126] Eaton CJ, Cohn F, Bollinger CC. Laminaria tent as a cervical dilator prior to aspiration-type therapeutic abortion. Obstet Gynecol 1972;39:535–7 [Evidence Grade: II-3].

[127] Bryman I, Granberg S, Norstrom A. Reduced incidence of postoperative endometritis by the use of Laminaria tents in

connection with first trimester abortion. Acta Obstet Gynecol Scand 1988;67:323–5 [Evidence Grade: I].

[128] Munsick RA, Fineberg NS. Cervical dilation from multiple laminaria tents used for abortion. Obstet Gynecol 1996;87:726–9 [Evidence Grade: II-2].

[129] Manabe Y, Mori T, Yoshida Y. Decidual morphology and F prostaglandin in amniotic fluid in stretch-induced abortion. Obstet Gynecol 1984;64:661–5 [Evidence Grade: III].

[130] Krammer J, O'Brien WF. Mechanical methods of cervical ripening. Clin Obstet Gynecol 1995;38:280–6 [Evidence Grade: III].

[131] Bokstrom H, Wiqvist N. Preoperative dilatation of the cervix at legal abortion with a synthetic, fast-swelling hygroscopic tent. Acta Obstet Gynecol Scand 1989;68:313–8 [Evidence Grade: II-3].

[132] Skjeldestad FE, Tuveng J. Cervical dilatation with Lamicel in first trimester therapeutic abortion. Int J Gynaecol Obstet 1990;33:153–7 [Evidence Grade: I].

[133] Darney PD, Dorward K. Cervical dilation before first-trimester elective abortion: a controlled comparison of meteneprost, laminaria, and hypan. Obstet Gynecol 1987;70:397–400.

[134] Bartz D, Maurer R, Allen RH, Fortin J, Kuang B, Goldberg AB. Buccal misoprostol compared with synthetic osmotic cervical dilator before surgical abortion: a randomized controlled trial. Obstet Gynecol 2013;122:57–63 [Evidence Grade: I].

[135] Borgatta L, Barad D. Prolonged retention of laminaria fragments: an unusual complication of laminaria usage. Obstet Gynecol 1991;78:988–90 [Evidence Grade: III].

[136] Liang ST, Woo JS, Tang GW. Ultrasonic localization of a displaced laminaria tent. Am J Obstet Gynecol 1983;146:988–9 [Evidence Grade: III].

[137] Hern WM. Laminaria versus Dilapan osmotic cervical dilators for outpatient dilation and evacuation abortion: randomized cohort comparison of 1001 patients. Am J Obstet Gynecol 1994;171:1324–8 [Evidence Grade: I].

[138] Wells EC, Hulka JF. Cervical dilation: a comparison of Lamicel and Dilapan. Am J Obstet Gynecol 1989;161:1124–6 [Evidence Grade: I].

[139] Wiebe ER, Rawling MJ. Vaginal misoprostol before first trimester abortion. Int J Gynaecol Obstet 1998;60:175–6 [Evidence Grade: I].

[140] Mittal S, Sehgal R, Aggarwal S, Aruna J, Bahadur A, Kumar G. Cervical priming with misoprostol before manual vacuum aspiration versus electric vacuum aspiration for first-trimester surgical abortion. Int J Gynaecol Obstet 2011;112:34–9 [Evidence Grade: I].

[141] Edwards D, Aitken R, Begg A, MacKay P, Marchant R. Predilatation of the cervix before suction curettage for therapeutic abortion in early pregnancy. Aust NZ J Obstet Gynaecol 1994;34:103–4 [Evidence Grade: II-3].

[142] Sharma M. Sublingual misoprostol for cervical priming in surgical first trimester pregnancy termination. J Obstet Gynecol India 2011;61:531–3 [Evidence Grade: I].

[143] Singh K, Fong YF, Prasad RN, Dong F. Vaginal misoprostol for pre-abortion cervical priming: is there an optimal evacuation time interval? Br J Obstet Gynaecol 1999;106:266–9 [Evidence Grade: I].

[144] Singh K, Fong YF, Prasad RN, Dong F. Evacuation interval after vaginal misprostol for preabortion cervical priming: a randomized trial. Obstet Gynecol 1999;94:431–4 [Evidence Grade: I].

[145] Burnett MA, Corbett CA, Gertenstein RJ. A randomized trial of laminaria tents versus vaginal misoprostol for cervical ripening in first trimester surgical abortion. J Obstet Gynaecol Can 2005;27:38–42 [Evidence Grade: I].

[146] Vimala N, Mittal S, Kumar S. Sublingual misoprostol before first trimester abortion: a comparative study using two dose regimens. Indian J Med Sci 2004;58:54–61 [Evidence Grade: I].

[147] Panchal HB, Godfrey EM, Patel A. Buccal misoprostol for cervical ripening prior to first trimester abortion. Contraception 2010;81:161–4 [Evidence Grade: II-2].

[148] Oppegaard KS, Qvigstad E, Nesheim BI. Oral versus self-administered vaginal misoprostol at home before surgical termination

of pregnancy: a randomised controlled trial. BJOG 2006;113:58–64 [Evidence Grade: I].

[149] Inal MM, Ertopcu K, Arici A, Ozelmas I. The effect of oral versus vaginal misoprostol on cervical dilatation in first-trimester abortion: a double-blind, randomized study. Eur J Contracept Reprod Health Care 2003;8:197–202 [Evidence Grade: I].

[150] Saxena P, Sarda N, Salhan S, Nandan D. A randomised comparison between sublingual, oral and vaginal route of misoprostol for pre-abortion cervical ripening in first-trimester pregnancy termination under local anaesthesia. Aust N Z J Obstet Gynaecol 2008;48:101–6 [Evidence Grade: I].

[151] Shetty J, Chawla R, Pandey D, Kamath A, Guddattu V. Sublingual misoprostol: a better choice for cervical priming before manual vacuum aspiration. Indian J Med Sci 2010;64:356–62 [Evidence Grade: I].

[152] Parveen S, Khateeb ZA, Mufti SM, Shah MA, Tandon VR, Hakak S, et al. Comparison of sublingual, vaginal, and oral misoprostol in cervical ripening for first trimester abortion. Indian J Pharmacol 2011;43:172–5 [Evidence Grade: I].

[153] Caliskan E, Filiz T, Yucesoy G, Coskun E, Vural B, Corakci A. Sublingual versus vaginal misoprostol for cervical ripening PRIOR TO manual vacuum aspiration under local anaesthesia: a randomized

study. Eur J Contracept Reprod Health Care 2007;12:372–7 [Evidence Grade: I].

[154] Ho PC, Ngai SW, Liu KL, Wong GC, Lee SW. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. Obstet Gynecol 1997;90:735–8 [Evidence Grade: I].

[155] Patel A, Talmont E, Morfesis J, Pelta M, Gatter M, Momtaz MR, et al. Adequacy and safety of buccal misoprostol for cervical preparation prior to termination of second-trimester pregnancy. Contraception 2006;73:420–30 [Evidence Grade: II-3].

[156] Hall G, Ekblom A, Persson E, Irestedt L. Effects of prostaglandin treatment and paracervical blockade on postoperative pain in patients undergoing first trimester abortion in general anesthesia. Acta Obstet Gynecol Scand 1997;76:868–72 [Evidence Grade: I].

[157] Gagne A, Guilbert E, Ouellet J, Roy V, Tremblay JG. Assessment of pain after elective abortion relating to the use of misoprostol for dilatation of the cervix. J Obstet Gynaecol Can 2010;32:244–53 [Evidence Grade: II-1].

[158] Chambers DG, Mulligan EC, Laver AR, Weller BK, Baird JK, Herbert WY. Comparison of four perioperative misoprostol regimens for surgical termination of first-trimester pregnancy. Int J Gynaecol Obstet 2009;107:211–5 [Evidence Grade: II-2].