



## Original research article

# Adjunct mifepristone for cervical preparation prior to dilation and evacuation: a randomized trial<sup>☆,☆☆,★</sup>

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## Abstract

**Objective:** The objective was to investigate mifepristone as a potential adjunct to cervical preparation for surgical abortion after 19 weeks of gestation, with the aim of improving procedure access, convenience and comfort.

**Methods:** This is a site-stratified, block-randomized, noninferiority trial of 50 women undergoing surgical abortion between 19 and 23 6/7 weeks of gestation randomized to receive either one set of osmotic dilators plus mifepristone the day prior to procedure (mifepristone group) or two sets of osmotic dilators (placed 18–24 h apart) in the 2 days prior to procedure (control group). All subjects received preprocedure misoprostol. Primary outcome was procedure time. Secondary outcomes included preoperative cervical dilation, ease of procedure, and side effects and pain experienced by subjects.

**Results:** Mean gestational age was similar between groups (20 weeks); more nulliparous subjects were randomized to the mifepristone group (46% vs. 12%,  $p=.009$ ). Mean procedure times were similar: mifepristone group 11:52 (SD 5:29) vs. control group 10:56 (SD 5:08); difference in means  $-56$  s, with confidence interval (95% CI  $-4:09$  to  $+2:16$ ) not exceeding the 5-min difference we a priori defined as clinically significant. Preprocedure cervical dilation did not differ and was  $>3$  cm for the majority of subjects in both groups. There was no difference ( $p=.6$ ) in ease of procedure reported by providers. Preoperative (postmisoprostol) pain and postoperative pain levels were greater with mifepristone ( $p=0.02$  and  $p=0.04$  respectively). Overall subject experience was not different ( $p=0.80$ ), with most reporting a “better than expected” experience.

**Conclusions:** Mifepristone with one set of osmotic dilators and misoprostol did not result in longer procedure times or less cervical dilation than serial (two sets) of osmotic dilators and misoprostol, and has the potential to improve access to second trimester abortion without compromising safety.

**Implications:** Use of mifepristone for cervical preparation before surgical abortion after 19 weeks allows for fewer visits and fewer osmotic dilators without compromising cervical dilation or increasing procedure time.

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**Keywords:** Mifepristone; Second-trimester abortion; Surgical abortion; Dilation and evacuation; Osmotic dilators

## 1. Introduction

With an estimated 1.06 million abortions performed in the United States in 2011 [1], abortion is one of the most common surgical procedures. According to the Centers for Disease

Control and Prevention [2], of the 765,651 abortions performed in the United States in 2010, the large majority were performed in the first trimester, 6.9% between 13 and 20 weeks of gestation and only 1.2% (approximately 9200) performed at greater than 21 weeks. Although 23% of abortion providers perform procedures after 20 weeks of gestation [1], these providers are often concentrated in urban areas and coastal cities, complicating access for many women, especially those who live at great distances from such providers.

The risk of complications with dilation and evacuation (D&E) — including uterine perforation, bleeding, infection, retained products of conception and cervical injury — increases as gestational age increases, with a disproportionate two thirds

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of all abortion complications occurring during second-trimester abortion [3]. Preprocedure cervical preparation, using a combination of osmotic dilators and pharmaceutical methods, is associated with a decreased risk of complications [4–7]. A survey of US abortion providers in 2006–2007 showed that 86% of providers used osmotic dilators and 74% use both osmotic dilators and misoprostol for preprocedure cervical preparation [8]. There is insufficient evidence to define the number of dilators or length of time required for cervical preparation for D&E, but after 19–20 weeks, expert opinion recommends at least 1 day of cervical preparation [4]; one or two sets of osmotic dilators placed 24–48 h prior to the procedure is common clinical practice [9]. Protocols requiring multiple-day preparation may be particularly burdensome for patients traveling to obtain an abortion, requiring more time off work and money for hotel accommodations, in addition to the discomfort of repeated outpatient procedures to place osmotic dilators.

Mifepristone is a synthetic steroid that acts as an antiprogesterone, competitively binding to progesterone receptors and preventing endogenous progesterone from binding [10,11]. Pretreatment with mifepristone likely increases uterine sensitivity to prostaglandins like misoprostol [12–14]. When given prior to first-trimester surgical abortion, mifepristone has been shown to cause significant increase in cervical dilation compared to placebo [15,16].

Use of mifepristone for second-trimester induction abortion has been shown to decrease morbidity and reduce the interval of induction to abortion (fetal expulsion) [16–21]. The data on its effect on cervical dilation prior to second-trimester surgical abortion are much more limited. One placebo-controlled study by Carbonell et al. [22] showed an increase in cervical dilation and a decrease in procedure time when mifepristone was used in addition to osmotic dilators and misoprostol prior to D&E between 12 and 19 weeks of gestational age. A randomized controlled trial by Borgatta et al., comparing mifepristone and misoprostol with osmotic dilators and misoprostol for abortion from 15 to 18 weeks, showed equivalence in procedure time with mifepristone compared to osmotic dilators [23]. These works suggest that mifepristone contributes to the expeditiousness of these procedures by increasing cervical dilation or pliability, or both. However, while more than 89% of abortions after 20 weeks of gestation in the United States are performed by D&E [2], there is little research on mifepristone for cervical preparation prior to D&E, particularly at greater than 19 weeks of gestation. We hypothesized that subjects who receive 1 day of cervical preparation using mifepristone and one set of osmotic dilators and misoprostol will have procedure times that are not significantly longer than cervical preparation with two sets of osmotic dilators over two days plus misoprostol.

## 2. Methods

We recruited subjects with singleton, viable intrauterine pregnancy presenting for scheduled outpatient abortion between 19 and 23 6/7 weeks of gestation (by ultrasound

dating) at Stanford Hospital and Clinics or Santa Clara Valley Medical Center from June 2012 to June 2013. Subjects had to be fluent in English or Spanish, > 18 years of age, able to give informed consent and comply with study protocol. Exclusion criteria included allergy to any study medication. The Stanford and the Santa Clara Valley Medical Center Institutional Review Boards approved the study.

We enrolled subjects at their initial consultation, at least 2 days prior to their scheduled procedure, and obtained informed consent. We randomized subjects, using a computer-generated, site-stratified, variable block size randomization sequence to receive either (a) two sets of osmotic dilators placed 18–24 h apart starting 2 days prior to their scheduled procedure (control group) or (b) one set of osmotic dilators and 200 mg oral mifepristone the day prior to their procedure [18] (mifepristone group). Using opaque, numbered envelopes, allocation was revealed to research participants and coordinators at the time of randomization. We administered 1 mg intraamniotic digoxin the day prior to procedure and 400 mcg of buccal misoprostol 90 min prior to abortion to all subjects (per standard practice at both institutions). All procedures were performed by a provider blinded to the treatment arm, in an operating room, under deep sedation or general anesthesia using standard extraction techniques.

We chose procedure time as our primary outcome, as inadequate cervical preparation would likely manifest itself by longer procedure times reflecting the need for further cervical dilation and manipulation. A noninferiority design was used. The primary outcome was mean procedure time, and clinical inferiority was defined a priori as 5 min longer. This was chosen as a time difference that would be meaningful to the provider. Prior studies have shown procedure time to be normally distributed with standard deviations of approximately 5 min [5,22]. We calculated that 22 subjects in each group were required to show that the mean procedure time for the intervention group was no more than 5 min longer than the control group, with a power of 0.9 and a one-tailed alpha of 0.05. We planned to recruit 50 subjects, anticipating 10% loss of subjects due to dropout or disqualification.

We used synthetic osmotic dilators (Dilapan-S, 4 mm) for both groups, placed through the internal cervical os after administration of a paracervical block. The mifepristone group received mifepristone (200 mg) and had 4–5 osmotic dilators placed the day prior to the abortion, while the control group had 2–4 osmotic dilators placed 2 days prior to the procedure and another 4–5 osmotic dilators added the day prior to the scheduled abortion (total 6–9). We administered a 100-mm visual analog scale (VAS) with anchors of *no pain* to *worst pain imaginable* at baseline and after speculum insertion, paracervical block and osmotic dilator insertion. VAS was also administered twice on procedure day: preoperatively (after misoprostol) and 30–60 min postprocedure. An additional VAS with anchors *worse than I expected* to *better than I expected* was used to assess overall experience.

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