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Mifepristone vs. osmotic dilator insertion for cervical preparation prior to surgical abortion at 14–16 weeks: a randomized trial☆,☆☆,★

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Abstract

Background: Cervical preparation is recommended before second-trimester abortion. We investigated the use of a pharmacologic method of preparation, mifepristone, as compared to osmotic dilators for surgical abortions at 14–16 weeks.
Study Design: This was a randomized, parallel-group study with concealed allocation. Women were allocated to receive osmotic dilators or mifepristone 200 mg orally 24 h prior to abortion. The study population was 50 women seeking surgical abortion at 14–16 menstrual weeks in a hospital-based abortion service. The primary outcome was the length of time to perform the procedure; the study had 80% power to detect a difference of more than 3 min in procedure time. Secondary outcomes included cervical dilation, side effects and acceptability.
Results: The mean abortion time for the osmotic dilator group was 8.00 min [95% confidence interval (CI) 6.75–11.47], and that for the mifepristone group was 9.87 min (95% CI 8.93–11.36). Side effects of pain were more common in the osmotic dilator group.
Conclusion: Mifepristone did not increase the time for abortion by more than the prespecified margin (3 min). Women preferred mifepristone to osmotic dilators.

Keywords: Abortion; Second trimester; Mifepristone; Osmotic dilators; Laminaria; Cervical priming

1. Introduction

Cervical preparation is recommended before second-trimester surgical abortion [1,2]. The purpose of the preparation is to soften and open the cervix so that instruments can be safely introduced. Osmotic dilators are one of the most widely used methods of cervical preparation. Dilator insertion can be uncomfortable, and many women experience cramping and pain while the dilators are in place. Dilator insertion also requires a trained provider. To avoid dilator insertion, pharmaceutical alternatives have been studied. One alternative is misoprostol, a prostaglandin that a woman takes several hours prior to a planned surgical procedure. However, misoprostol can have side effects including cramping, nausea and pain, and the efficacy for cervical preparation in the second trimester is not well established [2].

Mifepristone, a progesterone receptor modulator, is used in the first trimester and second trimester as part of medical abortion procedures. Compared to regimens that use misoprostol alone, mifepristone increases the efficacy of medical abortion in the first trimester [3] and decreases the induction-to-abortion interval in the second trimester [4]. Mifepristone alone has also been shown to be effective for cervical preparation before first-trimester surgical abortion [5–7].

The purpose of this study is to determine whether mifepristone taken the day before abortion is comparable to osmotic dilators for patients undergoing a surgical termination of pregnancy between 14 and 16 weeks. If mifepristone proves to be effective, it will have the

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advantages of allowing women to avoid dilator insertion the day prior to abortion, or a wait of several hours for the misoprostol to take effect, while still gaining adequate cervical preparation.

The primary hypothesis is that mifepristone is not significantly inferior to osmotic dilators using the measure of total abortion time. We chose to measure procedure time as the primary outcome, as we felt that procedure time was an important facet of procedure acceptability, both to clinicians and to patients. However, recognizing that the time required to perform an abortion is only one aspect of acceptability, we also assessed patient discomfort before, during and after the abortion, and patient and provider opinions about the process.

2. Materials and methods

Women aged 18–45 years requesting an induced abortion between 14 and 16 menstrual weeks were eligible for the study. All women had ultrasound dating of the pregnancy prior to study entry. Women were excluded from the study if they had fetal demise, ruptured membranes, spontaneous abortion, active substance abuse or did not speak English or Spanish. The study was approved by the Boston University Medical Center Institutional Review Board. Informed consent was obtained from all participants prior to the start of study procedures by one of the investigators.

Study procedures began on the day prior to the abortion. After eligibility was confirmed and informed consent was given, women were allocated to one of two groups: the osmotic dilator group or the mifepristone group. The 1:1 randomization was computer generated, using block sizes varying between 6 and 10. Allocation was carried out using sequentially numbered opaque vials; the vials concealed the group assignment until they were opened. The vials were prepared by the research pharmacy. Once allocation had occurred, treatment was not blinded.

Women in the osmotic dilator group had osmotic dilators placed 20–24 h prior to scheduled abortion. The procedure was as follows: women were first given ketorolac 60 mg im or ibuprofen 800 mg orally. The cervix was cleansed with povidone–iodine solution, and the cervix was infiltrated with 10 mL 1% lidocaine. Between three and six dilators were placed in the cervix based on clinician preference. Both laminaria and Dilapan (GEL-MED International spol s.r.o.) dilators were used. Doxycycline 200 mg orally was given after the dilators were inserted. Women were asked to rate the pain of insertion on an 11-point scale.

Women in the mifepristone group received mifepristone 200 mg orally with ingestion observed. No antibiotics or other medications were used.

Women in both groups were scheduled to return at 20–24 h after treatment for their abortion procedure. They answered a short questionnaire about overnight and morning symptoms prior to the abortion. All procedures were performed by experienced attending physicians or family planning fellows at Boston Medical Center.

For women in the dilator group, the dilators were removed immediately before the procedure or after speculum placement, according to operator preference. For all women, the time of speculum placement was recorded. A cervical block of 20 mL 1% buffered lidocaine with 4 U vasopressin was used for all women. A 14-mm suction cannula was used first. If the 14-mm cannula passed, the abortion was completed with suction and forceps. If the 14-mm cannula did not pass, cervical dilation was measured starting with a 39Fr Pratt dilator, followed by sequentially smaller dilators until a dilator passed easily. The operator could then dilate mechanically as much as deemed appropriate. The time that suction began was recorded. The time of completion of the procedure was defined as the time of speculum removal, which was also recorded. Suction was always used as the first intrauterine procedure; forceps were used at any time after the initial use of suction as needed.

After the procedure was completed, women were asked about the amount of discomfort during the procedure and their preferences for cervical preparation.

The primary outcome was the time from speculum placement to speculum removal ("procedure time"). Secondary outcomes included the length of time from the initial use of suction to speculum removal ("operative time") and cervical dilation at the beginning of the procedure. Secondary outcomes of discomfort were assessed with pain scores or by collapsing descriptive outcomes into binary outcomes. An 11-point scale (values from 0 to 10) was used to assess pain at a particular point in time, while descriptive categories were used to assess symptoms during a prolonged period, e.g., "overnight." Opinions about the method of cervical preparation were assessed with 5-point Likert scales. Physicians were asked to rate the ease of procedure on a 5-point scale.

The study was structured with a noninferiority design. The primary outcome, procedure time measured in minutes, was defined as inferior if the mean time for the mifepristone group was more than 3 min longer than the time for the osmotic dilator group, using a Student's t test. The 3-min figure was chosen because we felt that 3 min would be noticeable to the operator. The mean procedure time was expected to be 10 min. A one-sided t test with a 95% confidence interval (CI) and 80% power yielded a sample size of 24 women in each group. We planned to enroll 25 women in each group in case there were any withdrawals. Data were analyzed as intent-to-treat using SAS (Version 9, SAS Institute, Inc., Cary, NC, USA). Outcomes related to time were expressed as means and 95% CIs. A multiple regression analysis was performed to evaluate the relationship between the primary outcome and covariates, i.e., parity, gravidity and gestational age at the time of the procedure. Secondary outcomes were evaluated with χ^2 tests. A value of $p<.05$ was considered to be significant.