American Journal of Obstetrics and Gynecology (2006) **194**, 425–30

ELSEVIER

American Journal of
Obstetrics & Gynecology
www.ajog.org

Cervical preparation using laminaria with adjunctive buccal misoprostol before second-trimester dilation and evacuation procedures: A randomized clinical trial

Alison B. Edelman, MD, John G. Buckmaster, MD, Martha F. Goetsch, MD, Mark D. Nichols, MD, Jeffrey T. Jensen, MD

Department of Obstetrics and Gynecology, Oregon Health and Science University, Portland, OR

Received for publication April 5, 2005; revised July 6, 2005; accepted August 8, 2005

KEY WORDS
Dilation and evacuation
Second-trimester abortion
Laminaria
Misoprostol

Objective: This study was undertaken to determine whether buccal misoprostol improves cervical preparation achieved with laminaria before second-trimester dilation and evacuation procedures.
Study design: A randomized, double blind, placebo-controlled trial of preoperative cervical preparation with overnight laminaria and either buccal placebo or 400 μg buccal misoprostol approximately 90 minutes before second-trimester surgical abortion. Block randomization was used to provide balanced enrollment into 2 separate gestational age study groups: early (13-$15^{6/7}$) and mid (16-$20^{6/7}$) second trimester. Surgeons tested maximal cervical dilation by inserting the largest dilator that could be passed through the cervical os without force. Subject demographics and preprocedure symptoms were tracked.
Results: Groups were similar in regard to age, gravity, parity, delivery type, and gestational age. Data were analyzed from 125 women in the 13 to $15^{6/7}$ (30 misoprostol, 32 placebo) and 16 to $20^{6/7}$ (31 misoprostol, 32 placebo) gestational age groups. Overall, misoprostol treatment did not improve the initial mean dilation achieved with laminaria alone in either the 13 to $15^{6/7}$ (46.0 *fr* ± 5.0; placebo 45.0 *fr* ± 6.2, $P = .68$) or 16 to $20^{6/7}$ (50.9 *fr* ± 5.6, placebo 48.9 *fr* ± 5.2, $P = .16$) groups. However, a subanalysis of gestations 19 weeks or more demonstrated significantly greater dilation in the misoprostol group (53.6 *fr fr* ± 5.3, placebo 48.5 *fr* ± 5.0, $P = .01$). Subjects receiving misoprostol reported significantly more cramping than those receiving placebo (13-$15^{6/7}$ weeks misoprostol 25/30, 83%; placebo 17/32, 53%, $P = .02$; 16-$20^{6/7}$ week misoprostol 25/31, 81%, placebo 16/32, 50%, $P = .02$).
Conclusion: Cervical dilation with laminaria is augmented by 400 μg buccal misoprostol in gestations 19 weeks or more, but not in earlier gestations. Misoprostol causes more abdominal cramping.

Adequate cervical preparation has decreased the morbidity associated with second-trimester surgical terminations.[1,2] By eliminating the need for, or reducing the force needed to pass cervical dilators, cervical preparation with laminaria tent placement reduces the risk of complications associated with surgical abortion.[1-3] With increasing gestational age, the period for cervical preparation with laminaria can extend up to 48 hours. This extensive preprocedure preparation is cumbersome and time consuming for the physician

Reprints not available from the authors.

0002-9378/$ - see front matter © 2006 Mosby, Inc. All rights reserved.
doi:10.1016/j.ajog.2005.08.016

and patients may experience an increase in financial burden with time away from work and expenses incurred from travel and lodging.[4] Thus, alternative strategies designed to reduce or eliminate the need for laminaria represent important areas of research in abortion care.

Traditionally, cervical preparation for second-trimester abortions has been accomplished with serial placement of osmotic dilators. Recently, vaginal, oral, and buccal administration of misoprostol has proven successful for cervical preparation in first- and second-trimester surgical and medical abortions. In a randomized, double-blind, placebo-controlled trial of surgical abortion between 7 and 14 weeks' gestation, MacIsaac et al[5] found vaginally administered misoprostol produced cervical dilation superior, and oral misoprostol equivalent, to laminaria. Overall, vaginal administration results in more consistent absorption and better cervical dilation than oral dosing.[6-10] However, several studies have documented a preference by women for an oral route of delivery.[8,11]

The sublingual and buccal spaces offer alternative delivery sites designed to improve patient acceptability while minimizing side effects obtained with oral dosing. Pharmacokinetic studies demonstrate that sublingual dosing results in higher peak and area under the curve (AUC) concentrations than oral or vaginal administration, with oral administration showing the greatest variability.[6] Schaff et al[12] found that buccal administration of misoprostol resulted in significantly lower peak and AUC concentrations than sublingual. However, the greater activity of sublingual administration results in more gastrointestinal side effects (nausea, vomiting, diarrhea) than vaginal use.[13] Despite excellent clinical results after sublingual dosing, most subjects in 2 randomized trials expressed preference for the alternative administration choice (vaginal or oral).[14,15] In contrast, women receiving buccal misoprostol reported no difficulty placing the product in their cheek pouch, and indicated that the tablet had a chalky texture, but did not have a bad taste.[16] Therefore, buccal administration may represent a favorable alternative to oral or vaginal dosing.

We hypothesized that a combined misoprostol/laminaria approach should improve cervical preparation before second-trimester surgical abortions. The purpose of this study is to evaluate whether the addition of buccal misoprostol dosed 90 minutes before second-trimester surgical abortion improves cervical dilation produced by overnight laminaria.

Material and methods

A randomized, double-blind, placebo-controlled trial was conducted at the Lovejoy Surgicenter in Portland, Ore, from September 2002 to October 2004. The Institutional Review Board at Oregon Health and Sciences University approved the study protocols.

Women requesting termination of pregnancy with a gestation between 13 and $15^{6/7}$ weeks and 16 and $20^{6/7}$ weeks were recruited only after their decision to proceed with an abortion was confirmed. All women who met the following criteria were invited to participate: age 18 years or older, good general health, English speaking, and confirmation of gestational age by ultrasound. Exclusion criteria included subject refusal, inability to receive deep conscious sedation, or a contraindication to misoprostol. We excluded woman with pregnancies beyond $20^{6/7}$ because they undergo a 2-day cervical preparation with laminaria at this clinic.

Preprocedure counseling and evaluation were consistent with clinic protocols. Participants completed a demographics form before their procedure. Anesthesia consisted of deep conscious sedation by a certified nurse anesthetist using midazolam, propofol, fentanyl, and bag/mask ventilation. No paracervical block was used. Oxytocin (40 units in 1000 mL normal saline) was routinely administered in gestations 17 weeks and over at the start of the procedure.

Randomization occurred 1 day before the procedure and the same day as laminaria placement. Surgeons performing the procedures and staff counseling and enrolling subjects were blinded to treatment allocation. If clinically feasible, laminaria placement was limited to 1 in number for the 13 to $15^{6/7}$-week study, and 2 for the 16 to $20^{6/7}$-week study (Size LL, Nippon Laminaria Co). Some subjects received placement of an additional laminaria if the clinician determined successful retention of the laminaria required an additional laminaria stick. Subjects were randomized to receive either 400 μg of misoprostol or 500 mg of magnesium oxide (placebo). Women were instructed to self-administer the study medication in the buccal pouch 60 to 90 minutes before their procedure.

An investigator not involved with recruitment generated a separate randomization sequence by computer for each gestational age group. Only this investigator, the study coordinator, and the study nurse had knowledge of the randomization sequence. This investigator prepared all data sheets and medication packets without the knowledge of the investigators enrolling women. The data sheets and medication tablets were each placed in sealed opaque envelopes. The medication and subject data sheets were labeled with, and subjects enrolled by consecutive numbers. No identifiers of treatment group were placed on subject data sheets or the medication, only the number in order of enrollment.

Two experienced abortion providers performed the procedures using electric suction aspiration combined with traditional extraction techniques under deep conscious sedation. Surgeons tested maximal cervical dilation by finding the largest dilator that passed through the cervical os without force. They systematically started with the largest cervical dilator (61 mm in circumference)