Transcervical Balloon Compared to Osmotic Dilators Prior to Surgical Abortion: a Non-Inferiority Randomized Trial

Study Protocol and Statistical Analysis Plan

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Protocol

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Project Title: Transcervical Balloon compared to Osmotic Dilators prior to Surgical Abortion: a Non-Inferiority Randomized Trial

We will conduct an unblinded, randomized, non-inferiority trial of 40 participants undergoing second trimester abortion between 18 and 23 weeks of gestation at Stanford Health Care. Participants will be approached during their initial consultation for abortion, after consent for the abortion has been obtained**.** They will sign consent and be randomized on the day of cervical preparation, one day prior to their D&E. We will use 1:1 randomization using a computer-generated variable block sequence to ensure balance of treatment groups.

We will include participants of at least 18 years of age presenting to clinic for second trimester abortion at 18 to 23 weeks and 6 days gestation confirmed by ultrasound (which will include 17 weeks and 6 days gestation on day of cervical preparation, one day prior to D&E, with or without digoxin). We will include participants who are able to provide informed consent and comply with study protocol, English or Spanish-speaking, and a candidate for outpatient cervical preparation. Exclusion criteria will include anyone with an allergy to misoprostol, mifepristone or any study medication, premature rupture of membranes, intrauterine fetal demise, placenta previa, suspected abnormal placentation or evidence of infection at the time of enrollment. **Participants will be excluded on day of cervical preparation, after randomization, if their initial cervical exam is 2cm dilated and 50% effaced or more.**

Participants randomized to the osmotic dilator group will receive between 2 to 5 Dilapan-S using Table 1 as guidance, depending on gestational age. Those randomized to the Foley balloon group will have a Foley catheter inserted until the balloon lies beyond the internal os that will be filled with 30 mL of sterile water or saline.[1–3]

Placement of balloon or osmotic dilators will be performed in dorsal lithotomy position, with use of a speculum, standard 10-12mL paracervical block, and tenaculum or atraumatic grasper with use of adjunct initial dilation if needed (ie: os finder, sound). Adjunctive medications will be used based on our cervical preparation protocol (Table 1). Participants will receive mifepristone 200mg orally within 1 hour of osmotic dilator/balloon placement.[4,5] All participants will receive misoprostol 400 ug buccal 2-3 hours prior to their scheduled D&E.[5,6] Per our institutional practices, participants over 22 weeks gestation will be offered digoxin for feticide, administered upon request in earlier gestations, and use will be recorded. If the participant receives digoxin, it will be administered after dilator placement, and after the participant is asked about their pain level. Although downward traction applied to the balloon

has been associated with a shorter time to expulsion, it has been associated with more pain and bleeding.[3,7]. Given these unfavorable effects, and the potential challenges of maintaining downward traction as an outpatient, initial gentle traction will be applied with the catheter taped to the participant's medial thigh; however, participants will not be instructed to maintain tension as an outpatient.

Our primary outcome will be procedure duration (speculum insertion to removal). Prior studies have demonstrated that procedure time is normally distributed with a standard deviation of 5 minutes.[8,9] We will define 5 minutes as our non-inferiority threshold. To achieve 80% power with a one-sided alpha 2.5% to detect this difference, we require 16 participants per group and 32 total. Anticipating loss to follow up, we will plan to enroll 20 participants per group.

Description of the data to be collected and what statistical procedures will be used to answer the hypothesis and research question.

Day prior to abortion: We will collect contact information, baseline demographics and history (age, BMI, race, education, indication for abortion, parity, mode of prior deliveries, prior abortion, prior osmotic dilators, number of weeks gestation, prior cervical procedures, prior surgeries, medical problems, medications, allergies). We will record baseline pain prior to positioning patient for cervical preparation. We will collect information on initial digital cervical exam (dilation/effacement/consistency/position), time of osmotic dilator or balloon placement, number of Dilapan-S if applicable, dilator placement duration, provider ease of placement by VAS, participant reported pain after procedure (within 5 minutes of speculum removal) by VAS, reported maximum pain during procedure by VAS. If digoxin is administered, it will only be done after dilator placement and all pain levels are collected.

Day of abortion. Preoperative information will also include maximum reported pain overnight prior to misoprostol administration, time of misoprostol intake, documentation of time of osmotic dilator or Foley balloon removal or expulsion (total time with dilator in place), symptoms overnight, reported maximum pain overnight by VAS, reported number of ibuprofen and Norco pills taken overnight, patient satisfaction by VAS, and if they would recommend their type of dilation for future patients.

Abortion: We will record digital cervical exam (dilation/effacement/consistency/position), need for additional mechanical dilation, total duration of procedure (speculum insertion to removal), time from insertion of first intrauterine instrument (suction cannula or forceps) to final removal of intrauterine instrument (suction cannula), type of anesthesia, primary surgeon level (senior resident in their last half of final year, fellow, faculty), surgeon satisfaction with dilation by VAS, surgeon's ease with procedure by VAS, EBL, complications (cervical laceration, hemorrhage, perforation, infection, intact expulsion).

Post procedure: Prior to discharge, at least 60 minutes but before 120 minutes after procedure (time to be recorded), participants will be asked about overall experience by VAS, and current and maximum pain since procedure by VAS.

Table 1: Cervical preparation protocol based on gestational weeks

Gestational weeks	Misoprostol (400mcg buccal 2-3h prior to D&E)	Mifepristone (200 mg PO within 1h prior to dilator placement)	# of Dilapan-S	Digoxin
18 – 19w6d	Yes	Yes	2-3	By request
20 – 21w6d	Yes	Yes	3-4	By request
22 – 23w6d	Yes	Yes	4-5	Offered