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Original research article

Self-administered lidocaine gel for local anesthesia prior to osmotic dilator placement: a randomized trial☆,☆☆,★,★★

Gillian B. Schivone *,[1], Klaira Lerma, Corinne Montgomery, Paul Wright, Jennifer A. Conti, Paul D. Blumenthal, Kate A. Shaw

Stanford University, Department of Obstetrics and Gynecology, Division of Family Planning Services and Research, 300 Pasteur Drive, HG 332, Palo Alto, CA, USA 94305

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ABSTRACT

Objective(s): To compare pain scores during cervical dilator placement prior to dilation and evacuation (D&E) with patient-administered vaginal lidocaine gel versus lidocaine paracervical block (PCB).
Study design: We conducted an unblinded randomized trial of women ≥18 years of age undergoing surgical abortion at ≥16 weeks' gestation in two outpatient clinics. We randomized participants to receive self-administered lidocaine gel 2% 20 mL intravaginally 15–30 min before procedure initiation or lidocaine 1% 12 mL PCB immediately prior to dilator placement. Participants rated their pain at various time points using a visual analog scale (VAS), including anticipated and baseline pain, speculum insertion, tenaculum placement, cervical dilator placement (primary outcome) and speculum removal.
Results: We enrolled 72 women and analyzed data for 69 participants. Sociodemographic characteristics and VAS scores at all time points, except for anticipated pain, were similar between groups. The median pain score with dilator placement was 48 mm in the gel group and 61 mm in the PCB group ($p=.23$). Procedure times for the gel group and PCB group were 3.7 min and 5.2 min, respectively ($p<.01$). Lidocaine gel was noninferior to PCB for reported pain scores (VAS) with dilator placement, with a difference in means of −8 mm (95% CI −21, 5) favoring the gel.
Conclusions: Self-administration of lidocaine gel prior to placement of cervical dilators for D&E is noninferior to paracervical lidocaine block for local anesthesia and is a potential alternative to PCB for pain management with osmotic dilator placement.
Implications: Lidocaine gel and similar products represent noninvasive, nonpainful methods of local anesthesia for a variety of outpatient gynecologic procedures. Given our noninferiority findings, if gel anesthetics are available, they should be considered as an alternative to paracervical block.

1. Introduction

In the United States, approximately 11% of abortions are performed in the second trimester [1], primarily (87%) by dilation and evacuation (D&E) [2]. A critical factor for preventing complications in second-trimester D&E is adequate cervical preparation, which is commonly accomplished by preoperative placement of osmotic dilators. Dilator placement can be painful, with one study reporting pain scores ranging from 40 to 70 mm on a 100-mm visual analog scale (VAS) [3]. Although there is no standardized analgesic or anesthetic treatment used during this procedure, approximately 73% of clinicians in a national survey of abortion providers reported using a paracervical block (PCB) [4]. Soon et al. [5] demonstrated reduced pain with osmotic dilator insertion using a PCB as compared to a sham block. However, PCB itself is painful, resulting in pain scores of 25–60 mm on a 100-mm VAS [6–9].

A self-inserted analgesic prior to dilator placement could replace a painful injection, thus eliminating injection-associated pain and increasing patient-centeredness [6,10]. We performed this trial to evaluate if women's pain with cervical dilator placement following self-insertion of vaginal lidocaine gel would be noninferior to pain with the procedure following PCB. We also performed an exploratory pharmacokinetic study in normal female volunteers with vaginal lidocaine

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* Corresponding author.
E-mail addresses: gschivone@wustl.edu (G.B. Schivone), klerma@stanford.edu (K. Lerma), corinnemontgomery@stanford.edu (C. Montgomery), jacquelinebarbic@gmail.com (P. Wright), jconti@stanford.edu (J.A. Conti), pblumen@stanford.edu (P.D. Blumenthal), kateshaw@stanford.edu (K.A. Shaw).
[1] Current affiliation: Washington University School of Medicine, Department of Obstetrics and Gynecology, Division of Family Planning.

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gel administration. The presumed serum lidocaine toxicity level is approximately 5 mcg/mL [11]. Although nontoxic serum lidocaine levels are present after nasopharyngeal lidocaine gel placement, similar data are not available with vaginal lidocaine gel placement [12,13]. We hypothesized that vaginal lidocaine gel administration would not result in toxic serum lidocaine levels.

2. Materials and methods

2.1. Study design and allocation

We conducted this noninferiority, open-label randomized trial at the Stanford University Gynecology Clinic and the Family Planning Specialists Medical Group (FPS). FPS is an independent outpatient abortion clinic in Oakland, California. We obtained institutional review board approval from Stanford University prior to initiation. We included participants who were ≥18 years of age undergoing second-trimester surgical abortion at ≥16 weeks of gestation. We excluded participants who elected moderate sedation for dilator placement, had an allergy to lidocaine or had a pregnancy complicated by rupture of membranes. Research personnel obtained study consent after participants consented for an abortion procedure, and randomized them to one of two groups by computer-generated block randomization in permuted blocks of four and six. We maintained allocation concealment with opaque, sequentially numbered envelopes, opened immediately after enrollment. We elected not to use a sham PCB for subject blinding, as we wanted to directly compare these two types of cervical anesthesia without introducing other potential sources of pain [5,9].

We instructed participants in the lidocaine gel group to self-insert lidocaine gel 2% 20 mL vaginally (400 mg total) 15–30 min before the procedure using a 20-mL sterile, Luer-lock syringe. Research coordinators explained the proper insertion technique using a photograph of gel insertion on a pelvic model. Participants in this group received no additional cervical anesthesia. Clinicians placed the PCB in the following standardized manner: lidocaine 1% 12 mL (120 mg) was injected through a 22-gauge spinal needle, with 2 mL injected superficially at the tenaculum site (6 or 12 o'clock on the cervix) followed by immediate tenaculum placement and then injection of the remaining 10 mL into two equal aliquots at 4 and 8 o'clock along the cervicovaginal junction. The injection was continuous from superficial to deep (1–2 cm) to superficial (injecting with insertion and withdrawal). Dilator placement began immediately after application of the block. To limit health care provider variability, a group of five attending and two fellow physicians performed all procedures.

2.2. Measures

The primary study outcome was pain perceived on a 100-mm VAS at the time of cervical dilator placement. Secondary outcomes included pain perceived at additional time points also measured with a VAS: anticipated pain with the procedure as a whole (measured 30 min before the procedure); baseline pain (measured immediately prior to the procedure); and pain at the time of speculum placement, tenaculum placement and speculum removal. We also measured global satisfaction with the procedure on a VAS prior to discharge. Additionally, we assessed the incidence of complications and provider reported ease of insertion of dilators. We defined major complications as any problem that resulted in the patient requiring an additional procedure in the clinic or transfer to the hospital. Trained research personnel collected all data.

The minimum clinically significant difference in pain scores on a 100-mm VAS is 13–16 mm [14–16]. Pain scores at the time of laminaria insertion range from 40 to 70 mm, with standard deviations of 22–23 mm [3]. Utilizing a noninferiority limit of 15 mm, a standard deviation of 22, an alpha of 2.5 and 80% power, we required a total of 68 participants to determine a clinically significant difference. We added an additional 5% for a total of 72 participants to account for protocol deviation and participant dropout.

2.3. Statistical analysis

Research coordinators collected and managed all study data using REDCap, an electronic data capture tool hosted at the Stanford Center for Clinical Informatics. We compared demographic characteristics between the two groups with descriptive statistics using χ^2 test or Student's t test, as appropriate. We calculated both mean and median VAS scores to be consistent with prior similar literature — and to account for the fact that pain scores on a VAS are non-normally distributed — utilizing Student's t test and Mann–Whitney U test, respectively. We utilized a difference of means calculation to determine noninferiority. We also analyzed median pain scores by parity with a Mann–Whitney U test. Finally, we performed a multivariable analysis to evaluate potential confounders and determine independent predictors of pain at the time of cervical dilator placement utilizing age, body mass index (BMI), gestational age and parity as variables.

2.4. Serum lidocaine substudy

We recruited an additional 10 female, nonpregnant, healthy volunteers for participation in our serum lidocaine substudy. Research personnel consented participants, and a clinic nurse obtained IV access in each participant and drew a baseline serum lidocaine level. We instructed participants to place lidocaine gel 2% 20 mL vaginally in the same manner as the participants in the main study (Section 2.2). We collected blood samples from the participant's IVs at 5, 10, 15, 25, 45 and 60 min after gel placement. Samples were kept on ice and shortly thereafter analyzed at Stanford Hospital Center's clinical laboratory. The laboratory utilizes an assay that detects serum lidocaine levels above 0.5 mcg/mL; any level below 0.5 mcg/mL is considered "undetectable."

3. Results

From July 2016 to April 2017, we assessed 108 women for eligibility and enrolled 72 qualifying and consenting participants utilizing a per protocol analysis plan with a noninferiority design (Fig. 1). We did not include two gel group patients in the analysis who did not have dilators placed; one had a severely stenotic cervix that could not be dilated mechanically, and the other had difficulty with placement due to a combination of anatomical and pain management reasons. One participant in the CB group changed her mind after randomization and opted not to proceed with abortion. Demographic characteristics of the remaining 69 women (34 in the gel group and 35 in the PCB group) were similar (Table 1). Women in the gel group had the gel in place 31±12 min before dilator placement.

Table 2 demonstrates pain scores throughout the study procedures. Women who received lidocaine gel demonstrated a noninferior median pain score with dilator placement as compared to women who had a PCB (49 vs. 61, respectively, p=.23). The gel group participants also demonstrated noninferior pain scores at all other time points except for median anticipated pain (46 vs. 61, respectively, p=.02). Median pain scores were similar between groups when stratifying by parity. For nulliparous women, median pain scores were 38 (7–92) in the gel group and 62 (7–100) in the PCB group (p=.21); for parous women, median pain scores were 53 (1–95) and 61 (0–92) in the gel and PCB groups, respectively (p=.63). In multivariable analysis, none of the examined variables predicted higher pain scores with dilator placement.

Utilizing a difference in means calculation, lidocaine gel was noninferior to PCB by our noninferiority margin of 15 mm, with a difference in means of −8 mm (95% CI −21, 5) favoring the gel.

We identified no lidocaine toxicity event or major complications with either anesthetic application. Participants in the serum lidocaine

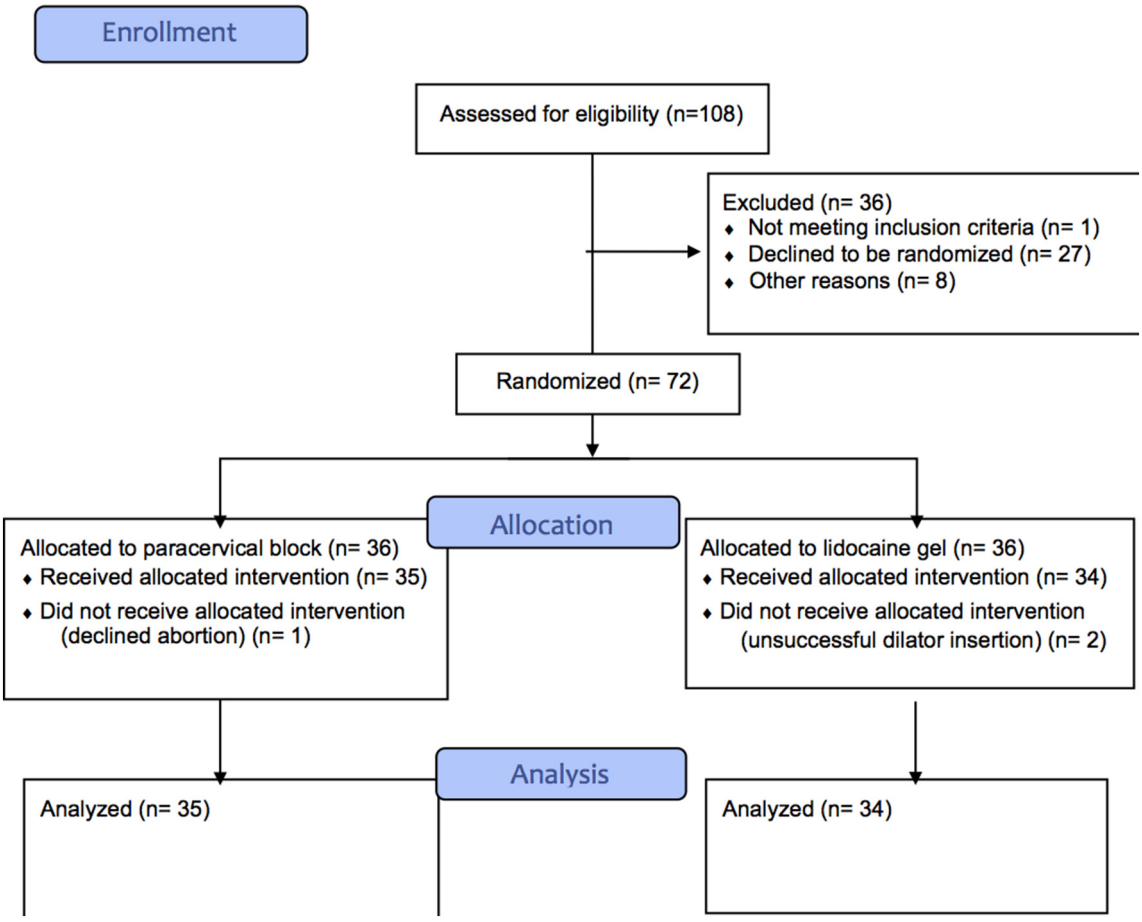

Fig. 1. Flow of participants.

substudy had serum lidocaine levels <0.05 mcg/mL at all time points. Attending-level clinicians performed more dilator insertions in the gel group than the PCB group (33/34 [97%] vs. 25/35 [71%], respectively, p<.01). Procedure times the gel group and PCB group were 3.7 min and 5.2 min, respectively (p<.01). Women in both groups received the same median number of dilators (3 [range 1–5] vs. 3 [range 1–6], respectively, p=.54). Using a VAS, clinicians reported similar median levels of dilator insertion difficulty between groups (12 [range 0–100] in the gel group vs. 11 [range 0–92] in the PCB group p=.55). Participants in each group noted similar VAS scores for overall pain, satisfaction with the procedure and likelihood to recommend the procedure (Table 3).

Table 1
Sociodemographic and clinical characteristics of women undergoing osmotic dilator insertion for second-trimester abortion with lidocaine gel or PCB (n=69)

	Lidocaine Gel (n=34)	PCB (n=35)	p value
Age (years)[a]	28±8	27±7	.41
BMI (kg/m^2)[a]	26±5	28±6	.25
Gestational age (weeks + days)[b]	19+0 (16+0–23+3)	19+3 (16+0–24+0)	.41
Parity[c]			.73
Nulliparous	16 (47)	15 (43)	
Parous	18 (53)	20 (57)	
Race[c]			.20
White	14 (41)	19 (54)	
Black or African American	14 (41)	9 (26)	
Other	6 (18)	7 (20)	
Ethnicity[c]			.59
Hispanic or Latina	11 (32)	12 (34)	
Non-Hispanic or Latina	22 (65)	23 (66)	
Unknown/unreported	1 (3)	0 (0)	

All data are presented as n (%), mean ± standard deviation or median (range).
[a] Student's t test.
[b] Mann–Whitney U test.
[c] χ^2 test.

4. Discussion

We found that patient-administered vaginal lidocaine gel is noninferior to PCB for local anesthesia with cervical dilator placement prior to D&E. Strengths of the study include the randomized, noninferiority trial design with ethnic and racial diversity among participants. We also included a substudy addressing the pharmacokinetics of vaginal lidocaine gel as this had not been investigated previously. Serum

Table 2
Median pain scores (VAS) at various times for women undergoing osmotic dilator insertion for second-trimester abortion with lidocaine gel or PCB (n=69)

	Lidocaine gel n=34	PCB n=35	p value
Anticipated pain	46 (1–86)	61 (14–96)	.02
Baseline pain	1 (0–27)	3 (0–42)	.05
Speculum insertion	21 (0–68)	28 (0–87)	.24
Tenaculum placement	36 (1–90)	44 (0–93)	.43
PCB	-	56 (0–95)	-
Dilator placement	49 (1–95)	61 (0–100)	.23
Speculum removal	25 (0–88)	39 (0–80)	.17

All data are presented as median (range).
All data reported on a VAS in mm.
Statistical analyses with Mann–Whitney U test.

Table 3
Median scores (VAS) for overall pain, satisfaction and likelihood to recommend for women undergoing osmotic dilator insertion for second-trimester abortion with lidocaine gel or PCB (n=69)

	Lidocaine gel n=34	PCB n=35	p value
Overall pain	48 (2–86)	62 (0–90)	.34
Overall experience	73 (4–100)	55 (2–100)	.63
Likelihood to recommend	84 (8–100)	78 (2–100)	.84

All data are presented as median (range).
All data reported on a VAS in mm.
Statistical analyses with Mann–Whitney *U* test.

lidocaine levels up to 1 h after placement of the gel were <.05 mcg/mL in all participants, suggesting that this intervention resulted in lidocaine levels far below the level of toxicity (approximately 5 mcg/mL) [11].

Limitations of the study include a lack of subject blinding, which may affect patient VAS scores and clinician behavior. We considered attempting patient blinding with placebo gel and a sham PCB. However, Renner et al. found that subjects in their study, despite receiving a sham block, could differentiate their group allocation [9]. Additionally, Soon at al noted that patients experienced pain with a sham block, which could have artificially decreased the difference in pain scores between our two groups [5]. A benefit of the lidocaine gel is the lack of pain with administration as there is no injection.

Another limitation is the possibility of variable lidocaine levels due to participant difficulty with gel self-administration. This issue could be improved with application of the gel in a suppository or concentrated gel pack. Given the necessity of additional time for the lidocaine gel to take effect, we would recommend that patients place the gel at the beginning of their clinical visit, allowing the gel to absorb during their visit. A potential issue with generalizability is our use of a lidocaine 1% 12 mL PCB. A nationwide survey of abortion providers by the National Abortion Federation noted a fairly even split among clinicians in terms of preferred PCB dosing: 36% use a volume of 20 mL, 12% use a volume of 15 mL, and 27% use a volume of 10 mL [17]. It is possible that a study comparing lidocaine gel and a lidocaine 20 mL PCB may not have the same results as we report here.

Limitations of the serum lidocaine substudy include the variability of gel placement as noted previously, as well as the fact that we completed this aspect of the study with nonpregnant healthy volunteers. There are limited studies regarding lidocaine toxicity in pregnancy to which we could have compared our results. This study should be repeated in pregnant patients to confirm the validity of our findings.

Overall, our results suggest that vaginal lidocaine gel is a noninvasive and noninferior alternative to PCB for local anesthesia with osmotic dilator placement and should be considered in patients to avoid the drawbacks of cervical injection.

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References

[1] Induced abortion in the United States. Guttmacher Institute; 2014 [Retrieved August 24, 2015].
[2] Newmann S, Dalve-Endres A, Drey EA. Society of Family Planning. Clinical guidelines. Cervical preparation for surgical abortion from 20 to 24 weeks gestation. Contraception 2008;77:308–14.
[3] Mercier RJ, Liberty A. Intrauterine lidocaine for pain control during laminaria insertion: a randomized controlled trial. Contraception 2014;90:594–600.
[4] Morrell KM, Castaño PM. Analgesia or anesthesia use during osmotic cervical dilator placement: a survey of providers. Contraception 2012;86:173–86.
[5] Soon R, Tschann M, Salcedo J, Stevens K, Ahn HJ, Kaneshiro B. Paracervical block for laminaria insertion before second-trimester abortion: a randomized controlled trial. Obstet Gynecol 2017;130:387–92.
[6] Conti JA, Lerma K, Shaw KA, Blumenthal PD. Self-administered lidocaine gel for pain control with first-trimester surgical abortion. Obstet Gynecol 2016;128:297–303.
[7] Kan AS, Ng EH, Ho PC. The role and comparison of two techniques of paracervical block for pain relief during suction evacuation for first-trimester pregnancy termination. Contraception 2004;70:159–63.
[8] Renner RM, Jensen JT, Nichols MD, Edelman AB. Pain control in first-trimester surgical abortion: a systematic review of randomized controlled trials. Contraception 2010;81:372–88.
[9] Renner RM, Nichols M, Jensen JT, Li H, Edelman A. Paracervical block for pain control in first-trimester surgical abortion: a randomized controlled trial. Obstet Gynecol 2012;119:1030–7.
[10] Li HWR, Wong CYG, Lo SST, Fan SYS. Effect of local lignocaine gel application for pain relief during suction termination of first-trimester pregnancy: a randomized control trial. Hum Reprod 2006;21:1461–6.
[11] Blanco L, Reid P, King T. Plasma lidocaine levels following paracervical infiltration for aspiration abortion. Obstet Gynecol 1982;60:506–8.
[12] Nydahl PA, Axelsson K. Venous blood concentration of lidocaine after nasopharyngeal application of 2% lidocaine gel. Acta Anaesthesiol Scand 1988;32:135–9.
[13] Soda K, Shimanuki K, Yoshida Y, Seo N, Yamanaka T, Sakurabayashi I, et al. Serum lidocaine and MEGX concentrations after pharyngeal anesthesia for gastroscopy. Endoscopy 1994;26:347–51.
[14] Jensen MP, Chen C, Brugger AM. Interpretation of visual analog scale ratings and change scores: a reanalysis of two clinical trials of postoperative pain. J Pain 2003; 4:407–14.
[15] Rowbotham MD. What is a "clinically meaningful" reduction in pain? Pain 2001;94: 131–2.
[16] Todd KH, Funk KG, Funk JP, Bonacci R. Clinical significance of reported changes in pain severity. Ann Emerg Med 1996;27:485–9.
[17] O'Connell K, Jones HE, Simon M, Saporta V, Paul M, Lichtenberg ES, et al. First-trimester surgical abortion practices: a survey of National Abortion Federation members. Contraception 2009;79:385–92.