



Contents lists available at ScienceDirect

Contraception: X

journal homepage: <https://www.journals.elsevier.com/conx>

Oral sedation for pain with cervical dilator placement: a randomized controlled trial☆☆☆



Jessica K. Lee^{a,*}, Anne E. Burke^b, Katrina Thaler^b, Jennifer A. Robinson^b, Carolyn Sufrin^b

^a Department of Obstetrics, Gynecology and Reproductive Sciences, University of Maryland School of Medicine, 11 S. Paca Street Suite 400, Baltimore, MD 21201

^b Department of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Bayview Medical Center, A Building, Room 121, 4940 Eastern Ave., Baltimore, MD 21224

ARTICLE INFO

Article history:

Received 13 May 2020

Received in revised form 10 December 2020

Accepted 13 December 2020

Available online xxxx

Keywords:

Cervical dilators

Laminaria

Second-trimester abortion

Dilation and evacuation

Pain management

ABSTRACT

Objective: Assess oral sedation versus placebo for pain control with cervical dilator placement.

Study design: We randomized participants presenting for dilation and evacuation to lorazepam 1 mg/oxycodone 5 mg or placebo 45 min before cervical dilator placement. Our primary outcome was median visual analog scale (VAS) pain score after dilator placement using a 100-mm VAS. We used our outcome data to calculate median pain score changes from baseline to better reflect pain score differences between study groups. Planned sample size was 30 participants per group, for a total of 60.

Results: We randomized 27 participants; 9 received sedation and 11 placebo. Median pain score increase from baseline to last dilator placement was 20 [interquartile range (IQR) 8–29] and 31 (IQR 15–81) in the oral sedation and placebo groups, $p = .16$.

Conclusion: We were unable to enroll our desired sample size, and our sample is underpowered to make any conclusions. Our results suggest that oral sedation may provide some benefit for pain relief with dilator insertion and indicate that further research might be worthwhile especially in settings that do not routinely provide these analgesics.

Implications: We had difficulty with study recruitment because many patients desired oral sedation for pain management for cervical dilator placement and declined randomization. Randomized trials of pain management with a placebo arm may find recruitment challenging especially if default clinical care already includes a pain management option that patients would have to opt out of.

© 2021 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Introduction

Approximately 11% of abortions in the United States are performed in the second trimester [1], most commonly via dilation and evacuation (D&E). Cervical preparation with osmotic dilators is a recommended effective practice for D&E beyond 14 weeks [2].

Few studies have examined pain management during or after cervical dilator placement. Paracervical block and self-administered vaginal lidocaine gel reduce pain, and intrauterine lidocaine and gabapentin do not reduce pain with cervical dilator placement [3–6]. No prior studies examined the effect of oral sedation. We aimed to assess if oral sedation decreases pain scores during and immediately after cervical dilator placement.

☆ **Clinical Trial Registration:** [ClinicalTrials.gov](https://clinicaltrials.gov), www.clinicaltrials.gov, NCT03202550.

☆☆ Declaration of interests: The authors declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in the paper.

* Corresponding author.

E-mail addresses: JKLee@som.umaryland.edu (J.K. Lee), Aburke@jhmi.edu (A.E. Burke), Kstouff3@jhmi.edu (K. Thaler), Jrobin87@jhmi.edu (J.A. Robinson), Csufrin1@jhmi.edu (C. Sufrin).

2. Materials and methods

We conducted a randomized, double-blind, placebo-controlled trial from July 2017 to May 2019. The Johns Hopkins Institutional Review Board approved the study, which was registered at [ClinicalTrials.gov](https://clinicaltrials.gov) (NCT03202550).

Before and during the study period, our clinic offered all patients undergoing dilator placement who had a support person for after the visit the option of oral sedation (lorazepam 1 mg/oxycodone 5 mg orally), which falls under the category of minimal sedation. To participate in the study, participants had to be willing to forego oral sedation, a part of our clinic's usual dilator pain management regimen.

We enrolled patients 18–50 years with gestational ages from 17 weeks 0 day to 23 weeks 6 days presenting for a D&E requiring cervical dilator placement. We required that participants have a support person to accompany them home after the visit. We excluded patients using benzodiazepines or opioids or with an allergy or contraindication to any study drugs.

We randomized participants to receive lorazepam 1 mg/oxycodone 5 mg orally or two oral placebo pills 45 min prior to dilator placement. We stratified randomization by gestational age with block size of four

and a 1:1 allocation ratio. We blinded clinicians, clinic and research staff, and participants to group allocation. All participants received ibuprofen 600 mg orally. A physician administered a paracervical block with a total of lidocaine 1% 20 mL and placed cervical dilators per our clinic algorithm (Appendix 1).

Participants reported the primary outcome, pain score immediately after cervical dilator placement, using a 100-mm visual analog scale (VAS) anchored by “no pain” (score of 0) and “worst pain ever” (score of 100). We planned to enroll a sample size of 30 per group to provide 80% power with a 5% two-sided alpha error rate to identify a 20-mm or greater difference [7] (standard deviation of 27 mm) in the primary outcome between groups.

Our secondary outcomes were pain scores at seven other time points during or after the procedure, dilator placement procedure time and number of dilators inserted relative to goal number. We used our pain outcome data to calculate median pain score changes from baseline to better reflect pain score differences between study groups. Providers reported perceived ease of dilator placement. Fifteen minutes after the procedure, participants completed an additional questionnaire assessing their symptoms and which study treatment they believed they received. Study staff reviewed participant medical records to document adverse events occurring within 24 h of the dilator placement. We collected study data using the secure, web-based application REDCap electronic data capture tools [8,9].

We performed an intention-to-treat analysis using the Wilcoxon rank-sum test for our primary outcome. We conducted additional data analyses using Student’s *t* test and Fisher’s Exact Tests as appropriate.

3. Results

From July 2017 to May 2019, we enrolled 33 patients and randomized 27 participants. Due to factors including not receiving the intervention (inability to swallow study drugs or declining to proceed with the study), receiving an unknown intervention (pharmacy error) or missing primary outcome data, 9 participants received oral sedation and 11 received the placebo (Fig. 1). We were not able to enroll the target sample size after 2 years despite increasing participant incentives and increasing patient education regarding study participation. Many patients desired oral sedation for pain management and did not want to be randomized and give up the usual option of oral sedation which we

Table 1
Baseline characteristics of participants randomized to receive oral sedation or placebo for cervical dilator placement prior to dilation and evacuation

Characteristics	Oral sedation n = 9	Placebo n = 11	p value ^a
Age			
Average (years)	25.7 ± 5.1	25.8 ± 5.6	.98
Gestational age			
Average	19 wk 5 d ± 8.1 d	19 wk 3 d ± 11.3 d	.73
<20 weeks	4 (44%)	6 (55%)	1.00
≥20 weeks	5 (56%)	5 (45%)	
Race/ethnicity			
Black	8 (89%)	9 (82%)	1.00
White	0 (0%)	1 (9%)	
Hispanic/Latino	0 (0%)	1 (9%)	
Other	1 (11%)	0 (0%)	
Parity			
Nulliparous	2 (22%)	4 (36%)	.64
Multiparous	7 (78%)	7 (64%)	
Education level			
High school/GED or less	5 (56%)	7 (64%)	.84
Some college	3 (33%)	2 (18%)	
College or more	1 (11%)	2 (18%)	
Total household income level			
Less than \$25,000	6 (67%)	5 (46%)	1.00
\$25,000–\$34,999	1 (11%)	2 (18%)	
\$35,000–\$49,999	2 (22%)	2 (18%)	
Greater than \$50,000	0 (0%)	2 (18%)	
Insurance			
Medicaid	8 (89%)	8 (73%)	.59
Private	1 (11%)	3 (27%)	
Illicit drug use in the past 30 days			
No	8 (89%)	9 (82%)	1.00
Yes (marijuana)	1 (11%)	2 (18%)	

^a *t* test/Fisher’s Exact Test.

offer as our clinic default. We stopped the study given these challenges with slow recruitment.

We present participant characteristics in Table 1. We show median VAS pain score changes from baseline for cervical dilator placement in Table 2. We found that median pain score change from baseline after cervical dilator placement was lower in the oral sedation group than in the placebo group (*p* = .16). We also noted lower median pain score changes from baseline for all other time points in the oral sedation

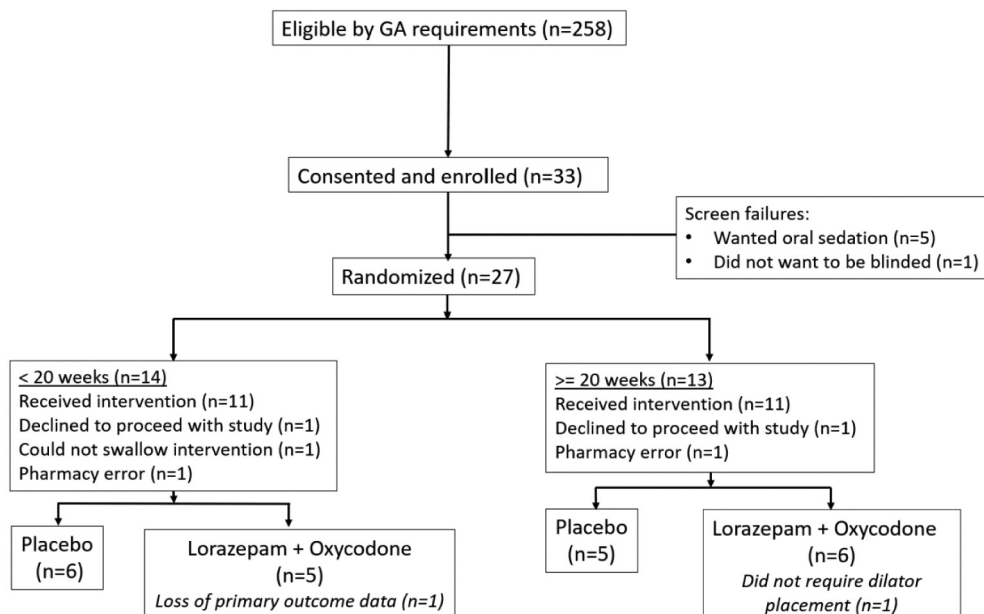


Fig. 1. Flow diagram of study participants receiving oral sedation or placebo for cervical dilator placement prior to dilation and evacuation. GA = gestational age.

Table 2

Median VAS^a pain score changes from baseline among participants randomized to receive oral sedation or placebo for cervical dilator placement prior to dilation and evacuation

Time point pain measured	Oral sedation Median (range) ^b n = 10	Placebo Median (range) n = 11	p value ^c
Before speculum	-1 (-6, 0)	-2 (-4, 0)	.65
Speculum placement	1 (0, 5)	14 (0, 43)	.18
Tenaculum placement	0 (-1, 46)	13 (4, 53)	.38
Paracervical block	7 (0, 45)	46 (4, 65)	.29
After first dilator placement	5 (0, 36)	27 (4, 53)	.14
After last dilator placement	20 (8, 29)	31 (15, 81)	.16
15 min after last dilator	0 (-2, 47)	25 (7, 46)	.34

^a VAS = visual analog scale. Median pain score change reported in millimeters on a 0- to 100-mm VAS.

^b Data are median [interquartile range (25%, 75%)].

^c p value obtained from a Wilcoxon rank-sum test.

compared to the placebo group.

We found that total procedure length (speculum placement to last dilator placement) was similar between the study groups (p = .70), as was the report of symptoms (vomiting, dry heaving, dizziness, drowsiness) (p = .77). Fifty-five percent of participants correctly guessed their allocation, with exact tests for a binomial probability of .5 indicating that blinding was maintained in our study.

We found similar ability to insert the desired number of dilators per our algorithm between study groups [two participants were unable to have the desired number of dilators inserted in the oral sedation group, four in the placebo group (p = .64)]. We observed no difference in adverse events between the two groups with only one adverse event in the study, a cervical laceration in the placebo group (p = 1.00).

4. Discussion

We attempted to perform a randomized trial to evaluate if oral sedation lowered pain experiences with dilator placement prior to D&E. We had to stop the study after enrolling only about one third of the planned population due to difficulties with enrollment due to study design. Our limited findings suggest that oral sedation may provide some benefit for pain relief with dilator insertion; however, our sample is underpowered to make any conclusions.

Study limitations include that we were not able to enroll the target sample size. We recognize that other clinics or institutions may not offer oral sedation as a standard option as our clinic does; our recruitment challenges are likely due to patients declining to opt out of usual care to participate in the study. This may impact the generalizability of our preliminary results. Additionally, many patients did not have someone to escort them home after the visit. Patients may find it challenging to arrange an escort for both the day of dilator insertion and day of D&E.

Our study was underpowered, but we did show some benefit for pain relief with dilator insertion in participants who received oral sedation. We struggled with recruitment because our study required participants to give up the usual care option of oral sedation and to be willing to be randomized to placebo. This is an important lesson for study design: that a trial that takes away usual care will be difficult to enroll

for. Larger studies evaluating our study objective would be helpful in the future, but they may run into similar difficulties with enrollment if usual care involves oral sedation. In the setting of the current opioid epidemic and the challenges of finding an escort home after oral sedation, it remains important to study effective pain management options and patient-centered preferences for cervical dilator placement that include both opioid and nonopioid interventions.

Funding

This work was supported by the Society of Family Planning Research Fund (grant SFPRF 17-05).

Acknowledgments

We sincerely thank Torri Ross, B.S.N., M.P.H., and Lauren Beal, M.P.H., for their contributions to study recruitment and enrollment.

Appendix 1. Dilator calculation algorithm for participants randomized to receive oral sedation or placebo for cervical dilator placement prior to dilation and evacuation

Weeks gestational age	Dilators
15½ weeks – 17 weeks 0 day	2 dilapan, 1 laminaria
17 weeks 1 day – 19½ weeks	3–4 dilapan, 1 laminaria
>19½ weeks–20½ weeks	5 dilapan, 1 laminaria
>20½ weeks–22 weeks 0 day	6–8 dilapan, 1 laminaria
22 weeks 1 day – 23½ weeks	9 dilapan, 1 laminaria

At provider discretion, mifepristone 200 mg may also be provided (must be done after the 15-min post dilator insertion time point pain and symptom assessment).

References

- [1] Jones RK, Kost K, Singh S, Henshaw SK, Finer LB. Trends in abortion in the United States. *Clin Obstet Gynecol* 2009;52:119–29.
- [2] Fox MC, Krajewski CM. Cervical preparation for second-trimester surgical abortion prior to 20 weeks' gestation: SFP guideline #2013-4. *Contraception* 2014;89:75–84.
- [3] Mercier RJ, Liberty A. Intrauterine lidocaine for pain control during laminaria insertion: a randomized controlled trial. *Contraception* 2014;90:594–600.
- [4] Soon R, Tschann M, Salcedo J, Stevens K, Ahn HJ, Kaneshiro B. Paracervical block for laminaria insertion before second-trimester abortion. *Obstet Gynecol* 2017;130:387–92.
- [5] Schivone GB, Lerma K, Montgomery C, Wright P, Conti JA, Blumenthal PD, et al. Self-administered lidocaine gel for local anesthesia prior to osmotic dilator placement: a randomized trial. *Contraception* 2019;99:148–51.
- [6] Creinin MD, Schimmoeller NR, Matulich MC, Hou MY, Melo J, Chen MJ. Gabapentin for pain management after osmotic dilator insertion and prior to dilation and evacuation: a randomized controlled trial. *Contraception* 2020;101:167–73.
- [7] Rowbotham MC. What is a “clinically meaningful” reduction in pain? *Pain* 2001;94:131–2.
- [8] Harris PA, Taylor R, Minor BL, Elliott V, Fernandez M, O'Neal L, et al. The REDCap consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
- [9] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap) – a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.