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

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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.

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 (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/oxycodeone 5 mg orally), which falls under the category of minimal sedation. To participate in the study, patients 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/oxycodeone 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 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 prior to dilation and evacuation. 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

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### Table 1

| Characteristics                      | Oral sedation | Placebo | p valuea |
|--------------------------------------|---------------|---------|----------|
| Age (Average years)                  | 25.7±5.1      | 25.8±5.6| .98      |
| Gestational age                       |               |         |          |
| Average < 20 weeks                    | 19 wk 5 d ± 8.1 d | 19 wk 3 d ± 11.3 d | <.73 |
| ≥20 weeks                            | 4 (44%)       | 6 (55%) | 1.00     |
| Race/ethnicity                        |               |         |          |
| Black                                 | 8 (89%)       | 9 (82%) | 1.00     |
| White                                 | 0 (0%)        | 1 (9%)  | 1.00     |
| Hispanic/Latino                       | 0 (0%)        | 1 (9%)  | 1.00     |
| Other                                 | 1 (11%)       | 0 (0%)  | 1.00     |
| Parity                                |               |         |          |
| Nulliparous                           | 2 (22%)       | 4 (36%) | .64      |
| Multiparous                           | 7 (78%)       | 7 (64%) | .84      |
| 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%) |          |

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* t test/Fisher’s Exact Test.
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Table 2
Median VAS* 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)a | Placebo Median (range) | p valueb |
|-------------------------|-------------------------------|------------------------|----------|
| Before speculum         | 1 (−1, 0)                     | −2 (−4, 0)             | .65      |
| Speculum placement      | 1 (0, 5)                      | 14 (0, 42)             | .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      | 20 (8, 29)                    | 31 (15, 81)            | .16      |
| 15 min after last dilat | 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.

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.

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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).

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