UNIVERSITY OF CALIFORNIA SAN DIEGO

# Addition of Buprenorphine to Paracervical Block Prior to Osmotic Dilator Insertion for Dilation and Evacuation: A Randomized Controlled Trial

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by

Nicole Economou

Committee in charge:

Professor Michael Pratt, Chair
Professor Nancy Binkin
Professor Erik Groessl
Professor Sheila Mody

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The thesis of Nicole Economou is approved, and it is acceptable in quality and form for publication on microfilm and electronically.

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The findings from the research study on which this thesis is based is currently being prepared for submission for publication. The thesis author was the primary investigator and author of this material.

ABSTRACT OF THE THESIS

Addition of Buprenorphine to Paracervical Block Prior to Osmotic Dilator Insertion for Dilation and Evacuation: A Randomized Controlled Trial

by

Nicole Economou

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Professor Michal Pratt, Chair

**Background**: Pain during osmotic dilator insertion is rated as moderate to severe, even with use of a 1% lidocaine paracervical block (PCB). Buprenorphine, a partial mu-opioid receptor agonist, can improve the analgesic properties of a local anesthetic and also prolong the duration of local anesthetic effect when administered in a perineural block.

**Methods**: This is a multi-site, randomized, double-blind controlled trial conducted from May 2020–May 2021. Participants presenting for dilation and evacuation who required osmotic dilators for cervical preparation were randomized 1:1 to receive a 1% buffered lidocaine PCB or a 1% buffered lidocaine + 0.15mg buprenorphine PCB. The primary outcome was pain scores during osmotic dilator insertion as rated on an 11-point numeric rating scale. Secondary outcomes included pain at additional time points and side effects. We used a Mann-Whitney *U* test to compare median pain scores between groups.

**Results**: We randomized 57 participants. There was no difference in median pain scores between the lidocaine + buprenorphine and the lidocaine alone PCB groups during osmotic dilator insertion (3.5 vs. 4, $p$=0.88). There were no differences in median pain scores at any time point after dilator insertion. Participants receiving buprenorphine had a higher incidence of vomiting post-dilator insertion (70% vs. 21%, $p$=0.0007).

**Discussion**: Addition of buprenorphine to a 1% lidocaine paracervical block did not reduce pain at the time of osmotic dilator insertion or at any time point post-insertion. The addition of buprenorphine to a PCB may increase rate of side effects, particularly vomiting, without any pain control benefit.

# 1. INTRODUCTION

Dilation and evacuation (D&E) is the most common method of second trimester abortion in the United States.[1] Cervical preparation prior to the procedure is essential in order to allow passage of operative instruments and pregnancy tissue safely through the cervix and to decrease the risk of complications, including cervical laceration and uterine perforation.[1–4] Optimal cervical dilation can be accomplished in multiple ways. The first is by mechanical dilation, when the cervix is dilated at the start of the procedure with metal or plastic dilators. In the first trimester, mechanical dilation alone is often used to complete abortion procedures. However, the greater amount of dilation required for second trimester procedures may require additional force which can increase the risk of cervical trauma, including cervical lacerations, and the risk of uterine perforation.[1] Therefore, more gradual dilation with osmotic dilators is often used prior to second trimester procedures.

In the second trimester, cervical preparation is typically achieved with placement of osmotic dilators in the cervix prior to the procedure. Over time, osmotic dilators absorb surrounding fluid from the cervical stroma and expand, in turn exerting radial pressure on the cervix to cause dilation and stimulate release of local prostaglandins. There are two types of osmotic dilators commonly used: laminaria tents and Dilapan-S. Laminaria tents are made from the stems of seaweed (Laminaria japonica or Laminaria digitata), which are dehydrated and sterilized. Available in a variety of sizes, laminaria swell to 3 to 4 times their initial diameter, reaching maximum effect after 12-24 hours.[5] Dilapan-S is a synthetic osmotic dilator which also swell to 3-4 times their initial diameter, but in a much more rapid timeframe compared to laminaria; it achieves dilation to 2-3 times the initial dilator diameter in only 2 to 4 hours.[5] While laminaria tents are relatively inexpensive and effective, drawbacks to their use include variability

in product, potential allergy, theoretical risk of infection, and need for a two-day abortion procedure to achieve maximal dilation.[4] Dilapan-S is increasingly used for same-day abortion procedures due to rapidity of dilation, however the high cost can be prohibitive for some providers.

Women have described the pain of osmotic dilator insertion as moderate to severe yet there have been few studies aimed at addressing pain during osmotic dilator insertion.[6–9] A lidocaine paracervical block is commonly used for pain control during other gynecologic procedures including procedures involving cervical dilation during dilation and curettage.[10,11] One randomized controlled trial found that use of a paracervical block with 1% lidocaine decreased pain with osmotic dilator insertion compared to a sham block.[7] Because the dilators slowly expand after insertion, there is continued discomfort for several hours after placement. Research has shown that pain after osmotic dilator insertion peaks at 2 hours post-insertion with use of a 1% lidocaine paracervical block and this local anesthetic is not sufficient to provide lasting pain relief.[12] Systemic medications, such as gabapentin and narcotic analgesics, have been studied to treat post-insertional dilator pain, however these treatments were not more effective than placebo.[12,13]

There are many adjunct treatments to optimize the duration of local analgesia from a peripheral nerve block. Buprenorphine, a partial mu-opioid receptor agonist, is a high potency, lipophilic opioid and has a high binding capacity for the mu-opioid receptor.[14,15] Because of the high binding capacity, buprenorphine has the longest duration of action of all opioids. When administered perineurally in combination with a local anesthetic, buprenorphine has been found to drastically increase the duration of analgesia at several anatomic sites, including axillary and subclavian brachial plexus blocks and infragluteal sciatic nerve blocks.[14–20] With the addition of

buprenorphine at doses of 0.15 – 0.3mg, there is significant prolongation of the anesthetic sensory blockade up to three times the duration of the local anesthetic alone.[14] The use of perineural buprenorphine is well established for postoperative analgesia.[14,15]

Buprenorphine itself also has local anesthetic properties. Buprenorphine blocks voltage gated sodium channels and inhibits C-fiber action potentials, thereby contributing to an analgesic effect.[21,22] One study using buprenorphine in conjunction with bupivacaine for a subclavian perivascular brachial plexus block found that the addition of buprenorphine improved the quality of the local anesthetic in terms of a denser sensory blockade at the time of administration.[18] Therefore, buprenorphine not only prolongs the duration of local anesthetic effect but also improves the analgesic properties when administered in a perineural block.

The addition of buprenorphine to a perineural local anesthetic has not been studied in a paracervical block. This study is the first trial to assess the efficacy of buprenorphine to provide analgesia for a gynecologic procedure. This medication has the additional benefit of providing long lasting pain relief for procedures that cause continued discomfort after the end of the procedure. The hypothesis of this research study is that the addition of 0.15mg of buprenorphine to a 1% lidocaine paracervical block will improve pain during osmotic dilator insertion and provide continued pain relief for several hours after osmotic dilator insertion.

This study has important public health implications for decreasing post-procedural pain and therefore need for post-procedural opioid analgesics. In 2018, prescription opioids accounted for 32% of all opioid overdose deaths.[23] Research has shown that the amount of opioids prescribed for post-surgical pain is higher than actual patient consumption.[24,25] Unused or leftover opioid prescriptions present a problem in terms of community misuse and diversion, particularly for adolescents.[26–29] In the last 5 years, there has been a renewed interest to find

effective, non-opiate analgesics for post-operative and procedural pain, particularly for obstetric and gynecologic procedures.[24,30–32] There is a growing recognition of the importance of limiting opioid prescriptions after surgery in order to prevent communication diversion of narcotics. There is no evidence to suggest that prescription opiates reduce pain more than non-opiate medications for medication abortion and after insertion of cervical dilators as preparation for second trimester dilation and evacuation.[12,13,31,33–35] Despite the lack of evidence, opiates are still widely prescribed for pain control for second trimester procedures. One nationwide study in 2009 found that 36% of clinicians prescribed narcotics after second trimester surgical abortions.[36] There remains a need to find effective pain control options to decrease the need for post-procedural narcotic analgesics; non-opiate and non-systemic interventions for pain control during cervical preparation, such as the intervention described in this study, may be helpful to curb the prescribing of opiates.

## 2. METHODS

### 2.1 Participant Recruitment and Allocation

This is a randomized, double-blind, placebo-controlled trial conducted at the University of California, San Diego Health (UCSD) and Planned Parenthood of the Pacific Southwest (PPPSW). We enrolled patients who presented to UCSD or PPPSW seeking D&E between 14 weeks 0 days and 23 weeks 6 days gestations and who required cervical preparation with overnight osmotic dilators as determined by the evaluating clinician. Patients were included if they were 18 years of age or older, spoke English or Spanish, and had a cell phone with text message and data capabilities to answer surveys. Participants were excluded if they had: pre-viable preterm rupture of membranes as an indication for the D&E, allergy to the study medications or ibuprofen, narcotic use in the preceding 24 hours (including prescription opiates, buprenorphine, methadone), recreational or illicit drug use in the preceding 24 hours (including marijuana), request for sedation during osmotic dilator insertion, acute or chronic liver disease, severe lung disease, or were incarcerated. We also excluded patients for whom same day D&E was planned. The UCSD Institutional Review Board approved this study prior to beginning recruitment, and all participants gave written consent to participate prior to study enrollment. The trial was also registered prospectively at ClinicalTrials.gov: Identifier NCT04254081.

After informed consent was obtained, baseline demographic information was collected from all eligible participants which included the patient's age, race and ethnicity, obstetric history, gestational age, reason for D&E, history of cervical procedures, baseline pain score, and chronic pain severity.[37] Participants were randomized 1:1 to receive a paracervical block with 20mL of 1% buffered lidocaine or a paracervical block with 20mL of 1% buffered lidocaine plus 0.15mg of buprenorphine. Block randomization was performed using a computer-generated

random sequence in alternating blocks of 4 and 6 stratified by vaginal parity – vaginally nulliparous (no prior vaginal deliveries) and vaginally parous (at least 1 prior vaginal delivery). The computer-generated randomization codes with the type of paracervical block were placed in sealed, sequentially numbered, opaque randomization envelopes. Only after confirming participant eligibility and obtaining consent was the participant assigned a study identification number and the randomization envelope selected.

**2.2 Study Design**

A study clinician not performing the procedure opened the designated randomization envelope. This clinician prepared the designated paracervical block into two 10 mL syringes. The study clinician then brought the paracervical block into the clinic room where the procedure was performed by a different clinician who was blinded to study assignment. Buprenorphine is a clear injectable solution and therefore a paracervical block with lidocaine and buprenorphine appears visually identical to a lidocaine paracervical block. Participants all received oral ibuprofen 800mg prior to the procedure.

Clinicians performing osmotic dilator insertion included obstetrics and gynecology residents, family planning fellows, family planning attending physicians, and advance practice clinicians. Family planning attending physicians supervised trainees performing the procedure. To ensure standardization of technique, a study team member reviewed the paracervical block injection technique with the clinician performing the osmotic dilator insertion. Clinicians injected the 2mL of the designated block on the anterior lip of the cervix. The remainder of the block (18 mL) will be injected at four points around the cervix, initially starting superficial and advancing to a depth of 3 centimeters, which is consistent with the literature on performing paracervical blocks during suction D&C. The clinician could place the tenaculum on the cervix

either before or after performing the paracervical block per their preference. To better standardize psychosocial aspects of pain during the procedure, the physician performing osmotic dilator insertion was given standard sentences to say, such as "you may or may not feel some sensation" at each potentially painful step of the procedure. The number and type of osmotic dilators placed were at the discretion of the clinician. Mechanical dilation with rigid dilators prior to inserting the osmotic dilators was performed at the discretion of the clinician. If participants were planned to have 2 sets of osmotic dilators, they were only enrolled for the study with the placement of the first set of osmotic dilators. At both sites, participants were prescribed ibuprofen 600mg to use as needed for post-procedural discomfort. Additionally, participants were routinely prescribed narcotic medications for severe pain – either hydrocodone 5mg + acetaminophen 325mg (Norco) or acetaminophen 300mg + codeine 30mg (Tylenol #3).

**2.3 Measures**

The primary study outcome was difference in median pain scores rated on an 11-point numeric rating scale (NRS) at the time of osmotic dilator placement. The numeric rating scale grades pain on an integer only scale from 0 (no pain) to 10 (pain as bad as it could possibly be). Secondary outcomes included pain on the NRS at additional procedural timepoints; pain and 1-, 2-, and 6-hours post-dilator insertion on the NRS; and overall procedural satisfaction on a Likert scale. The incidence of side effects and any major complications with dilator insertion was also recorded. We evaluated pain scores by asking each participant to verbally provide a pain score on a scale of 0-10 at different points during the procedure (baseline, speculum insertion, paracervical block administration, pain with mechanical dilation, pain with osmotic dilator insertion, pain at 5 minutes post-insertion, and overall procedural pain). Participants were also asked about any side effects that they experienced at any point during or after the procedure.

Trained research staff recorded all baseline and procedural data in REDCap on an electronic tablet during the clinic visit.[38]

Participants received an automated text message with a link to a survey at 1-, 2-, and 6-hours post-dilator insertion. These surveys were identical and asked about pain scores on the NRS, side effects, and analgesic use (including narcotics) during the specified time period. The survey data was automatically captured in the REDCap database.

**2.4 Power Calculation and Statistical Analysis**

It is suggested that a 2-point reduction in pain on the numeric rating scale (NRS) is clinically meaningful.[39–42] In prior research, pain scores at the time of osmotic dilator insertion range from 40 to 70mm on the visual analog scale (a 100mm linear pain scale) with a standard deviation of 22 to 25mm.[6,9] In a study investigating the use of intravaginal lidocaine gel for pain control during osmotic dilator insertion, the median pain score in the placebo group on the VAS was 61mm with a range of 0 to 100mm.[9] This placebo group received a 1% lidocaine paracervical block and best mirrors our study population, however this study used the VAS. We extrapolated these findings to an anticipated pain score on the NRS by dividing by 10. The visual analog scale and the numeric rating scale have modest correlation; thus we have used the data from this study to inform our power calculation.[39]

In order to detect a clinically meaningful 2-point difference on the NRS at the time of osmotic dilator insertion with 80% power and a two-sided alpha of 0.05, we calculated that a total of 52 patients (26 per study group) was needed. The sample size was doubled to allow for stratification by vaginal parity. To account for protocol deviation and participant dropout, we planned to enroll an additional 10% which resulted in a final sample size of 114 participants.

Although we aimed achieve this final sample size of 114 in order to perform analysis across two different strata, enrollment was impacted by the COVID-19 pandemic due to limitations on research activities at one of our study sites. Due to slower than expected accrual, we made the decision to stop enrollment at 57 participants as this provided statistical power to assess the primary study outcome. We explored differences in pain scores across strata as an exploratory analysis.

Baseline characteristics between the treatment groups were analyzed with descriptive statistics using chi squared test or Fisher's Exact test for categorical variables and t-test for continuous variables. The primary and secondary outcomes were continuous variables and analyzed using t-tests or Mann-Whitney *U* tests depending on the distribution of the data as appropriate. The primary outcome was evaluated per intent-to-treat analysis. A multivariable analysis was performed to evaluate for potential confounders and to assess predictors of pain at the time of osmotic dilator insertion. These variables included age, body mass index (BMI), indication for D&E, vaginal parity, gestational age, clinician level inserting dilators, and ease of dilator placement. R (Version 1.4.1103) was used for statistical analysis.[43]

## 3. RESULTS

From May 2020 to May 2021, we assessed 115 people for eligibility and randomized 57 consenting participations (Figure 1). All randomized participants were included in the intention to treat analysis. Demographic characteristics of the participants were similar between the two groups (Table 1). Participants had similar numbers of osmotic dilators placed in each group; a combination of laminaria and Dilapan-S were used, though a similar proportion of participants in each group had more than 50% of Dilapan-S placed in relation to laminaria (Table 1).

Table 2 shows NRS pain scores at different procedural time points. Participants who received a paracervical block with lidocaine + buprenorphine had no difference in median pain scores at the time of osmotic dilator insertion compared to participants receiving a lidocaine alone paracervical block (3.5 vs, 4 respectively, $p$=0.88). When stratifying by vaginal parity, median procedural pain scores were also similar between the two groups (Table 3). Compared to the lidocaine alone group, patients in the lidocaine + buprenorphine group who had a prior vaginal delivery had a trend toward lower median pain scores during mechanical dilation (4.5 vs. 6, $p$=0.05) and lower median pain scores overall (5 vs. 7, $p$=0.07). Clinicians reported similar levels of difficulty with dilator insertion between the two groups as measured on a Likert scale. Of participants receiving a lidocaine alone paracervical block, clinicians rated that it was difficult to place dilators in 17% of participants versus 21% of participants in the lidocaine + buprenorphine group; clinicians rated that it was easy to place dilators in 55% of participants in the lidocaine alone group versus 53% in the lidocaine + buprenorphine group ($p$=0.92).

There were no differences in median pain scores between the two groups at several time points after osmotic dilator insertion (Table 4). Similarly, when stratifying by vaginal parity, the median pain scores between the two groups at multiple post-procedural time points were similar.

Overall satisfaction scores, rating of expected pain versus actual pain, and likelihood to recommend the paracervical block to a friend also did not differ between the lidocaine alone and lidocaine + buprenorphine groups (Table 5).

In the multivariable analysis, indication for procedure predicted higher pain scores at the time of osmotic dilator insertion. Participants who were having a D&E for a fetal anomaly or for fetal demise were more likely to have higher pain scores compared to participants who were having a D&E with no maternal or fetal indication. All other predictors (age, ethnicity, BMI, prior vaginal delivery, clinician inserting dilators, ease of dilation) did not impact pain scores at the time of osmotic dilator insertion.

The use of narcotics for pain post-dilator insertion did not differ between the two groups. Because participants were prescribed different analgesic medications depending on the study site, the total dose of narcotics, expressed in morphine milligram equivalents (MME), was examined as a standardized measure. The total MME was similar between the lidocaine alone and the lidocaine + buprenorphine groups (2.6 versus 2.5, $p$=0.35). The use of ibuprofen post-dilator insertion was also similar between groups.

The lidocaine + buprenorphine group had a higher incidence of vomiting at any time after dilator insertion compared to the lidocaine alone group (70% vs. 21%, $p$=0.0007, Figure 2). At 2 hours post-insertion, there was a trend toward higher incidence of nausea and dizziness, however these differences were not significant (Figure 3). At any time after dilator insertion, the two groups had similar rates of nausea, headache, palpitations, and sleepiness (Figure 2). No participant experienced major side effects such as respiratory depression or loss of consciousness. There were no major complications with dilator insertion.

## 4. DISCUSSION

This research demonstrated that adding buprenorphine 0.15mg as an adjunct to a 1% lidocaine paracervical block did not decrease median pain scores during osmotic dilator insertion prior to D&E. There was also no difference in pain scores at any time point after dilator insertion. There was also a higher incidence of side effects in the lidocaine + buprenorphine group, particularly for vomiting.

Strengths of this study include the randomized, double-blind design. Neither the participant, clinician performing the dilator insertion, or study personnel administering the pain scale questionnaires were aware of the paracervical block assignment. Additionally, our study population was ethnically diverse and included a majority of Hispanic participants in both groups. By utilizing a text message-based survey platform, we were able to capture pain scores and side effects prospectively at several different time points after dilator insertion instead of relying on retrospective recall.

Limitations of this study include variation in number and type of osmotic dilators placed for cervical preparation. Due to the increased cost of Dilapan-S, there is a growing trend toward using more laminaria for cervical preparation. Because laminaria expand more slowly than Dilapan-S, the "peak" of post-dilator insertion pain at 2 hours demonstrated in prior research using primarily Dilapan-S was not shown in our data.[12,13] In this study, there was a consistent median pain level at almost all time points after dilator insertion which may reflect the use of laminaria in combination with Dilapan-S (Table 4).

Additionally, we found in the multivariable analysis that patients with a fetal anomaly or fetal demise as an indication for the D&E were significantly more likely to experience higher pain scores with osmotic dilator insertion. We did not measure pre-procedure anxiety scores in

this study; other research has found that anxiety levels can impact perceived pain scores. It is unclear from our research if the increase in pain scores were from pre-procedure anxiety levels as we did not measure this, or other factors related to the pregnancy. This presents an avenue for future research, as other interventions for pain control and anxiety may be available depending on the particular needs of this population.

Much of the information about buprenorphine as an adjunct for local pain control is found in the anesthesia literature. With the addition of buprenorphine at doses of 0.15 – 0.3mg, there is significant prolongation of the anesthetic sensory blockade up to three times the duration of the local anesthetic alone.[14,15] From previous literature, the most frequently cited side effect with perineural administration of buprenorphine was post-operative nausea and vomiting.[44] We found that this was similar in our study, particularly in relation to vomiting post-dilator insertion (Figure 3). In prior studies demonstrating an increase in nausea and vomiting, the data was confounded by patient use of oral opiates at home to control pain.[17] Our data showed that there was no difference in narcotic use as measured by MME between groups suggesting that the side effect of vomiting was likely due to the buprenorphine and not necessarily due to post-procedure narcotic use.

Most studies have cited an incidence of nausea and vomiting on the order of 10-50%. Use of a lower dose of buprenorphine (0.15mg) had a lower prevalence of nausea and vomiting in a review of multiple studies (4/50 patients).[45] Although we used the lower dose of buprenorphine in this study, we still noted an increase in vomiting and a trend toward an increase in nausea in the buprenorphine additive group. It is possible that there is more systemic absorption of medication when used in a paracervical block compared to perineural blocks at other anatomic sites. Most peripheral nerve blocks are performed using ultrasound guidance to avoid large

vessels, especially with brachial plexus and sciatic nerve blocks. Although visualization is used to avoid large vessels, there is still likely a small amount that is absorbed systemically at other anatomic sites given the occurrence of nausea and vomiting in other studies. Because a paracervical block is performed blindly and there is a higher concentration of vessels around the cervix, we chose to study the 0.15mg dose of buprenorphine as this dose has still been shown to significantly prolong post-procedure analgesia.[14,44,45] Even with this lower dose, there was still an increased incidence of side effects. The plexus around the cervix has high vascularity and there may be more systemic absorption of perineural anesthesia than at other anatomic sites. Similar to previous research, there were no cases of respiratory depression in our study with the addition of buprenorphine to a perineural block.[44]

This study is the first to assess the use of buprenorphine in a paracervical block for pain control during a gynecologic procedure. Both the 0.15mg and 0.3mg doses have been shown to be effective in prolonging analgesia and reducing use of post-operative analgesics. In this study, we did not find a difference in median pain scores with the addition of buprenorphine to a 1% lidocaine paracervical block at the time of osmotic dilator insertion or at any time points post-insertion. There was an increase in side effects experienced in the lidocaine + buprenorphine group. The addition of buprenorphine to a 1% lidocaine paracervical block does not decrease pain during or after osmotic dilator insertion and may increase side effects. Despite most participants rating their pain as mild 2 hours post-dilator insertion (median pain score 3, IQR 1-5), participants still used narcotic medications to control their pain. There remains a need to find effective, long-lasting pain control options during and after osmotic dilator insertion both to improve patient's experiences and to reduce the use of narcotics post-procedure.

The findings from this research study on which this thesis is based is currently being prepared for submission for publication. The thesis author was the primary investigatory and author of this material.

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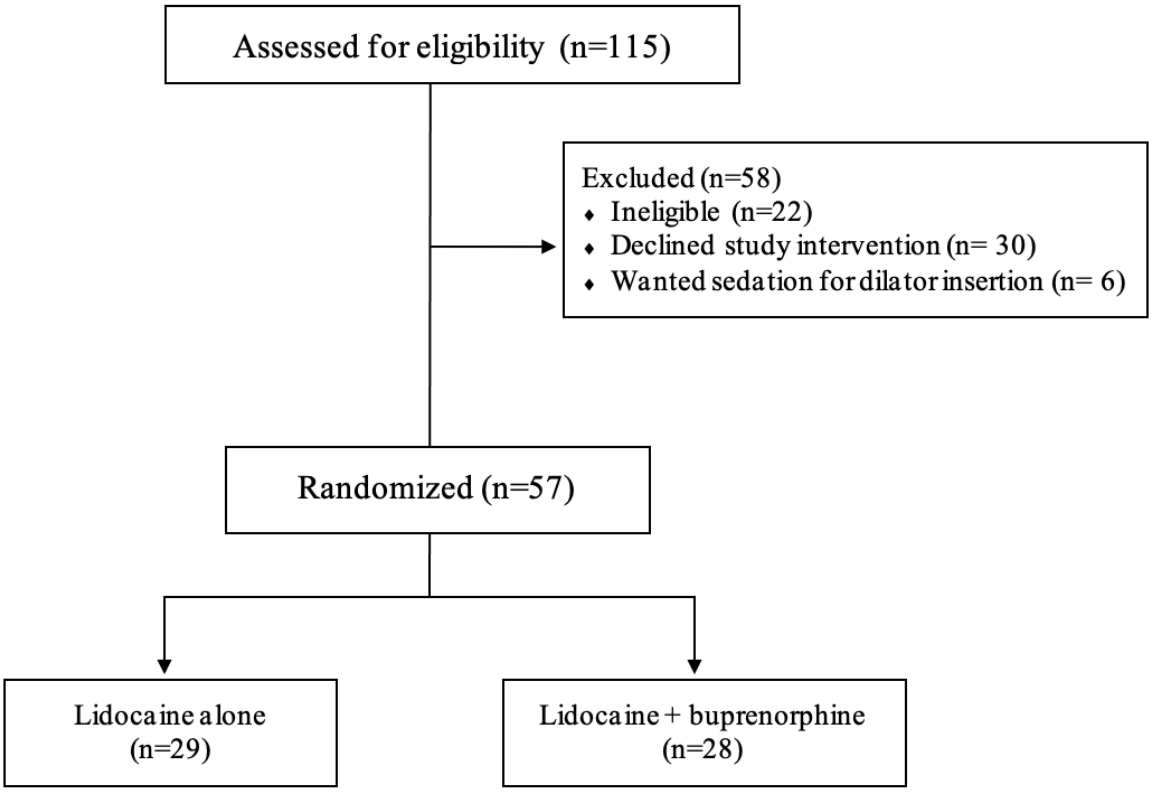


**Figure 1.** Flow of Participants

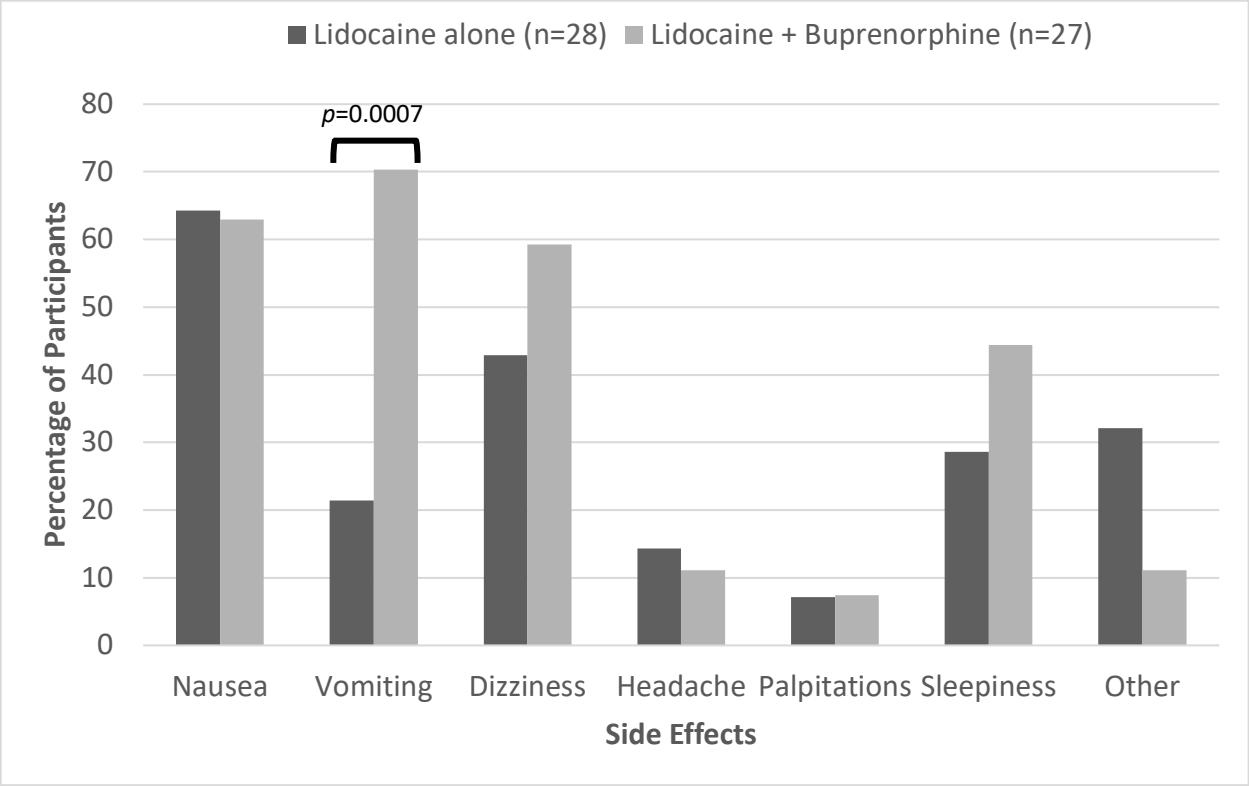


**Figure 2**. Side effects experienced by participants at any time after osmotic dilator insertion. Significance level $p<0.007$ with post-hoc Bonferroni correction.

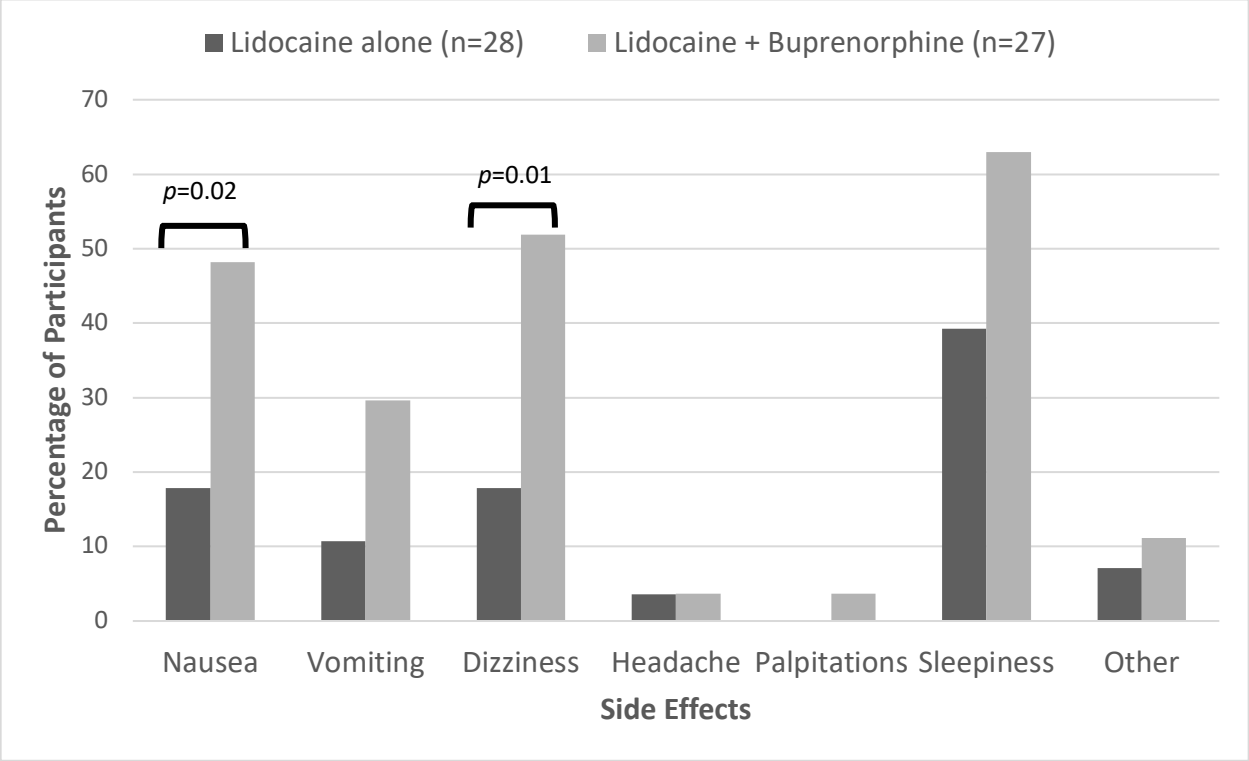


**Figure 3**. Side effects experienced by participants within 2 hours of osmotic dilator insertion. Significance level $p<0.007$ with post-hoc Bonferroni correction.

**Table 1**. Baseline demographic characteristics

| | **Lidocaine alone (n=29)** | **Lidocaine + Buprenorphine (n=28)** | ***p*-value** |
|---|---|---|---|
| **Age** (mean ± SD)[‡a] | 30.4 ± 6.5 | 30.0 ± 7.1 | 0.79 |
| **BMI** [a] | 26.4 ± 4.8 | 30.8 ± 8.8 | 0.07 |
| **Gestational age** [a] | 19w0d ± 2w4d | 19w2d ± 2w4d | 0.80 |
| **Reason for abortion**[b] | | | 0.78 |
| Undesired pregnancy | 20 (69.0) | 20 (71.4) | |
| Fetal anomaly | 5 (17.2) | 5 (17.9) | |
| Fetal demise | 4 (13.8) | 3 (10.7) | |
| **Vaginal Parity**[b] | | | 0.89 |
| Vaginally nulliparous | 14 (48.3) | 15 (53.6) | |
| Vaginally parous | 15 (51.7) | 13 (46.4) | |
| **Race/Ethnicity**[b] | | | 0.45 |
| White | 6 (20.7) | 4 (14.3) | |
| Black or African American | 1 (3.4) | 1 (3.6) | |
| Hispanic or Latina | 15 (51.7) | 19 (67.9) | |
| Asian | 5 (17.2) | 1 (3.6) | |
| Other or multiracial | 2 (6.9) | 3 (10.7) | |
| **Education**[b] | | | 0.93 |
| Some high school | 2 (6.9) | 1 (3.6) | |
| High school or equivalent | 9 (31.0) | 10 (35.7) | |
| Some college | 11 (37.9) | 10 (35.7) | |
| College or higher | 7 (24.1) | 6 (21.4) | |
| **Chronic Pain Classification**[b] | | | 0.60 |
| Grade 0 (pain free) | 8 (27.6) | 4 (14.3) | |
| Grade I (low disability, low intensity) | 17 (58.6) | 20 (71.4) | |
| Grade II (low disability, high intensity) | 2 (6.9) | 3 (10.7) | |
| Grade III (high disability, moderately limiting) | 1 (3.4) | 1 (3.6) | |
| Grade IV (high disability, severely limiting) | 1 (3.4) | 0 (0) | |
| **Patients receiving >50% Dilapan-S in relation to laminaria**[b] | 12 (41.4) | 13 (46.4) | 0.91 |
| **Clinician level**[b] | | | 0.71 |
| Resident | 4 (13.8) | 6 (21.4) | |
| Advance practice clinician | 17 (58.6) | 16 (57.1) | |
| Fellow or Attending | 8 (27.6) | 6 (21.4) | |

[‡] Data presented as *n* (%) or mean ± standard deviation. Missing data do not contribute to estimated *p*-values.

[a] Two sample *t*-test

[b] $\chi^2$-squared test

w = weeks; d = days

**Table 2.** Numeric Rating Scale procedural pain scores

| | **Lidocaine alone (n=29)** | **Lidocaine + Buprenorphine (n=28)** | ***p*-value*** |
|---|---|---|---|
| **Baseline pain** | 0 (0, 0) | 0 (0,0) | 0.88 |
| **Speculum placement** | 1 (0, 3) | 2 (1, 4) | 0.21 |
| **Paracervical block** | 4 (2, 6) | 3 (2, 6) | 0.52 |
| **Mechanical dilation (if performed)** | 4.5 (2.75, 6)^ | 5 (2, 7.5)^ | 0.88 |
| **Osmotic dilator insertion** | 4 (2, 7) | 3.5 (1, 6) | 0.82 |
| **Overall pain** | 5 (3, 7) | 5 (4, 7) | 0.92 |

Data presented as median (IQR)
NRS = Numeric rating scale (range 0-10)
*Comparisons analyzed using Mann-Whitney *U* test
^ Dilation not performed in 5 participants

**Table 3**. Numeric Rating Scale pain scores stratified by vaginal parity

| | Vaginally Nulliparous | | | Vaginally Parous | | |
|---|---|---|---|---|---|---|
| | **Lidocaine alone** (n=14) | **Lidocaine + Buprenorphine** (n=15) | *p*-value* | **Lidocaine alone** (n=15) | **Lidocaine + Buprenorphine** (n=13) | *p*-value* |
| **Baseline pain** | 0 (0, 0.75) | 0 (0, 0) | 0.39 | 0 (0,0) | 0 (0,0) | 1.0 |
| **Speculum placement** | 1.5 (0, 3) | 3 (1, 3.5) | 0.30 | 1 (0, 3) | 1.5 (0, 3.5) | 0.61 |
| **Paracervical block** | 4.5 (3, 6) | 3 (2, 5) | 0.34 | 5 (3, 6) | 3 (0.5, 4) | 0.09 |
| **Mechanical dilation** | 5 (2, 7.25) ^ | 4 (2, 8) ^ | 0.72 | 6 (4.25, 7) # | 4.5 (2, 7) # | 0.05 |
| **Osmotic dilator insertion** | 3.5 (0.25, 6.75) | 4 (2, 6) | 0.66 | 4 (3, 8) | 3 (2.5, 5) | 0.16 |
| **Overall pain** | 6 (4, 7.75) | 5 (4, 6) | 0.32 | 7 (5, 8) | 5 (2.5, 5.5) | 0.07 |

Data presented as median (IQR)
NRS = Numeric rating scale (range 0-10)
# Dilation not performed in 3 participants
^ Dilation not performed in 2 participants
*Comparisons analyzed using Mann Whitney *U* test

**Table 4.** Numeric Rating Scale pain scores post-dilator insertion

| Time after dilator placement | *n* | **Lidocaine Alone** *n*=29 | *n* | **Lidocaine + Buprenorphine** n=28 | ***p*-value*** |
|---|---|---|---|---|---|
| **5 minutes** | 29 | 2 (1, 3) | 28 | 2.5 (1, 4) | 0.89 |
| **1 hour** | 24 | 3.5 (1.75, 5.25) | 18 | 2 (1, 3) | 0.21 |
| **2 hours** | 28 | 3.5 (1, 5) | 25 | 3 (1, 5) | 0.71 |
| **6 hours** | 27 | 3 (0.5, 4.5) | 24 | 3 (1.75, 5.25) | 0.63 |
| **18-24 hours** | 28 | 2 (0, 4) | 27 | 2 (1, 3) | 0.29 |

Data presented as median (IQR)
NRS = Numeric rating scale (range 0-10)
D&E = Dilation and Evacuation
*Comparisons analyzed using Wilcoxon rank sum test (Mann Whitney *U* test)

**Table 5.** Overall satisfaction scores

| | **Lidocaine Alone** n=29 | **Lidocaine + Buprenorphine** n=28 | ***p*-value*** |
|---|---|---|---|
| **Overall satisfaction** | | | 0.25 |
| Very satisfied | 13 (44.8) | 14 (50.0) | |
| Satisfied | 14 (48.3) | 9 (32.1) | |
| Slightly satisfied | 0 (0) | 3 (10.7) | |
| Slightly dissatisfied | 1 (3.4) | 2 (7.1) | |
| Dissatisfied | 0 (0) | 0 (0) | |
| Very dissatisfied | 1 (1.8) | 0 (0) | |
| **Expected pain** | | | 0.29 |
| Less than expected | 17 (58.6) | 22 (78.6) | |
| About the same as expected | 6 (20.7) | 2 (7.1) | |
| More than expected | 5 (17.2) | 4 (14.3) | |
| Much more than expected | 1 (3.4) | 0 (0) | |
| **Would have same block for a procedure in the future** | | | 0.44 |
| Definitely yes | 23 (79.3) | 25 (89.3) | |
| Probably yes | 4 (13.8) | 2 (7.1) | |
| Not sure | 1 (3.4) | 0 (0) | |
| Probably no | 1 (3.4) | 0 (0) | |
| Definitely no | 0 (0) | 1 (3.6) | |
| **Would recommend to a friend** | | | 0.55 |
| Definitely yes | 26 (89.7) | 25 (89.3) | |
| Probably yes | 0 (0) | 1 (3.6) | |
| Not sure | 3 (10.3) | 2 (7.10) | |

*Comparisons analyzed using $\chi^2$-squared test