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Gabapentin for Pain Management after Osmotic Dilator Insertion and prior to Dilation and Evacuation: A Randomized Controlled Trial

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Abstract

Objective: To evaluate if gabapentin 600 mg reduces pain after osmotic dilator placement the day before a dilation and evacuation (D&E) procedure.

Study Design: We conducted a double-blind, placebo-controlled, randomized (stratified by vaginal parity) trial among women undergoing osmotic dilator placement before D&E at 15 to 23 5/7 weeks gestation. Subjects received gabapentin 600 mg or placebo 30 minutes before dilator placement, with re-dosing 8 hours later. We assessed pain after dilator placement using a numeric rating scale (NRS; scale 0-10) at 5 minutes, 2, 4, and 8 hours, and at presentation for D&E. The primary outcome was median NRS pain score change from baseline to 8 hours after dilator placement. Secondary outcomes included gabapentin-related side effects and analgesic use.

Results: Of 121 randomized women, we excluded three subjects (allergic reaction [placebo], randomization error, no NRS data), leaving 60 gabapentin and 58 placebo subjects. Of 110 (93%) women who provided 8-hour data, median pain score changes from baseline did not differ between gabapentin and placebo groups overall (2 vs. 2.5, p=0.52), in vaginally nulliparous women (2 vs. 4, p=0.10) or in parous women (2 vs. 1.5, p=0.37). We found no statistically significant differences in median pain score change from baseline to any timepoint overall or when stratified by parity. Beginning at 2 hours after dilator placement, more gabapentin than placebo users experienced dizziness (29/53[55%] vs. 11/53[21%], p=0.001) and tiredness (34/54[63%] vs. 17/54[31%], p=0.002). The proportion of women using narcotics did not differ between gabapentin (35/60[58%]) or placebo (40/58[69%]) users (p=0.26).

Conclusions: Gabapentin does not reduce pain with overnight osmotic dilator placement prior to D&E and causes drug-related side effects.

Keywords: gabapentin; abortion; dilation and evacuation; osmotic dilators; pain; text message

Implications Statement: Women experience pain, mostly mild to moderate, with overnight cervical dilator placement at 15-23 5/7 weeks gestation. About 2/3 of women will use a limited quantity of narcotics if provided. Gabapentin does not decrease the pain with or following dilator placement and does not decrease narcotic use.

1.0 Introduction

Osmotic dilators are commonly used for cervical preparation prior to dilation and evacuation (D&E) procedures. Cervical anesthesia reduces pain with dilator placement [1]; however, most research to date has focused on dilators and ease of D&E completion, evaluating pain as a secondary outcome [2-5]. Insertion of dilators can be more painful than pharmacological cervical preparation, and accounts of how this pain changes over time vary [3,4,6]. One trial evaluating use of intrauterine lidocaine for pain relief during laminaria placement asked participants 30 minutes before D&E to self-report their maximum pain level using a visual analog scale (VAS) since dilator insertion; mean pain scores for the post-laminaria interval were higher than those recorded at laminaria insertion (44 vs 32 p=.04) [2]. Women's experience with pain during the time between dilator insertion and D&E remains an under-evaluated aspect of their abortion experience.

Multimodal pain management is an area of interest across many procedural fields. Providers vary in their strategies for pain management after dilator insertion and may recommend over-the-counter analgesics alone or prescribe oral narcotics. Given the potential for narcotic addiction, studies have been investigating non-narcotic analgesic adjuncts such as gabapentin for various obstetric and gynecologic procedures. Gabapentin is an attractive medication because it is low-cost, non-addictive, and has few medical contraindications for use [7]. Studies regarding preoperative use of gabapentin in abdominal hysterectomy have demonstrated decreased post-operative narcotic use, decreased nausea and vomiting, and increased patient satisfaction [8-13]. A systematic review demonstrated a significant benefit of pre-operative gabapentin for preemptive analgesia for abdominal hysterectomy [14]. Data regarding preoperative gabapentin use in other contexts, such as Cesarean delivery and laparoscopic ovarian cystectomy, are less consistent [15-20]. The heterogeneity of gabapentin dosing and overall pain regimen along with study design limitations make these data challenging to generalize to abortion procedures. The goal of this study is to evaluate the effect of gabapentin on pain experienced after osmotic dilator placement prior to D&E.

2.0 Materials and methods

We conducted this randomized, double-blind, placebo-controlled trial at the University of California, Davis Medical Center. We enrolled women 15 weeks 0 days to 23 weeks 5 days gestation on the day prior to a planned D&E procedure for whom the surgical plan included osmotic dilator placement for overnight cervical preparation. We included women 18 years or older, English-speaking, with an active cell phone with text messaging capabilities, and a ride home from clinic. We excluded women currently taking gabapentin, with an allergy to gabapentin or our standard clinic analgesics (ibuprofen or acetaminophen with codeine), with active renal disease, or currently using narcotics. The UC Davis Institutional Review Board approved this study and all study subjects gave written consent prior to enrollment.

After obtaining baseline demographic information, we randomized subjects 1:1, with stratification based on vaginal parity, to receive two doses of gabapentin 600 mg or placebo. Subjects took the first study drug dose after randomization and instructed to take the second dose 8 hours after dilator placement. The UC Davis Investigational Drug Service (IDS) over-encapsulated the study drug and placebo tablets to create identical-appearing medication. The IDS performed the randomization allocation using a computer-generated random sequence in blocks of four for two groups (vaginally nulliparous and vaginally parous), prepared sequentially numbered vials for each group with appropriate treatment, and maintained the randomization log to ensure drug allocation concealment until study completion.

Family Planning fellows or Obstetrics and Gynecology residents under the supervision of Family Planning faculty aimed to place osmotic dilators 30-60 minutes after intake of the first study drug dose. All physicians followed a standardized clinic protocol for dilator placement (online Appendix Figure 1) using 4 mm Dilapan-S® and cervical anesthesia with lidocaine 1% 20 mL. We used adjunctive mifepristone for gestations 22 or more weeks or if the physician placed fewer than the preferred number of dilators. Subjects in this study did not receive misoprostol. We gave each subject prescriptions for 20 tablets each of ibuprofen 800 mg (1 tablet every 8 hours as needed) and acetaminophen with codeine

300/30 mg (1-2 tablets orally every 4-6 hours as needed) with instructions to use these medications as needed for pain management after dilator insertion.

We evaluated pain using an 11-point numeric rating scale score (NRS; scale 0-10) and assessed gabapentin-specific side effects of tiredness and dizziness. We asked each subject to verbally provide a baseline NRS score and side effect responses at the time of study drug intake and then at 5 minutes after dilator placement. Each subject received text messages at 2, 4, and 8 hours after dilator placement to ascertain current NRS scores for pain, perceived tiredness or dizziness, and the quantity of interval analgesic use (ibuprofen and acetaminophen with codeine). The 8-hour text included a prompt to take the second dose of study drug. Upon presentation for D&E procedure the subsequent day (approximately 18-24 hours after dilator placement), we asked the subject to verbally provide a NRS pain score, current tiredness or dizziness, and analgesic use since the 8-hour text message.

The primary outcome was median change in NRS score from baseline to 8 hours post dilator insertion. We assessed median change in individual pain score from baseline, as opposed to median group scores at each time point, because using median change in individual pain score has been adopted in other fields as the preferred standard for evaluating pain management [20]. Secondary outcomes included pain score change at other time points, difference in pain scores by gestational age, study drug side effects, and analgesic use. Additionally, we assessed median group pain scores at all post-dilator placement time points to describe women's pain experience with overnight dilator placement. Because narcotic pain medications can impact both pain and side effects, we also performed an analysis of these outcomes in women who did not use narcotics.

We estimated a sample size based on a prior study that utilized an 11-point NRS to assess immediate post dilator pain as a secondary outcome, reporting a mean score of 5.2 ± 1.2 [4]. We calculated 12 women per group would demonstrate a clinically meaningful pain difference of 2-points on NRS with 80% power and $\alpha=0.05$ [21]. We doubled the sample to allow for stratification by vaginal parity, and then doubled the size again to 48 per group to allow for adequate evaluation of the primary

and secondary outcomes. We increased the sample by 20% to account for incomplete follow-up or other limitations, yielding a final sample of approximately 120 women.

We performed a modified intention-to-treat analysis, including only women who provided any follow-up NRS information. We compared baseline characteristics among treatment groups using Fisher's Exact Test or Chi-square test as indicated, t-test for continuous variables, and Mann Whitney U for comparing median pain scores. We categorized pain scores post hoc as none, mild (1-3), moderate (4-6), or severe (7-10). We completed analyses using SPSS version 25 (Armonk, NY).

3.0 Results

We randomized 121 women from March 2017 to April 2018 and excluded 3 women from the outcome analysis, one due to randomization error, one due to an allergic reaction after dilator placement who had received placebo, and one who did not provide any follow-up NRS data (Figure 1). The characteristics of the 118 women (60 in the gabapentin group and 58 in the placebo group) who completed the study are presented in Table 1. The mean gestational age for the population was 19 weeks 3 days. Physicians completed dilator placement 42.3 ± 11.2 minutes after initial study drug intake in the gabapentin group and 44.2 ± 9.8 minutes in the placebo group (p=0.33). Nine (15%) and 15 (26%) women, respectively, received mifepristone. The final study evaluation occurred 22.8 ± 2.0 hours and 22.9 ± 1.8 hours, respectively, after dilator placement (p=0.91).

Median change in NRS pain score from baseline is presented in Table 2. Fifty-eight (97%) women in the gabapentin group and 52 (88%) women in the placebo group provided 8-hour NRS responses, the primary outcome. Median change in pain score from baseline to 8 hours post-dilator placement did not differ (2 vs. 2.5, p=0.52); this absence of effect persisted at all time points after dilator placement (5 minutes, 2 hours, 4 hours, and 18-24 hours). When evaluating median change in NRS scores by parity, we found no statistical differences between gabapentin and placebo users at any time point, though we did observe a clinically significant difference of 2 points at 5 minutes, 4 hours and 8 hours (Table 2).

When evaluating population median values at each time point, we also found no differences in scores at all post-dilator placement time points among treatment groups stratified by vaginal parity except for a 2-point difference at 8 hours in vaginally nulliparous women (online Appendix Figure 2). Participants provided a very wide range of pain scores at each time point.

Women who received gabapentin reported more dizziness or tiredness, both of which reached statistical significance compared to placebo beginning at 2-hours after dilator placement (Figure 2). More gabapentin than placebo users experienced dizziness at 2 (29/53[55%] vs. 11/53[21%], p=0.001), 4 (22/55[40%] vs. 5/50[10%], p=0.001) and 8 hours (15/57[26%] vs. 3/52[6%], p=0.004) and tiredness at 2 (34/54[63%] vs. 17/54[31%], p=0.002) and 4 hours (37/54[69%] vs. 18/51[35%], p=0.001).

Table 3 describes the proportion of women who used pain medication during the time from dilator placement to evaluation in the pre-operative area based on the 118 women who provided responses to analgesic use questions. Most (98 [83%]) women used some analgesia, with 85 (73%) women reporting any ibuprofen use and 75 (64%) reporting any acetaminophen with codeine use. Women who reported higher NRS pain scores more commonly used acetaminophen with codeine than ibuprofen or no pain medication (Table 3). Acetaminophen with codeine use did not differ between gabapentin (35/60[58%]) and placebo (40/58[69%]) users (p=0.26). Use of ibuprofen or acetaminophen with codeine did not differ by parity, with ibuprofen use by 45 (76%) vaginally nulliparous and 40 (68%) vaginally parous women (p=0.4) and acetaminophen with codeine use by 40 (68%) and 35 (59%), respectively (p=0.4). Few women (n=12, 10%) reported using six or more acetaminophen with codeine tablets, distributed equally among vaginally nulliparous (n=6) and parous (n=6) subjects; the maximum number used was 11.

When stratifying by gestational age (≤19 weeks 6 days or ≥ 20 weeks 0 days), we found no difference in maximum reported NRS pain score (median 5 vs 6, p=0.57) or any acetaminophen with codeine use (46/74 [62%] vs. 29/44 [66%], p=0.70). When evaluating pain and side effect outcomes in women who did not use any narcotic (25 gabapentin and 18 placebo subjects), we found no difference in median 8-hour NRS change from baseline (1 vs. 2, p=0.41), maximum reported NRS pain score (median

3 vs 3, p=0.96), or side effect profiles between gabapentin and placebo users (data not shown). Sub-analysis of the women who received mifepristone showed no difference between gabapentin and placebo users in median 8-hour NRS change from baseline (3 vs. 3, p=0.93), maximum reported NRS pain score (median 7 vs 7, p=0.86) or any acetaminophen with codeine use (5/9 [56%] vs. 10/15 [67%], p=0.68).

We describe the overall pain experience of women with overnight dilator placement by reporting median NRS pain scores and severity for the placebo group only in Table 4. Two of these women reported zero on NRS pain scale at all time points; both were less than 20 weeks gestation and vaginally parous.

4.0 Discussion

Gabapentin 600 mg with repeat dosing at 8 hours did not improve pain with overnight osmotic dilators prior to D&E procedure. Gabapentin had some clinical effect as demonstrated by the timely reports of dizziness and tiredness among women who received gabapentin compared to placebo, primarily over the first four hours after initial ingestion. Since both time points occurred in the afternoon prior to onset of a typical evening sleeping schedule, we conclude that the excess dizziness and tiredness are consistent with known drug side effects. These effects did not result in less narcotic use by women receiving gabapentin.

In the subset of vaginally nulliparous women, median pain score changes at 5 minutes, 4 hours, and 8 hours from baseline met our *a priori* designated 2-point clinical difference when comparing gabapentin and placebo groups. Although we recruited a study sample large enough for these differences to be assessed, the outcomes did not achieve statistical significance. We believe the lack of statistical significance is related to the very wide range in responses in both groups, demonstrating the variability in pain experience for each patient. Although gabapentin may provide a benefit for vaginally nulliparous women, we found these women experienced more dizziness and tiredness without a resultant decrease in narcotic use. Thus, the relevant benefit may be negligible. Further research of nulliparous women may identify who may benefit from gabapentin prior to osmotic dilator placement.

The lack of a clear benefit with gabapentin use correlates with a recently reported double-blind randomized trial demonstrating that gabapentin did not reduce postoperative pain with first trimester surgical abortion [22]. When considering these findings together with the benefit of pre-emptive gabapentin for pain reduction with abdominal hysterectomy [8-14], and the slight and variable pain reduction benefit with cesarean delivery [15-20], perhaps gabapentin is more beneficial for incision-related (sensory) pain and less for uterine cramping related (visceral) pain.

The medical literature lacks primary data on women's pain experience with dilator placement. Our placebo group provides explicit information about the pain experience with overnight dilators. Nulliparous women generally experience moderate pain after Dilapan-S placement, commonly peaking at 2 hours, and may remain the same for at least 6 more hours. Pain for multiparous women appears to peak at 4 hours and decline thereafter. This information will aid providers in patient counseling regarding pain expectations in the hours following osmotic dilator placement. Future studies should more carefully assess the pain course in vaginally nulliparous women more than 8 hours after dilator placement.

The broad range of pain scores indicates that some women experience more severe pain. By the time of presentation for D&E the next day, the pain level reported is lower than what is reported at 8 hours after dilator placement in parous women but not in nulliparous women, of whom about 20% are still reporting severe pain. We found a correlation of the maximum pain score with acetaminophen with codeine use but not with ibuprofen use, demonstrating that women who experience severe pain will use a narcotic when available, albeit generally fewer than 6 tablets. In our practice we now prescribe fewer narcotic tablets initially and have instituted a mechanism for providing additional analgesics overnight to women who continue to experience pain after finishing their supply.

We measured our dilator placement pain score 5 minutes after dilator placement to assess pain free of other factors, including anxiety, that could affect pain at the moment of placement. Prior studies have evaluated pain score at time of speculum removal. Schivone et al [23] enrolled 69 women 18 weeks or greater (mean 19 weeks) in an open-label randomized trial comparing lidocaine gel and lidocaine 1% 12 mL paracervical block for pain control during dilator placement. The investigators reported a median

visual analog scale pain score (based on a 10 cm line) of 2.5 cm with gel and 3.9 cm with the paracervical block (p=0.17) with peak pain in both groups during dilator placement. Borgatta et al [4] enrolled women 14-16 weeks gestation who received ibuprofen or ketorolac and a cervical anesthetic with lidocaine 1% 10 mL prior to placement of 3-6 osmotic dilators (both laminaria and Dilapan, mean 5), resulting in a mean NRS pain score of 5.2 (95% CI 4.0-6.4). Our median NRS pain score 5 minutes after dilator placement of 1-2 is much lower than reported in both studies, likely reflecting how quickly the pain decreases for most women after speculum removal. Of note, the Borgatta et al [4] study did not prescribe oral narcotics to have at home; 2/25 (8%) women made visits to the emergency department overnight to obtain narcotic pain medication. The need for narcotics in this study may reflect the use of more dilators than needed at this gestational age, potentially resulting in more pain [24].

A strength of our study is its large size which allowed ample numbers to evaluate overall outcomes as well as differences related to parity. Additionally, physicians minimized variation by maintaining a standardized osmotic dilator placement protocol across the five family planning subspecialists, two fellows, and residents who provided care to study participants. The study was limited by the enrollment criteria stipulating that participants must have a ride home from the outpatient osmotic dilator placement visit and must have a private cell phone not shared by others; both criteria could disproportionately restrict enrollment of women with limited support or resources. Additionally, the findings may be specific to the dilator regimen used in these participants and may not apply to other osmotic dilator protocols.

Though use of adjunctive non-opioid analgesics remains an important focus for abortion care, we showed that gabapentin does not provide benefit for osmotic dilator-associated pain compared to placebo. Women experienced gabapentin side effects but no primary benefit in pain reduction or decrease in narcotic use. We also describe that some women experience significant pain with overnight dilator placement and may utilize a narcotic prescription. The decision to prescribe narcotics should be individualized based on discussions with the patient. The description of the pain women experience

following dilator insertion and the associated analgesic use will allow clinicians to provide better counseling and adequately titrate pain medication prescriptions.

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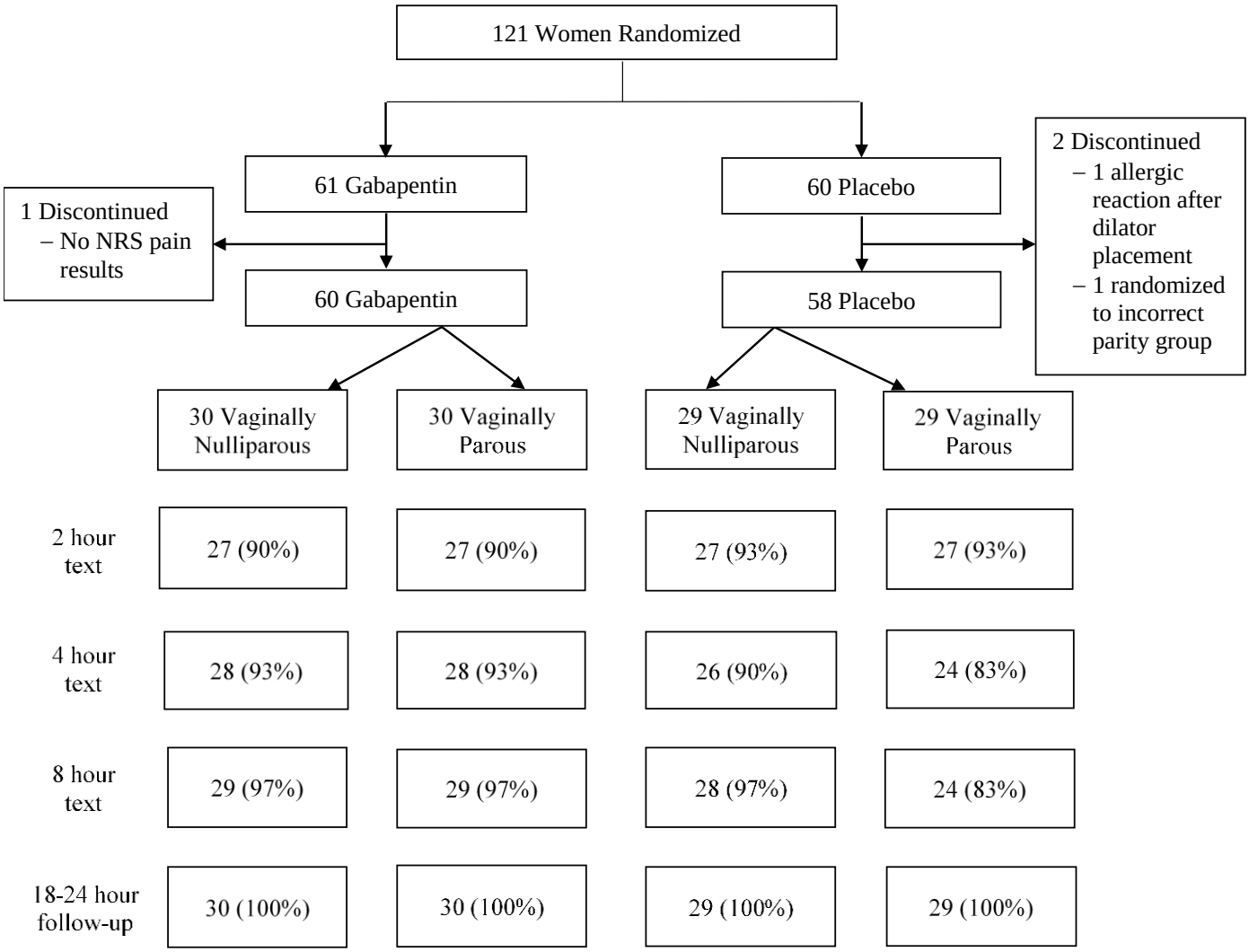
Figure 1. Flow and follow-up completion of subjects receiving gabapentin or placebo with cervical dilator placement before dilation and evacuation procedure



NRS = Numeric rating scale

Figure 2. Gabapentin-related side effects of dizziness and tiredness in subjects receiving gabapentin or placebo with osmotic dilator placement before dilation and evacuation procedure (N=118)

Figure 2A. Dizziness after osmotic dilator placement

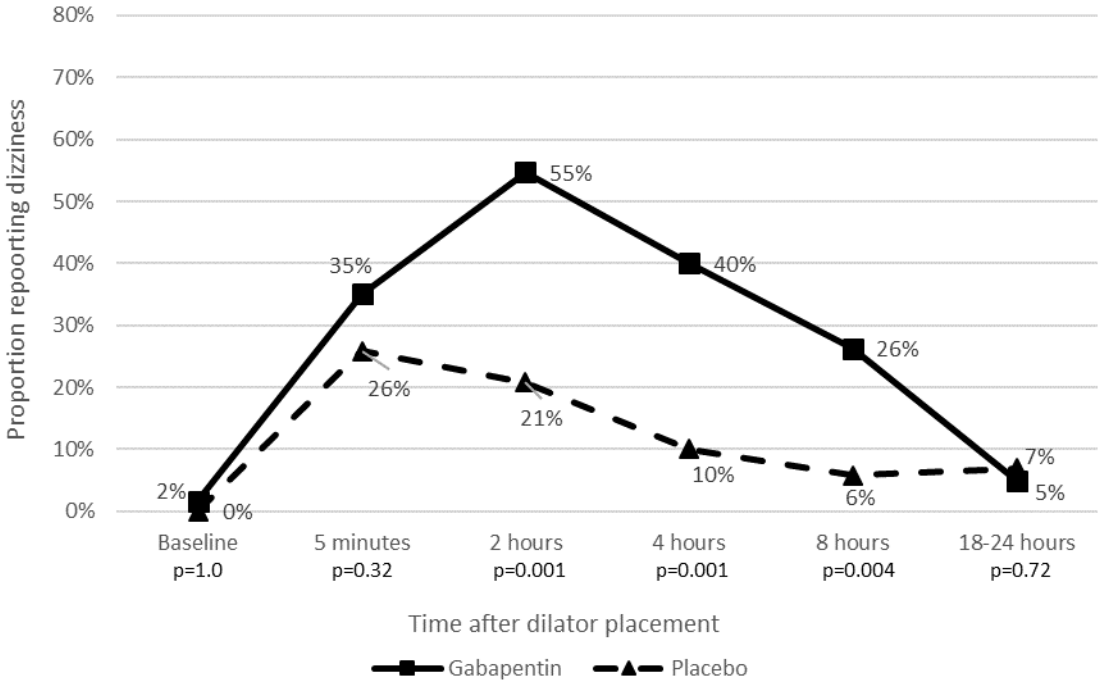
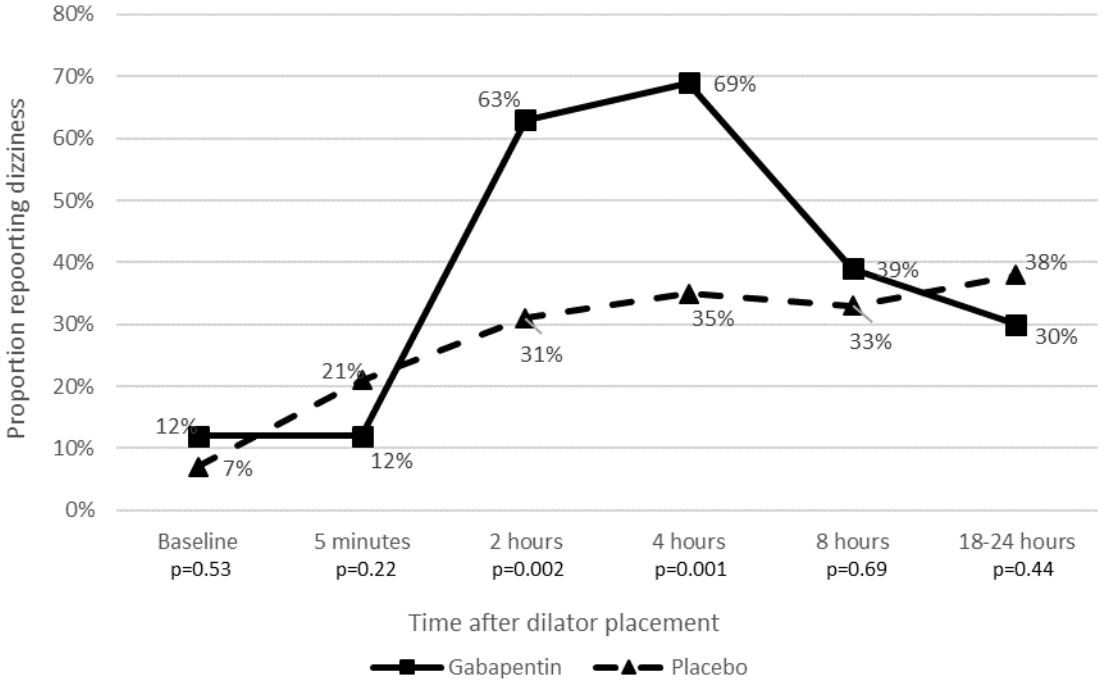


Figure 2B. Tiredness after osmotic dilator placement



Measured using an 11-point numeric rating scale (scale 0-10).

Table 1. Baseline characteristics of subjects randomized to receive gabapentin or placebo with cervical dilator placement before dilation and evacuation procedure

Characteristic	Gabapentin n=60	Placebo n=58	P value
Age (years)	25.4±5.6	27.2±6.1	0.09
Gestational age			0.25
15w0d – 19w6d	41 (68%)	33 (57%)	
20w0d – 23w5d	19 (32%)	25 (43%)	
Reason for abortion			0.20
Unwanted pregnancy	53 (88%)	51 (88%)	
Fetal anomalies	7 (12%)	7 (12%)	
Race			0.09
White	23 (38%)	34 (59%)	
Black	11 (18%)	11 (19%)	
Asian	7 (12%)	3 (5%)	
Mixed	14 (23%)	5 (9%)	
Other	4 (7%)	2 (3%)	
Declined	1 (2)	3 (5%)	
Ethnicity			0.32
Hispanic	43 (72%)	42 (72%)	
Non-Hispanic	17 (28%)	14 (24%)	
Declined	0	2 (3%)	
Education			0.017
Has not completed high school	6 (10%)	4 (7%)	
High school or equivalent	30 (50%)	15 (26%)	
Some college	16 (27%)	32 (55%)	
College or higher	8 (13%)	6 (10%)	
Declined	0	1 (2%)	
Gravidity			0.86
1	14 (23%)	10 (17%)	
2	15 (25%)	13 (22%)	
3	11 (18%)	13 (22%)	
4	5 (8%)	7 (12%)	
5	4 (7%)	3 (5%)	
6	4 (7%)	7 (12%)	
7 or more	7 (12%)	5 (9%)	
Prior vaginal delivery			0.93
0	30 (50%)	29 (50%)	
1	16 (27%)	13 (22%)	
2	8 (13%)	9 (16%)	
3 or more	6 (10%)	7 (12%)	
Prior Cesarean delivery			0.97
0	45 (75%)	44 (76%)	
1	9 (15%)	9 (16%)	

2 or more	6 (10%)	5 (9%)	
Prior miscarriage	12 (20%)	11 (19%)	1.0
Prior abortion	22 (37%)	27 (47%)	0.35
History of anxiety	6 (10%)	9 (16%)	0.42
History of depression	3 (5%)	5 (9%)	0.49
History of chronic pain	0	2 (3%)	0.24
History of drug use			0.71
None	46 (77%)	42 (72%)	
Marijuana	7 (12%)	11 (19%)	
Methamphetamine	4 (7%)	3 (5%)	
Multiple drugs	3 (5%)	2 (3%)	

Data presented as mean ± standard deviation or n (%).
w=weeks; d=days

Table 2. Median change in NRS pain score from baseline among women with osmotic dilators in place prior to dilation and evacuation procedure

	Time after dilator placement	Gabapentin n=60		Placebo n=59		p-value*
		n	Median NRS pain score change	n	Median NRS pain score change	
Total population (N=118)	5 minutes	60	1 (-6, 10)	58	2 (-5, 8)	0.42
	2 hours	54	3.5 (-8, 9)	54	4 (-2, 10)	0.57
	4 hours	56	3 (-8, 9)	50	3.5 (-3, 10)	0.39
	8 hours	58	2 (-3, 8)	52	2.5 (-5, 10)	0.52
	18-24 hours	60	0.5 (-8, 7)	58	1 (-2, 9)	0.23
Vaginally nulliparous (n=59)	5 minutes	30	0 (-6, 8)	29	2 (-2, 7)	0.09
	2 hours	27	4 (-8, 9)	27	5 (0, 9)	0.26
	4 hours	28	3 (-8, 9)	26	5 (-1, 8)	0.35
	8 hours	29	2 (-3, 8)	28	4 (-2, 7)	0.10
	18-24 hours	30	0.5 (-8, 6)	29	1 (-2, 9)	0.12
Vaginally parous (n=59)	5 minutes	30	2 (-5, 10)	29	2 (-5, 8)	0.54
	2 hours	27	3 (-1, 9)	27	2 (-2, 10)	0.81
	4 hours	28	3 (-3, 7)	24	2.5 (-3, 10)	0.93
	8 hours	29	2 (-2, 7)	24	1.5 (-5, 10)	0.37
	18-24 hours	30	0.5 (-3, 7)	29	1 (0, 8)	0.95

Data presented as median (range)
NRS = Numeric rating scale (overall range 0-10)
*Mann Whitney U test

Table 3. Maximum NRS pain score with osmotic dilators and use of acetaminophen with codeine and/or ibuprofen

Categorization of NRS pain score	Number of women reporting NRS and analgesic data n=118	Used acetaminophen with codeine* n=75 (64%)	p value[†]	Used Ibuprofen only n=23 (20%)	p value[‡]	Used no analgesics n=20 (17%)	p value[§]
Severe (7-10)	46 (40%)	37 (49%)	<0.01	5 (22%)	0.94	4 (20%)	0.02
Moderate (4-6)	34 (29%)	23 (31%)		6 (26%)		5 (25%)	
Mild (1-3)	33 (28%)	15 (20%)		10 (43%)		8 (40%)	
None (0)	5 (4%)	0		2 (9%)		3 (15%)	

Data presented as n (%)
NRS = Numeric rating scale (overall range 0-10)
*Includes women who used both acetaminophen with codeine and ibuprofen
[†] Chi-square test; p-value is compared to no use of acetaminophen with codeine
[‡] Chi-square test; p-value is compared to use of no pain medication
[§] Chi-square test; p-value is compared to use of any pain medication

Table 4. Population median NRS pain scores and proportion with severe pain stratified by vaginal parity among women receiving placebo with osmotic dilator placement before dilation and evacuation procedure

Time after dilator placement	Vaginally Nulliparous (n=29)			Vaginally Parous (n=29)			p-value*
	Number responding	NRS Median (range)	Severe pain[†]	Number responding	NRS Median (range)	Severe pain[†]	
Baseline	29	0 (0, 6)	0	29	0 (0, 6)	0	0.72
5 minutes	29	2 (0, 9)	3 (10%)	29	2 (0, 8)	3 (10%)	0.88
2 hours	27	6 (0, 10)	9 (33%)	27	3 (0, 10)	7 (26%)	0.09
4 hours	26	5 (0, 8)	7(27%)	24	3.5 (0, 10)	5 (21%)	0.19
8 hours	28	5 (0, 10)	5 (18%)	24	2 (0, 10)	2 (8%)	0.008
18-24 hours	29	2 (0, 10)	6 (21%)	29	2 (0, 8)	2 (7%)	0.51

Data presented as median (range)
NRS = Numeric rating scale (overall range 0-10)
*Mann Whitney U test comparing medians
[†] Severe pain is NRS score of 7-10

Online Appendix Figure 1. Pre-operative Cervical Preparation: Use of Dilapan and Mifepristone

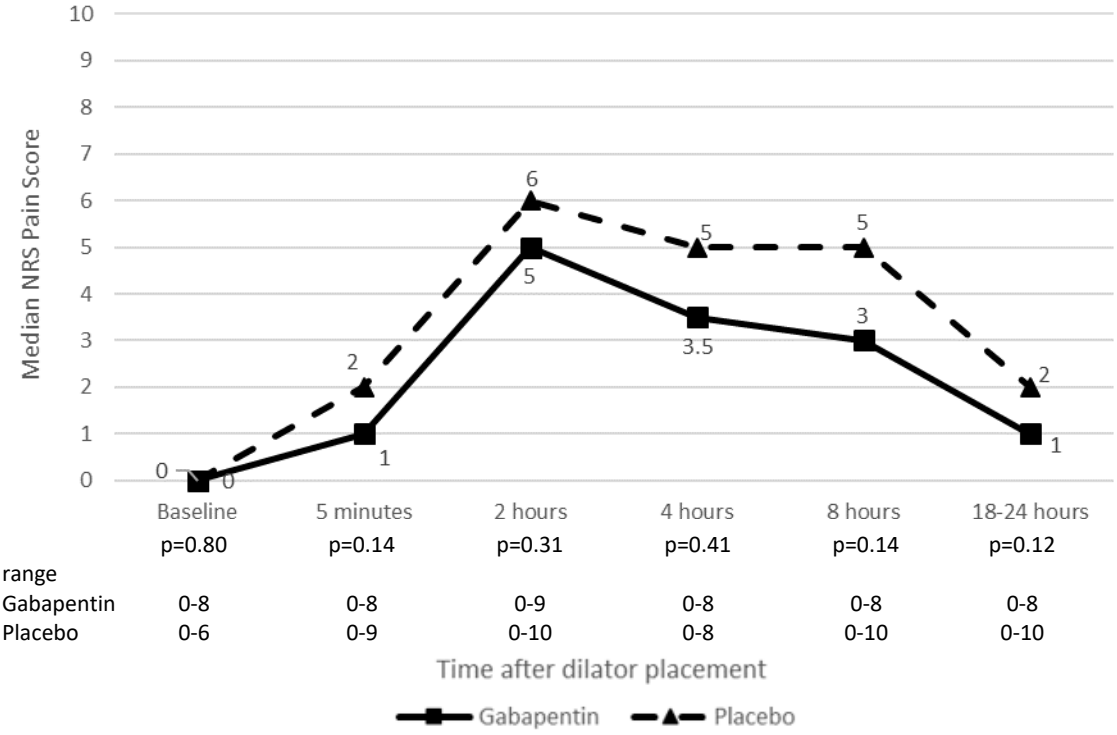
Gestational Age (weeks)	Treatment Option
15	Dilapan #2
16-17+	Dilapan #3
18-19+	Dilapan #4
20-20+	Dilapan #5
21-21+	Dilapan #6
22-23+	Dilapan #7-8 AND Mifepristone*

Gestational Age (weeks)	Provide adjunctive **mifepristone*** if only placed:	Use **second set** of dilators if only placed:
12-13+	--	--
14-15+	--	--
16-17+	1 dilator	--
18-19+	2 dilators	1 dilator
20-20+	3 dilators	2 dilators
21-21+	4 dilators	3 dilators
22-23+	--	4 dilators

* Mifepristone 200 mg one day before procedure

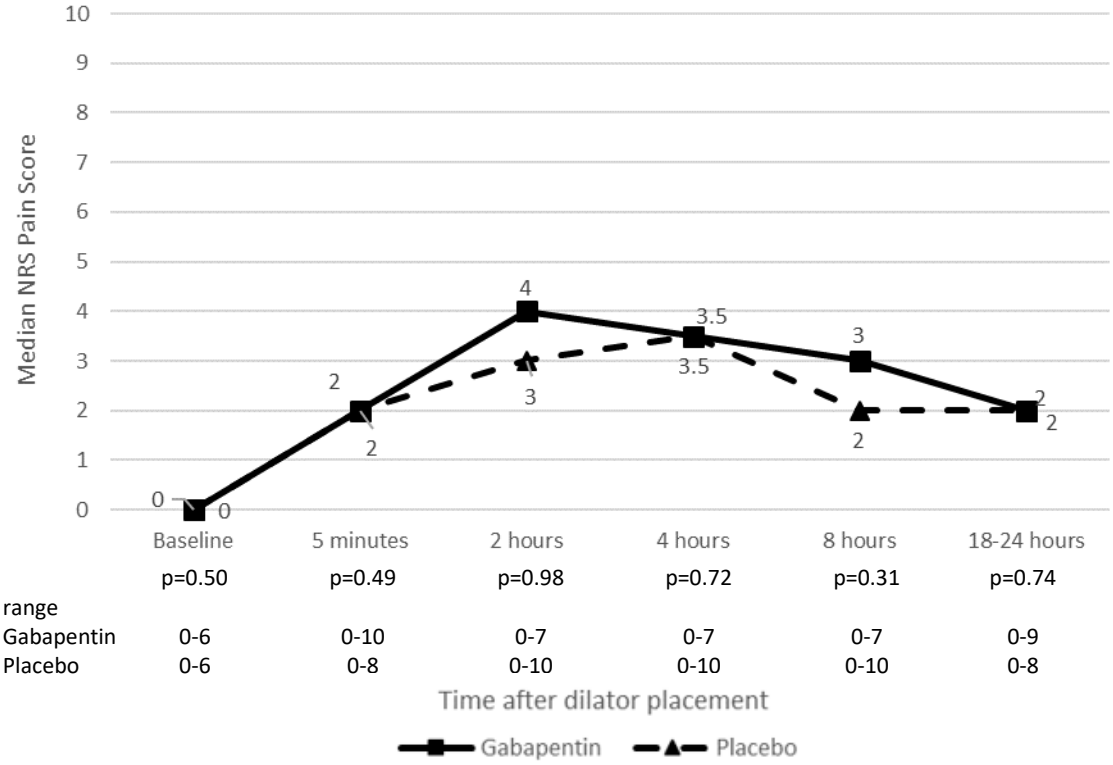
Online Appendix Figure 2. Population median pain scores among subjects receiving gabapentin or placebo with osmotic dilator placement before dilation and evacuation procedure

Figure 2A. Vaginally nulliparous women (n=59)



	Baseline	5 minutes	2 hours	4 hours	8 hours	18-24 hours
	p=0.80	p=0.14	p=0.31	p=0.41	p=0.14	p=0.12
range						
Gabapentin	0-8	0-8	0-9	0-8	0-8	0-8
Placebo	0-6	0-9	0-10	0-8	0-10	0-10

Figure 2B. Vaginally parous women (n=59)



	Baseline	5 minutes	2 hours	4 hours	8 hours	18-24 hours
	p=0.50	p=0.49	p=0.98	p=0.72	p=0.31	p=0.74
range						
Gabapentin	0-6	0-10	0-7	0-7	0-7	0-9
Placebo	0-6	0-8	0-10	0-10	0-10	0-8

NRS = Numeric rating scale (overall range 0-10).