Gabapentin as an adjunct for pain management during dilation and evacuation: A double-blind randomized controlled trial

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PROJECT SUMMARY

Justification.

Over 900,000 abortion procedures are performed annually in the United States [1]. For many women, pain relief during abortion is inadequate despite the use of non-steroidal anti-inflammatory drugs, local anesthetics, opioids, and/or moderate sedation. Research on pain control during abortion has focused on methods for relief during first-trimester suction curettage with little research dedicated to pain during dilation and evacuation (D&E). Gabapentin (Neurontin®) has emerged as an effective adjunct to pain management for a variety of surgical procedures. Gabapentin is inexpensive and is also effective in reducing anxiety, nausea, and vomiting. The addition of pre-operative gabapentin to moderate sedation during D&E may lead to increased patient satisfaction and pain relief without significantly increasing risk or cost.

Proposed Research.

We propose a randomized controlled double-blinded trial evaluating the use of adjunct gabapentin versus placebo in addition to moderate sedation during D&E. We hypothesize that 600 mg oral gabapentin administered pre-operatively at the time of cervical preparation initiation will improve intra-operative pain control. We also hypothesize that it will improve pre- and post-operative pain, anxiety, nausea, vomiting, and overall satisfaction with pain management during D&E. We hypothesize that the doses of moderate sedation agents required to obtain adequate sedation will be decreased in patients receiving gabapentin versus placebo. We also plan to compare the risk of adverse events with adjunct gabapentin versus placebo with moderate sedation.

To test our hypotheses we plan to enroll 130 participants who will be randomized 1:1 to receive either 600 mg gabapentin or placebo at the initiation of cervical preparation. Baseline participant characteristics will be recorded. Pain will be assessed pre-operatively, at 3 intraoperative time points, and postoperatively by 100 mm visual analog scale (VAS). We plan to assess satisfaction with pain control, nausea, vomiting, and anxiety preoperatively and post-operatively, using 5-point Likert scales and the State Trait Anxiety Inventory, respectively. A final assessment will be made by phone on post-operative day one to evaluate overall satisfaction and perform a final screen for adverse events.

New features.

No publications have evaluated the use of gabapentin during abortion care, although multiple studies are currently underway investigating gabapentin's effects during first trimester abortion and during overnight cervical osmotic dilators. To our knowledge, this will be the first evaluation of gabapentin in conjunction with moderate sedation for pain relief during same-day second trimester abortion.

Problems anticipated.

Gabapentin does have a sedating effect and, when used in conjunction with moderate sedation and oral opioids, may lead to increased sedation. We have chosen a relatively low dose of gabapentin to minimize this potential risk. We also plan to limit daily recruitment to minimize disrupting clinic flow and ensure that the study coordinator is available to conduct all assessments on all participants.

1. DESCRIPTION OF THE PROJECT

1.1 Rationale and objectives of the study

1.1.1 Rationale

Over 900,000 induced abortions are performed in the United States annually and 8.6% are dilation and evacuation (D&E) over 13 weeks gestation [1][2] . As over half of abortions are surgical

in nature, the Society of Family Planning has identified "pain management preferences for abortion" as a research priority [3]. The vast majority of the research on pain management during abortion has been conducted in the first trimester. Safe and efficacious options for pain management during abortion include local anesthetics, NSAIDs, anxiolytics, opioids, sedatives, hypnotics, and general anesthesia. Most studies evaluating paracervical block, NSAIDs, oral sedation, and IV sedation demonstrate efficacy in pain reduction [4]. Despite reduction in pain with NSAIDs, paracervical block, and IV sedation, many women still experience inadequate pain relief at the time of surgical abortion.

Gabapentin (Neurontin®), has recently emerged as an effective adjunct to pain management for a variety of surgical procedures but has yet to be studied for perioperative pain control during second-trimester abortion. Gabapentin is a gamma-amino butyric acid (GABA) analog and is approved by the U.S. Food and Drug Administration (FDA) for treatment of post-herpetic pain and seizure disorders. Off-label uses include the treatment of neurologic, chronic and surgical pain. The primary mechanism of action is believed to be modulation of voltage-gated calcium channels and inhibition of release of neurotransmitters [5].

Gabapentin is successfully being used as an adjunct to pain control during both inpatient and outpatient surgical procedures, such as hysterectomy, orthopedic, and ear-nose-throat (ENT) procedures. It is relatively inexpensive. The addition of pre-operative gabapentin to moderate sedation during D&E may lead to increased patient satisfaction and pain control without significantly increasing risk or cost. It may also reduce anxiety, nausea, and vomiting and allow providers to use lower doses of sedatives, improving anesthetic safety.

1.1.2 Objectives and hypotheses

Objective 1: To compare the effect of gabapentin 600 mg to placebo on intraoperative pain during D&E under moderate sedation.

We hypothesize that administration of gabapentin will lower reported pain during D&E compared to placebo.

Objective 2. To compare the effect of gabapentin 600 mg to placebo on the total dose of IV sedation (fentanyl and midazolam) during D&E.

We hypothesize that administration of gabapentin will reduce the total dose of IV sedation agents compared to placebo.

Objective 3. To compare the effect of gabapentin 600 mg to placebo on pre- and post-operative pain, anxiety, nausea, vomiting, and overall satisfaction with pain management.

We hypothesize that administration of gabapentin will result in lower pre- and post-operative pain, anxiety, nausea, and vomiting, and higher satisfaction with pain management compared to placebo.

Objective 4. To compare the adverse events and risks of gabapentin to placebo.

We hypothesize that pre-operative administration of gabapentin will not increase adverse events compared to placebo.

1.2 Previous similar studies

A number of well-designed studies have evaluated pain management during first-trimester abortion. A combination of paracervical block and IV sedation is more effective than paracervical block alone, with the combination resulting in a mean pain score of 43-46 mm (SD 23-26) on a 100-mm visual analog scale (VAS) during first-trimester abortion [6]. In a prospective randomized controlled trial (RCT) of IV sedation (midazolam 2 mg and fentanyl 100 mcg) compared to oral sedation for first-trimester abortion, patients receiving IV sedation had significantly lower pain scores with a mean score of 36.3 (SD 26.5) vs. 61.2 (SD 25.2) on a 100-point scale [7]. Other RCTs evaluating IV sedation used lower doses of IV agents, with and without paracervical block, and found higher mean pain scores, with confidence intervals ranging from 3.7 to 5.5 on a 10-point scale [8], [9]. We could find no published studies dedicated to pain control during second-trimester abortion.

Within the last decade many studies have evaluated the use of gabapentin in prevention and treatment of peri-operative pain. The largest meta-analysis on prophylactic gabapentin was published in 2015 [10]. Of the 133 included studies, over 20 involved gynecologic procedures. Pre-operative doses of gabapentin ranged from 100 mg to 1200 mg. They found that pre-operative gabapentin was associated with reduced anxiety, pain scores, and opioid use in the first 24 hours after surgery. It was also associated with reduced nausea, vomiting, and pruritus and increased patient satisfaction and sedation. Despite increased sedation with gabapentin use, there was no significant association between respiratory depression and gabapentin use. Six randomized controlled trials have examined the relationship between pre-operative gabapentin and respiratory depression and none found an association [11]–[16]. An earlier meta-analysis of gabapentin prior to abdominal hysterectomy included 14 trials and concluded that pre-operative gabapentin reduced post-operative morphine consumption, pain, and nausea [17].

Evaluation of the effect of gabapentin on intraoperative outcomes and in combination with sedation is limited. A single study investigating pre-operative gabapentin during deep sedation for ENT surgery found decreased consumption of intraoperative sedation agents (fentanyl), decreased use

of rescue analgesic, and reduced intraoperative pain scores [18]. They did note increased dizziness in the gabapentin group. Gabapentin has also been found to improve pain scores and decrease consumption of fentanyl when used for pain control during intensive care unit admission [15]. Dose-finding studies have been limited by inadequate sample size, but their findings suggest that pre-operative doses of at least 600 mg to 900 mg provide post-operative benefit [5].

1.3 Design and methodology

1.3.1 Research design and General Methodological Approach

We propose a randomized controlled double-blinded trial comparing oral gabapentin 600 mg to placebo among patients undergoing outpatient same-day dilation and evacuation under moderate sedation. We propose to give the study drug (gabapentin or placebo) shortly after the initiation of same-day cervical preparation and a minimum of one hour prior to D&E. The primary study outcome is maximum pain during D&E as recorded by 100-mm VAS (Table 1). Secondary outcomes include total doses of IV sedation, pain at three time points during D&E, perioperative pain, anxiety, nausea, vomiting, patient satisfaction with pain management, oxygen saturation during moderate sedation, and administration of sedation reversal agents. We will also contact patients by phone on post-operative day 1 (POD1) to assess for prolonged or delayed side effects, adverse events and overall satisfaction with pain control.

Study medications will be administered by study staff, Planned Parenthood of Metropolitan Washington DC (PPMW) staff, or MedStar Washington Hospital Center (MWHC) staff after initiation of cervical preparation. The MedStar Health Research Institute (MHRI) pharmacy will prepare identical capsules containing gabapentin 600 mg or methylcellulose placebo. The pharmacy will package the capsules in sequentially numbered opaque sealed envelopes according to a computer-generated 1:1 randomization scheme prepared by MHRI. Study staff involved in administering medications and assessing outcomes, clinical staff (health care associates, nurses, physicians), and participants will be blinded to randomization assignment. Randomization assignment will only be revealed at the time of data analysis or in the case of a serious adverse event. As there is no standard or optimal dose of pre-operative gabapentin, we have chosen to use a dose of 600 mg with the aim of maximizing pain relief while minimizing the sedative effect. This is the same dose currently being investigated during first-trimester abortion at Emory University.

Administration of analgesics, anesthetics, and anti-emetics will be standardized. Patients will generally receive the following oral pre-procedure regimen: naproxen 500 mg, ~~tramadol 50 mg,~~

alprazolam 0.25 mg, promethazine 25 mg, and azithromycin 500 mg. Medications may be adjusted per provider judgement and patient characteristics, such as allergies. At the time of D&E, providers will administer a paracervical block using 20 mL of 1% lidocaine with 4 units vasopressin. Initial doses of moderate sedation at both sites will be 1 mg midazolam and 50 mcg fentanyl. Additional doses are sometimes required intraoperatively to achieve adequate pain relief and will be left to provider discretion. Total doses of moderate sedation will be capped at 5 mg midazolam and 200 mcg fentanyl. Total doses of midazolam and fentanyl will be documented.

Assessments and tools:

Pain will be assessed using 100-mm VAS. We will assess pre-operative pain using VAS while the patient awaits moderate sedation administration in the procedure room. We will assess intra-operative pain at the following time points: within one minute after speculum placement, within one minute after the initiation of uterine suction aspiration, and within one minute after speculum removal. An assessment of "maximum" intra-operative pain will be made 3- 5 minutes after speculum removal. VAS will be used to assess post-operative pain 30 minutes (range 20-40 minutes) after the procedure. Assessments of anxiety will be made using 20-items of state anxiety from the State Trait Anxiety Inventory (STAI), a validated tool for measurement of anxiety that is used frequently in abortion research [19], [20]. Anxiety will be assessed prior to administration of moderate sedation and 30 minutes post-procedure. Nausea, vomiting, and satisfaction with pain control will be assessed using 5-point Likert scale prior to the administration of moderate sedation and 30 minutes post-procedure. Lowest intra-operative oxygen saturation as measured via pulse oximeter and administration of reversal agents will be recorded. Adverse events will be monitored and include, but are not limited to, seizure-like activity, need for sedation reversal agent, respiratory depression (oxygen saturation <90%), use of uterotonics, aspiration of emesis, or transfer to hospital. Overall satisfaction with pain control will also be assessed on POD1 using a 5-point Likert scale. Participants will receive financial compensation in the form of a $40 gift card on the day of the procedure for their time and participation. After completion of the phone assessment on POD1, participants will be mailed a $10 gift card.

Table 1: Assessments

Time	**VAS**	**STAI**	**Nausea, vomiting, and satisfaction 5-point Likert**
Pre: Prior to moderate sedation	X	X	X

Intra-op: Within 1 minute after speculum insertion	X		
Intra-op: Within one minute after initiating uterine aspiration	X		
Intra-op: Within 1 minute after speculum removal	X		
Max pain experienced during abortion procedure, assessed 3-5 min after speculum removal (Primary outcome)	X		
Post: 30 min after D&E completion	X	X	X
POD1			X (satisfaction only)

1.3.2 Criteria for the selection of subjects

Inclusion criteria include:

- English proficiency
- 18 years of age or older
- Gestational age 14 weeks 0 days to 19 weeks 6 days
- Ability to provide informed consent
- Desire to proceed with outpatient D&E under moderate sedation

Exclusion criteria include:

- Contraindications to outpatient abortion or moderate sedation
- Current use of gabapentin (Neurontin®) or pregabalin (Lyrica®)
- Severe renal disease, per patient report
- Allergy or sensitivity to gabapentin or pregabalin

1.3.3 Subject recruitment and allocation

A total of 130 participants will be recruited from two sites at the time of abortion provision: MedStar Washington Hospital Center Family Planning and Preventative Care (MWHC) and Planned Parenthood of Metropolitan Washington DC (PPMW). PPMW has a diverse patient population, with a

majority of women being African American and age 20-29 years old. We will recruit from the PPMW clinic on the day they provide second trimester termination procedures. MWHC patients are generally referred from their general obstetrician's office or self-referred for abortion and are seen in a private outpatient office. We will recruit eligible patients on days when we are not recruiting at PPMW. Baseline characteristics of the outpatient center at WHC and at PPMW in 2012 are shown below:

Table 2: Patient demographics

Age (years)	WHC	PPMW
<20	4%	12%
20-24	11%	38%
25-29	11%	25%
30-39	68%	21%
40 or more	6%	5%
Race		
Black, non-Hispanic	22%	65%
White, non-Hispanic	61%	16%
Hispanic	11%	8%
Multiracial	0%	8%
Other/unknown	6%	3%

In both recruitment settings, D&E is offered as a same-day procedure under moderate sedation with fentanyl and midazolam. Standard care at both sites includes cervical preparation with misoprostol and/or osmotic dilators, initiated at least two hours prior to D&E. Patients will be recruited after gestational age is confirmed to be 14 through 19 weeks, after eligibility for moderate sedation is confirmed , and after patients have provided informed consent for surgical abortion (Appendix A). This occurs after the patient has completed ultrasound, counseling, lab studies, and documentation of medical history. Patients will generally be recruited after initiation of cervical preparation, as this is a time when clinic flow will not be disrupted by study recruitment. Some participants may be recruited before cervical preparation initiation, as clinic flow permits, but no participant will receive study medications until after cervical preparation has begun.

Patients will be approached by study staff in a private room where eligibility will be assessed and consent will be obtained. A detailed explanation of the study will be provided and written informed consent will be obtained (Appendix B). The patient will be given a copy of her signed informed consent. After the consent is signed, eligibility for the study will be confirmed. Enrollment will be limited to 4 participants per site per day to minimize the impact on clinic flow. Permission to conduct this study has been obtained from the medical directors at both sites and will be approved by Planned Parenthood Federation of America research committee as well as the MHRI IRB.

A MHRI statistician not involved in the conduct of the study will produce the allocation sequence using a computer generated random sequence. The MedStar Health Research Pharmacy will prepare sequentially numbered sealed opaque allocation packets containing the appropriate study medications within opaque capsules. The packets will not be assigned to a participant until eligibility is confirmed. Randomization assignment will only be revealed at the point of data analysis, serious adverse event, or if interim assessment is needed.

1.3.4 Description of the drugs and devices to be studied

Gabapentin (Neurontin®) is FDA-approved for the treatment of post-herpetic neuralgia and seizure disorder. Off-label uses include chronic refractory cough, neuropathy, hot flashes, restless leg syndrome, social anxiety disorder, and post-operative pain. Although its chemical structure is similar to GABA and it was originally suspected to be a GABA analog, the primary mechanism of action is suspected to be via central nervous system voltage-gated calcium channels and the inhibition of excitatory neurotransmitter release [21]. In the U.S., it is available as 100 mg, 300 mg, and 400 mg capsules or 600 mg or 800 mg tablets and is intended for oral consumption. Although originally brought to market as Neurontin® by Pfizer, gabapentin is now available as a generic from multiple pharmaceutical companies. A single 600 mg tablet costs less than $5 wholesale. Oral consumption leads to a peak serum concentration in 2-4 hours with a half-life of 5-8 hours [5].

Gabapentin has an impressive safety record. It is metabolized renally and should be dose-adjusted for renal impairment [5]. Drug interactions are uncommon but include decreased absorption when consumed with antacids [5]. The most commonly reported side effects include dizziness, somnolence, ataxia, and edema and are more pronounced with chronic use and dose $\geq$ 1200 mg [22]. Adverse events are uncommon and include seizure or worsening depression at the time of chronic gabapentin use cessation [5]. Recently, concerns regarding respiratory depression have been raised due

to one retrospective review [23]. In this study, most patients were greater than 50 years old and the average length of surgery was 3 hours. Patients who received gabapentin were slightly more likely to have respiratory depression in recovery (17.5% vs 15.8%, p=0.11). It was only with multivariate analysis that a statistically significant difference was noted. Given the methods, this finding may reflect uncontrolled bias, possibly resulting from anesthesiologists giving gabapentin to patients most at risk of respiratory events to reduce narcotic need. Characteristics associated with respiratory depression after gabapentin use were being elderly, underlying conditions that affect breathing, and concurrent use with opioids [23]. The results of this study contradict a large meta-analysis which showed increased sedation but no increase in respiratory depression with pre-operative gabapentin [10].

1.3.5 Admission procedure

After eligibility has been confirmed and informed consent has been obtained, participants will complete a questionnaire assessing demographic information and medical history (Appendix C). Relevant baseline characteristics including age, gravidity, parity, race, ethnicity, and weeks of gestation will be collected. We will also document pre-existing psychiatric disorders such as depression, anxiety, bipolar disorder and chronic pain syndromes.

She will then be assigned to the next sequentially numbered randomization packet. After initiation of cervical preparation, the participant will consume the study drug from the packet with water or clear juice. Time of administration will be recorded on the patient's chart and will occur at least one hour before the planned procedure. All medications given throughout the clinic experience will be recorded. Method(s) of cervical preparation will be recorded. Antibiotic, anti-emetic, and analgesic administration will be standardized but medications may be adjusted to the need of each woman to accommodate patient characteristics such as allergies and without regard to her enrollment in this study.

1.3.6 Follow-up procedure

The pre-operative assessment will be completed by the study coordinator immediately prior to initiation of moderate sedation (Appendix D), which usually occurs in the procedure room. The intra-operative assessments will be administered by the study coordinator during the procedure at the specified time or point during the procedure (Appendix E). The times of all assessments will be noted. The time of speculum removal will be considered the time of procedure completion.

A same-day post-operative assessment will be completed by the participant 30 minutes (20-40 min range) after procedure completion in the recovery room (Appendix F). After completion of the post-operative assessment patients will receive a $40 gift card and be reminded that they will receive a phone call the following day.

A phone call will be made to all participants on the day following their procedure to administer the POD1 assessment (Appendix G). The participant phone number will be tested at the time of enrollment and three attempts will be made to reach participants by phone on POD1. Participants will be provided with a phone number for the study coordinator should they have trouble receiving phone calls. Patients that complete the POD1 assessment will be mailed a $10 gift card.

1.3.7 Criteria for discontinuation

Participants may withdraw at any time by refusing to participate in further assessments or by electing not to continue with pregnancy termination.

We expect loss to follow up for all primary and most secondary outcomes to be rare as most assessments are made on the date of study enrollment. We expect some loss to follow up for the POD1 assessment but will take the following steps to minimize this loss: testing of participant phone numbers at the time of enrollment, providing a reminder about the phone call prior to clinic discharge, agreeing in advance on a convenient time for the follow up phone call, providing participants with the study coordinators phone number, and provision of a gift card by mail after completion.

Patients who experience serious adverse events will be discontinued from the study and allocation may be revealed to ensure appropriate management of medical conditions. An adverse event (AE) is defined as any health-related reaction, effect, toxicity or abnormal laboratory result that a study participant experiences during the course of the study, irrespective of relationship to the study intervention. A serious adverse event (SAE) is defined as any experience that is fatal or life threatening, requires in-patient hospitalization or prolongation of an existing hospitalization, or results in a persistent or significant disability or incapacity.

A data safety monitoring board (DSMB) will be assembled. A DSMB meeting will be triggered by a case of respiratory compromise requiring sedation reversal (naloxone or flumazenil). This board will consist of clinicians and researchers knowledgeable in abortion care, moderate sedation, and gabapentin. The following individuals have agreed to serve on the DSMB:

- Mitch Creinin, MD, Professor of Obstetrics and Gynecology, Division Director of Family Planning, University of California Davis

- Gillian Dean, MD, MPH, Senior Director of Medical Services, PPFA
- Sue Carlisle, MD, PhD, Professor of Anesthesia/Dean, University of California San Francisco

If triggered to meet, they will review the cumulative data to date and provide advice regarding the safety of continuing, modifying, or discontinuing the study.

The study may be discontinued at any time by IRB or clinical management at either participating institution or the Office for Human Research Protection. One of the co-investigators (AB) will review all adverse events. If there is a suspicion for increased risk, study allocation may be revealed for a preliminary analysis and if related to the study intervention, the study could be prematurely ended.

1.3.8 Laboratory and other investigations

No laboratory studies will be performed for the clinical trial.

1.3.9 Data management

Data will be collected on paper by the research coordinator. Original documents will be stored in a locked cabinet at the Medstar Health Research Institute. Data will be collected on password protected iPads using the REDCap application for iPad. The iPads and REDCap database will be accessible only by the primary, co-investigators, and research coordinator via password protection. The study personnel who will be collecting and entering the data have extensive experience working with confidential medical information and will follow standard institutional procedures for data handling, verification, cleaning, and storage. Appropriate firewall and virus scanning software are installed and updated routinely by the hospital support staff.

1.3.10 Data analysis

Data analysis will be conducted using Stata. The baseline characteristics of the populations will be described. Intention-to-treat analysis will be performed. Primary continuous outcome (pain score on 100-mm point VAS) for the two treatment groups will be compared using T-tests, and if appropriate, by non-parametric analysis. Secondary outcomes will be compared using Chi-square and T-tests, as applicable. Baseline characteristics will be evaluated for potential interaction or confounding with primary and secondary outcomes. If we observe 5 serious adverse events (SAE) requiring sedation reversal agents before enrolling 50 participants, we will ask the statisticians to unblind allocation and

perform an interval analysis to assess for a relationship between study arm and risk of SAE. Once 50 participants are enrolled, we will ask the same analysis after 6 events occur. These numbers of events are based on the concept that if all of the events are in one treatment arm we would find a statistically significant difference in SAE risk between the arms. For reference, sedation reversal is used in less than 1% of D&Es at both sites. Participants may request that their data not be used for analysis if a request is received prior to analysis as mentioned in the consent form. MedStar Health Research Institute (MHRI) statisticians will be consulted to assist with the analysis as needed.

1.3.11 Number of subjects and statistical power

Based on the literature which showed a mean pain score of 3.6 with IV sedation [7], and considering that D&E is expected to be more painful than first-trimester uterine aspiration, we estimate a mean pain score of 45 and a SD of 25 using a 100-point scale for patients in the control group. 30% reduction in pain has been accepted as clinically significant [24]. With 80% power and alpha of 0.05, we will need to include 59 participants in each arm (118 total) to detect a decrease of 13 points on a 100-point scale, approximately 30% reduction in pain. As the primary outcome is assessed on the same day as enrollment, we do not expect significant loss to follow up. Accounting for the possibility of withdrawals or incomplete data, we plan to enroll 130 women. Enrollment of 3-5 patients per week will allow recruitment to be completed in approximately 26-43 weeks (6-10 months).

1.3.12 Study limitations

We are aware that the standard regimen for moderate sedation during second trimester abortion at our facilities (naproxen, tramadol, alprazolam, fentanyl, and midazolam) may provide greater pain relief and sedation than other commonly used regimens and thus may limit our ability to detect an improvement in pain relief. However, our experience is that a significant proportion of women have inadequate pain control despite receiving the standard regimen and therefore they may benefit from gabapentin. The fact that gabapentin has been shown to reduce total narcotic use after major surgery is reassuring. Our sample size limits our ability to detect rare outcomes or complications such as medication adverse reactions.

1.3.13 Duration of project

We anticipate completing the process of IRB approval and training of staff to be complete by the early summer of 2017, at which time enrollment will commence. We expect recruitment and data

collection to last 7-9 months. Data analysis and manuscript preparation will take an additional 2-3 months.

Table 3: Timeline

	2017										2018					
	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun
Material development																
IRB Review																
Contracts, Hiring																
Staff training																
Recruitment and data collection																
Data cleaning and analysis																
Report and manuscript writing																

1.4 Project management

Dr. Ashley Brant (fellow) and Dr. Pamela Lotke (fellowship director and principal investigator) will have ultimate responsibility for this study and will serve as the primary contacts. Other faculty mentors include Dr. Matthew Reeves, Dr. Peggy Ye, and Dr. Rachel Scott. This study will not involve other institutions. The staff at PPMW and MWHC have participated in prior similar studies and are familiar with the data collection and study participation processes. We will have pre-study meetings with the staff at both PPMW and MWHC to explain the study and discuss work flow.

1.5 Links with other projects

None

1.6 Main problems anticipated

The frequency of intraoperative pain assessments will require the study coordinator to remain in the room throughout the procedure and therefore we will limit recruitment to 4 patients per day per site to minimize disruptions to clinic flow. This will also reduce the chance of missing data from

perioperative assessments as a result of the coordinator's unavailability. We also anticipate some loss to follow up at the time of the POD1 assessment; this assessment is a secondary outcome and we are taking steps to minimize loss as described in section 1.3.6. Our final concern relates to the potential for over-sedation with the combination of gabapentin and opioids, which could impact both patient safety and clinic flow if discharge is delayed. Although dose-finding studies have not identified an ideal dose, we suspect that a one-time dose of 600 mg will improve pain control without significantly contributing to sedation. Sedation reversal agents are available at both sites. Adverse events, including respiratory depression, will be monitored, reviewed, and allocation revealed if necessary.

1.7 Expected outcomes of the study and dissemination of findings

This study will contribute to the body of literature on pain control during abortion. It will begin to fill the chasm of evidence on pain control during D&E. This may lead to increased use of gabapentin for family planning procedures. It will also contribute to our knowledge regarding the safety of gabapentin as an adjunct to moderate sedation in an outpatient setting; which may be applicable to other gynecologic procedures as well as other medical and surgical specialties. If found to be effective as an adjunct to moderate sedation, gabapentin may further improve pain control for abortion procedures performed without IV sedation. We expect that adjunct use of gabapentin will improve women's experiences and satisfaction with abortion care.

We plan to present the results of this study at the North American Forum on Family planning or a similar national medical conference. The manuscript will be submitted to *Contraception* or a similar journal for peer review and publication.

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2. ETHICAL CONSIDERATIONS

After the proposal is submitted to the Fellowship in Family Planning, we will submit the application for this protocol to MHRI/MWHC IRB. We will also submit the proposal to PPMW for approval through the appropriate channels. Approval through Planned Parenthood Federation of America (PPFA) will also be sought prior to study initiation.

3. BUDGET

3.1 Line-Item Budget

PROJECT BUDGET									
Title: Gabapentin as an adjunct for pain management during dilation and evacuation: A double-blind randomized controlled trial									
Time Period:		Year 1				Year 2			
A. PERSONNEL									
Name	**Role**	**Effort**	**Stipend/ Salary**	**Fringe**	**TOTAL**	**Effort**	**Salary**	Fringe	**Total**
Matthew Reeves, MD MPH	Co-Investigator	5%	In-kind		$0	5	In-kind		0
Ashley Brant, DO, MPH	Co-Investigator	20%	In-kind		$0	20	In-kind		0
Pamela, Lotke, MD	Principal Investigator	5%	In-kind		$0	5	In-kind		0
Peggy Ye, MD MPH	Co-Investigator	5%	In-kind		$0	5	In-kind		0
Rachel Scott, MD	Co-Investigator	5%	In-kind		$0	5	In-kind		0
Preeti Dhillon	Research Coordinator	60%	$69,000	20.9	$50,053	58%	$71,070	20.9	$24,918.00
			Total Personnel		$50,053				$24,918.00
B. MATERIALS AND SUPPLIES			**Cost**	**N**					
Office Supplies (paper, ink)			$258.00	1	$258.00				
Ipad			$400.00	2	$800.00				
			Total Materials Cost		$1,058.00				0
C. PARTICIPANT COSTS			**Cost**	**N**					
Participant Reimbursement Randomized			$40.00	130	$5,200.00				
Follow up phone call			$10.00	130	$1,300.00				
			Total Participant Costs		$6,500				0

E. TRAVEL			**Cost**	**N**					
Research Coordinator travel, parking					$1,000				
			Total Travel		$1,000				0
F. OTHER COSTS									
			Cost	**N**					
Pharmacy Start-Up					$1,500				
Medication Preparation and Dispensing	$5.00/ dose		$5.00	130	$650				
Acquisition Costs for Medications and Materials					$150				
Research Room Fees at PPMW					$8,000				
Stamps			$271.00	1	$271.00				
Biostatistics	$150/hour		$150.00	26	$3,900.00				
			Total Other Costs		$14,471				0
			TOTAL		**$73,082**				**$24,918.00**
			Total amount for YEAR 1 and YEAR 2						**$98,000**

The budget is also submitted as a separate excel file.

3.2 Budget Justification

3.2.A. Personnel

Pamela Lotke, MD, MPH: Principal Investigator. Dr. Lotke will be responsible for administration and oversight of all aspects of this project. She will assist in the training of staff and participate in study operations. She will oversee recruitment and provide administrative oversight at WHC FPPC.

Ashley Brant, DO, MPH: Family Planning Fellow. Dr. Brant will also be responsible for administration and oversight of all aspects of this project. She will assist in the training of staff and participate in study operations, and will take the lead in preparations of reports, data analysis, and manuscript submission. She will assist the research coordinator in preparation for study initiation, subject recruitment, study enrollment and completing all study related activities

Preeti Dhillon, MPH: Research Coordinator: 18 Calendar Months at 60% effort in year 1 and 58% in year 2. The MedStar Clinical Research Center (MCRC) research coordinator will coordinate implementation of the protocol, oversee administrative and research activities including recruitment,

retention, patient contact, data entry, patient registration, preparation of IRB protocol submissions, renewals and amendments, and ensure regulatory documents are filed properly under the immediate supervision of the Principal Investigator.

Matthew Reeves, MD, MPH: Faculty mentor and research advisor. Dr. Reeves will provide support in overall project design and assist in data analysis, preparation of reports, and manuscript submission.

Peggy Ye, MG, MPH: Faculty mentor and research advisor

Rachel Scott, MD, MPH: Faculty mentor and research advisor

3.2.B Equipment

None

3.2.C Materials and Supplies

$258 for office supplies that will be used for the questionnaires.

Two iPads will be purchased and used for data collection, each costing $400, for a total of $800.

3.2.D Participant Costs

Patients will receive $40 during the randomization visit and $10 for the follow-up phone visit, for a total of $50 per participant. Total cost is expected to be $6,500.

3.2.E Travel

$1,000 to cover mileage and parking cost of research coordinator at off-site visits to Planned Parenthood

3.2.F Other

Pharmacy expenses: $1500 for pharmacy start-up fee, $650 for preparation and dispensing of drugs, $150 for acquisition cost of medication and materials. Totaling $2,300.

A biostatistician at MHRI will be consulted to provide statistical expertise regarding overall project design, analysis, and results dissemination. She/He will oversee final data analysis to ensure appropriate statistical methods are utilized.

$271 for mailing gift cards to the patients after follow up call visits.

PPMW will receive $8,000 for use of their facilities during the study. This is intended to cover the use of a private space for recruitment and enrollment as well as storage needs. It also provides payment for PPMW staff time for medication administration and potential additional monitoring that may be required during the procedure and during the recovery period. Finally, it covers potential impact to health center revenue from effects on patient flow.

4. APPENDICES

Appendix A: Recruitment script and eligibility assessment
Appendix B: Informed consent
Appendix C: Demographics and history
Appendix D: Pre-operative assessments
Appendix E: Intraoperative assessments
Appendix F: Post-operative assessments
Appendix G: Post-operative day 1 assessment

Appendix A: Recruitment script and eligibility assessment

"We would like to invite you to participate in a study that is evaluating a FDA-approved medication called gabapentin and the effect that it has on pain you may have during your abortion procedure. Your participation is completely voluntary and will not influence the care you receive at the clinic. If you choose to participate, you will be given a pill, either gabapentin or a sugar pill prior to the abortion, in addition to usual pain medications. Neither you nor the research or clinic staff will know whether you received the Gabapentin or placebo. We will then ask you to rate your pain, nausea, anxiety, and satisfaction with pain control. You will also be asked to report any additional side effects that you experience. These assessments will take place while you are here at the clinic and will not delay or prolong your care today. You will be reimbursed with a $40 gift card today for your participation. You will also receive a phone call tomorrow to ask again about pain and side effects. After you complete the phone call, you will receive a $10 gift card in the mail. If you are interested in participating, we will give you a consent form to read and we will go through the study in detail with you. Whether or not you choose to be in the study will not affect your care at the clinic. Are you interested in participating in the study?"

Eligibility assessment:

1.	Is your age ≥ 18 years?	❑ **Yes**	❑ No
2.	Do you plan to undergo surgical abortion with moderate/ IV sedation?	❑ **Yes**	❑ No
3.	Is your gestational age ≥ 14 weeks and < 20 weeks? (Study coordinator will confirm in medical record)	❑ **Yes**	❑ No
4.	Are you fluent in English and able to provide informed consent?	❑ **Yes**	❑ No
5.	Do you have an allergy, sensitivity or other reason why you cannot receive Gabapentin?	❑ **No**	❑ Yes
6.	Do you have any contraindications to outpatient surgical abortion using moderate/IV sedation?	❑ **No**	❑ Yes
7.	Are you currently taking gabapentin (Neurontin) or pregabalin (Lyrica)?	❑ **No**	❑ Yes
8.	Do you have any renal (kidney) disease?	❑ **No**	❑ Yes
9.	Has the fetus/baby died?	❑ **No**	❑ Yes

To be eligible, participant must answer "Yes" to questions 1-4 and "No" to questions 5-9.

Appendix B: Informed consent

MedStar Health Research Institute Informed Consent for Clinical Research

INTRODUCTION

We invite you to take part in a research study called *Gabapentin as an adjunct for pain management during dilation and evacuation: A Randomized Controlled Trial*. You were selected as a possible participant in this study because you are at or above 18 years of age and have decided to have an abortion and are equal to or more than 14 weeks pregnant. Please take your time to read this form, ask any questions you may have and make your decision. We encourage you to discuss your decision with your family, friends and your doctor(s).

WHAT IS THE PURPOSE OF THIS STUDY?

This study is being done to evaluate the effect of gabapentin (600 mg) on pain during second trimester abortion with moderate sedation**.** The addition of gabapentin to moderate sedation during second trimester abortion may lead to increased patient satisfaction and pain relief without significantly increasing risk or cost. It may also reduce anxiety, nausea, and vomiting and allow providers to use lower doses of other pain medications, improving anesthetic safety.

WHAT ELSE SHOULD I KNOW ABOUT THIS RESEARCH STUDY?

It is important that you read and understand several points that apply to all who take part in our studies:

- Taking part in the study is entirely voluntary and refusal to participate will not affect any rights or benefits you normally have;
- You may or may not benefit from taking part in the study, but knowledge may be gained from your participation that may help others; and
- You may stop being in the study at any time without any penalty or losing any of the benefits you would have normally received.

The nature of the study, the benefits, risks, discomforts and other information about the study are discussed further below. If any new information is learned, at any time during the research, which might affect your participation in the study, we will tell you. We urge you to ask any questions you have about this study with the staff members who explain it to you and with your own advisors prior to agreeing to participate.

WHO IS IN CHARGE OF THIS STUDY?

The investigator is Dr. Pamela Lotke. The research is being sponsored by The Society for Family Planning (SFP). MedStar Health Research Institute is being paid by SFP, to conduct this study with Dr. Pamela Lotke as the primary investigator.

WHO CANNOT PARTICIPATE IN THIS STUDY?

You cannot be in this study if any of the following apply to you:

- Contraindications to outpatient abortion or moderate sedation
- Current use of gabapentin (Neurontin®) or pregabalin (Lyrica®)
- Severe renal disease
- Allergy or sensitivity to gabapentin
- Fetal Demise

WHAT IF I AM PRESENTLY PARTICIPATING IN ANOTHER RESEARCH STUDY?

Are you presently participating in any other research studies? Yes ☐ No ☐

If yes, please state which study(ies)_____

While participating in this study, you should not take part in any other research project without approval from the people in charge of each study. This is to protect you from possible injury arising from such things as extra blood drawing, extra x-rays, interaction of research drugs, or similar hazards.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About **130** people will take part in this study, worldwide.

WHAT HAPPENS IF I AGREE TO BE IN THE STUDY?

If you agree to take part in this study, taking into consideration allergies to medications, you will receive the standard oral pain medications and you will be "randomized" into one of the following study groups:

- Gabapentin 600 mg
- Placebo (a "sugar" pill without any medication)

Randomization means that you are put into a group by chance. It is like flipping a coin. Neither you nor the investigators will choose what group you will be in. You will have a one in two chance of being placed in either group.

Neither you nor the investigator will know what group you are in.

If you choose to participate in the study:

- You will be asked some questions about your background and medical history.
- You will be randomized into one of the two study groups.
- You will be given/take the assigned medication prior to your surgical procedure.
- You will complete a questionnaire immediately prior to the start of sedation.
- You will answer questions about your pain during the procedure.
- You will complete a questionnaire 20-40 minutes following your procedure.
- You will complete a questionnaire over the phone the day following your procedure.

The procedures/treatments in this study that are considered experimental/investigational are:

- Study drug (gabapentin or placebo)

For procedures/treatments that are not experimental/investigational:

- Your abortion procedure and sedation. Your participation in the study will not affect how your abortions is performed or how sedation is given.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study from the time of enrollment until completion of the follow-up phone visit one day after your surgical procedure. You should expect a call from a research staff member the day after your surgical procedure.

The investigator may decide to take you off this study if it is believed to be in your best interest, you fail to follow instructions, new information becomes known about the safety of the study, or for other reasons the investigator or sponsor believes are important.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the investigator and your regular doctor first so they can help you decide what other options may be best for your medical care once you are off study.

If you suddenly withdraw from the study, there are no consequences to you but we may not be able to use any of the information gathered from your participation.

WHAT ARE THE RISKS AND SIDE EFFECTS OF THIS STUDY?

If you decide to participate in this study, you should know there may be risks. You should discuss these with the investigator and/or your regular doctor and you are encouraged to speak with your family and friends about any potential risks before making a decision. Potential risks and side effects related to this study include:

Risks and side effects ***that may occur*** include:

- Dizziness and drowsiness. These side effects are uncommon and are more common with long-term use of high doses of gabapentin.

Risks and side effects ***that rarely occur*** include:

- Temporary loss of muscle control, swelling, seizure. These side effects are very rare and are more common with long-term use of high doses of gabapentin.

If you are assigned to receive placebo, we want you to know that you will be taking an inactive ingredient made to look and taste as if it was an active medication. In general, placebo is assigned to individuals in research studies, so that the researchers can better evaluate the true overall effect of the study medication(s). Unlike the gabapentin, placebo will not reduce pain associated with the procedure.

Please tell the investigator about all medications including over-the-counter drugs or herbal supplements you are taking, even if you don't think they are important.

There may also be risks and side effects other than those listed above that we cannot predict. Many side effects go away in a short time after the gabapentin is stopped, but, in some cases, side effects can be serious, long lasting and/or life threatening. If you have any unwanted side effects, you should ask the investigator whether there are any medications or other things that may be done to make the side effect less uncomfortable.

For more information about risks and side effects, please ask Dr. Pamela Lotke.

ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

You may or may not get any direct benefit from being in this study. We cannot promise that you will experience any benefits from participating in this study. We hope the information learned from this study will benefit others in the future.

WHAT OTHER OPTIONS ARE THERE?

Instead of being in this study, you have these options:

- You may undergo your surgical abortion outside of this study.
- You always have the option to not be in this study or to refuse any medical treatment.

WHAT ABOUT CONFIDENTIALITY?

Your personal health information (PHI) will be kept private to the extent allowed by law. Study records identifying you will be kept confidential and will not be made publicly available. You will not be identified by name in any publications resulting from this study. You will be asked to sign a separate form that will give permission to the investigator, representatives from government agencies, including the Food and Drug Administration (FDA), institutional review boards, the sponsor and/or the sponsor's representative(s), and certain other people, agencies or entities, to look at and review the records related to this study including your personal health information and the information discovered during this study. This separate form explains in greater detail who will have access to your records, what type of information will be reviewed and for what purposes, how long your permission for others to review and release your records will last, and how you may withdraw your permission if necessary. If you do not wish to sign this permission form you will not be allowed to participate in this study.

Information, that does not include personally identifiable information, concerning this clinical trial has been or may be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered clinical trials. This data bank can be accessed by you and the general public at www.ClinicalTrials.gov. Federal law requires clinical trial information for certain clinical trials to be submitted to the data bank.

WILL I BE PAID FOR PARTICIPATING IN THIS STUDY?

You will be paid for being in this study. Participants will be given a $40 gift card after completing all in-patient study related procedures and an additional $10 will be provided to participants upon completion of the follow-up telephone questionnaire. Payments of $600 or more in one year will be reported to the IRS. Materials and information obtained from you in this research may be used for

commercial or non-commercial purposes. It is the policy of Medstar Washington Hospital Center, MedStar Health Research Institute, MedStar Health, Inc. and its affiliated entities not to provide financial compensation to you should this occur.

WHAT ARE THE COSTS?

You do not have to pay anything to be in this study. However, if taking part in this study leads to procedures or care not included in the study, it may lead to added costs for you or your insurance company. You will not be charged for the medications and tests that are part of this research study.

You, or your insurance company, will be charged for any other portion of your care that is considered standard of care. You may be responsible for any co-payments and deductibles that are standard for your insurance coverage.

WHAT IF I'M INJURED OR BECOME ILL DURING THE STUDY?

We will make every effort to prevent injuries or illness from occurring while you are in the study. In the case of an injury, illness, or other harm occurring to you during, or resulting from, the study, you should seek medical treatment. You should also contact the study doctor as soon as possible. You or your insurance company will be charged for any continuing medical care and/or hospitalization that are not a part of the study.

If you suffer an injury related to the study drug or study procedures, the reasonable costs of necessary medical treatment of the injury will not be reimbursed by the Society for Family Planning to the extent these costs are not covered by your insurance or other third party coverage.

No funds have been set aside, by Medstar Washington Hospital Center, the MedStar Health Research Institute, MedStar Health, or its affiliated entities to repay you in case of injury, illness, or other harm occurring during, or resulting from the study, and their current policies do not provide for payments for lost wages, cost of pain and suffering, or additional expenses. By agreeing to this you do not give up your rights to seek compensation in the courts.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

- You have the right to be told about the nature and purpose of the study;
- You have the right to be given an explanation of exactly what will be done in the study and given a description of potential risks, discomforts, or benefits that can reasonably be expected;
- You have the right to be informed of any appropriate alternatives to the study, including, if appropriate, any drugs or devices that might help you, along with their potential risks, discomforts and benefits;
- You have the right to ask any questions you may have about the study;
- You have the right to decide whether or not to be in the study without anyone misleading or deceiving you; and
- You have the right to receive a copy of this consent form.

By signing this form, you will not give up any legal rights you may have as a research participant. You may choose not to take part in or leave the study at any time. If you choose to not take part in or to leave the study, your regular care will not be affected and you will not lose any of the benefits you would have received normally. We will tell you about new information that may affect your health, welfare, or willingness to be in this study.

WHO DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the investigator, Dr. Pamela Lotke, at 202-877-2235. If you are having a medical emergency, you should call 911 or go directly to the nearest emergency room.

For questions about your rights as a research participant, contact the MedStar Health Research Institute. Direct your questions to the Office of Research Integrity at:

Address:	MedStar Health Research Institute 6525 Belcrest Rd. Suite 700 Hyattsville, MD 20782	Telephone : Toll Free: Fax	(301) 560-2912 (800) 793-7175 (301) 560-7336

SIGNATURES

As a representative of this study, I have explained the purpose, the procedures, the possible benefits and risks that are involved in this research study. Any questions that have been raised have been answered to the individual's satisfaction.

_____ _____
Signature of Person Obtaining Consent Date of Signature

Printed Name of Individual Obtaining Consent: _____

I, the undersigned have been informed about this study's purpose, procedures, possible benefits and risks, and I have received a copy of this consent. I have been given the opportunity to ask questions before I sign, and I have been told that I can ask other questions at any time. I voluntarily agree to be in this study. I am free to stop being in the study at any time without need to justify my decision and if I stop being in the study I understand it will not in any way affect my future treatment or medical management. I agree to cooperate with Dr. Pamela Lotke and the research staff and to tell them immediately if I experience any unexpected or unusual symptoms.

_____ _____
Participants signature Date of Signature

Printed Name of Participant _____

_____ _____
Signature of Witness Date of Signature

Printed Name of Witness: _____

As the Principal Investigator (or designee) for this research study, I attest that the participant has voluntarily agreed to be part of this study, the risks and benefits of the study have been fully explained, and any questions have been addressed to the participant's satisfaction.

_____ _____
Principal Investigator's Signature Date of Signature

[Note: if not the principal investigator, a sub-investigator who has delegation of authority or who may adjudicate adverse events should sign for the PI; must be signed within 5 business days of consenting the participant

Appendix C: Demographics, medical history, chart review

Subject ID:	Date:	Time:	Interviewer:

Section one: Demographics

1) What is your date of birth? (MM/DD/YYYY): __ __ / __ __ / __ __ __ __

2) Which of the following BEST describes your racial/ethnic background?

☐ White/Caucasian
☐ Black or African American
☐ Asian
☐ Other, Mixed, or Multi-racial
☐ Don't know/don't want to answer

3) Do you consider yourself to be Hispanic/Latina/Latino?

☐ NO
☐ YES

4) What level of education have you completed?

☐ Less than high-school
☐ High-school diploma or GED
☐ Some college
☐ Associates degree or Technical Certification
☐ Bachelors degree
☐ Masters degree/Doctoral degree

5) What is your best estimate of the total yearly income in your household? Include all family members from all sources, before taxes, in [last calendar year]. By "combined family income," I mean your income PLUS the income of all family members living in this household (including cohabitating partners, and armed forces members living at home.

☐ <$10,000
☐ $10,001-25,000
☐ $25,001-50,000
☐ $50,001-75,000
☐ $75,001-100,000
☐ >$100,001
☐ Don't know/refused

6) What is your insurance type?

☐ Medicaid/Medicare
☐ Private insurance
☐ Other, specify_____
☐ Uninsured
☐ Don't know/refused

Section two: Medical history

7) Have you ever been pregnant before?

☐ NO
☐ YES → Answer questions a-e below

a. Number of miscarriages or ectopic pregnancies_____
b. Number of C-sections? _____
c. Number of vaginal deliveries? _____
d. Number of abortions? ____ (if 0, skip to question 9)
e. Number of medical abortions: ____
f. Number of surgical abortions: ____

8) Do you have any of the following medical conditions?

		If yes, do you take medication for it?	Name of medication(s):
1. Anxiety	☐NO ☐ YES	☐NO ☐ YES	
2. Depression	☐NO ☐ YES	☐NO ☐ YES	
3. Other mental health diagnosis (bipolar, schizophrenia, PTSD): Name of condition(s): _____ _____	☐NO ☐ YES	☐NO ☐ YES	
4. Medical conditions that may cause chronic pain (fibromyalgia, rheumatoid arthritis, etc.): Name of condition(s): _____ _____	☐NO ☐ YES	☐NO ☐ YES	

9) Do you currently take any of the following medications?

	Past month	**Number of tablets in last month**	

		1-9	10-19	20 or more	
1. Opiate Pain medication (including oxycodone, Percocet, oxycontin, methadone, etc.)	☐NO ☐ YES	☐	☐	☐	Name: _____
2. Benzodiazepine pain medication (including Xanax, Valium, Ativan, etc.)	☐NO ☐ YES	☐	☐	☐	Name: _____

10) Do you, or have you ever, used any of the following substances?

	Past month	**Frequency, average during the last month**		
1. Cigarettes	☐NO ☐ YES	☐ ≤ 1/2 PPD	☐ >½ to 1 PPD	☐ > 1 PPD
2. Alcohol	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
3. Marijuana	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
4. Cocaine/Crack	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
5. Heroin	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
6. Methamphetamine	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
7. Any other illicit drugs to get high	☐NO ☐ YES	☐ < 2 times/week	☐ 2-3 times/week	☐ ≥ 4 times/week
	Name of drugs:			

11) Have you ever been physically or sexually assaulted?
- ☐ NO
- ☐ YES, Sexually Assualted
- ☐ YES, Physically Assaulted
- ☐ YES, Both sexually and physically assaulted

12) Are you having an abortion because of a fetal diagnosis?
- ☐ NO
- ☐ YES. Please describe: _____

INTRODUCTION TO VISUAL ANALOG SCALE

For these questions, we are going to ask you to make an X on a line. For example, let's say you are asked how much you like Oreo cookies:

How much do you like Oreo cookies? (make an X on the line)

very little _____ very much

You answer the question by making an "X" on the line according to how much you like or dislike Oreo cookies.

If you liked Oreo cookies a lot, then you might make an "X" on the line like so:

very little ——————X—————— very much

If you liked Oreo cookies more than life itself(!), then you might make an "X" on the line like so:

very little ——————————X very much

If you <u>hated</u> Oreo cookies, then you might make an "X" like so:

very little X—————————— very much

If you thought Oreo cookies were just "OK," then you might make an "X" like so:

very little ————X———— very much

The idea is that if you like Oreo cookies, you make an "X" on the line closer to the phrase "very much;" the closer you make the "X," the more you are saying you like Oreo cookies. If you don't like Oreo cookies, you make an "X" on the line closer to the phrase "very little;" the closer you make the "X," the more you are saying you don't like Oreo cookies.

13) How much do you like Oreo cookies? (make an X on the line)

very little _____ very much

14) How much pain do you experience with your menstrual periods? (make an X on the line)

very little _____ very much

15) How much pain do you anticipate having during your procedure? (make an X on the line)

very little _____ very much

16) How much pain you are experiencing at this time? (make an X on the line)

very little _____ very much

Medical Record Review

1) Date of birth (MM/DD/YYYY): ____ / ____ / ____
2) Gestational age: ____ weeks _____ days
3) Height: ____
4) Weight: ____ kg/lbs
5) Medications administered:

Type: (include antibiotics, misoprostol, uterotonics, pain and nausea medication)	Route -Oral -IV -Rectal -Vaginal -Paracervical	Dose	Timing - Pre-op - Intra-op - Post-op	Time	Notes
☐ Azithromycin	☐ Oral	☐ 500 mg	☐ Pre		
☐ Alprazolam	☐ Oral	☐ 0.25 mg	☐ Pre		
☐ Promethazine	☐ Oral	☐ 25 mg	☐ Pre		
☐ Naproxen	☐ Oral	☐ 500 mg	☐ Pre		

6) Time of cervical preparation initiation:
    a. Misoprostol: Dose_____ Route: _____ Time: _____ AM / PM
    b. Osmotic dilators: Time: _____ AM / PM
        i. Number of Dilapan-S: _____
        ii. Number of laminaria: _____
7) Time of study medication: _____ AM / PM

8) Medications during D&E
   a. Paracervical block agents: please indicate if volume other than 20 mL: _____
      ☐ Lidocaine 1%
      ☐ Vasopressin 4 units
      ☐ Bicarbonate
   b. Fentanyl total dose: _____ mcg
   c. Versed total dose: _____ mg

9) Was a sedation reversal agent administered (ex: flumazenil, naloxone)?
   ☐ Yes
   ☐ No
   a. If yes, what agent(s) and dose was administered? _____mg__

Appendix D: Pre-Operative Assessments

Subject ID:	Date:	Time:	Interviewer:

1) How much pain you are experiencing at this time. (make an X on the line)

very little _____ very much

2) How satisfied are you with your pain relief at this time?	Very unsatisfied 1	Somewhat unsatisfied 2	Neutral 3	Somewhat satisfied 4	Very Satisfied 5
3) How much nausea are you experiencing at this time?	No nausea 1	Very little 2	Mild 3	Moderate 4	Severe nausea 5
4) How much vomiting are you experiencing at this time?	No vomiting 1	Very little 2	Mild 3	Moderate 4	Severe vomiting 5

5) Have you experienced any other symptoms, besides pain, since you were given the study medications?
   ☐ NO
   ☐ YES. If yes, please describe: _____
   _____

State Trait Anxiety Inventory (STAI) – State Items

Read each statement and select the appropriate response to indicate how you feel right now, that is, at this very moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

		Not at all	**A little**	**Somewhat**	**Very much so**
1	I feel calm	1	2	3	4
2	I feel secure	1	2	3	4
3	I feel tense	1	2	3	4
4	I feel strained	1	2	3	4
5	I feel at ease	1	2	3	4
6	I feel upset	1	2	3	4
7	I am presently worrying over possible misfortunes	1	2	3	4
8	I feel satisfied	1	2	3	4
9	I feel frightened	1	2	3	4
10	I feel uncomfortable	1	2	3	4
11	I feel self confident	1	2	3	4
12	I feel nervous	1	2	3	4
13	I feel jittery	1	2	3	4
14	I feel indecisive	1	2	3	4
15	I am relaxed	1	2	3	4
16	I feel content	1	2	3	4
17	I am worried	1	2	3	4
18	I feel confused	1	2	3	4
19	I feel steady	1	2	3	4
20	I feel pleasant	1	2	3	4

Appendix E: Intraoperative assessments

Subject ID:	Date:	Time:	Interviewer:

Time of speculum insertion: ____:____ AM/PM

1) After speculum placement.
   How much pain are you experiencing right now? (make an X on the line)

very little _____ very much

Patient unable to complete VAS due to sedation and seems comfortable ☐Yes ☐No
Patient unable to complete VAS due to sedation and seems uncomfortable ☐Yes ☐No
Patient refuses to complete VAS and seems comfortable ☐Yes ☐No
Patient refuses to complete VAS and seems uncomfortable ☐Yes ☐No

2) During uterine aspiration.
   How much pain are you experiencing right now? (make an X on the line)

very little _____ very much

Patient unable to complete VAS due to sedation and seems comfortable ☐Yes ☐No
Patient unable to complete VAS due to sedation and seems uncomfortable ☐Yes ☐No
Patient refuses to complete VAS and seems comfortable ☐Yes ☐No
Patient refuses to complete VAS and seems uncomfortable ☐Yes ☐No

Time of speculum removal: ____:____ AM/PM

3) After speculum removal.
   How much pain are you experiencing right now? (make an X on the line)

very little _____ very much

Patient unable to complete VAS due to sedation and seems comfortable ☐Yes ☐No
Patient unable to complete VAS due to sedation and seems uncomfortable ☐Yes ☐No
Patient refuses to complete VAS and seems comfortable ☐Yes ☐No
Patient refuses to complete VAS and seems uncomfortable ☐Yes ☐No

4) 3-5 minutes after procedure completion.
What was the maximum pain you experienced during your abortion?
(make an X on the line)

very little _____ very much

Patient unable to complete VAS due to sedation and seems comfortable	☐Yes	☐No
Patient unable to complete VAS due to sedation and seems uncomfortable	☐Yes	☐No
Patient refuses to complete VAS and seems comfortable	☐Yes	☐No
Patient refuses to complete VAS and seems uncomfortable	☐Yes	☐No

5) Please record the lowest oxygen saturation as recorded by the pulse oximeter during the procedure (to be completed by the research coordinator)

_____%

Appendix F: Post-operative assessments

20-40 min after procedure completion

Subject ID:	Date:	Time:	Interviewer:

1) How much pain are you experiencing right now? (make an X on the line)

very little _____ very much

2) How satisfied are you with your pain relief at this time?	Very unsatisfied 1	Somewhat unsatisfied 2	Neutral 3	Somewhat satisfied 4	Very Satisfied 5
3) How much nausea are you experiencing at this time?	No nausea 1	Very little 2	Mild 3	Moderate 4	Severe nausea 5
4) How much vomiting are you experiencing at this time?	No vomiting 1	Very little 2	Mild 3	Moderate 4	Severe vomiting 5

5) Have you experienced any other symptoms, besides pain, since you were given the study medications?
☐ NO
☐ YES. If yes, please describe: _____
_____

State Trait Anxiety Inventory (STAI) – State Items

Read each statement and select the appropriate response to indicate how you feel right now, that is, at this very moment. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your present feelings best.

		Not at all	**A little**	**Somewhat**	**Very much so**
1	I feel calm	1	2	3	4
2	I feel secure	1	2	3	4
3	I feel tense	1	2	3	4

4	I feel strained	1	2	3	4
5	I feel at ease	1	2	3	4
6	I feel upset	1	2	3	4
7	I am presently worrying over possible misfortunes	1	2	3	4
8	I feel satisfied	1	2	3	4
9	I feel frightened	1	2	3	4
10	I feel uncomfortable	1	2	3	4
11	I feel self confident	1	2	3	4
12	I feel nervous	1	2	3	4
13	I feel jittery	1	2	3	4
14	I feel indecisive	1	2	3	4
15	I am relaxed	1	2	3	4
16	I feel content	1	2	3	4
17	I am worried	1	2	3	4
18	I feel confused	1	2	3	4
19	I feel steady	1	2	3	4
20	I feel pleasant	1	2	3	4

6) Would you choose this method of pain control if you need to have this procedure again?
   ☐ NO
   ☐ YES

7) Would you recommend this method of pain control to other women who are having this procedure?
   ☐ NO
   ☐ YES

Time of discharge from recovery: ____ : ____ AM/PM

Appendix G: Post-operative day 1 assessment

Subject ID:	Date:	Time:	Interviewer:

8) On a scale of 1 to 5, where 1 is very unsatisfied and 5 is very satisfied, how satisfied were you with the pain relief you experienced yesterday?
   - ☐ 1 very unsatisfied
   - ☐ 2
   - ☐ 3
   - ☐ 4
   - ☐ 5 very satisfied

9) Did you experience any complications or side effects yesterday or today?
   - ☐ NO
   - ☐ YES

   If yes, please explain: _____
   _____
   _____
   _____
   _____

10) Would you choose this method of pain control if you need to have this procedure again?
   - ☐ NO
   - ☐ YES

11) Would you recommend this method of pain control to other women who are having this procedure?
   - ☐ NO
   - ☐ YES