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**PROTOCOL TITLE:** Postpartum Perineal Pain after Obstetric Anal Sphincter Injuries: A Randomized Clinical Trial

**PRINCIPAL INVESTIGATOR:**

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1.5

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04/23/2019

## **OBJECTIVES:**

To assess the incidence of perineal pain in postpartum patients 1 week after obstetric anal sphincter injuries (OASIS).

We hypothesize that perineal pain at 1 week postpartum will be reduced by the administration of epidural morphine with or without intravenous ketamine after OASIS compared to on-demand analgesic management.

## **BACKGROUND:**

Obstetric anal sphincter injuries (OASIS) encompass both third and fourth degree perineal tears. These tears can have a significant impact on women's quality of life in the short and long term.<sup>1</sup> One of the most distressing immediate complications of this severe perineal injury is perineal pain. A study by Macarthur et al. revealed that the frequency of perineal pain for patients with OASIS was 100%, 91%, and 20% on day 1, day 7, and 6 weeks' postpartum, respectively.<sup>2</sup> Perineal pain can lead to urinary retention, defecation problems, and postpartum depression in the immediate postpartum period.<sup>3</sup> In the long term, women with perineal pain may have dyspareunia and altered sexual function.<sup>1</sup>

Severity of acute pain after childbirth predicts not only persistent pain, but also postpartum depression.<sup>4</sup> Using a Present Pain Intensity (PPI) scale, Macarthur et al. confirmed that on postpartum day 1, women with OASIS were more likely to use the words "distressing" or "worse" to describe their perineal pain compared to women with intact perineum (48% vs. 13%).<sup>2</sup> Unfortunately, the recommendations for the analgesic management of women with OASIS has not been differentiated from women that undergo vaginal delivery with no trauma or lesser trauma (first and second degree perineal lacerations).

Epidural morphine has long been used for the analgesic management of patients after cesarean delivery, and has also been reported to reduce the need for oral pain medication in the first 24 hours following vaginal delivery.<sup>5</sup> Ketamine, an N-methyl-D-aspartate (NMDA) and glutamate receptor antagonist that decreases central sensitization and pain memory, has also been used at low-doses for multimodal analgesic management of women after cesarean delivery. In a study by Bauchat et al., women who received ketamine reported lower pain score 2-weeks postpartum.<sup>6</sup> Ketamine also has been described as having antidepressant and anti-inflammatory effects, which could mitigate the risk of postpartum depression and improve analgesia in this subset of patients.<sup>7</sup>

We propose a randomized controlled trial to study the effects of three interventions (placebo, low dose intravenous ketamine plus epidural morphine, or epidural morphine alone) in women with OASIS, on acute and chronic pain as well as on patient centered outcomes.

## **INCLUSION AND EXCLUSION CRITERIA:**

Inclusion: age >18 years of age, English-speaking, vaginal delivery (spontaneous or assisted) of a full-term fetus (>37 weeks' gestation), OASIS as assessed by obstetrical provider, functional epidural analgesia at time of delivery, patient amenable to follow-up at their obstetrician's office or at the specialty perineal clinic within the first week postpartum.

Exclusion: previous pelvic surgery, history of chronic pelvic pain, history of recurrent urinary tract infections, women with known malformations of their urinary tract, true allergies to ketamine and/or morphine, preeclampsia or hypertensive disorder at the time of delivery, obstructive sleep apnea.

**STUDY-WIDE NUMBER OF PARTICIPANTS:**

The total number of participants to be accrued with OASIS is 160.

**STUDY-WIDE RECRUITMENT METHODS:** N/A

**MULTI-SITE RESEARCH:** N/A

**STUDY TIMELINES:**

Subjects will be followed within one week of delivery to 12 months postpartum. The incidence of 3rd and 4th degree perineal lacerations at Prentice Woman's Hospital for the last 3 years has been: 327 (YR 2014), 281 (YR 2015), 218 (YR 2016). Therefore, we anticipate to complete enrollment in approximately 1 year, taking into consideration loss to follow-up and recruitment constraints.

**STUDY ENDPOINTS:**

**Primary endpoint:** Perineal pain assessed by verbal rating scale (VRS) in postpartum patients within 1 week after obstetric anal sphincter injuries.

**Secondary endpoints:** Presence of postpartum depression within 1 week after delivery, assessment of maternal-infant bonding, MEDoc Pathway Device pain sensory results within 1 week after delivery, presence of postpartum depression 6 weeks after delivery, perineal pain at 6 weeks after delivery, maternal quality of life 3 months after delivery, and female sexual function 3 months after delivery, perineal pain 3,6, and 12 months after delivery.

**PROCEDURES INVOLVED:**

Prospective, double-blinded, randomized clinical trial.

Randomization: Patients will be approached after repair of OASIS has been completed, and prior to the epidural catheter removal. After informed consent, eligible patients will be randomized to 1 of 3 possible paired interventions:

- 1) Epidural saline + intravenous saline
- 2) Epidural morphine 3mg + intravenous saline
- 3) Epidural morphine 3mg + intravenous ketamine 0.3mg/kg (based on pre-delivery weight)

The subjects will be randomized to a 1/5 chance for group 1 and a 2/5 chance for group 2 and group 3. Randomization and study drug preparation will be conducted by the pharmacy on Prentice 10<sup>th</sup> floor. The epidural catheter will be removed after study drug or placebo administration, and the patient will be transferred to postpartum unit following standard institutional protocol.

Post-neuraxial morphine order set will be ordered for postpartum analgesia and monitoring.

## Anesthesia OB – Post Neuraxial Morphine Order Set

Component	Order Details
<b>MEDICATION - Communication</b>	
The following orders indicate that the patient is to receive no sedatives or opioids except those ordered by Anesthesiology for the next 12 hours.	
<input checked="" type="checkbox"/> 1 - No Sedatives	Start: T;N, For: 12 Hour
<input checked="" type="checkbox"/> 1 - No Opioids Except by Anesthesia	Start: T;N, For: 12 Hour
<b>MEDICATIONS - Oxytocin</b>	
Update order comment and notify nurse to increase oxytocin to a maximum of 36 Units/Hour (600 mL/hour) if uterine atony continues.	
<input checked="" type="checkbox"/> oxytocin 30 Unit + Sodium Chloride 0.9% 500 mL	IV Infusion, Titrate Parameters: Titrate per OB Protocol, Start: 9/6/2017 10:27, Titrate per OB Protocol, 500 mL (Bag Vol)
<b>MEDICATIONS - Pain</b>	
<input type="checkbox"/> ketorolac (Toradol)	30 mg, Dose Form: Inj, IV Push, Q 6 Hours, For: 12 Hour
<input type="checkbox"/> acetaminophen-HYDROcodone (Norco 10 mg-325 mg oral tablet)	1 Tab, Dose Form: Tab, PO, Q 4 Hours, PRN, Pain-Mild (pain score 1-3)
<input type="checkbox"/> acetaminophen-HYDROcodone (Norco 10 mg-325 mg oral tablet)	2 Tab, Dose Form: Tab, PO, Q 4 Hours, PRN, Pain-Moderate (pain score 4-6)
<b>MEDICATIONS - Multi-modal Anti-Emetics</b>	
Choose dexamethasone only if NOT administered in the Operating Room.	
<input type="checkbox"/> dexamethasone (Decadron)	10 mg, Dose Form: Inj, IV Push, Once, For: 12, Hour, PRN, Nausea/Vomiting
<input type="checkbox"/> ondansetron (Zofran)	4 mg, Dose Form: Inj, IV Push, Q 6 Hours, For: 12, Hour, PRN, Nausea/Vomiting
<input type="checkbox"/> prochlorperazine (Compazine)	10 mg, Dose Form: Inj, IV Push, Once, For: 12, Hour, PRN, Nausea
<b>MEDICATIONS -Other</b>	
<input type="checkbox"/> nalbuphine (Nubain)	2.5 mg, Dose Form: Inj (PF), IV Push, Q 6 Hours, For: 12, Hour, PRN, Pruritus
<input type="checkbox"/> nalbuphine (Nubain)	5 mg, Dose Form: Inj (PF), IV Push, Q 6 Hours, For: 24, Hour, PRN, Pruritus
<input type="checkbox"/> naloxone (Narcan)	200 mcg, Dose Form: Inj, IV Push, As Needed, For: 12, Hour, PRN, CNS/Respiratory Depression
<b>NURSING</b>	
<input checked="" type="checkbox"/> Respirations	Q 1 Hour, 12 Hour
<input checked="" type="checkbox"/> Respirations	Q 2 Hours, 12 Hour, T;N+720
<input checked="" type="checkbox"/> Call Anesthesia	If respiratory rate is less than 8 per minute or in respiratory distress and naloxone is administered, if refractory to treatment.
<b>RESPIRATORY SERVICES</b>	
<input type="checkbox"/> O2 Therapy - Nasal Cannula	2 lpm

## Study timeline:

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Phase	Sequence of Events	Interventions or Assessment Variables	
I  Information will be collected during patient hospitalization	PPD 0	Checklist followed by study team member for eligibility assessment	<i>Hypothesis testing</i>
	Post-delivery (Following 3 <sup>rd</sup> stage of labor) Eligibility confirmed, repair of perineal laceration completed, confirmation of hemodynamic stability.	Patient approached by member of study team for informed consent Study drug randomization and administration -Demographics -Obstetrical Data -Anesthesia Data - Richmond Agitation Sedation Score – 15-30 min after intravenous drug administration - Addiction Research Center Inventory and lysergic acid (LSD) questionnaire - Plan to breastfeed. If yes, how long they plan to breastfeed? (<3 months, 3-6 months, >6 months). If multiparous, did they breastfeed in the past? If yes, for how long? When (<3 months, 3-6 months, >6 months) and why did they stop?	
	PPD 1	-Perineal pain scores (VRS) -Need for additional analgesic intake for management of perineal pain (yes or no)  • Total analgesic consumption (opiates/nsaids) - McGill Pain Questionnaire -Brief Pain Inventory (BPI) Short Form	.

II  Information will be collected in-person during patient's perineal clinic visit	PPD 2-7	<ul style="list-style-type: none"> <li>-Perineal pain scores (VRS)</li> <li>-Need for additional analgesic intake for management of perineal pain (yes or no) <ul style="list-style-type: none"> <li>• Total analgesic consumption (opiates/nsaids)</li> </ul> </li> <li>-McGill Pain Questionnaire</li> <li>-Brief Pain Inventory (BPI) Short Form</li> <li>-Edinburgh Postnatal Depression Scale (EPDS)</li> <li>-Maternal Postnatal Attachment Scale (MPAS)</li> <li>- If plan was to breastfeed, is patient currently breastfeeding? yes or no? If not, why did she stop?</li> <li>-MEDoc pathway</li> <li>Hot and Cold Sensory Threshold Assessment test will be performed</li> </ul>	<ul style="list-style-type: none"> <li>-Edinburgh Postnatal Depression Scale (EPDS), Maternal Postnatal Attachment Scale (MPAS): if perineal pain is not well –controlled, the patient will be at increased risk for depression. It will also impact the patient's ability to bond with the newborn.</li> <li>-MEDoc device is predictive of chronic pain</li> </ul>
III  Information will be collected remotely via electronic and/or printed surveys, depending on the patient's preference	6 weeks	<ul style="list-style-type: none"> <li>- Perineal pain scores (VRS)</li> <li>-Need for additional analgesic intake for management of perineal pain (yes or no) <ul style="list-style-type: none"> <li>• Total analgesic consumption (opiates/nsaids)</li> </ul> </li> <li>-McGill Pain Questionnaire</li> <li>-Brief Pain Inventory (BPI) Short Form</li> <li>- If plan was to breastfeed, is patient currently breastfeeding? yes or no? If not, why did she stop?</li> <li>-Edinburgh Postnatal Depression Scale (EPDS)</li> <li>-Maternal Postnatal Attachment Scale (MPAS)</li> <li>-Patient Reported Outcome Measurement Information System (PROMIS) 29</li> </ul>	
IV	3 months	-Perineal pain score (VRS)	

Information will be collected remotely via electronic and/or printed surveys, depending on the patient's preference		<ul style="list-style-type: none"> <li>-Need for additional analgesic intake for management of perineal pain (yes or no) <ul style="list-style-type: none"> <li>• Total analgesic consumption (opiates/nsaids)</li> </ul> </li> <li>-Physical therapy treatment (yes or no)</li> <li>-The McGill Pain Questionnaire</li> <li>-Brief Pain Inventory (BPI) Short Form</li> <li>- If plan was to breastfeed, is patient currently breastfeeding? yes or no? If not, why did she stop?</li> <li>-Edinburgh Postnatal Depression Scale (EPDS)</li> <li>-Maternal Postnatal Attachment Scale (MPAS)</li> <li>-Patient Reported Outcome Measurement Information System (PROMIS) 29</li> <li>- Female Sexual Function Index (FSFI)</li> </ul>	
V	6 Months	<ul style="list-style-type: none"> <li>-Perineal pain score (VRS)</li> <li>-Physical therapy treatment for pelvic pain (yes or no)</li> <li>- If plan was to breastfeed, is patient currently breastfeeding? yes or no? If not, why did she stop? -</li> <li>Patient Reported Outcome Measurement Information System (PROMIS) 29</li> <li>- Female Sexual Function Index (FSFI)</li> </ul>	
VI	12 Months	<ul style="list-style-type: none"> <li>-Perineal pain score (VRS)</li> <li>-Physical therapy treatment for pelvic pain(yes or no)</li> <li>- If plan was to breastfeed, is patient currently breastfeeding? yes or no? If not, why did she stop?</li> </ul>	

		-Patient Reported Outcome Measurement Information System (PROMIS) 29 - Female Sexual Function Index (FSFI)	
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Phase I will involve the collection of data points from patient interview, chart review, and surveys during the initial hospitalization. Phase II entails the administration of a brief questionnaire and surveys to the patient during their 1 week follow up appointment in the specialty perineal clinic.

Thermal pain test (threshold measurement) will be performed during the first follow up visit if the subject attends the the PEAPOD clinic. The Medoc PATHWAY Pain & Sensory Evaluation System (Medoc Ltd, Israel, Durham NC)) with advanced thermal stimulator (ATS) will be used to apply 6 thermal stimuli to participants' left volar forearm, 5cm from the wrist. The thermal baseline temperature will be set to 32°C. The Medoc system order of stimuli (3 cold and 3 warm) with a rest period between stimuli.

At the start of each trial, the thermode increases or decreases in temperature at the rate of 1°C per second and participants are instructed to push a button when the stimuli is considered painful. After participants press the button, the thermode returns to baseline temperature and the next trial begins. The participants are also given a separate shut off button which terminates the testing.

The second part of the test (summation) will include a single stimulus with the thermode set at 5°C with a 45 second timed stimulus. Subjects will use a verbal rating scale (VRS) to rate the painfulness of the stimulus at 10 second intervals (anchored with “no pain” 0 and 100 “worst pain imaginable”)

Phases III and IV will rely on the collection of patient data using a brief questionnaire and surveys at 6 weeks and 3 months postpartum.

Phases V and VI will rely on perineal pain score (VRS) responses at 6 and 12 months post-delivery.

A pre-survey notification message (via phone or email) will be sent to patients prior to phases III and IV. A personalized cover letter will be included with the surveys. Non-respondents will be contacted using combination of messages and surveys.

#### **DATA AND SPECIMEN BANKING: N/A**

#### **DATA AND SPECIMEN MANAGEMENT:**

The primary outcome of this study is the proportion of women with pain (VRS > 4, on a 0 to 10 scale) with activity at 7±3 days postpartum. Based on the study of Macarthur et.al<sup>2</sup> evaluating pain following perineal injury following childbirth, we estimated that 55% of women would have pain (VRS > 4, on a 0 to 10 scale) at 7 days. We assumed an absolute reduction of 25% in pain in women receiving epidural morphine 3mg + intravenous saline compared to epidural saline +

intravenous saline, and an absolute reduction of 30% in pain in women receiving epidural morphine 3mg + intravenous ketamine 0.3 mg/kg compared to epidural saline + intravenous saline. Groups sizes of 30:60:60 will be required to detect a difference in an effect size of 0.25 (Cramér's  $\omega$ ) at a power of 0.8 and an alpha of 0.05 using  $\chi^2$  statistic. A sample of 150 subjects will be randomized using a 1:2:2 randomization to epidural saline plus intravenous saline, epidural morphine + intravenous saline, and epidural morphine + intravenous ketamine groups. We will recruit up to 160 patients to account for subjects that decline participation and lost to follow-up.

The completed data forms will be kept in folders with only the study ID number as an identifier. These folders will be placed in a secure, locked cabinet in the Office of the Section of Obstetrical Anesthesiology located in Prentice Women's Hospital 9th floor. REDcap will be used for data entry. Only study team members will have access to the data files. Data will be password protected using a Department of Anesthesiology dedicated computer which is backed up nightly by the departmental server which is located on the 5<sup>th</sup> floor Arkes Pavilion. The access is controlled by key card and password protected by the departmental data manager.

Only the study ID number will be used to identify participants during data analysis. The data will be stored in the departmental computer until the completion of the study, including the final data analysis. Members of the anesthesia team collecting these data will be educated on the process prior to approaching prospective participants. Data both electronic and paper will be destroyed 5 years after the study has been completed using current standards and vendors.

#### **PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS:**

A data safety monitoring board consisting of the Department of Anesthesiology Director of Research, a Urology/Gynecology faculty member, and a statistician along with the study research personnel will periodically evaluate the data collected to determine whether participants remain safe. Safety data and adverse event data will be reviewed using the medical record and data collection form. It will be reviewed every 50 subjects or if one of the study subject experiences a rapid response team intervention and review. Data will be compared between groups using the  $\chi^2$  statistic or the Fisher's exact test. A  $P < 0.05$  will be required to reject the null hypothesis.

#### **WITHDRAWAL OF PARTICIPANTS:**

A subject can request withdrawal from the study at any time. A clinical research team member will contact the PI by secured-email to inform her about the event that led to early study termination. No further research procedures will be performed, and if the subject additionally requests, all data to that point will not be used.

#### **RISKS TO PARTICIPANTS:**

The risk of the study drugs:

##### **Morphine:**

More Frequent: itching, nausea, vomiting, urinary retention, constipation, dizziness, hypotension, depression of cough reflex and slowing of respirations

Rare risk: respiratory depression leading to respiratory arrest

**Saline:** hypernatremia

**Ketamine:**

Most Frequent: delirium, hallucinations, mood changes, nightmares, tachyarrhythmia, tonic-clonic epilepsy, vocalization

Less Frequent: bradycardia, hypertension, respiratory depression, vomiting, increased intraocular pressure, flashbacks several weeks post operatively

Rare: anaphylaxis, anorexia, diplopia, injection site irritation, laryngismus, nausea, nystagmus, obstructive pulmonary disease, skin inflammation, skin rash

These side effects are uncommon with the lower dose range used in this study.

The risk of the use of the Pathway Pain & sensory evaluation system (Medoc, Dunham, NC) include slight redness on the skin from securing the sensor to the arm with velcro.

There is the risk of the subject becoming emotionally uncomfortable answering some of the surveys' or questionnaires.

Participants are at risk for loss of confidentiality. Strict measures will be in place to ensure that no loss of confidentiality occurs. All participants will be assigned a participant study number that will be used to identify them. One document will link the participant name to their participant number, and this will be kept in a password-protected computer in a locked office in the Prentice Women's Hospital. Only study team members will have access to the study data.

**POTENTIAL BENEFITS TO PARTICIPANTS:**

Improved pain relief after obstetrical and anal sphincter injuries.

Decreased oral opioid consumption which will result in less problems with post-birth constipation from opioids.

**VULNERABLE POPULATIONS:**

Pregnant to postpartum, breastfeeding women

**COMMUNITY-BASED PARTICIPATORY RESEARCH: N/A**

**SHARING OF RESULTS WITH PARTICIPANTS:**

Individual participant results will not be shared with others.

**SETTING:**

This study will be conducted on the Labor and Delivery suite on the 8th of Prentice Women's Hospital as well as in the subject's obstetric offices at NM. Data analysis will occur on the NM campus in the Department of Anesthesiology 9th floor office of Prentice Women's Hospital and on the 10th floor Arkes Pavilion in the Department of Anesthesiology administrative offices

### **RESOURCES AVAILABLE:**

The Section of Obstetrical Anesthesiology actively provides 24-hour care to 90% of over 12,000 obstetric patients admitted to the Labor and Delivery Unit at Prentice Women's Hospital. Dr. Feyce Peralta, the principal investigator for this study, is an Assistant Professor in the obstetrical anesthesiology section who regularly supervises and provides care to patients in labor and delivery. The Section of Obstetrical Anesthesiology also has a dedicated group of clinical research nurses who assist with daily recruitment and follow-up of patients in clinical anesthesiology trials. All study team members have CITI training.

The PEAPOD (Peripartum Evaluation and Assessment of the Pelvic Floor Around the Time of Delivery) clinic, is a specialty perineal clinic dedicated to women who suffer from birth trauma at Northwestern Memorial Prentice Women's hospital, as well as hospitals throughout the Chicagoland area. Dr. Lewicky-Gaupp, an Associate Professor in the Division of Female Pelvic Medicine and Reconstructive Surgery, is the Medical Director of the clinic. Together with physical therapists, sex counselors and psychologists, this transdisciplinary clinic (which is one of only a handful in the United States) has changed the standard of postpartum care for women who suffer OASIS. Not only does this clinic serve as a resource for new mothers, it has provided a platform for multidisciplinary research studies in this unique and under-studied patient population. Patients that suffer obstetric anal sphincter injuries (OASIS) during birth are frequently referred to this clinic for evaluation and treatment. Dr. Lewicky-Gaupp will provide follow-up evaluation of these patients in the PEAPOD clinic.

The Asher Center for the Study and Treatment of Depressive Disorders, directed by Katherine L. Wisner, MD MS, is a clinical research women's mental health program at Northwestern's Department of Psychiatry and Behavioral Sciences. Dr. Wisner holds academic appointments in the Departments of Psychiatry and Behavioral Sciences and Obstetrics and Gynecology. The Asher Center includes 10,000 square feet of research space which accommodates investigators and staff performing and mental health evaluations and research. This space is integrated with a 5,000 square foot clinical care program staffed by an interdisciplinary team of psychiatrists, psychologists, a maternal-fetal medicine research scholar, nurses, and trainees. The Asher Center is located one block from Prentice Women's Hospital. The Asher Center includes two examination rooms specifically furnished with space for examination of mothers and infants, with digital weight scales accurate to .01 g. Two conference rooms (for 12 or 30 people) with audiovisual equipment are available for staff meetings and for other work-related functions. The family room includes comfortable sofas, rocking chairs, and toys for children of all ages. The Center has diaper changes and waste containers in all restrooms. Quiet rooms for breastfeeding women and a kitchen with sink, refrigerator, microwave and snacks are also available.

Dr. Wisner and Asher Center staff will provide consultation regarding use of the depression assessments and interpretation of depression measures and data, as well as participate in manuscript development. Our resources will be utilized for emergent psychiatric situations that may arise, such as suicidality.

### **PRIOR APPROVALS:**

The Department of Anesthesiology Research Committee

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**RECRUITMENT METHODS:**

Subjects will be approached and recruited by a member of the anesthesia research team after delivery of their baby and have been identified as experiencing an obstetric anal sphincter injury on the 8<sup>th</sup> floor Labor and Delivery Unit at Prentice Women's Hospital. The study team members will use Dashboard from the Labor and Delivery Unit at Prentice Women's Hospital and obstetric medical histories to identify potential participants. Subjects who are willing to participate in the study will provide written consent. There will be no materials used to recruit patient. There will be no payment to participants.

**NUMBER OF LOCAL PARTICIPANTS:**

The total number of participants to be accrued is 160.

**CONFIDENTIALITY:**

Data will be stored in a department computer and departmental server which are both password protected. Each study subject will be assigned a study code number. The code will be used to link study data to patient identification (name) in a separate database. Subject data will be stored on secured password-protected computers at Northwestern University and Department of Anesthesiology servers. Paper data will be completed by research study team members and will be entered into REDCap. The paper folders will be stored in Arkes Pavilion 10th floor Department of Anesthesiology administrative office via key card controlled front door and key controlled closet. Data access will be password protected and only available to study investigators via REDCap. REDCap access will be controlled by the Principal Investigator. Data both electronic and paper will be destroyed 5 years after study closure using current department protocol and current vendor.

**PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS:**

The subject will have multiple interactions with the study team members. The first interaction will be to discuss and obtain written informed consent; then multiple times over the next 12 months for brief periods (less than 5 minutes). These brief interactions limit the amount of intrusion into the subject's recovery process.

The research study team is only to be allowed to view the data sheets, REDCap and Powerchart for selected data within the parameters of the study.

**COMPENSATION FOR RESEARCH-RELATED INJURY: N/A****ECONOMIC BURDEN TO PARTICIPANTS:**

Subjects will not be paid or charged extra for the care they receive as part of this study. All subjects will be charged for the standard care they receive including the cost of the epidural labor analgesia that they would receive if they had not participated in this study. This cost will be billed to their insurance providers. Similarly, insurance will be billed for clinic visit to the PEAPOD clinic, as it has become standard of care for patient with OASIS to be seen within the first postpartum week to ensure that wound complications are discovered early.

**CONSENT PROCESS:**

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The consent process will take place in the Labor and Delivery Unit, 8<sup>th</sup> Floor, at Prentice Women's Hospital. This will be performed by a member of the research study team. There is no waiting period since subjects are in the hospital for delivery of their baby. SOP HRP 090 will be followed. The research study team will spend greater than 10 minutes discussing the study. With each subject ample time will be allowed for patient to answer questions regarding the study and the consent document. The subject will also be informed that there is no conflict of interest between the PI and the protocol. The PI will not receive financial remuneration nor will the study participation affect the subject's financial charges for their care.

For Non-English-Speaking Participants

N/A

Waiver or Alteration of Consent Process:

N/A

Participants who are not yet adults (infants, children, teenagers)

N/A

Cognitively Impaired Adults

N/A

Adults Unable to Consent

N/A

#### **PROCESS TO DOCUMENT CONSENT IN WRITING:**

The participant will be required to sign a consent form for participation in the study.

#### **DRUGS OR DEVICES:**

The study drugs are FDA approved. The departmental data manager and the 10<sup>th</sup> floor pharmacy Prenticed Women's Hospital will have the randomization table. The study drugs will be prepared and dispensed by the 10<sup>th</sup> floor pharmacy, and administered by a physician. The anesthesiologist, nurses and study research personnel will be blinded to the study group.

The MEDoc pathway device is owned by Northwestern University and has been tested and stickered by Biomedical Engineering at Northwestern Hospital. The device is stored in Arkes Pavilion on the 10<sup>th</sup> floor Department of Anesthesiology Administrative suite in a locked research closet.

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4. Eisenach JC, Pan PH, Smiley R, Lavand'homme P, Landau R, Houle TT. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. *Pain* 2008;140:87-94.
5. Goodman SR, Drachenberg AM, Johnson SA, Negron MA, Kim-Lo SH, Smiley RM. Decreased postpartum use of oral pain medication after a single dose of epidural morphine. *Reg Anesth Pain Med* 2005;30:134-9.
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7. De Kock M, Loix S, Lavand'homme P. Ketamine and peripheral inflammation. *CNS Neurosci Ther* 2013;19:403-10.