University of Pittsburgh
Department of OB/GYN
300 Halket Street
Pittsburgh, PA 15213
412.641.1403

CONSENT TO ACT AS A SUBJECT IN A RESEARCH STUDY

TITLE: **Preoperative pudendal nerve block and levator ani muscle injection for improved pain control after vaginal reconstructive surgery: a three-arm, randomized, double-blind, placebo-controlled trial**

PRINCIPAL INVESTIGATOR: Lauren Giugale, MD
Department of Obstetrics, Gynecology and Reproductive Sciences
Division of Urogynecology
Magee Womens Hospital
412-270-1046

STUDY COORDINATOR: Judy Gruss, RN
412-641-7850

SOURCES OF SUPPORT Magee-Womens Research Institute - Clinical Trainee Research Award

Why is this study being done?

Pain control is an important part of care after surgery for pelvic organ prolapse. Pelvic organ prolapse is the dropping or sagging of the pelvic organs (like the bladder or uterus). This study is being done to find a method that will improve pain control after vaginal prolapse surgery. One approach to pain control is injecting local anesthesia near the site of surgery. We are looking at the injection of local anesthesia and a small dose of steroid in the muscles of the pelvis during surgery to see if we can lessen postoperative pain after vaginal surgery.

The local anesthetics bupivacaine and short-acting steroid dexamethasone have both been used in other areas of surgery with safe results and improvement in recovery after surgery. However, there is less information available on the effects of these medications during vaginal prolapse surgery. In this study, these medications will be injected by your surgeon after you are already asleep for surgery with the goal of decreasing the overall response to pain. This study will help doctors understand if this is an effective way to potentially decrease the pain that patients experience after prolapse surgery.

Who is being asked to take part in this study?
Approximately 75 women from the Magee-Womens Hospital of UPMC who are at least 18 years old and undergoing vaginal surgery for pelvic organ prolapse will be asked to participate in this study.

What are the procedures of this study?
1. If you agree to participate in this study, research staff will review your record to make sure you are eligible for the study. They will record some information from your record on study forms that do not contain your name or any other identifying information. Things that they will record include your age, race/ethnicity, body mass index, smoking status, medical and surgical history, and postoperative care. You may be asked to confirm or provide information that is missing or incomplete.

2. You will be randomly assigned to receive pelvic injections with either a placebo (saline solution, but no active medication), bupivacaine local anesthetic alone, or a solution containing both bupivacaine and dexamethasone. You will have a 1 in 3 chance of receiving the placebo medication and a 2 in 3 chance of receiving an active medication. Neither you nor your surgeon will know if you receive the drug or the placebo. Bupivacaine is approved by the FDA (US Food and Drug Administration) for local anesthesia and dexamethasone is approved by the FDA as an anti-inflammatory agent. The combination of bupivacaine and dexamethasone is not FDA-approved for use in vaginal prolapse surgery. The procedures to inject these solutions are performed after you are already asleep, but before the surgery for prolapse has started. Your surgeon will perform these injections. The injections do not affect the rest of your prolapse surgery. You will receive two injections within the vagina and two injections outside of the vagina. The medication is injection into the small muscles that surround the vagina. Additionally, each surgeon is familiar with the procedures for injecting the medication and has performed similar procedures previously. Your care after this surgery will not be changed based on which of the three injections you receive. Your care after surgery will be the same as it would be if you did not enroll in this research study.

3. You will be asked to fill out 3 short surveys before surgery for a baseline assessment (this will take approximately 7 minutes). After surgery, we are interested in your pain, any nausea or vomiting, and your bladder function. You will be asked to rate your pain on a score of 0-10 and also be asked questions regarding the amount of nausea and vomiting you had after surgery (this will take approximately 3 minutes and you will complete these forms before you leave the hospital). As part of normal postoperative care, your bladder will be tested after surgery to assess whether you can void on your own. This study will not interfere with whether or not you have a bladder test, but we will record the results of your bladder function.

4. We are also interested in understanding your pain and how many pain medications you are taking once you are at home after surgery. At home, you will be asked about your pain level and asked to record how many pain pills you take during the first 3 days after surgery and record a final pain level 1 week after surgery. Lastly, we are interested in knowing when you are "back to normal" after surgery, and you will be asked questions about when you are able to do certain activities (like cleaning and cooking) after surgery. You will answer these questions at 1 week, 2

weeks, 6 weeks and 12 weeks after surgery to tell us how you are doing. The forms completed at home should take you approximately 5 minutes to complete. After you have completed all of the forms, you will send these forms to our office in an envelope provided. You may also bring these forms with you to your follow-up visit.

5. Study staff will contact you to remind you to schedule your follow-up visit and return the survey forms, as well as answer any study related questions you may have.

6 Because we want to follow our study patients closely, we ask that if you seek treatment for any possible postoperative problem, that you are treated by your surgeon whenever possible. You will also be asked to alert the study team if you have any problems after surgery. In case you need to seek treatment from another care provider, we ask that you contact the study team after receiving that care to provide us with an update. We will provide a card with our contact information.

7. The study team will contact you periodically over the 12 weeks after surgery to answer any questions you have and remind you to fill out your study surveys. They will also remind you to return the forms and to follow-up with your doctor 6 weeks after surgery.

8 At your routine 6-week postoperative visit, the research team may collect any completed surveys that you have, in the event that you have brought them with you instead of mailing them in to the office.

9. At 12 weeks after your surgery, you will complete the last survey and mail the completed form into the office. This will mark the end of the research study.

What is the duration of participation in this study?
If you agree to participate and are eligible, your participation will be requested from the day of your surgery through 12 weeks following your surgery. You will only receive medication in the operating room on the day of surgery. The remainder of the study duration involves follow-up after surgery.

What are the possible risks and discomforts of this study?
Risks of transobturator and transvaginal injections: Many of the risks associated with the study injections are similar to the risks associated with prolapse surgery itself. These include bleeding, infection, damage to nearby structures (bladder and bowel), and need for further surgery. Hematomas (blood collections) may form at the injection sites, which usually resolve spontaneously. Rarely, a hematoma will need further surgical management.

Risks of bupivacaine: If either too much medication is used or if the medication enters the blood stream, there can be toxicity related to injection of local anesthesia. Minor symptoms of toxicity include ringing in the ears or a metallic taste in the mouth, however severe symptoms of toxicity could include heart problems. Precautions are taken to limit the dose of bupivacaine that you receive and to make sure the injection is going into a muscle and not into a blood vessel. Numbness and tingling and occasional pain in the groin, buttock and leg can occur with

injections of local anesthesia. These symptoms are usually temporary and related to the anesthetic effect of the bupivacaine. While uncommon, if you are having difficulty walking after the procedure, we will have you evaluated by physical therapy prior to discharge from the hospital to ensure safety. Lastly, although rare, allergic reaction to bupivacaine can occur. You will be monitored by anesthesiology closely while receiving any study medications and any adverse reaction to study medication will be managed immediately.

Risks of dexamethasone: While other studies looking at the use of dexamethasone during surgery have not demonstrated any increased risk of infection or delayed wound healing, this is a theoretical risk. You receive antibiotics at the time of surgery to minimize the risk of infection. Additionally, the effects of dexamethasone are short compared to other steroid medications. Upon discharge after surgery, you should watch for warning signs of infection including vaginal bleeding, discharge, fevers or chills and call the research team (number provided) and Urogynecology office for any concerns. An increase in blood glucose levels has been demonstrated following the administration of steroids. However, the increase in serum glucose levels is small and temporary. For this reason, we are not allowing anyone with diabetes to participate in this study.

Risks of survey completion: You will be asked to complete a number if surveys within 12 weeks after your surgery to assess your postoperative recovery. The answers to your questions will remain confidential and do not impact the care you will receive from your doctor. You do not have to complete survey questions that make you uncomfortable.

Risks of study data collection: There is the possibility of loss of confidentiality. In very rare cases, people not associated with this research study may inadvertently see your identifiable research results. We will do everything in our power to prevent this from happening by keeping all research records in locked files, and filing medical information by a research record number, rather than by your name or social security number. The codebook containing your name and number will be kept by the Study Coordinator in a separate secure location.

Will I benefit from taking part in this study?

If you receive bupivacaine or bupivacaine and dexamethasone as part of the study, you may experience decreased pain after surgery. If you receive a placebo injection, you may benefit from decreased exposure to medications. The information obtained from this study will give us an understanding of whether or not these injections should be used routinely to decrease pain after prolapse surgery.

Will anyone know that I am taking part in this study?

All records pertaining to your involvement in this study are kept strictly confidential (private) and any data that includes your identity will be stored in locked files. Your identity will not be revealed in any description or publications of this research. Medical records will not be shared with anyone not directly involved in your medical care. Safeguards will be used to minimize breach of confidentiality. This will include labeling all data with a study number rather than your name or other direct identifiers.

What treatments or procedures are available if I decide not to take part in this research study?
You do not have to participate in this study. If you do not participate in this study, you will have your vaginal prolapse surgery performed by your doctor as scheduled without any changes. You will receive all other care provided to patients receiving pelvic reconstructive surgery.

If I agree to take part in this research study, will I be told of any new risks that may be found during the course of the study?
You will be promptly notified if, during the conduct of this research study, any new information develops which may cause you to change your mind about continuing to participate.

Will my insurance provider or I be charged for the costs of any procedures performed as part of this research study?
You and/or your insurance will be charged, in the standard manner, for the surgery, hospital stay, office visits, and procedures performed for your routine medical care. This includes any visits to your doctor for postoperative care or postoperative complications. You will be responsible for any co-pays, coinsurances, or deductibles associated with your clinical visits.

Neither you, nor your insurance provider, will be charged for the costs of any of the procedures performed for the purpose of this research study. These procedures include the levator muscle injections, pudendal nerve blocks, survey completion and medical record abstraction. You will not be charged for the bupivacaine, dexamethasone or placebo medications administered as part of this study.

Will I be paid if I take part in this research study?
You do not receive any payment as part of the research study.

Who will pay if I am injured as a result of taking part in this study?
University of Pittsburgh researchers and their associates who provide services at the University of Pittsburgh Medical Center (UPMC) recognize the importance of your voluntary participation in their research studies. These individuals and their staff will make reasonable efforts to minimize, control, and treat any injuries that may arise as a result of this research. If you believe that the research procedures have resulted in an injury to you, immediately contact Dr. Giugale at the number listed on the first page. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by the hospitals of UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation.

Will this research study involve the use or disclosure of my identifiable medical information?
This research study will involve the recording of past, current and/or future identifiable medical information from your hospital and/or other health care provider (for example, your physician's office records). This information that will be recorded will be limited to information concerning the surgical procedure (for example, diagnostic information, lab and scanned results, medications, medical history). This information will be used to determine your eligibility for

this study and to follow your response once you are enrolled in the study.

Who will have access to identifiable information related to my participation in this research study?
In addition to the investigators listed on the first page of this authorization (consent) form and their research staff, the following individuals will or may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study:

Authorized representatives of the UPMC hospitals or other affiliated health care providers may have access to identifiable information (which may include your identifiable medical information) related to your participation in this research study for the purpose of (1) fulfilling orders, made by the investigators, for hospital and health care services (e.g., laboratory tests, diagnostic procedures) associated with research study participation; (2) addressing correct payment for tests and procedures ordered by the investigators; and/or (3) for internal hospital operations (i.e. quality assurance).

Authorized representatives of the University of Pittsburgh Research Conduct and Compliance Office may review your identifiable research information (which may include your identifiable medical information) for the purpose of monitoring the appropriate conduct of this research study.

In unusual cases, the investigators may be required to release identifiable information (which may include your identifiable medical information) related to your participation in this research study in response to an order from a court of law. If the investigators learn that you or someone with whom you are involved is in serious danger or potential harm, they will need to inform, as required by Pennsylvania law, the appropriate agencies.

For how long will the investigators be permitted to use and disclose identifiable information related to my participation in this research study?
The investigators may continue to use and disclose, for the purposes described above, identifiable information (which may include your identifiable medical information) related to your participation in this research study for a minimum of seven years after final reporting or publication of a project.

Is my participation in this research study voluntary?
Your participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above, is completely voluntary. (Note, however, that if you do not provide your consent for the use and disclosure of your identifiable information for the purposes described above, you will not be allowed to participate in the research study.) Whether or not you provide your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Your doctor may be involved as an investigator in this research study. As both your doctor and a research investigator, s/he is interested both in your medical care and the conduct of this research study. Before agreeing to participate in this research study, or at any time during your study participation, you may discuss your care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your doctor.

May I withdraw, at a future date, my consent for participation in this research study?
You may withdraw, at any time, your consent for participation in this research study, to include the use and disclosure of your identifiable information for the purposes described above. (Note, however, that if you withdraw your consent for the use and disclosure of your identifiable medical record information for the purposes described above, you will also be withdrawn, in general, from further participation in this research study.) Any identifiable research or medical information recorded for, or resulting from, your participation in this research study prior to the date that you formally withdrew your consent may continue to be used and disclosed by the investigators for the purposes described above.

To formally withdraw your consent for participation in this research study you should provide a written and dated notice of this decision to the principal investigator of this research study at the address listed on the first page of this form.

Your decision to withdraw your consent for participation in this research study will have no effect on your current or future relationship with the University of Pittsburgh. Your decision to withdraw your consent for participation in this research study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

If I agree to take part in this research study, can I be removed from the study without my consent?
If the investigators feel that you cannot complete the study requirements safely (for example, you have an allergic reaction to a study medication), they may withdraw you from the study.

FDA Clinical Trial Registry
A description of this clinical trial will be available on http://www.clinicaltrials.gov as required by US Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

****

VOLUNTARY CONSENT:

All of the above has been explained to me and all of my current questions have been answered. I understand that, throughout my participation in this research study, I am encouraged to ask questions about any aspect of this research study including the use and disclosure of my identifiable medical record information. Such future questions will be answered by the investigators listed on the first page of this form.

Any questions I have about my rights as a research participant or the research use of my medical information will be answered by the Human Subject Protection Advocate of the IRB Office, University of Pittsburgh (1-866-212-2668).

By signing this form, I agree to participate in this research study and provide my authorization to share my medical records with the research team. A copy of this consent form will be given to me.

_____ _____

Subject's Signature Date

CERTIFICATION OF INFORMED CONSENT

I certify that I have explained the nature and purpose of this research study to the above-named individual, and I have discussed the potential benefits and possible risks of study participation. Any questions the individual has about this study have been answered, and we will always be available to address future questions as they arise. I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Printed Name of Person Obtaining Consent Role in Research Study

_____ _____

Signature of Person Obtaining Consent Date