Official Title of Study: Reduction of Bladder Injection Pain with Belladonna Opiate Suppository: A Randomized, Double-Blind, Placebo-Controlled Trial (ROBIN Trial)

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# RESEARCH CONSENT FORM

## Reduction of Bladder Injection Pain with Belladonna Opiate Suppository: A Randomized, Double-Blind, Placebo-Controlled Trial (ROBIN Trial) Protocol # 5 November 2015



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[redacted]

You are being asked to join a research study. Participating in research is different from standard medical care. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at Associates in Women's Health.

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read it carefully and ask as many questions as you need to, before deciding about this research.

You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating. You may be asked to sign a new consent form if this occurs.

This research study will take place at the Wichita Women's Pelvic Surgery Center at Associates in Women's Health (3232 E. Murdock St., Wichita, KS 67208) with Edgar LeClaire, MD, FACOG as the researcher. About ***26 people*** will be in this study. Your expected length of participation is about two weeks.

### Why am I being asked to take part in this study?

You are being asked to take part in this study because we hope to learn if we can improve pain associated with Onabotulinumtoxin A (BoNT), also known as Botox (Allergan®), injections into the bladder.

### Why is this study being done?

Overactive bladder (OAB) and urge urinary incontinence (UUI) affect 17% of women in the United States. Bladder injection with Onabotulinumtoxin A (BoNT), also known as Botox (Allergan®), is an effective, Food and Drug Administration (FDA) approved for the treatment of OAB and Neurogenic Bladder (NB) that has failed first-line medical

management. Additionally, the American Urologic Association endorses BoNT bladder injection for the treatment of refractory Painful Bladder Syndrome (also known as Interstitial Cystitis). This procedure involves placing a camera into the bladder (cystoscope) and injecting BoNT in 10-30 places in the bladder. Currently, Lidocaine (a numbing medicine) gel is commonly used to improve discomfort during a cystoscopy. While this helps reduce some discomfort during cystoscopy procedures, its effectiveness during BoNT injections have not been well studied. Additionally, methods to address bladder injection pain have not been very well addressed in research.

Belladonna & opiate suppositories (B&Os) have been commonly used to treat spastic lower urinary tract pain. B&O suppositories have been used safely in robotic prostatectomy (surgery removing of part or all of the prostate gland) studies and have shown improved pain control. The overall goal of this study is to improve the patient experience and methods to control pain during the BoNT injection procedure.

**What is being tested in this study?**
This study is testing whether using a B&O suppository can improve patient discomfort during BoNT injections into the bladder. The current standard pain control protocol is to use local Lidocaine inside of your bladder, which helps with pain from the urethra (opening of your bladder into your vagina) but does not help as much with pain caused by bladder cramping from irritation. There is a commonly used medicine in the form of a suppository that works to both relax the bladder and reduce the brain's experience of pain. This suppository, a B&O suppository, contains belladonna and opiate. Belladonna is found in plants and has been safely used throughout history for many different treatments. Opiates are naturally occurring pain medicine. These suppositories are currently used for other urology procedures, but have not yet been studied for use during in-office bladder injections of BoNT. This study will test how effectively the medicine decreases pain during the procedure. This study will use a B&O suppository that is made up of belladonna and morphine.

B&O suppositories are not currently approved by the FDA. However, this is because the medication was developed and regularly used before the existence of the FDA, and thus they were grandfathered in and did not have to be evaluated by the FDA. It is routinely and safely used in this practice and many others, however it is technically an investigational drug. This means it is still being studied to find out what a safe/effective dose is.

Using this test drug during the procedure will NOT replace the use of numbing medicine. You will receive numbing medication (viscous Lidocaine) prior to undergoing the bladder injection procedure.

**How long will I be in the study?**
Your participation in this study is expected to last about 2 weeks. You will be asked to complete the in-office procedure and one follow-up visit two weeks after the procedure. The two-week follow-up visit will occur regardless of whether you decide to participate in this study, and is part of standard care.

**What will I be asked to do?**
If you decide to participate in this study, you will be asked to read and sign this consent form before any study procedures take place.

You will be randomly assigned (like rolling the dice) to one of 2 groups. A computer will decide which group you are in.

**Group 1: Receive the B& O suppository 40 minutes prior to procedure**

**Group 2: Receive a placebo suppository 40 minutes prior to procedure**

You will have a 1 in 2 chance (50 %) of receiving B&O suppository or placebo. A placebo has no active ingredients, but is made to look like the study drug. Neither you nor the investigator will know which treatment you are receiving. In the event of an emergency, the investigator will be able to find out what treatment you are receiving. From this point forward, the B&O suppository and placebo will both be referred to as "study drug."

There is a difference between the standard pain control protocol and participating in this study. With standard care, you will undergo the in-office procedure in which Dr. Edgar LeClaire will inject BoNT into your bladder. You will be asked to void before you are to leave the clinic the day of the procedure, and attend a follow-up appointment two weeks after your procedure.

As a participant in this study, the procedures that involve research include the use of the suppository (either the B&O or placebo) during the procedure. You will be asked to complete forms regarding your pain levels and function. Additionally, we would like to collect your medical history from your clinic medical record.

**The use of a B&O suppository to provide additional pain control during this procedure is experimental at this time.**

Below, you will find a schedule of events listing all procedures that will occur at each study visit. Following the table, you will find a description of the study procedures.

| | |
|---|---|
| **Appointment #1** | • You and Dr. LeClaire have determined that the bladder injection therapy is the next step in your clinical are for overactive bladder, neurogenic bladder, or refractory interstitial cystitis.<br>• You have agreed to undergo the bladder injection therapy and you meet the criteria to participate.<br>• You will be offered consent to participate in this study (this consent form). |
| **Appointment #2** | • You will be treated with BoNT injections with Lidocaine, according to standard care.<br>• You will be assigned, at random, to either receive a B&O suppository, or a placebo suppository. ***(RESEARCH)***<br>• During the procedure, you will be asked to assess your pain level. ***(RESEARCH)***<br>• You will be asked to complete a voiding trial after the procedure is done, which is part of standard care. You will be asked your satisfaction with pain management during the procedure. |
| **Appointment #3** | • You complete your two-week follow-up appointment with Dr. Edgar LeClaire, and a voiding trial during the appointment, which is part of your standard of care. |

**What are the possible risks or discomforts?**
Participating in this study includes some risk and possible discomfort. The study intervention may cause side effects or other problems such as drowsiness, nausea, or discomfort. The researchers will be checking your medical information during the study to watch for side effects. However, you should tell the research team about anything that is bothering you or any changes in your health since the last visit. The researchers may be able to take steps to reduce side effects. You may experience none, some, or all of the side effects listed below. There may be other side effects or risks that are not yet known.

*Adverse reactions:* Occur rarely with an undefined frequency but may include palpitations (irregular heartbeat), dizziness, drowsiness, pruritus (itching), urticarial (rash), constipation, nausea/vomiting, urinary retention (inability to completely empty the bladder), blurred vision, photophobia (sensitivity to light).

The loss of anonymity is a risk associated with research projects that involve human subjects. The researchers working on this study will take every precaution to guard patient identity. The study doctors and the research staff will review and collectively summarize the information for this study. No patient will be identified by name and protections will be in place to keep individual information confidential and anonymous.

Researchers believe a minimal risk is associated with psychological, economic, social, and legal aspects of this study.

There are risks that the study drug may not add additional benefit from the current standard of care. There is little data to suggest that this drug will be beneficial, but large studies directly comparing drug to placebo are lacking. Thus, we cannot predict every possible side effect and outcome. The B&O suppository may increase urinary retention associated with the BoNT therapy, but you will be closely monitored for this. Your follow-up study will include urodynamics (testing to assess your bladder and urethra are performing adequately) and a scan of your bladder to assess for increased urinary retention. This side effect can be treated, will most likely resolve, and is not life-threatening or fatal.

Risks of placebo are similar to the risks of the treatment arm, including the risks associated with the BoNT procedure. Although using a B&O suppository during the BoNT procedure has not been studied by the manufacturer (Allergan®), Dr. Edgar LeClaire uses the suppository as his regular practice. Thus, if you are assigned to the placebo group, you may theoretically experience more discomfort or pain during the procedure. However, you will still receive the standard numbing medication (Lidocaine) to help with pain.

Allergic Reaction Risks

Sometimes, people have serious allergic reactions to drugs. A severe allergic reaction could be life-threatening and may result in death. Symptoms of allergic reactions include:

- Swelling of mouth, throat or eyes
- Rash
- Difficulty breathing
- Coughing
- Wheezing
- Sudden drop of blood pressure
- Seizures
- Flushing
- A fast pulse
- Sweating

You should call 911 if you think you are having a severe allergic reaction. Please also contact the study team if you have any of these or other side effects during the study.

**Pregnancy Risks**

You cannot be in this study if you are pregnant or nursing a baby. You cannot be in this study if you are trying to get pregnant. There may be pregnancy risks that are not known yet. For this reason, you must tell the study doctor right away if you get pregnant during the study. If you are at a risk for being pregnant, you will be given a pregnancy test as part of Dr. LeClaire's standard care.

**Are there benefits to being in this study?**

You may or may not benefit from this study. Researchers hope that the information from this research study may be useful in the treatment of other patients with overactive bladder or neurogenic bladder. Additionally, the information collected from this study

may help clinicians better control pain during in-office procedures.

**Will it cost anything to be in the study?**
As a participant in this study you will not bear any cost that is outside your standard medical care. You or your insurance will be billed for the parts of the study that are standard medical care, such as your office visits related to your medical care and the BoNT injection therapy. Your insurance or government health program may not cover certain items if you are part of a research study. You may want to talk to your insurance company before deciding to participate.

**Will I get paid to participate in the study?**
You will receive a $25 gift card if you chose to participate in this study. You will receive your gift card at the conclusion of your two-week follow-up visit to help cover travel/driver costs. If you decide to withdraw from this study before completing all study related procedures, you will not receive the gift card.

**Will the researchers get paid for doing the study?**
The Principal Investigator and the researchers associated with this study will not receive payment or compensation outside of standard treatment for conducting this study.

**What happens if I get hurt or sick during in the study?**
If you have a serious side effect or other problem during this study, you should immediately contact Dr. Edgar LeClaire [redacted]. If it is after 5:00 p.m., a holiday or a weekend, [redacted] go to the emergency room. A member of the research team will decide what type of treatment, if any, is best for you at that time.

If you have a bodily injury while participating in this study, treatment will be provided for you at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to your health insurance policy, your government program, or other third party, but you will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

**What happens if I think I have been harmed or hurt due to study related procedures?**
If you think you have been harmed as a result of participating in research at the University of Kansas School of Medicine – Wichita (KUSM-W) or one of its affiliates, you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160. You may also speak to someone on the telephone at 913-588-1240.

**Do I have to be in the study?**
Being in research is voluntary. You can choose whether or not to participate. Even if you decide not to join the study, you can still come to Associates in Women's Health for services and treatment.

**What other choices do I have?**
You can choose to not participate in the study. If you do not participate, you will receive the B&O suppository, as this is Dr. Edgar LeClaire's routine for pain control during the BoNT injection therapy. If for some reason you choose not to receive the B&O suppository, you will receive the standard pain control methods during the procedure, which is Lidocaine.

**How will my privacy be protected?**
The researchers will protect your information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. Your health information is protected by a federal privacy law called HIPAA (Health Insurance Portability and Accountability Act). By signing this consent form, you are giving permission for KUSM-W to use and share your health information. If you decide not to sign the authorization form, you cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study activities and from your medical record. You may be identified by information such as name, address, phone number, or date of birth. Your health information will be used at KUSM-W by Dr. Edgar LeClaire, members of the research team, and officials at KUSM-W who oversee research, including members of the KUSM-W Human Subjects Committee and other committees and offices that review and monitor research studies.

By signing this form, you are giving Dr. Edgar LeClaire and the research team permission to share information about you with persons or groups outside KUSM-W. Your information will be shared with representatives the U.S. Food and Drug Administration (FDA) and U.S. agencies that oversee human research (if a study audit is performed). The Wichita Medical Research and Education Foundation Institutional Review Board and the KUSM-W Human Subjects Committee may also need to review your records. These groups or agencies may make copies of study records for audit purposes. The purpose for using and sharing your information is to make sure the study is done properly and to evaluate the safety and effectiveness of B&O suppository.

The HIPAA privacy law may not apply to everyone who receives your health information. Your information might not be protected by HIPAA if persons outside KUSM-W disclose it. In some cases, there may be other laws that protect your information from improper use.

Your permission to use and share your health information will not expire unless you cancel it. Any research information that is placed in your medical record will be kept indefinitely.

While you are participating in this study, you may see any study information that is

placed in your KUSM-W medical record. However, some study information is kept only by the researcher. The records kept only by the researcher may not be available to you until the end of the study.

The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

**Can I stop being in the study?**
You may stop being in the study at any time. Your decision to stop will not prevent you from getting treatment or services at Associates in Women's Health. You will be informed of any significant new findings that might change your decision to continue to be part of the study.

You have the right to cancel your permission (revoke authorization) for researchers to use your health information. If you want to cancel your permission, please write to Dr. Edgar LeClaire. [redacted] If you cancel permission to use your health information, you will be withdrawn from the study. The researchers will stop collecting any additional information about you unless they need information about a side effect of B&O suppository. They may use and report information that was gathered before they received your cancellation.

**Could my participation be stopped early?**
This study might be stopped, without your consent, by the investigator, the Institutional Review Board, or by the FDA. Your participation also might be stopped by the investigator if it is in your best interest or if you do not follow the study requirements.

Your physician will decide about future treatment, if it is needed.

**Who can I talk to about the study?**
Before you sign this form, Dr. Edgar LeClaire or other members of the study team should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns or complaints after signing this form. If you have any questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (316) 293-2610. You may also write the Human Subjects Committee at 1010 N Kansas, Wichita, KS 67214. In addition you may contact Wichita Medical Research & Education Foundation in writing at 3306 E. Central Ave, Wichita, KS 67208 or by phone at (316) 686-7172.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law (NCT02600715). This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

## Indemnity Clause

No guarantee has been made to you as to the results that may be obtained. Wichita Women's Pelvic Surgery Center at Associates in Women's Health, the Wichita Medical Research and Education Foundation and other involved organizations do not provide free medical treatment or other forms of compensation for injuries incurred as a result of participating in this research.

## CONSENT

Dr. Edgar LeClaire or a member of the research team has given you information about this research study. They have explained what will be done and how long it will take. They explained any inconvenience, discomfort or risks that may be experienced during this study.

By signing this form, you say that you freely and voluntarily consent to participate in this research study. You have read the information and had your questions answered. ***You will be given a signed copy of the consent form to keep for your records.***

_____
Print Participant's Name

_____ _____ _____
Signature of Participant Time Date

_____
Print Name of Investigator

_____ _____
Signature of Investigator Date

_____
Print Name of Person Obtaining Consent

_____ _____
Signature of Person Obtaining Consent Date

_____
Participant ID Number