Document Title: Minimizing Pain During Office Intradetrussor Botox Injection: A Prospective Randomized Controlled Trial Comparing Two Protocols

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Approved by the Beth Israel Deaconess Medical Center Committee on Clinical Investigations:

Consent Approval Date: _____

Protocol Number: _____

Beth Israel Lahey Health
Mount Auburn Hospital

INFORMED CONSENT FORM TO TAKE PART IN A RESEARCH STUDY

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: Minimizing pain during office intradetrusor Botox injection: A prospective randomized controlled trial comparing two protocols
PRINCIPAL INVESTIGATOR: Eman Elkadry, MD
PROTOCOL NUMBER: 037-2019

KEY INFORMATION

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

Why am I being invited to take part in a research study?
We invite you to take part in a research study because you are receiving Botox bladder injections for a diagnosis of overactive bladder.

What should I know about a research study?
- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- Your participation is completely voluntary.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- Your refusal to participate will not result in any consequences or any loss of benefits that you are otherwise entitled to receive.
- You can ask all the questions you want before you decide.
- If you choose not to take part, or if you leave the study, your decision will in no way harm your relationship with any member of the research team or any other individuals at Mount Auburn Hospital.

SUBJECT'S NAME:
TITLE OF RESEARCH PROTOCOL: MINIMIZING PAIN DURING OFFICE INTRADETRUSOR BOTOX INJECTION: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL COMPARING TWO PROTOCOLS
PRINCIPAL INVESTIGATOR'S NAME: EMAN ELKADRY, MD
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Why is this research being done?
The purpose of this study is to compare two different treatment protocols on the pain associated with intradetrusor Botox injections. Before Botox injections into the bladder, patients generally have their bladder filled with lidocaine, an anesthetic which helps reduce the discomfort during the procedure. Lidocaine instillation into the bladder is the standard of care. This study examines whether adding sodium bicarbonate, which brings the solution closer to the normal physiologic pH, will help with pain during bladder Botox injections. All enrolled subjects will be provided with the Botox treatment and lidocaine instillation into the bladder, and only some patients will also receive sodium bicarbonate. The goal of this study is to assess whether adding sodium bicarbonate to the lidocaine solution improves pain with bladder Botox injections, which may benefit you and others in the future undergoing this procedure.

How long will the research last and what will I need to do?
We expect that you will be in this research study for one visit.

You will be asked to fill out a brief questionnaire regarding your pain during the Botox procedure after the procedure is finished.

More detailed information about the study procedures can be found under ***"*DESCRIPTION OF STUDY DETAILS*".***

Is there any way being in this study could be harmful to me?
Potential risks include bladder pain, worse procedural pain, however these are unlikely and are theoretical risks but have not been reported in the literature.

More detailed information about the risks can be found under ***"*RISKS AND DISCOMFORTS*".***

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include reduced pain with bladder Botox injections.

What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate or not to participate.

Instead of being in this study, your choices may include: standard bladder instillation.

DETAILED INFORMATION SECTION

Please read this consent form carefully and ask the investigators or study staff to explain any words or information that you do not clearly understand. Once you read this consent form and understand what your participation in this study will involve, you will be asked to sign this form if you wish to take part.

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You will be given a signed copy of the form to keep for your records.

DISCLOSURE OF SPECIAL INTERESTS OF MOUNT AUBURN HOSPITAL AND INVESTIGATORS
This study is being conducted by Dr. Eman Elkadry. There is no funding agency in this study. Neither MAH nor Dr. Elkadry has/have any additional interests in this research project.

WHOM TO CONTACT IF YOU HAVE QUESTIONS OR PROBLEMS

If you have any questions, concerns or complaints about this research or experience any problems, you should contact Dr. Eman Elkadry or Kathleen Rogers at [617] 354-5452.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS

You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

PURPOSE
The purpose of this study is to compare two different treatment protocols on the pain associated with intradetrusor Botox injections. Botox injections into the bladder is the standard of care for refractory overactive bladder. Patients in both arms of this study will be receiving the standard of care. Before Botox injections into the bladder, patients generally have their bladder filled with lidocaine, an anesthetic which helps reduce the discomfort during the procedure. Lidocaine instillation into the bladder is similarly the standard of care. This is a blinded study which means that neither you nor the study doctor will know if you are receiving the standard treatment or enhanced treatment with a buffered solution. A buffered solution is a solution that can keep the pH of a solution relatively consistent. Lidocaine is normally acidic. In this study, the sodium bicarbonate brings the solution closer to the normal physiologic pH. All enrolled subjects will be provided with the Botox treatment and lidocaine instillation into the bladder. The only difference will be the pre-treatment medications, some patients will receive sodium bicarbonate. As part of this study you will be asked to complete a brief questionnaire after treatment asking you about your experience and your pain during the procedure.

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STUDY PARTICIPANTS

You have been asked to be in the study *because you have a diagnosis of overactive bladder and are undergoing bladder Botox injections for treatment of this condition.*

Approximately 72 people will take part in this study at Mount Auburn Hospital. A total of 72 people will take part in this study at all study sites.

DESCRIPTION OF STUDY DETAILS

At the initial visit, you will be asked questions about your health, past surgeries, medications as part of your routine clinic visit. You will be asked questions about incontinence and sexual function, height and weight, and a pelvic examination including assessment of pelvic floor tenderness and strength. This will not be different for patients who are part of the study and for those who decline to participate in the study. If you qualify for this study and consent to participate, you will be randomized 1:1 at the time of your cystoscopy to the standard pretreatment instillation using lidocaine or the buffered instillation using lidocaine with sodium bicarbonate. You will then undergo intradetrusor Botox injections as is standard practice. At the completion of your bladder Botox injections, you will be asked to answer questions about your pain and your satisfaction.

If you agree to be in this study, you will be in this research study for about one visit.

After you sign the consent form, the following things will happen:

1. Screening Procedures: Screening procedures are tests and procedures that will be done to determine if you are eligible to take part in the research study. For this research study, the screening procedures include: review of medical history to determine your pelvic floor disorder.

2. Randomization Procedures:

   It is not clear at this time which of the treatments in this study would be better for you. For this reason, the treatment plan offered to you will be picked by chance [like the flip of a coin]. You will not be able to choose which treatment you receive. The chances of receiving either of the treatments are approximately equal. After the randomization, you will be assigned to one of the following groups:

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A) Standard lidocaine bladder instillation

B) Buffered lidocaine bladder instillation

If one treatment arm is found to be less effective than the other while you are taking part in the study, you will be informed and further treatment will be discussed.

Neither you nor your physician will know which treatment you are receiving. However this information can be learned in case of an emergency.

3. Research Procedures: If you qualify to take part in this research study, you will undergo these research procedures: You will undergo your bladder pretreatment instillation and bladder Botox injections as is the standard of care. You will either receive lidocaine alone or lidocaine with sodium bicarbonate. After your Botox injections you will complete a brief questionnaire.

4. Monitoring/Follow-Up Procedures. Procedures performed to evaluate the effectiveness and safety of the research procedures are called "monitoring" or "follow-up" procedures. For this research study, the monitoring/follow-up procedures include: routine post-procedure visits as is our standard clinical practice.

RISKS AND DISCOMFORTS

Potential risks include bladder pain, worse procedural pain. These are unlikely and are theoretical risks but have not been reported in the literature. Since there are limited studies on using buffered solution for pre-instillation, there may also be other side effects that we cannot predict because it is not possible to predict all potential side effects. Similar buffered solutions however are already commonly used for lidocaine injections and for bladder instillations for other indications including interstitial cystitis.

Loss of confidentiality

There is the potential for loss of confidentiality by participating in this study. Every effort will be made to protect the confidentiality of your identifiable information.

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CONFIDENTIALITY

Information learned about you during this research program will be maintained confidentially by the research staff as described in this form.

Information learned from your participation in this study and from your medical record may be reviewed and photocopied by the Food and Drug Administration (FDA) and/or other federal and state regulatory agencies, accreditation agencies, the BIDMC Committee on Clinical Investigations, the BIDMC Human Subjects Protection Office and others involved in research administration of Mount Auburn Hospital or the Beth Israel Deaconess Medical Center. Information resulting from this study and from your medical record may be used for research purposes and may be published; however, you will not be identified by name in such publications.

MEDICAL RECORD

Information from this study will not be placed in your medical record.

POSSIBLE BENEFITS

It is not possible to predict whether you will benefit directly from participation in this study. However, your participation may help others in the future as a result of knowledge gained from the research.

OTHER AVAILABLE OPTIONS

Taking part in this study is voluntary. Instead of being in this study, you have the following options: standard bladder instillation.

We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

IF YOU DECIDE NOT TO TAKE PART IN THE STUDY

Participation in this study is voluntary. You have the right to decide not to take part in this study. If you choose to participate, you have the right to leave the study at any time. Your decision to not

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participate will not result in any penalties or loss of benefits to you. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you decide not to participate in the study or decide to leave the study early, your decision will not affect your relationship with the research team or any other individual at Mount Auburn Hospital.

INVESTIGATORS RIGHT TO STOP THE STUDY

The investigators have the right to end your participation in this study if they determine that you no longer qualify to take part, or if it would be dangerous for you to continue, or if you do not follow study procedures as directed by the investigators. Mount Auburn Hospital or the funding source may stop the study at any time.

COSTS AND/OR PAYMENTS TO YOU

COSTS COVERED BY STUDY

There are no additional costs associated with this study as this is considered standard treatment. However, you and your insurance company will be charged for other tests, procedures or medications of this study that are considered standard treatment for your medical condition.

CO-PAYMENT/DEDUCTIBLE STATEMENT

You will be responsible for any co-payments or deductibles that are standard for your insurance coverage.

COST OF RESEARCH RELATED INJURY:

If you are injured as a direct result of your participation in this study you should contact the Investigator at the number provided under the section “Whom to Call if You Have Questions” in this form. You will be offered the necessary care to treat your injury. You or your insurance company will be billed for medical care and/or hospitalization related to this injury. You will be responsible for all co-payments and deductibles required under your insurance. MAH will consider reimbursement of injury related expenses not covered by your insurance on a case-by-case basis. At this time there is no plan to reimburse you for items such as lost wages or lost time from work. By signing this consent form you have not given up any legal rights.

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A description of this clinical trial will be available on www.ClinicalTrials.gov as required by U.S. law. 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.

AUTHORIZATION FOR USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION

As part of this study, we will be collecting, using and sharing with others information about you. Please review this section carefully as it contains information about the federal privacy rules and the use and disclosure of your information.

DESCRIPTION OF PROTECTED HEALTH INFORMATION [PHI]

By signing this informed consent document, you are allowing the investigators and other authorized personnel to use and disclose health information about you. This may include information about you that already exists (for example: your medical records and other sources of health information, demographic information, the results of any laboratory tests) as well as any new information generated as part of this study. This is your Protected Health Information.

PEOPLE/GROUPS AT MOUNT AUBURN HOSPITAL WHO WILL SHARE AND USE YOUR PROTECTED HEALTH INFORMATION

Your Protected Health Information may be shared with and used by investigators working on this study, including the supporting research team (such as research assistants and coordinators, statisticians, data managers, laboratory personnel, pharmacy personnel, and administrative assistants), and may also be shared with and used by other health care providers at MAH who have treated you in the past and have information relevant to the research, or who provide services to you in connection with the research.

PEOPLE/GROUPS OUTSIDE OF MOUNT AUBURN HOSPITAL TO WHOM YOUR PROTECTED HEALTH INFORMATION WILL BE DISCLOSED (SHARED) AND WHO MAY USE YOUR PROTECTED HEALTH INFORMATION

We will take care to maintain confidentiality and privacy about you and your Protected Health Information. We may share your Protected Health Information with the following groups so that they may carry out their duties related to this research study:

- The members and staff of Research Administration at BIDMC and the Committee on Clinical Investigations of Beth Israel Deaconess Medical Center, which is responsible for reviewing studies for the protection of the research subjects, so that it can carry out its oversight responsibilities with respect to the study.

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- The other hospitals and medical centers taking part in this study and research collaborators at those institutions.
- Other research collaborators and supporting research team members taking part in this study
- Any external health care providers who provide services to you in connection with this research
- Laboratories not affiliated with MAH that are involved in conducting tests related to the research
- Statisticians and other data monitors not affiliated with MAH
- The members and staff of any other IRBs (beyond the BIDMC Committee on Clinical Investigations) that oversee the research
- Centralized data collectors
- Your health insurance company
- The Food and Drug Administration [FDA], the Department of Health and Human Services [DHHS], the National Institute of Health [NIH], the Office for Human Research Protections [OHRP], and other federal and state agencies that may have jurisdiction over the research
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study (if applicable)

Those who receive your Protected Health Information during the course of the research may not be required by the federal privacy regulations to protect it, and they may make further disclosures to others and use your information without being subject to penalties under those laws.

PURPOSE: WHY WE ARE USING AND SHARING YOUR PROTECTED HEALTH INFORMATION

The reason for using and sharing your Protected Health Information is to conduct and oversee the current, secondary, and future research described in this Informed Consent Document. There are many other reasons beyond the research for which MAH may use or disclose your Protected Health Information. Not all of these reasons require your express written authorization. For example, we will use and share your Protected Health Information to ensure that the research meets legal, institutional and accreditation requirements and to conduct public health activities. The various ways in which MAH may use and disclose your protected health information without your authorization are explained in a document called the Notice of Privacy Practices. If you have not received a copy of MAH's Notice of Privacy Practices, please ask us for one and review it before signing this form. In addition to signing this document, you may also be asked to sign a BIDMC General Agreement form acknowledging that you have received the MAH Notice of Privacy Practices.

NO EXPIRATION DATE – RIGHT TO WITHDRAW AUTHORIZATION

Your authorization for the use and disclosure of your Protected Health Information in this Study shall

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never expire. However, you may withdraw your authorization for the use and disclosure of your Protected Health Information at any time provided you notify the Principal Investigator in writing. If you would like to take back your authorization so that your Protected Health Information can no longer be used in this study, please send a letter notifying the Principal Investigator of your withdrawal of your authorization to Dr. Eman Elkadry at 725 Concord Avenue, Suite 3500, Cambridge, MA 02138. Please be aware that the investigators in this study will not be required to destroy or retrieve any of your Protected Health Information that has already been used or disclosed before the Principal Investigator receives your letter, and they are permitted to continue to use and disclose your previously collected information as necessary to complete the research.

REFUSAL TO SIGN
Your clinical treatment may not be conditioned upon whether you sign the Authorization for Research. However, if you choose not to sign this informed consent document and authorization for the use and disclosure of your Protected Health Information, you will not be allowed to take part in the research study.

RIGHT TO ACCESS AND COPY YOUR PHI
If you wish to review or copy your Protected Health Information as it is made part of your medical record, you may do so after the completion or termination of the study by sending a letter to the Principal Investigator requesting a copy of your Protected Health Information. You may not be allowed to inspect or copy your Protected Health Information until this study is completed or terminated.

ADDITIONAL CONTACT FOR QUESTIONS OR CONCERNS
You may contact the Human Subjects Protection Office at [617] 975-8500 in the event that you would like to obtain information or to offer input about the research study. This office is independent of the investigator or investigator's research staff and can also assist with questions relating to your rights as a participant in research, which may include questions, concerns or complaints about your participation in the study.

THE FOLLOWING PARAGRAPHS CONTAIN SOME STANDARD INFORMATION WHICH GENERALLY APPLIES TO INDIVIDUALS PARTICIPATING IN A RESEARCH STUDY.

CONSENT FORM FOR CLINICAL RESEARCH

I have read the previous page[s] of the consent form and the investigator has explained the details of the study. I understand that I am free to ask additional questions.

If I wish additional information regarding this research and my rights as a research subject, or if I believe I

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have been harmed by this study, I may contact the Human Subjects Protection Office (HSPO).

I am aware that this is a research project and that unforeseen side effects may occur.

I understand that Mount Auburn Hospital has no formal program for compensating patients for medical injuries arising from this research. Medical treatment will be provided for injuries at the usual charge to me or to my insurer unless payment is otherwise provided for in this consent form.

I understand that participation in this study is voluntary and I may refuse to participate or may discontinue participation at any time without penalty, loss of benefits, or prejudice to the quality of care which I will receive.

I acknowledge that no guarantees have been made to me regarding the results of the treatment involved in this study, and I consent to participate in the study and have been given a copy of this form.

_____ _____

Signature of Subject or Legally Authorized Representative (Parent if the subject is a minor) Date

_____

Relationship of Legally Authorized Representative to Subject

The subject has been given the opportunity to read this consent form and to ask questions before signing, and has been given a copy.

_____

SIGNATURE OF INVESTIGATOR/Co-Investigator DATE

_____

PRINT INVESTIGATOR'S/Co-Investigator's NAME

A signing co-investigator must be listed on the study's approved Research Staffing Form at the time of consent.

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THE FOLLOWING SECTIONS ARE NOT NEEDED FOR ALL STUDIES AND SHOULD BE UTILIZED AS INDICATED:

If the subject is able to speak and understand English but is not able to read or write

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is able to understand English but is not physically able to read or write or see

I was present during the entire oral presentation of the informed consent and witnessed the subject's agreement to participate in the study.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

If the subject is not English speaking and signed the translated Short Form in lieu of the English consent document.

As someone who understands both English and the language spoken by the subject, I interpreted, in the subject's language, the researcher's presentation of the English consent form. The subject was given the opportunity to ask questions.

Signature of Interpreter: _____

Printed name of Interpreter: _____

Date: _____