

Title: Efficacy of Intrathecal Oxytocin to Speed Recovery After Hip Surgery

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Department/Section of Anesthesiology

EFFICACY OF INTRATHECAL OXYTOCIN TO  
SPEED RECOVERY HIP SURGERY

Informed Consent Form to Participate in Research  
James C. Eisenach, M.D., Principal Investigator

## INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you are scheduled to have hip replacement surgery. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

## WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to help researchers better understand patterns of recovery after **Hip Replacement** surgery. We will evaluate how pain, activity and reasoning responses determine patterns of recovery. We will also evaluate the effectiveness of a medication called Oxytocin. Oxytocin is commonly given by IV (into a vein) to treat certain types of pain. We believe that intrathecal or spinal oxytocin (given into the spinal fluid) may prove to be an excellent pain killer for certain types of pain which sometimes occur with cancer or follow nerve injury after accidents or surgery. At present, there are not good treatments for this type of pain and your participation in this study may help researchers better understand this type of pain and perhaps develop new ways of treating this pain. This is the fourth study in the United States to examine the effects of oxytocin given into the spinal fluid in the back.

Oxytocin has been approved by the US Food and Drug Administration (FDA), but the preparation and route of administration being used in this study has not been approved. At this time, there is not a form of Oxytocin that is available on the open market for spinal administration.

In this study spinal oxytocin will be compared to a placebo. A placebo is a substance, like a sugar pill, that is not thought to have any effect on diseases or medical conditions. In this study you will either receive the active study medication, oxytocin or placebo which is not active. Placebos are used in research studies to see if the drug being studied really does have an effect

We will ask you to complete several psychological questionnaires that tell us about your reasoning responses, thoughts, and emotional feelings.

### HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

A total of 120 people will take part in this study. In order to identify the 120 subjects needed, we may need to screen as many as 140 because some people will not qualify to be included in the study.

### WHAT IS INVOLVED IN THE STUDY?

You will be randomized into one of the following 2 study groups described below.

Randomization means that you are put into a group by chance. It is like flipping a coin. You will have a one in two chance of being placed in either group.

The groups are:

- 1) Intrathecal oxytocin
- 2) Intrathecal saline (placebo)

Neither you nor the investigator will know which study medication you are receiving. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

### PREOPERATIVE PROCEDURES

Once you have agreed to participate, you will be scheduled to come to our Headache and Pain Research Unit (HPRU) for 2 study visits. Each visit will last approximately 2 hours.

#### STUDY VISIT 1:

Approximately 2 weeks before your surgery we will have you come to the HPRU for your first study visit. During the first visit we will ask you about your medical history, existing pain and any medications that you are taking. If you are a female subject of child-bearing potential we will also administer a urine pregnancy test. We will ask you to complete a series of 13 questionnaires on the computer.

After you have completed the questionnaires we will train you to use an electronic tablet for daily diary entries and also in the use of an accelerometer (small device that is worn on your wrist like a watch to record your activity). The accelerometer tells us about your activity by counting the number of steps you take, the distance you walk and the quality of your sleep while you are wearing it.

You will also complete 1 electronic survey that asks you about how you make decisions or how impulsive you are. We will have you play a card game that also tells us how you make decisions. We will also have you play a game on an iPad that tells us how anesthesia and surgery affects your ability to pay attention.

All questionnaires/surveys are for research purposes only.

### DAY OF SURGERY AND IN-HOSPITAL CARE

The spinal procedure will be done per standard of care by anesthesiology faculty. After turning on your side, your back will be washed with antiseptic, local anesthetic will be injected to numb your skin, and a needle will be placed in the lower part of your back. Once the spinal needle is in place and just before the spinal medication is administered, a small amount (less than ½ teaspoon) of cerebrospinal fluid will be withdrawn (this is the clear fluid that fills the cavities of the brain and covers the surfaces of the brain and spinal cord). This sample will be used to test for neurotransmitters (chemical molecules that “ferry” nerve impulses across the synapse from one neuron to the next in the brain) this is important because the neurotransmitters tell us about how your brain processes pain. The study medication that you are randomized to will be added to the routine medication that the anesthesiologist will give you to make you numb for your surgery.

A member of the study team will contact you at 24 hours after your surgery to assess your pain level, have you play the iPad game and answer your diary questions.

We will also collect information from your medical record including the type of surgery you are having, the medications that you are taking, the type of anesthesia that you have for your surgery, the type of pain you have, the amount of pain medication that you use after your surgery and the number of days you are in the hospital after your surgery as well as any other significant events that happen during your hospital stay.

### HOSPITAL DISCHARGE

We will ask you to make a daily evening entry in the electronic diary beginning the day of your hospital discharge and continuing for 60 days. Each of the assessments will only require about 2 minutes of your time to complete.

The electronic diary (tablet) will be equipped with a pre-paid wireless card so that you may connect to the internet to access the diary for completion.

You will also be asked to wear your accelerometer daily for the first 8 weeks after your discharge.

A member of the study team will call you once a month for 6 months and at 12 months after your discharge and ask you questions about your pain, physical function and 1 questionnaire. This phone call should last about 10 minutes.

During your postoperative visits to your surgeon we will record information about your joint function.

### STUDY VISIT 2:

Approximately 8 weeks after your surgery, we will ask you to return to the HPRU. We will repeat the questionnaires that were performed during our first visit and ask you to return the electronic diary and the accelerometer.

You will also complete 1 electronic survey that asks you about how you make decisions or how impulsive you are and you will play a card game that tells us how you make decisions.

## HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 12-13 months.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences.

## WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. We will ask you to complete various psychological tasks, which may cause you to reflect on emotional experiences or feel emotional. If you find it necessary, a list of resources are included at the end of this consent form that you may find helpful. We will not be providing immediate feedback to you from your psychological questionnaires.

### **Oxytocin**

The safety of spinal oxytocin has been extensively examined in animals, with no evidence of any nerve damage or other lasting effects, nearly 1000 humans have received spinal oxytocin in China without reported problems. Although this all suggests that it is safe to administer oxytocin, the exact risks are unknown. We will monitor you for the following potential side effects such as your level of sleepiness, changes in your blood pressure, how fast your heart is beating, and your urge to breathe. "The study team will provide treatment for side effects, as necessary."

You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia).

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

The risk of harm or discomfort that may happen as a result of taking part in this research study is not expected to be more than in daily life or from routine physical or psychological examinations or tests. You should discuss the risk of being in this study with the study staff.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study.

## Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

## ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future; however it is possible that you may have some relief from your postoperative pain.

## WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

## WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes:

- Name
- Age (date of birth)
- Health history
- Current medications
- Questionnaires
- Surgical Experience (ie: surgeon, procedure, anesthesia, pain, medications, complications, length of hospitalization)
- Postoperative function

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

- 1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research.
- 2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center.
- 3) Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.
- 4) The study sponsor (National Institutes of Health) will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.
- 5) Representative from the Food and Drug Administration will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

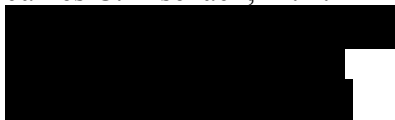
If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records. Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for an indeterminate period of time. This authorization does not expire and/or any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. James C. Eisenach that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

James C. Eisenach, M.D.



However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. 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 Web site at any time.

### WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including procedures related directly to the study will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

### WILL YOU BE PAID FOR PARTICIPATING?

You will be paid a total; of \$700 for completion of the entire study. If you complete only part of the study or withdraw during the study you will be paid according to the schedule below:

- \$100 for completion of the first HPRU study visit
- \$100 for completion of the second HPRU study visit
- \$100 for return of study supplies (electronic tablet, Actigraph™ and chargers)
- \$200 for completing at least 90% of the daily diary entries on the electronic tablet and wearing the Actigraph™ through 8 weeks after surgery at least 90% of required time
- \$200 for completion of all the scheduled study visits and telephone questionnaires

Once you have returned the Actigraph™ and the electronic diary (including the charger) and the wireless card your payment will be processed.

If you withdraw for any reason from the study before completion you will be paid according to the schedule of payment above after you have returned all study related items.



To receive payment, you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

### WHO IS SPONSORING THIS STUDY?

This study is being sponsored National Institutes of Health. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

### WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of \$25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of \$25,000 coverage for each claim and is limited to a total of \$250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [REDACTED].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Dr. James C. Eisenach at [REDACTED] during regular business hours and after hours you may page the study coordinator by calling [REDACTED] and entering the pager number [REDACTED].

### WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the

study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. The investigators also have the right to stop your participation in the study at any time. This could be because we have not been able to contact you or you are not completing your questionnaires and diaries as agreed upon. You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

### WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. James C. Eisenach at [REDACTED] during regular business hours and after hours you may page the study coordinator by calling [REDACTED].

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [REDACTED].

You will be given a copy of this signed consent form.

### SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed): \_\_\_\_\_

Subject Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_ am pm

Person Obtaining Consent: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_ am pm

Below is a list of resources that you may find helpful:

Emergencies:

Local Emergency Department

National Suicide Prevention Lifeline: 800-273-TALK (8255)

Non-Emergent:

Wake Forest Psychiatry (medical or counseling): 716-WAKE

Check with your insurance panel to identify therapists, doctors and other healthcare providers

Websites such as [www.findatherapist.com](http://www.findatherapist.com)

<http://www.findatherapist.com>

<http://www.therapists.psychologytoday.com>

<http://www.find-a-therapist.com>