Official Title: Generate a pharmacodynamic model of oxytocin for peripheral analgesic effects
NCT04431206
IRB Approval Date: 04/10/2023

Wake Forest®
School of Medicine

Department/Section of Anesthesiology

GENERATING A PHARMACODYNAMIC MODEL OF OXYTOCIN FOR PERIPHERAL ANALGESIC EFFECTS

INFORMED CONSENT FORM TO PARTICIPATE IN RESEARCH

James C. Eisenach, M.D., Principal Investigator

SUMMARY

You are invited to participate in a research study. The purpose of this research is to evaluate the change of oxytocin in the blood after administration of oxytocin by intravenous (IV) route and the effects it may have on thermal testing. You are invited to be in this study because you are a healthy subject or you have been diagnosed with advanced arthritis in your knee(s). Your participation in this research will involve 2 visits and last approximately 5 hours (total for both visits).

Participation in this study will involve receiving, IV administration of oxytocin and thermal testing. All research studies involve some risks. A risk to this study that you should be aware of is discomfort from the thermal/sensory testing and IV placement. Potential risks associated with receiving oxytocin are headache, facial flushing and a sensation of your heart pounding additional risks that are discussed later in this document.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. This is not a treatment study and there are no additional choices. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is James C. Eisenach, M.D. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: James C. Eisenach, M.D.
[redacted]

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

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 a healthy adult or you have advanced arthritis in your knee(s). 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 evaluate the effects oxytocin (naturally occurring hormone made in the brain that transmits messages) administered by intravenous (IV) route at a set rate may have on thermal testing. Oxytocin (intravenously or intramuscularly) is commonly given to pregnant women to cause labor to start or given after the delivery of an infant to stop the mother from bleeding. In this study we will be administering a dose of oxytocin over a 30 minute period. Oxytocin is being given to help researchers develop a model for evaluating the effect, if any on the response or your parasympathetic nervous system.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

We will enroll up to 18 people in the healthy subject group and up to 20 people in the advanced knee arthritis group. In order to identify the 32 subjects needed, we may need to screen as many as 200 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

You will have 2 study visits. Study visit 1 will be conducted in the Pain Research Unit at Piedmont Plaza II or the Clinical Research Unit (CRU) at Wake Forest Baptist Medical Center. Study visit 2 will be conducted in the Clinical Research Unit (CRU) at Wake Forest Baptist Medical Center. Study visit 1 will last approximately 2 hours and study visit 2 will last approximately 3 hours.

If you take part in this study, you will have the following tests and procedures:

PROCEDURES

Vital Signs: we will monitor your blood pressure, heart rate, respiratory rate and oxygen saturation (amount of oxygen in your blood).

Laboratory Testing: female participants of child-bearing potential will provide a urine sample to determine that they are not pregnant.

Thermal Heat Testing: we will train you to accurately describe pain from a small (about the size of a penny) and a large (about the size of a half dollar) probe. The tip of the heat probe that will be applied to the skin on your forearm is about the size of a penny. The tip of the heat probe

that will be applied to your calf is about the size of a half dollar. The thermal heat probe will be controlled by a computer that is programmed to deliver temperatures that range from skin temperature up to a temperature that is hot (122 ºF) and uncomfortable, but does not burn your skin.

Intravenous injection of Oxytocin: we will place an intravenous catheter and administer oxytocin.

Study Visit 1

You will report to the (CRU) at least 1 day prior to study visit 2. You will review and sign the Informed Consent (if you have not already done so). After informed consent is adequately obtained, a detailed medical history will be obtained. During this visit we will measure your blood pressure, heart rate, respiratory rate and we will place a clip on your finger which will measure the oxygen in your blood. Female participants of child-bearing potential will provide a urine sample for a pregnancy test. We will perform thermal heat training by applying thermal temperatures that range from 100°F to 122 °F with a 5 second presentation of varying temperatures to your forearm. We will ask you to rate each stimuli using an 11 point numerical verbal scale (NRS) anchored at 0 for no pain and 10 for the worst pain imaginable. After this training, we will then place a slightly larger probe on your lateral calf and warm the area to a temperature of 113°F for 5 minutes. During this five minute warming period we will ask you to give a pain rating each minute for any pain you are experiencing. If you do not experience pain during the initial thermal heating, we will move the thermal probe to a different location on your calf and repeat the testing and deliver a temperature of 115°F for 5 minutes. During the five minute warming period we will ask you to give a pain rating each minute for any pain you are experiencing. If you do not experience pain during this heating, we will move the thermal probe to a different location on your calf and repeat the testing and deliver a temperature of 117°F for 5 minutes. During the five minute warming period we will ask you to give a pain rating each minute for any pain you are experiencing.

Study Visit 2

On the second visit, you will report to the CRU, in the morning after having had nothing to eat or drink since midnight. Baseline vital signs (BP, HR, Resp, POX) will be obtained for a baseline measurement and then at 15, 30, and 60 minutes after the infusion was started. A peripheral intravenous (IV) catheter will be inserted into a vein in your arm and we will begin an IV fluid solution for the duration of the study. After obtaining baseline vital signs, we will obtain baseline measures from the thermal heat testing that was performed on your lateral calf study visit 1; oxytocin will be administered intravenously by pump over a period of 30 minutes. We will repeat the thermal testing; 113°F- 117°F temperature for 5 minutes on your lateral calf 5 additional times at different time points. This temperature will be determined from your testing on study visit 1. We will measure your vital signs 3 more times throughout the study.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for 2 visits, approximately 5 hours total.
We will call you daily for 5 days after study visit 2.

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. Risks and side effects related to the thermal testing and oxytocin we are studying include:

Heat Probe
You may experience brief pain during the thermal heat testing.

Needle Insertions
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.

Oxytocin
The dose of oxytocin we are using in this study and the route of administration are approved by the Food and Drug Administration (FDA). However the indication we are using oxytocin for in this study is not approved by the FDA. We will monitor you for many potential problems such as changes in your blood pressure, how fast your heart is beating, and your urge to breathe. We will treat any side effects that you may experience if the changes are enough to concern us.
There is the possibility of a feeling of being flushed (warm feeling), headache and increased heart rate with no significant change in blood pressure during or immediately after the infusion. These events have been reported by previous participants but were short lived, lasting approximately 12-15 minutes. Additionally the following events have been reported as associated with the administration of oxytocin in the laboring female population:

Anaphylactic reaction
Postpartum hemorrhage
Cardiac arrhythmia
Fatal afibrinogenemia
Nausea
Vomiting
Premature ventricular contractions
Pelvic hematoma
Water intoxication
Subarachnoid hemorrhage
Hypertensive episode
Uterine rupture

Additional precautions are used in the presence of specific anesthetic medications; we are not administering any of these medications during this research study.

Finally, you cannot participate in this study if you are allergic to latex, as there have been reports of allergic reactions to oxytocin injection in women with latex allergies.

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.

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.

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).
If you donate blood to the American Red Cross, you should talk with the study doctor about whether or not it is safe to do so while participating in this study. You should not donate blood more than 2 times per week and no more than approximately one pint (about 500 ml) of blood in an eight week period.

Reproductive Risks and other Issues to Participating in Research

Due to known 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.

WHAT OTHER CHOICES ARE THERE?

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

WHAT ARE THE COSTS?

All study costs, including any study medications and 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 YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by NIH which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

WILL YOU BE PAID FOR PARTICIPATING?

You will be paid $300 if you complete all the scheduled study visits. If you withdraw for any reason from the study before completion you will be paid as follows:

Completion of study visit 1: $25
Placement of IV: $25

Completion of all study related procedures: $250

In the event you do not qualify to continue in the study after study visit 1 (due to the thermal testing) we will compensate you $25 for your time.

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 by the National Institutes Health (NIH). 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 James Eisenach at [redacted] or after hours you should call the study coordinator at [redacted].

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** medical history and medication history.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

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.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

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. 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.

[redacted]

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.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

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.
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. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

This study will be enrolling students from the Wake Forest University Medical Center campus. In addition to your rights as a research participant noted in the previous section, as a student, you are under no obligation to participate in this study. You may refuse to participate or withdraw from the study at any time and for any reason without affecting your grades, performance evaluations, or assignments. You will not be pressured into participating in this research study by any statements or implied statements that your grades, performance evaluations or assignments will be affected by your willingness to enroll in the study. Your medical records/information will not be used by the faculty, administration or study staff to make decisions regarding the status of your medical benefits. If you have questions regarding your enrollment in the study and your status as a medical student, please contact the Office of Student Services for additional information.

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 Eisenach at [redacted] or after hours you should call 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] or the Research Subject Advocate 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 (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

WFU School of Medicine
Institutional Review Board
IRB Number:IRB00066136
Meeting Date Approved 4/10/2023
Version Valid Until: 4/9/2024