Title: The Effects of Intraocular Phenylephrine/Ketorolac Infusion on Retinal Thickness and Macular Edema in Cataract Surgery
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No Drop Cataract Surgery: The effect of Intraocular Phenylephrine/Ketorolac Infusion on Retinal Thickness and Macular Edema in Cataract Surgery.
Informed Consent Form to Participate in Research
Keith Walter MD; Principal Investigator

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help you and/or other people in the future. You are being asked to take part in this study because you are scheduled to undergo cataract surgery for one eye or both eyes within 1- 4 weeks of each other most likely 2 weeks apart. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask 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 test if we can eliminate the use of a post-operative eye drop. This would mean patients would no longer need to use any eye drops after cataract surgery. Over the last decade, we have reduced the number of drops needed from 3 prescriptions to just one anti-inflammatory drop, specifically a Non-Steroidal Anti-inflammatory Drug (NSAID). NSAIDS are drugs that help to control pain and inflammation. Issues with these drops include difficulty with placing the drops in the eye, using the drops as directed by the doctor, generic substitution and insurance coverage. A large number of patients aren't able to afford these drops, or these drops aren't covered by insurance. Pharmacists often substitute the prescribed drug for a generic version or a similar drug that does not work as well. Recently, Omidria (phenylephrine and ketorolac injection 1% / 0.3%) was approved by the Food and Drug Administration (FDA) for post-operative pain and inflammation in patients having cataract surgery. Omidria is a combination drug consisting of phenylephrine and ketorolac, and is used as an irrigating solution applied to the eye during cataract surgery. Ketorolac is a strong NSAID, and stops prostaglandins which cause pain, inflammation, and swelling. Animal studies have shown that Omidria can prevent prostaglandin production nearly 100% for over 12 hours post cataract surgery when given during surgery.

In the study we will be using Omidria with the fluid used in "washing" out the cataract. Since Omidria was FDA approved for cataract surgery 3 years ago, we use it quite often to help with pain, inflammation and the added benefit of maintaining a dilated pupil during surgery which helps to prevent complications from cataract removal. We now wonder if the post-operative topical NSAID eye drop is even needed. We would like to eliminate as many unneeded drops as

possible. We will be monitoring you post op to determine the success of your surgery and to measure your pain, inflammation and any unexpected swelling. These measures are standard for cataract surgery patients, and will be done routinely as part of your follow up exams after your cataract removal surgery even if you do not choose to participate in the study. If needed you may be prescribed a NSAID drop if you develop pain, inflammation or unexpected swelling after your surgery.

You can elect to enroll one or both eyes if you wish. You can withdraw from the study at any time, even if the first eye was already done successfully.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Up to 200 people will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in the research study you can choose to remain enrolled from the time of your first cataract surgery to about 6 weeks following your second cataract surgery which may be scheduled from 1 to 4 weeks (typically 2 weeks) after the first surgery.

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

Visit 1: Your first visit will be the clinic visit where you will be evaluated to see if you are eligible to be enrolled in the research study. If you meet all the criteria for the study, a study coordinator will discuss the study with you. You will be given plenty of time to review the consent and the opportunity to ask questions so you can make a decision on whether you would like to participate. This will likely be the same visit where you are evaluated for cataracts and determine to be eligible for cataract surgery.

Visit 2: Day of your first cataract surgery. On this day you will undergo your scheduled cataract surgery on the first eye. You will be given Omidria during your cataract surgery at no cost to you. This drug will be administered frequently to the eye to control the pupil size during cataract surgery and to control post-op pain.

Visit 3: 18-24 hours post cataract surgery. This is a standard post op required visit. On this day, you will be asked to come into the clinic where all the standard tests will be conducted, such as pupil size measurement, and intraocular pressure will be measured. Your vision and comfort levels will also be evaluated at this time. This is standard testing we do for any patient whether in the study or not.

Visit 4: 1-2 weeks post-surgery. This is a standard post op visit. Your vision and comfort levels will also be evaluated at this time, as well as intraocular pressure and inflammation checked and

recorded. A macular scan will be performed to check if there is any swelling.

Visit 5: 5-6 weeks post-surgery. This is also a standard post op visit. Your vision and comfort levels will also be checked at this time, as well as intraocular pressure and inflammation monitored and recorded. A macular scan will be performed to determine if there is any swelling.

If you have decided to have both eyes enrolled in the study, the same procedures will be done for the second eye. If you decide to enroll both eyes some visits will likely be done at the same time. For example, if you have the second eye done 2 weeks after the first, then when study eye 1 will be at visit #3 (two weeks); study eye 2 will be at visit #2 (one day). This means that you won't likely complete 10 visits if you enroll both eyes but only 6-8 total visits. The total number of visits is the same whether you elect to participate in the study or not.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for from the time of your first cataract surgery to 6 weeks following your second cataract surgery which may be scheduled from 1 to 4 weeks after the first surgery. If you choose to only enroll one eye then you will be enrolled in this study from the time of the surgery for the eye enrolled in the study until 6 weeks after your surgery.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the study doctor or study staff first to learn about any potential health or safety consequences. You will likely need to be prescribed topical medication, and continue to do our normal post op visits.

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. Allergies to Omidria or NSAIDs would prevent you from participating in this study, so please let the study staff know if you have a rash or hives from prior NSAIDs. You may be allergic to Omidria or NSAIDs, and be unaware. Allergies can be a threat to your health, including death which is rare. Systemic exposure to phenylephrine, a part of Omidria, could cause your blood pressure to rise. Your blood pressure will be monitored during your surgery, and treated if needed.

If you enroll, we do not plan on using any topical eye drops, such as NSAIDs or corticosteroids after your surgery. There may be complications or risks involved that can't be predicted. Some of those risks may include:

- Pain
- tenderness
- light sensitivity

- Blurred vision from macular edema or swelling in the back of the eye

Common side effects of Omidria may include:

- Inflammation inside your eye
- Increased Intraocular Pressure
- Posterior Capsule Opacification or a cloudiness behind the lens (seen in routine cataract surgery about 30% of the time and treatable in the office with a laser)
- Eye Irritation
- Foreign Body Sensation in Eyes or feeling as though something is in your eye

These risks are uncommon, but do occur with cataract surgery in general, and often occur even with topical drops are used. There is a small risk that you will still need these prescribed topical drugs, and that you will have to pay for them or use your insurance. All of these risks are treatable with additional drops or medications, or a laser treatment. Please discuss these risk and the treatment options with the study doctor.

There is a slight risk of a breach of confidentiality which is when your private information is disclosed without your consent. 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.

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.

Pregnant women are excluded from participation in this study. If you are a sexually active woman of childbearing potential and have not been using a reliable method of birth control, two negative pregnancy tests performed 15 days apart are required to check for possible early pregnancy prior to starting treatment.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you.
. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be: eliminating the need for eye drops before and after surgery. This may save you money, time and hassle of placing frequent drops for the month after surgery. Omidria is FDA approved for maintaining an acceptable pupil size during cataract surgery. This may make the surgery easier and faster for you and the surgeon.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to the study team members about all the choices you have. Instead of being in this study, you have these options:

- Use the routine eye drop, bromfenac, obtained from the pharmacy, starting 2 days before and continuing for at least 4 weeks after surgery.

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, such as the cataract surgery itself, the use of the laser, or a premium lens, which are not related to this study, will be your own responsibility. We will not bill you nor your insurance company for the additional post op visit, but your insurance will be billed for the cataract surgery as we would any non-study patient.

The cost of the Omidria will be covered by the study. You or your insurance company will not be billed for the Omidria used for the purposes of this study.. Any additional tests, will not be charged, and are part of the routine post-operative care we provide any patient undergoing cataract surgery.

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 except as authorized by you or as required by law. However, 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.

WILL YOU BE PAID FOR PARTICIPATING?
You will receive no payment or other compensation for taking part in this study.

WHO IS SPONSORING THIS STUDY?
This study is being sponsored by Dr. Keith Walter and the Department of Ophthalmology. In addition, Omeros will be providing the drug at no cost.

Dr. Walter has a relationship with Omeros and receives income, separate from this study, for consulting and speaking services for Omeros. Dr. Walter will not receive any additional income from Omeros for participating in this study.

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].

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 about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** patient name, age, gender, patient MRN, date of birth, gender, race, visual acuity, eye pressure, date of surgery, eye(s) involved, complications, pain scores, inflammation scores, macular thickness by OCT. , pupil sizes, eye color, intraocular pressure, and photo of your eyes

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will 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.

Laboratory test results and other medical reports created as a result of your participating in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with the research study.

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.

If you choose to participate in this study, your medical record at Wake Forest University 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.

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), 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.

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 will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. 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. Keith Walter MD 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:

Keith Walter MD
[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.

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 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 you need additional medication to control pain, inflammation or macular swelling. Additionally, if you fail to make the post op visits or are unable to participate in testing.

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. Keith Walter MD at [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.

I consent to a) one eye (right or left)
OR
b) both eyes

Circle One

Subject Name (Printed):_____

Subject Signature:_____Date:_____Time_____am pm

Person Obtaining Consent (Printed):_____

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