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STUDY TITLE: Celecoxib versus acetaminophen-codeine-caffeine for postoperative pain in primary elective open septorhinoplasty with osteotomies: A single-blinded randomized controlled trial.

Date Approved by Review Board, VERITAS IRB: January 30, 2020

Informed Consent Form for:

Patient Name: _____

Patient ID#: _____

This informed consent form is for adults between the ages of 18 - 80 who undergo Rhinoplasty surgery with Dr. Jamil Asaria, either at FACE Toronto, or Humber River Hospital, and who we are inviting to participate in a research study titled: **Celecoxib versus acetaminophen-codeine-caffeine for postoperative pain in primary elective open septorhinoplasty with osteotomies: A single-blinded randomized controlled trial.**

Principle Investigator: Blake Raggio, MD
Organization: FACE Toronto Cosmetic Surgery; Humber River Hospital Department of Surgery
Sponsor: Humber River Hospital Department of Surgery
Project (version): Celecoxib versus acetaminophen-codeine-caffeine for postoperative pain in primary elective open septorhinoplasty with osteotomies: A single-blinded randomized controlled trial (Version 1a)

This Informed Consent Form has two parts:

1. Information Sheet (gives you information about the study)
2. Certificate of Consent (this is where you sign if you agree to participate)

You are entitled to a copy of the full Informed Consent Form.

This will be stored in your medical records at FACE Toronto.

Part I: Information Sheet

Introduction

My name is Dr. Blake Raggio and I am conducting research on behalf of Dr. Jamil Asaria to determine if the non-opioid medication, celecoxib (tradename, CELEBREX), has equal post-operative pain control efficacy as the traditionally prescribed opioid medications, namely acetaminophen/codeine (Tylenol #3).

I am going to give you information and invite you to be part of a research study. You can choose whether or not you want to participate. We are asking you for your agreement to participate in the study. If you do not wish to take part in the research, you do not have to.

You may discuss anything in this form with your family, friends or anyone else you feel comfortable talking to. You can decide whether to participate or not after you have talked it over. You do not have to decide immediately.

There may be some words you don't understand or things that you want me to explain more about because you are interested or concerned. Please ask me to stop at anytime and I will take time to explain.

Purpose: Why are you doing this research?

We are seeking to determine if the non-opioid medication, celecoxib (tradename, CELEBREX), has equal post-operative pain control efficacy as the traditionally prescribed opioid medications, namely acetaminophen/codeine/caffeine (Tylenol #3).

Choice of participants: Why are you asking me?

We are only testing patients who undergo primary elective open septorhinoplasty with osteotomies by Dr. Jamil Asaria at either FACE Toronto or Humber River Hospital.

Participation is voluntary: Do I have to do this?

You don't have to be in this research if you don't want to be. Its up to you. If you decide not to be in the research, its okay and nothing changes. Even if you say "yes" now, you can change your mind later and its still okay.

What is this "test" drug and what do you know about it?

The medication we are testing in this research is called celexocib (tradename, CELEBREX), a nonsteroidal anti-inflammatory drug (NSAID) approved for analgesia in osteoarthritis, primary dysmennorhea, and acute pain settings including after surgery. CELEBREX has been tested before with adults who undergo plastic surgery and is well-tolerated and appears similarly effective to opioids regarding post-operative pain control. We now want to test the efficacy of CELEBREX for pain control after rhinoplasty compared to a routinely prescribed opioid medication, TYLENOL #3.

CELEBREX is made by the drug company Pfizer. Potential side effects include Cardiovascular Thrombotic Events, GI Bleeding/Ulceration/Perforation, Hypertension,

Heart Failure, Renal Toxicity, Hyperkalemia, Anaphylactic Reactions, Serious Skin Reactions, Hematologic Toxicity. With that being said, CELEBREX is generally well tolerated by patients and is overall considered safe to use for postoperative analgesia. In placebo-or active-controlled clinical trials, the discontinuation rate due to adverse events was 7.1% for patients receiving CELEBREX and 6.1% for patients receiving placebo. Among the most common reasons for discontinuation due to adverse events in the CELEBREX treatment groups were dyspepsia and abdominal pain (cited as reasons for discontinuation in 0.8% and 0.7% of CELEBREX patients, respectively). Some participants in the research will not be given the drug which we are testing. Instead, they will be given the drug codeine/acetaminophen/caffeine (TYLENOL #3), the drug which is most commonly prescribed by Dr. Asaria for pain control after rhinoplasty. There are several risks and side effect associated with TYLENOL #3, however, including neurologic (e.g., drowsiness) and gastrointestinal effects (e.g., constipation), as well as the potential for abuse and dependence.

Procedures: What is going to happen to me?
We are going to test the efficacy of CELEBREX versus TYLENOL#3 by giving some of the patients in the research study CELEBREX and the others are going to get TYLENOL#3. You will know which medicine you were given during the study. On the contrary, Dr. Asaria will not know which medicine you will be receiving. By doing the research like this, we can compare the efficacy of the medicines without being influenced by what we think or hope the research will show.

If you decide that you want to do this, there will be three things that happen:

1. You will be given a prescription for either study medication, CELEBREX or TYLENOL#3, with instructions for use during the immediate post-operative period.

2. During your first several days of recovery up until the day of your cast removal, you will keep a daily diary during your recovery recording your pain levels, the number of times the prescribed medication was used, and how often “rescue analgesics”(e.g., acetaminophen) were used in the event your pain was not adequately controlled with the study medication..

3. On the day of your cast removal, you will be photographed (similar to the pre-operative photographs), to evaluate the degree of swelling and bruising you have.

After the cast is removed on your first post-operative visit, your participation in the research will be finished.

Risks: Is this bad or dangerous for me? What happens if I experience complications?
CELEBREX is considered safe to use for post-operative pain control. It has already been tested on adults for use in acute pain after multiple types of surgical procedures, including orthopaedic and dental surgery and plastic surgery. In fact, some prominent Rhinoplasty surgeons prescribe CELEBREX as their primary pain control medication after surgery in

an attempt to limit the prescribing of opioids. If anything unusual were to happen to you, however, we need to know and you should feel free you page the on-call physician (pager number will be provided), or to call/e-mail the office anytime with your concerns or questions. If you get sick or have concerns or questions in-between the scheduled visits to clinic, you should let me or the staff nurse know. You don't have to wait for a scheduled visit.

Reimbursements: Do I get anything for being in the research?
No.

Confidentiality: Is everybody going to know about this?
We will not tell other people that you are in this research and we won't share information about you to anyone who does not work in the research study. Information about you that will be collected from the research will be put away and nobody but the researchers will be able to see it. Any information about you will have a number on it instead of your name (deidentified). Only the researchers will know what your number is and we will secure the data with encrypted software. It will not be shared with or given to anyone except Dr. Jamil Asaria, Dr. Blake Raggio (principal investigator), and other main contributors to the research study (e.g., statistician).

Sharing the Findings: Will you tell me or others the results?
When we are finished the research, you are entitled to learn what we reported.

We will also be telling more physicians, scientists and others, about the research and what we found by writing and sharing reports and by going to meetings with people who are interested in the work we do. Your identity will remain confidential in any publication that may result from this research. You will be identified by study code only; your name will not be used.

A description of this clinical trial will be available on http://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.

Right to Refuse or Withdraw: Can I choose not to be in the research? Can I change my mind?
You do not have to be in this research. No one will be mad or disappointed with you if you say no. Its your choice. You can think about it and tell us later if you want. You can say "yes" now and change your mind later and it will still be okay. Should you decide to withdraw from the research study, the data collected to the point of withdrawal remains part of the study database and may not be removed, as per the regulations and guidance set forth by the Food and Drug Administration (FDA) and Office of Human Research Protections (OHRP).

Who to Contact: Who can I talk to or ask questions to?

You can ask me questions now or later. You can ask the nurse or other involved staff any questions. You will be provided a number (416-479-4244) where you can reach us for more information regarding the study. Alternatively, if you are nearby the office, you can come and see us. If you want to talk to someone else that you know like your family, friends, or doctor, that is okay too.

This study has been reviewed by Veritas IRB. If you have any questions about your rights as a research participant or the Investigator's responsibilities, you may contact Veritas IRB 24 hours per day and 7 days per week at 514-337-0442 or toll-free at 1-866-384-4221. An Independent Review Board (IRB) is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the participant's rights and welfare in mind. If you have any study-related comments, complaints or concerns, you should first contact the study investigator. Please call the IRB if you need to speak to a person independent from the Investigator and the research staff, and/or if the Investigator and the research staff could not be reached.

If you choose to be part of this research, you are entitled to a copy of this document to keep for your own record. This document will be stored in your medical record as well.

PARTICIPANT LEVEL OF STUDY UNDERSTANDING:

- Do you understand that participation is voluntary? If so, please initial: _____
- Do you understand your participation in the study? If so, please initial: _____
- Do you understand that you may contact us at any time in the event of any adverse effects or postoperative complications? Is so, please initial: _____
- Do you understand that that you can ask questions anytime and how to contact us for more information about the study if needed? If so, please initial: _____

PART 2: Certificate of Consent

I understand the research is about testing CELEBREX versus TYLENOL#3 for pain control after rhinoplasty, and that I might be prescribed either medication post-operatively.
I understand that I will be given a "diary" to record some pain metrics during the recovery period.
I understand that I will have photographs of my face taken on the first post-operative visit after the nasal cast is removed, which will be used solely for research purposes and not shared.

STATEMENT BY THE PATIENT/PARTICIPANT:

[ ] I have read this information (or had the information read to me).
I have had my questions answered and know that I can ask questions at any time, either now or later, if I have them. I agree to take part in the research.

OR

[ ] I do not wish to take part in the research and I have not signed the consent below.

Patient:

_____

Printed Name Signature Date

STATEMENT BY THE RESEARCHER TAKING CONSENT:

I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the patient understands the aforementioned information and required participation.

I confirm that the patient was given an opportunity to ask questions about the study, and all the questions asked by him/her have been answered correctly and to the best of my ability.
I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this consent form is available for the participant and scanned into their medical record at FACE Toronto Cosmetic Surgery.

Researcher:

_____

Printed Name Signature Date