Consent to Participate in Research

Title of Research Project: Does precise delivery of remifentanil decrease coughing at emergence from anesthesia?

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Introduction

You are being invited to take part in this research study because you will be having either head and neck surgery, or eye surgery**.** This study is being conducted by the University of Vermont at the UVM Medical Center.

We encourage you to ask questions and take the opportunity to discuss the study with anybody you think can help you make this decision.

Key Information to Help You Decide Whether or Not This Study Is Right for You

- The purpose of this research is to reduce or avoid coughing at the end of surgery, when the breathing tube is removed from the patient's throat.
- Why we're doing this study: For surgery with general anesthesia, you are put to sleep. A breathing tube is put into your throat so that a machine will breathe for you while you are asleep. At the end of surgery, when the breathing tube is removed, patients sometimes cough. In patients who have had eye surgery or head and neck surgery, coughing can cause bleeding at the site of the operation.

Concise summary

We want to find a way to reduce or stop patients from coughing at the end of surgery when the breathing tube is taken out. The breathing tube is removed when you are waking up from anesthesia, and are at the point when you can breathe on your own. In most types of surgery, coughing at this point is common, and does not affect you very much, if at all. But for surgery involving the eye or the head and neck, coughing right after surgery can cause bleeding at the site of surgery.

This study will use a short-acting pain drug called remifentanil at the end of surgery to prevent coughing. We will give you this medicine for 5 to 30 minutes. The point of the study is to test if using a simple computer program to guide precise delivery of how much of the drug is given to you is effective at reducing or preventing coughing.

Here's what's involved: If you decide to be in the study, we will assign you to receive either remifentanil, or a placebo, which will be salt water. The choice of which one you get will be done randomly, like flipping a coin. We will start giving you the study drug or placebo near the

end of surgery. The medicine will be given by a pump, through an intravenous line into your arm. We will tell the pump how much medicine to give you based on your age, weight, height and sex. We will start the pump between 5 and 30 minutes before the end of surgery. The pump will run for between 10 and 40 minutes. A member of our study team will be in the operating room and will write down whether you coughed, and if so, how much you coughed. The study will end when you are brought to the recovery room.

There are a few risks. The main risk to you from being in this study is that your breathing may be slowed by the study drug, at the end of surgery. This happens in between 1 in 10 to 1 in 20 people. Slowed breathing should go away within 5 minutes after we turn off the study drug pump. The risk of harm to you is minimal, because you will be in the operating room, and your breathing will either still be assisted by the ventilator, or the anesthesiologist taking care of you will help you breathe. There's also a risk that your heartbeat will be slowed for a few minutes by the study drug, but this rarely happens in the amount of drug used in this study. If this does happen, the anesthesiologist taking care of you will stop the pump and take the appropriate steps to treat you. A mild lowering of blood pressure can occur in up to 1 in 5 people, and is common in patients under anesthesia. If this occurs, it will return to normal within 5 minutes after the study drug pump is turned off. Vomiting is common after surgery with with anesthesia, and may occur in fewer than 1 in 5 people, but your risk should be lower because your anesthesia provider will give you anti-vomiting medications. These risks are discussed in more detail in the following pages.

You don't have to participate. If you decide not to be in the study, you will have surgery and anesthesia in the usual way for your type of surgery.

The information above is only a brief summary of the study. If you are interested in learning more, please read the following pages for more detailed information about the study. If you decide to take part in the research, you will be asked to provide written consent at the end of this document.

Why Is This Research Study Being Conducted?

At the end of surgery, when a patient is starting to wake up from anesthesia, and the patient is to breathe on their own, the breathing tube is removed from the patient's throat. In most types of surgery, coughing at this point is common, and does not affect the patient very much. But for surgery involving the eye or the head and neck, coughing right after surgery may rarely cause bleeding at the site of surgery, which could slow your recovery and affect the outcome of the surgery. A number of methods have been tried to prevent or reduce coughing at this point, but of all the different methods described in medical journals, only remifentanil, a very short-acting opioid drug that is commonly used during anesthesia, showed any promise at decreasing the occurrence of coughing.

Just giving patients remifentanil is not enough, however: It has to be given by infusion, in precise amounts tailored to each patient's age, weight, height and sex, in order to reach the right target level of the drug in your body. Too little remifentanil will not prevent you from coughing, and too much can depress your breathing and will take more time for the drug to wear off, delaying your recovery in the operating room.

The actual amount of remifentanil needed varies between patients. In this study, we will use a simple computer program to calculate the amount of remifentanil needed to reduce coughing at the point of emergence from anesthesia. We will use your age, weight, height, and sex to tell the program to calculate the correct dose of remifentanil for you. We will then set up a standard drug infusion pump to give you that dose of remifentanil.

The purpose of the study is to see if we can use the computer program to give remifentanil with enough precision to reduce coughing at emergence from anesthesia.

What Is Involved In The Study?

This a randomized, placebo-controlled study. Randomized means that patients will be randomly assigned to one of two treatments, like flipping a coin to decide which one you will receive. A placebo is like a sugar pill, which is like a drug that has no effect. The reason for using a placebo is to divide patients into two groups, and see which group has less coughing at the end of surgery. You will be assigned at random to receive either remifentanil, or saline (salt water) if you are in the placebo group. It's also a double-blind study, which means that neither you nor the anesthesia provider will know which group you are in. Your anesthesia provider will take care of you in the same way they take care of all patients undergoing surgery with anesthesia.

You will receive the study drug through an intravenous (IV) line in your arm or hand. The IV line will be put in before surgery by a nurse in the preoperative area. This is standard for all patients having surgery. When you are in the operating room, we will set up the drug infusion pump and program it according to your age, weight, height and sex. We will then put the pump in "standby" mode until the end of surgery.

When the surgeon tells the anesthesia provider that you are within 5 to 30 minutes of the end of surgery, we will start the pump. When surgery is finished, the inhaled anesthetic gases used to keep you asleep for surgery will be turned off. You will start to recover from anesthesia, and when the anesthesia provider decides that you are ready, he or she will remove the breathing tube from your throat, just as they do for all patients having this type of surgery. We will stop the infusion either at this point, or at 15 minutes after the anesthetic gases were turned off, whichever comes first.

We will observe you and write down whether you coughed and how hard you coughed. We will also record the time at which the breathing tube was removed, the time to recovery from anesthesia, the length of the infusion, and how much of the study drug (remifentanil or salt water) you were given.

Once our study is complete, we will remove any identifiable private information that could be used to identify you. This is called de-identification. We will keep the de-identified information we collected for future use by us or another investigator, without additional informed consent. After the data is de-identified, no one will be able to use that data to know the identities of the patients who took part in this research project.

What Are The Risks and Discomforts Of The Study?

A major risk to you from this study is that your breathing could be temporarily slowed by the remifentanil. This condition should go away within 5 minutes of stopping the infusion of the study drug. This risk occurs in between 1 in 20 to 1 in 10 people. The only time this could happen is when are still in the operating room, where you will be monitored at all times by your anesthesia provider. Because you will still be in the operating room, the actual risk to you is extremely low. Your breathing will be assisted, either by the anesthesia machine, or by your anesthesia provider, if the breathing tube has been removed. Another risk is of a mild lowering of blood pressure, which can occur in up to 1 in 5 people, and is common in patients under anesthesia. If this occurs, it will resolve within 5 minutes of stopping the infusion, and your anesthesia provider will monitor your blood pressure during the entire time you are in the operating room. Vomiting after surgery with anesthesia is common, and may also occur in fewer than 1 in 5 people who are given remifentanil, but that risk is lower in this study because your anesthesia provider will give you anti-vomiting medications during surgery.

Remifentanil may cause a slow heartbeat. This rarely occurs in the dose of remifentanil that we are using in this study. If your heart rate slows to the point that your anesthesia provider thinks it could be harmful, we will stop the infusion of remifentanil, and your anesthesia provider will treat you if your condition requires it. An itchy sensation on your skin may occur for a few minutes after surgery; this happens in 1-2 in 100 people who receive remifentanil.

What Are The Benefits of Participating In The Study?

You may or may not receive a benefit from participation in this study. If you are randomized to the remifentanil group of this study, you may experience less coughing when the breathing tube is removed at the end of surgery. However, not all patients cough when the breathing tube is removed, regardless of the type of surgery. The knowledge gained in this research may improve future care of patients.

What Other Options Are There?

You are free to not participate in this study. If you decide not to participate, you will receive the same level of care provided to all surgery patients at UVM Medical Center.

Are There Any Costs?

There are no costs to you.

What Is the Compensation?

You will not be compensated for taking part in this study.

Can You Withdraw or Be Withdrawn From This Study?

You are free to withdraw from this study at any time, before or after sedation. If the anesthesia provider taking care of you feels that the study procedures are not in your best interest, you will be withdrawn from the study. If your surgery will end less than 5 minutes after the start of infusion, or if there is a clinical reason for removing the breathing tube while you are still under deep anesthesia, we will withdraw you from the study and not give you the infusion. If this happens, the anesthesia provider on duty will care for you in the usual manner. In addition, the researcher may discontinue your participation in this study at any time. If you decide to withdraw, we will delete your study data from our records.

What About Confidentiality of Your Health Information?

What health information will be used and disclosed for this study?
The health information we plan to collect for this study is listed below.

- Medical history and examinations
- Information that identifies you, such as your name, address, age, and sex
- Reports from hospital and clinic visits
- Lists of medications you are taking
- Details of your anesthesia care during surgery

Who is disclosing your health information for this research study?

- The University of Vermont Medical Center

Who will use your health information in this study?
Our research team will use your health information. We may also share it with those who assist with the conduct of the research or oversight of the activities for this study. The representatives from the institutions, organizations, and agencies are listed below.

- The University of Vermont and its Committees on Human Research
- Officials from agencies and organizations that provide accreditation and oversight of research
- The University of Vermont Medical Center
- Federal and state agencies that oversee or review research information, such as the U.S. Food and Drug Administration (FDA), the Department of Health and Human Services, the National Institutes of Health, and public health and safety authorities
- Your health insurer, for portions of the research and related care that are considered billable.

Your health information is protected by a federal law called the Health Information Portability and Accountability Act (HIPAA). Once your health information is shared outside of the University of Vermont Medical Center, we cannot guarantee that these laws will continue to apply. As a result, your health information could be further disclosed for other purposes. In the absence of a Certificate of Confidentiality, it is also possible for a court or other government official to order the release of study data. The confidentiality of your health information cannot be guaranteed if you agree it may be used in this study.

How long will your health information be used for research?
Your permission to use your health information will not end until the study is completed. During this study, you will not have access to study data. You may ask for your data once study activities are complete. You have a right to receive a copy of the information in your medical record at any time.

What if you decide not to give permission for research use of your health information? If you decide not to allow the use and disclosure of your health information, you may not take part in this study. Your decision will have no effect on your current or future medical care.

If you choose to stop taking part in this study in the future, you may cancel permission for the use of your health information. You should let the research team know that you are cancelling your permission. A member of the research team will assist you in making your decision effective. The study will delete any data collected about you for research purposes. However, you cannot get back information that was already shared with others.

Who can answer your questions about the use and disclosure of your health information?

If you have questions or concerns about the use and disclosure of your health information, you should ask a member of the study team at 802-847-2415 or the Privacy Officer at The University of Vermont Medical Center, Inc., at 802-847-2667.

Safeguarding Your Health Information

A record of your progress will be kept in a confidential form at the Department of Anesthesiology in the UVM Medical Center main campus. The security of your record will be maintained by the research team. The results of this study may eventually be published and information may be exchanged between medical investigators, but patient confidentiality will be maintained.

If your record is used or disseminated for government purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

Clinical Trials Registration

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.

What Happens If You Are Injured?

If you are injured or become ill as a result of being in this research, The UVM Medical Center, the hospital partner of the University of Vermont, will provide reasonable and usual medical care for that injury or illness. There will be no cost to you if the conditions listed below apply to your injury or illness. These conditions are:

1. The investigator, in consultation with the study sponsor, determines that your injury or illness results from the research and not from your underlying condition or its usual treatment.
2. You let the investigator know about the injury or illness when you first notice it; and
3. You follow medical advice about proper treatment options for the injury or illness.

The UVM Medical Center may claim payments for your medical treatment directly from the study sponsor or your insurance company when these payments are allowed.

For an injury or illness that results from being in this study, the University of Vermont and The UVM Medical Center will not offer you any other payments, such as lost wages or expenses, except for your medical care. Even though you may receive medical care at no cost to you under certain conditions if you are in this study, the UVM Medical Center and the University of Vermont do not admit to any responsibility for an injury or illness that results from being in the study.

If you agree to take part in this study and you sign this consent form, you are not giving up any of your legal rights.

Contact Information

You may contact Dr. Elie Sarraf, the Investigator in charge of this study, at 802-8472415 for more information about this study. If you have any questions about your rights as a participant in a research project or for more information on how to proceed should you believe that you have been injured as a result of your participation in this study you should contact the Director of the Research Protections Office at the University of Vermont at 802-656-5040.

Statement of Consent

You have been given and have read or have had read to you a summary of this research study. Should you have any further questions about the research, you may contact the person conducting the study at the address and telephone number given below. Your participation is voluntary and you may refuse to participate or withdraw at any time without penalty or prejudice to your present and/or future care.

You agree to participate in this study and you understand that you will receive a signed copy of this form.

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Signature of Subject Date

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Name of Subject Printed

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Signature of Principal Investigator or Designee Date

_____

Name of Principal Investigator or Designee Printed

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