Informed Consent

Phase I Assessment of Hypertonic Saline in Moderate to Severe Asthmatics

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: October 10, 2023
IRB Study # 17-3209
Title of Study: Phase I Assessment of Hypertonic Saline in Moderate to Severe Asthmatics
Principal Investigator: David Peden, MD
Principal Investigator Department: Pediatrics - Allergy Immunology and Rheumatology
Principal Investigator Phone number: 919-966-0768
Principal Investigator Email Address: david_peden@med.unc.edu
Funding Source and/or Sponsor: NIH National Heart, Lung, and Blood Institute (NHLBI)
Study Contact Telephone Number: (919) 966-5638
Study Contact Email: carole_robinette@med.unc.edu

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty. Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Mucus in the respiratory tract is an important part of asthma and can cause asthma symptoms to be severe. Currently there are no medications that specifically target mucus in patients with asthma. Hypertonic saline (HS) is concentrated salt water, also known 7% sodium chloride solution. In patients with other lung diseases like cystic fibrosis, which involves large amounts of mucus blocking the airways, inhaling HS helps to loosen the mucus and improve movement of mucus out of the lungs. In studies done at our center, HS has been used to help people cough up

samples of mucus-containing material called sputum. HS has been well tolerated by people with mild asthma. The purpose of this study is to see if HS improves movement of mucus out of the lungs in people with asthma that is more severe.

Are there any reasons you should not be in this study?
You should not be in this study if you have chronic lung problems (with the exception of asthma), other chronic health problems, if you have problems with blood clotting, if you are a smoker, or if you are pregnant, trying to get pregnant or breastfeeding.

How many people will take part in this study?
There will be approximately 28 people in this research study.

How long will your part in this study last?
There are 8 visits for this study, including a visit for the purpose of informed consent, and it should take approximately 3 and ½ months to complete all of these visits. In person visits 1, 3 and 6 will each last between 4 ½ and 5 hours. After each of these, you will return for a 1 hour follow up visit the next day. If at any time you have a flare-up of your asthma, we will delay your visit until you have been well for at least 4 weeks or if you test positive for Covid during the study, we will ask you to wait 90 days to finish; this may add to the total time for your participation. We will ask you to return 5-10 days after the last visit for a checkout visit that will last about 1 hour.

In total, you will have 8 study visits.
Consent Visit: 1.5 hours
Visit 1: 5hours
Visit 2: 1 hour
Visit 3: 5 hours
Visit 4: 1 hour
Visit 5: 5 hours
Visit 6: 1 hour
Visit 7: 1 hour

What will happen if you take part in the study?
We will have the consent visit by either by video or in person. If you agree to join the study, you can sign and date the document during our discussion. You will arrive at the research lab for the screening visit, or **Visit 1.** Please avoid taking non-steroidal medications, such as ibuprofen, naproxen or aspirin, and multivitamins, vitamins E and C, or herbal supplements for 4 days prior to each study visit. Also, please use all prescribed medications prior to your study visits, and please use your inhalers at approximately the same time of day on the days of your study visits. You must provide proof of being up to date with vaccination to Covid-19 prior to starting the study.

1. You will be given an opportunity to read the consent form, and the study will be explained to you. We will answer all of your questions.
2. We will then collect your **medical history**, including any **medications** that you take.
3. If you are female, you will have a **urine pregnancy test**, and it must be negative.

4. We will check your **vital signs**, including your temperature, your heart rate, your respiratory rate, blood pressure, and the oxygen concentration in your blood.
5. One of the study doctors will do a **physical examination** of your lungs, heart, eyes, ears, nose and throat.
6. Exhaled nitric oxide **(FeNO)** will be collected. Nitric oxide is a chemical that your body produces, and it can be increased with asthma. This test is done by having you exhale into a machine that measures the amount of NO your body produces.
7. You will do a **lung function** test for us, in which you will be asked to take a full breath in and blow it out as hard and as fast as you can. You will do this several times, and we will coach you through it each time.
8. You will fill out a **symptom questionnaire** that asks you to rate your symptoms (such as cough, fatigue, shortness of breath, etc) on a scale of 0 (no symptoms) to 3 (severe symptoms).
9. Then, you will have a baseline **Mucociliary Clearance Scan (MCC)**. You will be seated in front of a gamma camera, which is a device for measuring radioactivity. Before being seated we will tape two small, radioactive discs (Americium 241) to your upper and lower back in order to determine your position in front of the gamma camera. The Americium 241 discs are the same sources found in household smoke detectors and will expose you to a very tiny radiation dose (which is included in the total dose of radiation you are exposed to in the study). You will then be seated in front of a gamma camera and place a plate that contains a small amount of Cobalt 57 (a radioactive material) in front of your chest to create a picture of the shape of your lungs, similar to a weak chest X-ray. This scan will identify various regions of your lungs to help the researchers analyze data from the gamma camera scan. Then, a measurement of background radioactivity will be made for 15 minutes while you remain seated in front of the camera.
10. Next, you will be escorted into another room where you will inhale an aerosol of sulfur colloid labeled with the radioactive material, Technetium 99m. You will inhale the aerosol according to a prescribed breathing pattern that you will practice prior to aerosol inhalation. Aerosol inhalation will take about 5 minutes.
11. After inhaling the aerosol, you will then be seated in front of the gamma camera again for a measurement of radioactivity in your lungs. You will remain seated in front of the camera for a period of 120 minutes. During this time you will be allowed periodic breaks from sitting. The gamma camera will measure the rate that secretions clear from your lungs (mucociliary clearance rate).
12. When the MCC scan is complete, you will undergo a sputum induction procedure. To this, we will check your lung function, and then have you use 4 puffs of albuterol with a spacer. Then you will be asked to breathe a very heavy mist that we make in a machine called an ultrasonic nebulizer, for 7 minutes. At the end of the 7 minutes, you will blow your nose, rinse your mouth with water, and clear your throat. Then you will cough up any sputum that you feel is coming from your chest. You will do this 2 more times, with increasing concentrations of the salt water. We will check your lung function in between the levels to make sure your levels don't fall to an unsafe level. We will check your vital

signs again prior to sending you home. We will check your vital signs and lung function and ask you to fill out another symptom questionnaire before you leave. You will be discharged with an albuterol inhaler to use if you experience asthma symptoms after you leave the lab. You will also be given prednisone tablets to take if you experience very severe asthma symptoms, and a study coordinator will instruct you on how and when to take this medicine. You will be given the contact information for the on-call study physician, who is available 24 hours a day, 7 days a week.

13. At any time during the study, if you cough up mucus, we will collect it in a cup to send to the lab.

You'll come back the next day for a follow up visit and 30-minute camera scan (**Visit 2**). We will review any problems you may have had overnight as well as take your vital signs, measure your lung function and feNO, and ask you to fill out another symptom questionnaire.

You will return for your next visit (**Visit 3**) at least 1 week but no more than 6 weeks later. At this visit, we will:

1. Review any changes in your health or medications since the last visit.
2. Collect your vital signs, and have you complete a symptom questionnaire
3. Do a urine pregnancy test for females
4. Measure your FeNO
5. Perform lung function
6. Physical examination by a study physician
7. You will have another MCC scan in which you will undergo a lung transmission and background scan followed by inhaling a radiolabeled aerosol and sitting in front of gamma camera for 2 hours. You will be allowed intermittent breaks from sitting in front of the camera during the 2 hours.
8. While you are sitting at the camera, we will ask you to inhale 4 puffs of albuterol using a spacer
9. When you are finished with the MCC measurement, we will ask you to undergo a sputum induction.
10. Collect your vital signs, symptom questionnaire, and lung function before discharging you from the lab (with albuterol inhaler and prednisone tablets as in Visit 1).

You will return the next day for a follow up visit and 30 minute camera scan (**Visit 4**). We will review any problems you may have had overnight as well as take your vital signs, measure your lung function and FeNO, and ask you to fill out another symptom questionnaire.

You will return for your next visit (**Visit 5**) at least 1 week but no more than 6 weeks later. At this visit, we will:

1. Review any changes in your health or medications since the last visit.
2. Collect your vital signs, and have you complete a symptom questionnaire
3. Do a urine pregnancy test for females
4. Meassure your FeNO
5. Perform lung function
6. Physical examination by a study physician

7. You will have another MCC scan in which you will undergo a lung transmission and background scan followed by inhaling a radiolabeled aerosol and sitting in front of gamma camera for 2 hours. You will be allowed intermittent breaks from sitting in front of the camera during the 2 hours.
8. While you are sitting at the camera, we will ask you to inhale 4 puffs of albuterol using a spacer
9. A dose of 7% HS from the nebulizer will be given to you after the first 15 minutes of the 120 min scan
10. We will check your vital signs and have you complete a symptom questionnaire at 5 and 30 minutes after inhaling HS.
11. Depending on your symptoms, we may repeat a lung function test to see if your lung function has changed.
12. When you are finished with the MCC measurement, we will ask you to undergo a sputum induction.
13. Collect your vital signs, symptom questionnaire, and lung function before discharging you from the lab (with albuterol inhaler and prednisone tablets as in previous visits).

You will return the next day for a follow up visit and 30-minute camera scan (**Visit 6**). We will review any problems you may have had overnight as well as take your vital signs, measure your lung function and FeNO, and ask you to fill out another symptom questionnaire.

You will come back to the research lab 5-10 days later for **Visit 7,** for a check out visit. We will:

1. Review any changes in your health or medications
2. Check your vital signs, and have you do a symptom questionnaire
3. Measure your FeNO
4. Have you do a lung function test
5. If you have any health symptoms or concerns, a study doctor will do a physical examination.

All the samples we collect from you, including the sputum and blood, will be kept until all the analysis is complete.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

Hypertonic Saline (HS): There is a chance that inhaling HS could cause an asthma attack, with coughing, wheezing, or trouble breathing. We will check your lung function first before giving HS, and if it is too low, you will not be given HS. All participants will receive 4 puffs of albuterol before the HS dose is given. Albuterol may cause you to feel jittery for a short period of time, can cause a headache, can increase your heart rate, can irritate your throat and can make your nose run. We will monitor your symptoms and lung function regularly to make sure it is not dropping too low. If your lung function drops significantly or if you feel like you need rescue albuterol, we will administer more puffs of albuterol.

This research study involves exposure to radiation from 3 inhalations of radioaerosol and lung transmission scans for measurements of mucociliary clearance. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. The radiation dose you will receive in this study is 133 mRem, which is equal to the radiation exposure everyone receives from natural background sources in 162 days. For comparison, the average person in the United States receives a radiation exposure of 300 mRem per year from natural background sources, such as from the sun, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from participation in this research study is less than the amount you receive from these natural sources in one year. The amount of radiation you will receive in this study has a minimal risk and is below the dose guideline established by The University of North Carolina Radiation Safety Committee for research subjects. The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside this study that are a part of your medical care. Since radiation can be especially harmful to a developing fetus, it is important that pregnancy be avoided during this study by using effective birth control measures (either hormonal contraceptives, like birth control pills; or a barrier method, like condoms. You must inform one of the investigators if you have had any x-rays or other radiation exposure within the past year so that we do not exceed the yearly dose limits. If you wish, Dr. Peden will provide you with additional information and answer any questions you may have. If desired, additional information can be obtained from Marija Ivanovic, Ph.D, Chairman of the Radiation Safety Subcommittee of UNC Hospitals at 919-843-0717.

The tape that is used to hold the radioactive discs (Americium 241) to your upper and lower back can cause mild skin irritation.

There is no risk with the FeNO measurement.

With lung function measurement (called spirometry), you might have the sensation of being lightheaded, or feeling faint. You will be seated in a non-rolling chair for safety.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study and again if more than 7 days have passed. The study pays the cost of these tests.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

Your personal information, including your name, will go into a database called REDCap, which is designed for research studies. Only individuals who need to see your identifying information will have access to this part of the database. All study data will be coded with your study

number. Any hard copy item with any personal identifying information, such as the study worksheets, will be secured in a locked office when not in use. No one outside of the study staff will have access to these records. We will need to use your date of birth for the lung function program.

Participants will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What is a Certificate of Confidentiality?

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects 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 or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances: if you require medical treatment for any medical problems you might have related to the research.

The study team would like to message you by email, however you may say "no" to receiving these messages and still participate in this study. If you say "yes", messages may contain personal information about you and may be sent or received by the study team's personal electronic devices or in a method that is not able to be encrypted (protected) and there is the risk your information could be shared beyond you and the study team. This information may include information such as reminders and notifications to contact the study team.

If you wish to stop receiving unprotected communication from the study team or have lost access to your device, please notify the study team using the study contact information on the first page of this consent form. After the study is complete and all research activities finished, or you

withdraw from the study or request to stop receiving unprotected communication, you will no longer receive un-encrypted (un-protected) messages specific to this study.

_____ Yes, I consent to the study team utilizing the following email address to send communication:

_____

_____ No, I do not consent to receive un-protected communication from the study team.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?
You will be receiving $890 for taking part in this study.

Subjects will be paid for participation as detailed below:
Visit 1: $240
Visit 2: $40
Visit 3: $240
Visit 4: $40
Visit 5: $240
Visit 6: $40
Visit 7: $25
Completion bonus: $25

Total for completing all visits: $890

If you arrive for a study visit, and it must be rescheduled for any reason, you will be paid $25 for your time. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for

U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

You will be paid for your participation by check, we will just need to provide the w-9 form discussed above to University Accounts Payable. If you change your address, we'll need for you to complete a new form. You may have the payment directly deposited in your bank account, and we'll need your banking information to be able to do that. Please note that the checks are sent by University Accounting, so we will not be able to give it to you to at the end of your research visit. Checks may take a little longer than direct deposits, but typically can be expected via mail within ~4 weeks.

The University is seeking a vendor to work with which will allow us to give you pre-paid gift cards, pre-paid Visa or Mastercard including virtual cards. When this is available to the study team, you will have the option of being paid in this fashion.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research

Who is sponsoring this study?
This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____

Signature of Research Participant Date

_____

Printed Name of Research Participant

_____ _____

Signature of Research Team Member Obtaining Consent Date

_____

Printed Name of Research Team Member Obtaining Consent