Consent for Participation in a Clinical Research Study

Trial to Assess Chelation Therapy (TACT): Protocol # 1 U01 AT001156-01

YOU ARE ASKED TO READ THE FOLLOWING FORM TO MAKE SURE THAT YOU COMPLETELY UNDERSTAND WHAT WILL HAPPEN IF YOU AGREE TO TAKE PART IN THIS RESEARCH STUDY. SIGNING THIS FORM MEANS THAT THE STUDY HAS BEEN EXPLAINED TO YOU AND THAT YOU GIVE YOUR PERMISSION TO TAKE PART. THE FEDERAL GOVERNMENT REQUIRES YOUR APPROVAL IN WRITING BEFORE YOU TAKE PART IN ANY RESEARCH STUDY. IT IS IMPORTANT THAT YOU KNOW WHAT WILL TAKE PLACE AND WHAT RISKS ARE INVOLVED BEFORE YOU DECIDE WHETHER OR NOT TO TAKE PART IN THIS STUDY.

Introduction

You are being asked to take part in a research study to test the effectiveness of chelation therapy for patients who have survived a heart attack. The study will involve 2372 patients like you at up to 150 clinical centers. Your participation in the study will include 28 months of treatment, and up to 32 months of follow up.

Purpose of the Study

The purpose of this study is to determine whether these treatments benefit heart attack patients.

Background

Chelation therapy, as used in this study, consists of 40 treatments through a vein in your arm (infusion) of a solution of vitamins and dissolved materials that are thought to bind specific toxic elements circulating in your blood. These elements, known as heavy metals, include iron, copper, and calcium, and may contribute to the development of heart disease. The Food and Drug Administration has approved chelation therapy for treatment of lead poisoning, but not as a treatment for heart disease. Chelation therapy has been practiced in the community for many years. The present clinical practice of chelation therapy also involves the use of high-dose antioxidant vitamins, minerals, and nutritional supplements taken by mouth. However, like with chelation therapy, there is no evidence that these supplements are beneficial for patients like you. The Trial to Assess Chelation Therapy (TACT) will test chelation solution versus a placebo (a substance with no active ingredient) salt-water solution, and high-dose vitamins and minerals taken by mouth versus a low-dose vitamin.

Procedures

If you agree to take part in this study, you will be scheduled for a screening visit. During this visit, a complete medical history and a simple physical examination will be performed. We will also obtain samples of your blood (two tablespoonfuls) to check your blood cell counts as well as your kidney and liver function. You will be asked questions about how you rate your health, about your activities, how you are feeling emotionally and some questions about your working status, education, and income. We expect this screening visit to take about 90 minutes to carry out. Once the laboratory tests are complete, you will be contacted by the research staff and told whether you are eligible, and, if so, asked to schedule your first infusion visit.

Also, at the screening visit, you will be asked to fill out a Confidential Patient Information Form. This form will ask for specific information such as your name, address, phone number, social security number, and other identifiers that will be entered confidentially by the Study Coordinator. The information will be used by the research staff and the Economics and Quality of Life Coordinating Center at the Duke Clinical Research Institute to follow your care and check for changes in your health.

The research staff will call for a treatment assignment and you will be assigned randomly by a computer (by chance, like flipping a coin) to one of these four groups:

Chelation solution + High-dose supplements	Chelation placebo + High-dose Supplements	Chelation solution + Low-dose supplements	Chelation placebo + Low-dose supplements

All patients, including yourself, will receive a total of 40 infusions, beginning with one infusion per week for 30 weeks, followed by an additional 10 infusions given approximately once every 2 weeks to once every 2 months. It will take up to 28 months to complete all the required infusions. Each infusion consists of receiving the solution slowly through a needle in your vein. The needle will be inserted by trained medical personnel under sterile conditions and each infusion will last for 3 hours. You will have blood drawn for laboratory tests during 10 of your visits. Each time, you will have approximately 1 tablespoonful of blood drawn. During each visit, you will be asked how you feel, and whether you have had any complaints or other problems. In addition, the research staff will ask you whether you have had any new heart problems or hospitalizations, and will measure your blood pressure and perform a simple physical exam. Because of the time of the infusions, you should count on being at the clinic for

at least 5 hours. If you live far away from your doctor's office, you may spend a lot of time traveling back and forth.

If you are assigned to the chelation group you will receive a standard intravenous mixture established by the American College for Advancement in Medicine.

The components are as follows. Please review the list of components carefully and notify us if you have an allergy to any of them:

Additive	Role of Additive
Up to 3 grams of EDTA	Chelating agent
2 grams of magnesium chloride	To reduce local discomfort and replace losses
100 mg of procaine HCL	To reduce local discomfort
2500 units of heparin	To reduce local inflammation of veins
7 grams of ascorbate (Vitamin C)	For anti-oxidant properties
2 mEq Potassium	To replace losses
840 mg sodium bicarbonate	To act as a buffer and reduce discomfort
250mg pantothenic acid	For anti-oxidant properties
100mg of thiamine	For anti-oxidant properties
100mg of pyridoxine	To replace chelation losses

Because chelation therapy may also remove important vitamins and other nutritional elements needed by the body, all patients, including yourself, will be required to take vitamins and nutritional supplements. These supplements will be taken on a daily basis. You will be assigned by chance to receive either high-dose vitamin supplements or low-dose vitamin supplements. Neither you nor the research staff will know to which group you have been assigned. On the day of actual infusion, you will be asked to take these supplements 3-5 hours after the infusion to avoid the possibility of the supplements being removed by the chelation therapy. We will ask you to bring these supplements with you to every infusion visit, to ensure that you are taking them as required.

p 4 withheld in entirety
"proprietary info"

proprietary info

As part of this study you may be chosen at random to be interviewed by the research staff from the Economics and Quality of Life Center at the Duke Clinical Research Institute. These interviews, done over the phone, will be scheduled at 6 months, 1 year and 2 years after the initial enrollment to the study. The research staff will ask you questions regarding any changes in how you feel, in your ability to perform your daily activities, or in your working status. If you are chosen, the information will allow us to understand the possible effects of chelation and vitamins on the quality and economics of patients' lives. All of these data will be analyzed using coded information without your name or other identifiable information that could be made public. The calls will take about 15-25 minutes to complete.

After the 40 infusion visits have been completed, research staff from [redacted] will call you every 3 months until the end of the study to find out how you are doing and whether you have had any heart problems since the last call. You will also be asked about any hospitalizations or heart procedures you may have had between study visits. If you have been hospitalized during the follow-up period, it will be necessary for you to sign a release so that we can have access to any medical records related to that hospitalization. In addition, you will be asked to return for a visit each year and at the end of the study. At each visit, you will be asked questions about your medical condition and undergo a simple physical exam.

If you are a woman and are able to become pregnant, you are not eligible to participate in this study.

Your Responsibilities

As a participant in this study you are required to do the following:

- Take the 3 high-dose pills twice per day.
- Take the 1 low-dose capsule once per day.
- Allow at least 5 hours for each infusion visit.
- Bring your study vitamins in their original packaging (bottle and blister packs) to each infusion visit.
- On the day of your infusions, take your assigned vitamins 3-5 hours after your infusion.
- If someone on the research staff calls you on the telephone, please answer all their questions.
- Continue taking all other medications for your heart disease and other conditions as prescribed by your physician.

Risks and Side Effects

This treatment may cause the side effects listed below. However, there may be some side effects that we cannot predict.

EDTA, or ethylenediamine tetraacetate is in the chelation solution. It is approved for use by the FDA as a treatment for lead poisoning but not for coronary artery disease. It binds heavy metals like lead, copper, and iron, and allows them to be excreted in the urine. EDTA rarely may cause allergies, kidney problems, or if given too quickly may cause low calcium, muscular spasms, heart rhythm problems, and low blood pressure that might be serious. You will be monitored carefully for these side effects. The infusion will be monitored closely so it does not go in too quickly, and your blood pressure will be checked before, during, and after the infusion. If your kidney function is not good, you will not be allowed to participate in the study. If your kidney function gets worse during the infusions, then the dose of EDTA will be reduced, or the infusions will be stopped. As part of monitoring your kidney function, you will need to inform your study physician if you are unable to urinate for 12 hours. You may develop flu-like symptoms such as low-grade fevers, sneezing, muscle and joint aches, headaches and watery eyes. These symptoms usually occur 4 to 8 hours after receiving the infusion. These symptoms are usually seen when high doses of EDTA are given, or if the infusion rate is too rapid. Patients with diabetes have been reported to develop low blood sugar during the infusion. For this reason, if you are diabetic, we will ask you to snack before the infusion, and monitor you for symptoms of low blood sugar.

During the infusions, you may experience a "burning-like" sensation at the site of the infusion, or through the vein. Certain medications (such as magnesium and a local anesthetic) are added to the solution to reduce this discomfort.

EDTA has the ability to remove certain vitamins and minerals that are needed by your body. You will be provided with supplements to be taken by mouth that will replace these elements. Although the risk of removal of these minerals is small, this can cause symptoms such as fatigue, dry skin, tingling sensation in your hands and feet, a skin rash, diarrhea, and constipation. EDTA also may reduce the effectiveness of some of the medications you are taking.

As described earlier, magnesium chloride and potassium chloride are included in the infusion solution. Magnesium and potassium are essential salts that are components of all cells in the body. Potassium can cause burning at the site where the intravenous line is placed. However, there are no other likely side effects expected from the doses to be infused.

Vitamins B1, B6, pantothenic acid, and vitamin C also are included in the infusion solution. These essential vitamins have no significant side effects. However, vitamin C is being used at a higher dose than usual.

Heparin, also included in the infusion solution, is a commonly used blood thinner that is used to prevent clotting of the vein used for the intravenous infusion. The principal side effect of heparin at the doses used in this study is an allergy that could lead to bleeding or blood clots. You will be closely monitored for this, and the heparin will be stopped if an allergy seems to occur.

Procaine, also included in the infusion solution, is a local anesthetic that will prevent stinging or discomfort during the intravenous infusions. The main side effect is the possibility of allergy. Sodium bicarbonate is a naturally occurring substance that increases the ability of the kidney to excrete impurities. It is included in the infusion solution.

If your heart is weak, you may be at risk of developing fluid in your lungs as a result of the heart's inability to tolerate the amount of fluid that will be infused. People who already have a history of decreased heart function will be at greater risk. If you have had fluid in your lungs due to a weak heart within the last 6 months, you will not be permitted to participate in the study.

Since chelation therapy is given intravenously, you will have some discomfort at the needle puncture site. There is also a risk of bruising, swelling, and redness developing at the site of the intravenous infusion. Rarely, a serious blood infection may develop

that would require antibiotic treatment. It is very important for you to report any pain, swelling, or redness at the site of the needle punctures, as well as any fever or chills, to your doctor or study investigator. You may also experience these discomforts when having your blood drawn.

The oral anti-oxidant vitamin, mineral, and nutrient supplements being provided are well tolerated and have low risks of serious side effects. Beta-carotene, however, one of the supplements used, has been associated with a higher rate of cancer in patients who smoke. Smokers are not eligible to participate in this study, and it is important that you not start smoking while you are participating.

You or your legally authorized representative will be informed in a timely manner if new information becomes available that may affect your willingness to continue participation in this study.

Finally, there does remain the risk of serious unanticipated side effects that we cannot predict, because this type of study has never been carried out in so many patients.

If you experience one of these side effects, the sponsor (National Institutes of Health) and/or the Data Coordinating Center, (Duke Clinical Research Institute) may need to review your entire medical record.

If you have any questions about the risks or discomforts, contact [INSERT SITE INVESTIGATOR'S NAME AND PHONE NUMBER HERE].

Benefits

You may or may not receive any medical benefit from your participation in this study. In the future, other people with a similar condition may benefit from the knowledge obtained from this study.

Alternative Treatments

If you choose not to participate in this study, your other cardiac treatments as directed and recommended by your doctor will not be affected. You should continue to use proven standard medicines for heart attack patients whether or not you participate in this research study.

Right to Withdraw

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at [redacted]. If you do decide to withdraw, we ask that you contact Dr. [redacted] in writing and let [redacted] know that you are withdrawing from the study. [redacted] mailing address is [redacted]

Involuntary Withdraw

Your doctor may ask you to leave this study if he/she feels it is appropriate or necessary. Your doctor will notify you if this should occur. This in no way will affect your continued medical care and treatment by your physician. Should you decide to discontinue your study participation early, you are asked to contact [redacted] to arrange for final study visit procedures. In addition, the investigator, the sponsor, or the FDA, without regard to your consent, may terminate your participation in this study if either party believes it to be in your best interest. Such conditions may include, but are not limited to, a serious adverse reaction, a worsening of your condition, or lack of cooperation on your part.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the information from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

Costs

You or your insurance company will not be charged for the study treatments or for tests required by the study. All the study medications are provided free of charge to participating research subjects.

Should you have a complication of chelation therapy that requires medication or hospitalization, the study and/or its researchers will be unable to pay for those costs, and you and/or your insurance company will be responsible for the costs resulting from the complication.

You will not be paid to participate in this study.

If you do not sign this consent form, you will continue to receive care from your regular physician, but not as a part of this study.

Confidentiality

Study records that identify you will be kept confidential as required by law. Federal Privacy Regulations provide safeguards for privacy, security, and authorized access. Except as previously addressed in this consent, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier in study records disclosed outside of [INSERT SITE INSTITUTION NAME HERE]. For records disclosed outside of [INSERT SITE INSTITUTION NAME HERE], you will be assigned a unique code number. The key to the code will be kept in a locked file at the Duke Clinical Research Institute (DCRI).

As part of the study, Dr. [INSERT SITE INVESTIGATOR'S NAME HERE] and [CHOOSE HIS/HER] study team will report the results of your study-related laboratory tests to those named below. These test results will be reported to the TACT Clinical Coordinating Center, TACT Clinical Events Committee, Accu-Care Pharmacy Services, and OmniComm Systems.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include, for example, representatives from the Food and Drug Administration, representatives of [INSERT NAME OF PI HERE], the Institutional Review Board, DCRI associates, NCCAM and NHLBI. If your research record is reviewed by any of these groups, they may also need to review your entire medical record.

The following parties may review your study and medical records without your permission, or the permission of your legal representative, as they deem necessary:

Department of Health and Human Services (DHHS),
United States Food and Drug Administration (FDA),
Duke Clinical Research Institute (DCRI),
Quantum Healthcare Consultants,
OmniComm Systems,
Accu-Care Services Pharmacy,
[INSERT YOUR INSTITUTION NAME HERE]
[INSERT YOUR INSTITUTIONAL REVIEW BOARD'S NAME HERE]

In addition, the pharmacy preparing the study infusions (Accu-Care Services Pharmacy) and the prescribing study physician will know who you are.

In addition to signing this informed consent form, you are required to sign a separate consent form that allows your research doctor or investigator to receive your study medications directly from Accu-Care Services Pharmacy.

Record Retention

Your study results will be retained in your research record for 3 years after the end of the study. At that time either the research information not already in your medical record will be destroyed or information identifying you will be removed from such study results at the clinical site. Any research information in your medical record will be kept indefinitely.

Information that could identify you by name will not be used if the results of this study are published.

Injury

In case of injury please contact [INSERT SITE INVESTIGATOR'S NAME AND PHONE NUMBER (24-HR PHONE IF APPLICABLE)]. Immediate necessary care is available if you are injured as a result of taking part in this study. However, there is no provision for free medical care or for monetary compensation for such injury. Financial compensation for research-related injury or loss of wages is not available.

Statement of Consent

"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask the questions I have, and my questions have been answered to my satisfaction. I have been told whom to contact if I have additional questions. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time without affecting my future medical care. I have been told that I will be given a signed copy of this consent form."

_____ _____

Name of Subject Date

_____

Signature of Subject

_____ _____

Name of Legally Authorized Representative (if applicable) Date

_____

Signature of Legally Authorized Representative (if applicable)

_____ _____

Name of Person Obtaining Consent Date

_____

Signature of Person Obtaining Consent

_____ _____

Name of Witness (if applicable) Date

_____

Signature of Witness (if applicable)