Use of (-)-Epicatechin in the Treatment of Becker Muscular Dystrophy (Pilot Study)

NCT01856868

3/24/2014

Title of research study: UCD0113: An open-label pilot study of purified tea-derived epicatechin to improve mitochondrial function, strength and skeletal muscle exercise response in Becker Muscular Dystrophy

Investigator: Craig McDonald, MD

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you are an adult diagnosed with Becker muscular dystrophy.

What should I know about a research study?

(Experimental Subject's Bill of Rights)

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document.

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team:

Craig McDonald, MD Study PI at phone number 916-734-2923

Erik Henricson, MPH Co-PI at phone number 916-734-0384

UC Davis Department of Physical Medicine and Rehabilitation
4860 Y Street, Suite 3850
Sacramento, CA 95817

For emergencies please call the following 24-hour emergency number. Our study doctors are available 24 hour a day for these health related emergencies.

UC Davis Medical Center operator - (916) 734-2011

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If you call the UCDMC Hospital Operator, tell the Operator you are participating in a research study and you wish to talk to Dr. Craig McDonald. This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/IRBAdmin.You may talk to a IRB staff member at (916) 703-9151, IRBAdmin@ucdmc.ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

This research study will test an investigational drug called (-)-Epicatechin. (-)-Epicatechin is purified from tea as a nutritional extract. (-)-Epicatechin will be evaluated for the treatment of progressive muscle loss and impaired skeletal muscle function in Becker Muscular Dystrophy (BMD) patients. (-)-Epicatechin has been shown to improve muscle structure and function in previous studies of animals and humans.

How long will the research last?

We expect that you will be in this research study for 8 weeks for a total of 6 visits.

How many people will be studied?

We expect about 10 people here will be in this research study at UC Davis.

What happens if I say yes, I want to be in this research?

Study Procedures:

See below for a table of all the study procedures:

Event	Screening (Week -2 to Day 1)	Baseline (Day 1)	Week 2	Week 4	Week 8	Early Withdrawal
Informed consent	X					
Medical history	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X
Physical examination	X	X	X	X	X	X
Blood & urine collection and tests	X	X	X	X	X	X
ECG	X	X	X	X	X	
Other medications and dietary supplements	X	X		X	X	X
Adverse events		X	X	X	X	X
Functional assessments		X		X	X	X

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Muscle Biopsy		X			X	
Dispense Epicatechin		X	X			

Informed consent (30 mins) (At Screening)

Before we begin any procedure we will review this consent form with you and answer any questions that you might have. After you sign the consent form we will provide you with a copy.

Medical history and medications (10 mins) (At Each Visit)

We will ask you questions about medical conditions and medications that you are taking.

Vital signs and physical exam (30 mins) (At Each Visit)

We will measure your weight, height, blood pressure and breathing rate.

Blood & urine collection and tests (30 mins) (At Each Visit)

We will collect approximately 13 ml (about 2.6 teaspoons) of your blood and a urine sample for safety assessments.

Electrocardiogram (ECG) (15 mins) (At Each Visit)

A test to determine how well your heart is functioning

Adverse events (10 mins) (At Each Visit Following Screening)

We will ask you if anything has happened since the last visit that hurt or was out of the ordinary with regard to your health.

Functional assessments (3 hours) (At Each Visit Following Screening)

You will be asked to perform several exercise tests including the following measures:

- Six minute walk test—you will walk as fast as you can for 6 minutes around 2 cones
- Recumbent cycling test—you will exercise using a recumbent bicycle
- Strength test—we will measure the strength of your elbows and knees with a BIODEX ergometer
- Range of motion test—we will assess your range of motion by measuring the extension of your knees, ankles, elbows and wrists in front of a motion sensing system
- Breathing tests—you will perform PFTs (Pulmonary Function Tests) to assess how much air you can breathe in and out
- Timed Function Testing—we will assess your ability to rise from the floor, climb four standard stairs and walk or run for 10 meters
- Upper/Lower Extremity function—we will assess your ability to use your arms and legs
- Anthropometric Measurements—we will measure your waist and hip circumference
- Body Composition by Dual energy X-ray absorptiometry (DEXA)—we will ask you to lie still on the bed of the DEXA scanner. The scanning arm will pass over your body one or more times and will make a computerized X-ray image of your whole body. You will not feel anything during the scan, but you will be asked to lie very still.
- Multifrequency Bioimpedence Assessment (MFBIA)—we will assess the amount of total water and fat-free mass in your body. Electrodes are placed on your ankle and wrist.

Impedence is measured between upper and lower extremity electrodes. You will not feel anything during the test.

- Muscle Biopsy (60 mins) (At Baseline and Week 8)

The muscle biopsy samples will be collected by open biopsy according to standard hospital procedures. The minimum amount of muscle tissue required is a small piece of muscle of at least 0.5 x 1.0 x 1.0 cm. Biopsy at baseline will be collected from the halfway point of the biceps muscle. A second biopsy at 8 weeks will be collected from the same muscle at a place about 1 inch away from the first biopsy. The biopsies will be done with local anesthesia (numbing) like you would have for routine dental procedures. The doctor will close the incision with some small stitches or tape called "steri-strips." The biopsy will have a small scar about an inch long.

Study Medication-Epicatechin

You will swallow pills of (-)-epicatechin 50mg twice per day (100mg per day total dose). Study medication will be supplied as a clear 25mg gelatin capsule. You will take two capsules in the morning at approximately 7:30AM at least 15 minutes before the morning meal and two with the evening at approximately 7:30PM at least 1 hour after the evening meal.

What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible to:

Tell the doctor if you have any new or worsening medical symptoms or problems during the time you receive the study medication as part of this study. It is important that you tell the doctor even if symptoms or problems are mild or you do not think they are related to study drug.

Please call if you have any questions about study medication or about the use of other drugs during the time that you receive study medication.

Contact the doctor immediately if an overdose of study drug happens or is suspected.

What happens if I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you.

Instead of being in this research study, your choices may include participating in other available clinical trials or choosing not to participate at all.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you.

If you leave the research, contact the investigator so that the investigator can recommend proper follow up care.

If you stop being in the research, already collected data may not be removed from the study database. You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me?

Potential Risks

Risks of Study Medication (Epicatechin)

Hypotension (low blood pressure). Given the reported effects of (-)-epicatechin on blood vessels, it a potential risk may be associated with hypotension. With cocoa based studies, blood pressure reducing effects are only reported in humans that have high blood pressure. There is the possibility

that patients undergoing drug treatment for high blood pressure if given (-)-epicatechin may develop hypotension.

Migraines. The consumption of cocoa products has been associated with increased likelihood of migraine development. (-)-Epicatechin may increase the chances for migraine development in certain individuals.

Bleeding. Anti-clotting like effects have been described in a limited number of reports on the effects of cocoa, although no such reactions have been seen to date. It will be important not to take any "blood thinning" medications during the study without consulting the study doctor.

Risks of Blood Tests

The risks of blood drawing include soreness or bruising at the site of the needle. A local numbing cream (EMLA) will be applied to the area. There are no side effects associated with the use of this cream. Rarely, a more serious injury, such as hematoma (bleeding under skin) or infection may develop.

Risks of Muscle Biopsy

After the muscle biopsy you may feel pain at the place of the biopsy. Patients usually find the pain easy to tolerate and that they rarely need to take a painkiller although Tylenol or ibuprofen is appropriate as needed for the next 24 hours. The muscle biopsy may leave a small scar and it is possible that the strength of that muscle might be slightly reduced in the short term. Additional risks of the muscle biopsy include: bleeding, wound separation, and/or possible infection.

Risks of Strength Testing and Functional Assessments

At this time, there are no known risks associated with functional evaluation or muscle strength testing methods used in this protocol. However, you may experience mild muscle soreness the day after muscle testing.

Risks of Breathing Tests

These tests may cause dizziness and lightheadedness during and shortly after the test.

Risks of Electrocardiogram (ECG)

The ECG has no known risks.

Risks of DEXA

This study involves a low radiation exposure that is less than other diagnostic tests using ionizing radiation. The amount of radiation exposure received in this study is below the levels that are thought to result in a significant risk of harmful effects.

Risks of Multi-Frequency Bioimpedence Assessment (MFBIA)

There are no known risks of MFBIA testing.

Risks of Upper Extremity Range of Motion Evaluation

There are no known risks of upper extremity range of motion evaluation.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include:

- You may experience an increase in muscle strength or a delay in strength decline.

- You will receive additional care during study participation including muscle strength training, contracture measurements and spirometry during each study visit.
- Your medical and adverse event history will be closely monitored
- You will experience additional medical monitoring that will allow for increased interaction with medical staff above expected routine clinical care (i.e. the increased monitoring of safety labs)

It is possible the participants will not experience any direct benefit as a result of their study participation. However, the data collected during this trial may provide information that will benefit the scientific community as well as other individuals with BMD

What happens to the information collected for the research?

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB and other University of California representatives responsible for the management or oversight of this study.

The IRB and the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your medical records may be looked at by government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf) and in an attached document.

Can I be removed from the research without my OK?

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

There is no charge for you to participate in this study. Neither you nor your insurance carrier will be charged for your taking part in the research. All costs associated with the study will be paid by the department.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by or may be billed to your insurance company just like other medical costs. The University does not normally provide any other form of compensation for injury.

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

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Are there other research opportunities?

If you are interested in being contacted for future research, please provide your phone number and/or email. This is completely optional.

_____(initials) Yes, I am willing to be contacted for future research opportunities. My phone number and/or email is: _____.

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	Date
Printed name of person witnessing consent process	

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