Effect of EPA and HMB on Strength in ICU Patients

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Consent Form

Effect of EPA and HMB on Strength in ICU Patients

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are being asked to participate in a research study to determine if administration of either Hydroxymethylbutyrate (HMB), eicosapentaenoic acid (EPA), or the combination of HMB plus EPA can improve respiratory muscle strength in critically ill patients. You are being invited to take part in this research study because you have required mechanical ventilation. You will be one of 80 patients asked to participate in the study.

Because of your condition, you may not be able to make the decision to participate in this research. In this case, _____, your legally authorized representative will attempt to decide what you would do if you were able to choose whether or not to be in this study. Your legally authorized representative will determine whether your participation in the study is in your best interests.

WHO IS DOING THE STUDY?

The person in charge of the study is Dr. Gerald Supinski, a member of the Pulmonary Division of the Department of Medicine at the University of Kentucky. There may be other people on the research team assisting at different times during the study, including Dr. Leigh Ann Callahan, also a member of the Pulmonary Division of the Department of Medicine at the University of Kentucky.

WHAT IS THE PURPOSE OF THIS STUDY?

Patients that are on mechanical ventilators in medical intensive care units have extremely weak breathing and leg muscles. Currently there is no treatment to prevent or reverse this weakness. In animal studies, however, it has been shown that two nutritional supplements, hydroxymethylbutyrate (HMB) and eicosapentaenoic acid (EPA) can help prevent the development of muscle weakness in critical illness. The purpose of this study is to determine if one or both of these drugs can also prevent breathing and leg muscle weakness in patients on mechanical ventilators. The results of this study may be shared with the Food and Drug Administration (FDA) and other federal agencies, if required.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

If you have a pacemaker or implanted defibrillator you cannot participate in this study. If you have severe liver disease with variceal bleeding you also cannot participate in this study. If your clotting parameters are severely abnormal you can participate in the study but no muscle biopsy will be taken.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

These studies will be conducted in the intensive care unit at the University of Kentucky hospital. The total duration of the study is 22 days.

WHAT WILL YOU BE ASKED TO DO?

We will first measure the strength of your breathing muscles, the strength of a leg muscle, measure your lung function through the breathing machine, measure muscle size, and obtain a muscle biopsy from the side of your thigh. We will then administer one of four drug regimens. These drugs will be continued for ten days. On day eleven, breathing muscle strength, leg muscle strength, muscle size, and lung function will be reassessed and a second muscle biopsy from your thigh will be obtained. On day twenty-one, a final assessment of breathing muscle strength, leg muscle strength, muscle size, and lung function will be made.

To measure breathing muscle strength we will first ask you to swallow two tiny balloons attached to small plastic tubes. These balloons will be passed through the nose using a lubricating gel. The balloons will be advanced until one is the stomach and the second is in the esophagus. We will then place magnetic coils over the front of the right and left neck. We will then stimulate the nerves to the breathing muscles with a single magnetic impulse and measure the pressure in the balloons produced when the breathing muscles contract. We will repeat these measurements of a total of three times. The balloons will then be removed from the nose.

To measure leg muscle strength, we will place a force detector around the right lower leg and stimulate a muscle in the right thigh called the quadriceps muscle. Stimulation will be performed using a magnetic coil placed over the nerve to the quadriceps. We will measure muscle strength three times and then remove the force detector.

To assess lung function, we will press a button on the breathing machine which activates an automatic measurement of lung function.

To determine muscle size we will place a ultrasound probe over the lower chest and over the left thigh and measure muscle thickness.

To obtain the thigh muscle biopsy we will fist clean the skin with two different antibacterial solutions (betadine and alcohol). We will than anesthetize the skin over the muscle with a small volume of a numbing drug (lidocaine, one teaspoon). After five minutes a small 1/4 inch incision will be made in the skin. A special muscle biopsy needle will then be placed into the muscle and a small piece approximately ¼ inch wide will be removed by suction. We will apply pressure to the area for 10 minutes and then place a heavy bandage over the site.

The supplement regimens to be used are provided below. You will receive one of these four; the choice as to which you will get will be determined randomly and this choice will be made by the pharmacist involved in the study. The four choices are:

(1) Placebo this will be given as two tablespoons of salt water solution, 1.5 grams of amino acids and 0.2 teaspoons of corn oil every 12 hours,

(2) Hydroxymethylbutyrate (HMB); this will be given as two tablespoons of salt water solution, 1500 mg HMB and 0.4 teaspoons of corn oil every 12 hours,

(3) Eicosapentaenoic acid (EPA); this will be given as two tablespoons of salt water, 1.5 grams of amino acids and 1000 mg EPA every 12 hours,

(4) HMB and EPA; two tablespoons of salt water, 1500 mg HMB and 1000 mg EPA every 12 hours.

The following table summarizes what you will be asked to do:

Time	Nutritional Supplement	Testing
Day 1		Muscle strength, muscle size, muscle biopsy
Day 1-10	Supplement given for 10 days	
Day 11		Muscle strength, muscle size, muscle biopsy
Day 21		Muscle strength, muscle size

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

You are not a candidate for these measurements if you have a pacemaker since magnetic pulses can affect pacemaker function. You are also not a candidate if you have a history of severe liver disease or esophageal bleeding, since placement of the tubes into the esophagus can cause bleeding in these patients. You can participate in

the study but will not have a muscle biopsies performed if you have abnormal clotting parameters (i.e. elevation of the INR above 1.5, an aPTT 50% or more above the normal range, or a platelet count less than 60,000).

There have been no reported instances of side effects or complications from these measurements of muscle strength in patients without pacemakers or liver disease. While there are no major risks to the performance of these measurements, there may be discomfort from insertion of the balloons into the nasal passages or from magnetic stimulation of the nerves to the breathing muscles. The magnetic stimulation will create the sensation of muscles contracting in the chest or leg; this sensation will only last for a second after the magnet is activated.

Eicosapenataenoic acid (EPA) is a health food contained in fish oil. No major complications have ever been reported from use of this supplement at this dosage, but this food has been reported to occasionally cause nausea, diarrhea, heartburn, skin rash, itching, and joint, back, and muscle pain. At doses higher than the dose used in the study this agent may reduce blood clotting and can increase the anti-clotting effects of aspirin and Coumadin.

Hydroxymethylbutyrate (HMB) is a food supplement that has been used to build muscle in athletes and preserve muscle function in cancer patients. Small amounts are normally made by the body daily. This supplement has not been reported to cause side effects at any dosage studied.

There is a small risk of bleeding and/or infection secondary to performance of the leg muscle biopsy. To minimize these risks, a pressure bandage will be placed over the biopsy site and Dr. Supinski or Dr. Callahan will return daily to inspect the biopsy site for 7 days after this procedure.

In addition to the risks listed above, you may experience a previously unknown risk or side effect. As a result, a physician will be in attendance at all times during the study and will stop measurements if any harmful effects are observed. In addition, if you have serious nausea from administration of the drugs, these agents will be stopped.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

The two supplements being tested, HMB and EPA have been shown to preserve muscle strength in animal models of critical illness. It is hoped that these agents will also improve muscle strength in human patients that are critically ill. If these supplements improve your strength, they may help you recover from your illness faster and allow you to come off the ventilator sooner. Since this is the first time these agents have been tested in critically ill patients, however, there is no guarantee that they will improve your strength. In addition to a potential benefit to you, your willingness to take

part in this study may help doctors better understand and/or treat others who have your condition.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering. If you decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

There is currently no drug therapy that is being used in the University of Kentucky Medical Intensive Care Unit to prevent or reverse weakness in critically ill patients. If you do not participate in this study you will receive passive range of motion treatments by physical therapy, which is the standard care to improve muscle function at this time.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive for your condition. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study.

The University of Kentucky will not bill your insurance company, Medicare or Medicaid for any of the medical procedures done in this study. You also will not be billed for the supplements used in this study or the time of the personnel performing this study. The supplements are being provided at no cost to you.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will keep private all research records that identify you to the extent allowed by law. Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. The records for this study will be kept in a locked file cabinet to which only Dr. Supinski and Dr. Callahan have access. Unless required by law, your name will not be disclosed outside the hospital and research clinic. Dr. Supinski and staff; authorized representatives of Dr. Supinski; health authority inspectors, such as the US Food & Drug Administration and the National Institutes of Health, and authorized representatives of the University of Kentucky may look at or copy pertinent portions of records that identify you. If required, Dr. Supinski may contact your personal physician to collect additional medical information and your past medical history.

A description of this clinical trial will be available at ClinicalTrials.gov. 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.

CAN YOUR TAKING PART IN THE STUDY END EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. The individuals conducting the study may need to withdraw you from the study. This may occur if you are not able to follow the directions they give you, or if they find that your being in the study is of more risk than benefit to you. If you withdraw or are withdrawn from the study the study treatment will no longer be provided and may not be available.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may be able to take part in this study if you are currently involved in another research study, but only if that study does not involve taking any drugs. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

It is important that you follow carefully all the instructions given by Dr. Supinski and his staff regarding this study. If you believe you are hurt or if you get sick because of something that is due to the study, you should call Dr. Supinski at 859-494-3480 or page Dr. Supinski through 859-257-5522 immediately. Dr. Supinski will determine what type of treatment, if any, that is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Therefore, the medical costs related to your care and treatment because of research-related harm will be your responsibility. These costs may be paid by your insurer if you are insured by a health insurance company. You should ask your insurer if you have any questions regarding your

insurer's willingness to pay under these circumstances. These costs may also be paid by Medicare or Medicaid if you are covered by these services. If you have any questions regarding Medicare/Medicaid coverage you should contact Medicare by calling 1-800-Medicare (1-800-633-4227) or Medicaid (1-800-635-2570). A co-payment/deductible from you may be required by your insurer or Medicare/Medicaid even if they have agreed to pay these costs. The amount of this co-payment/deductible may be substantial. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

In no way does signing this consent form waive your legal rights nor does it relieve the investigators, Sponsor or involved institutions from their legal and professional responsibilities.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will not receive any rewards or payment for taking part in the study.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the investigator, Dr. Gerald Supinski at 859-494-3480. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

WHAT ELSE DO YOU NEED TO KNOW?

There is a possibility that the data/tissue/specimens/blood collected from you may be shared with other investigators in the future. If that is the case the data/tissue/specimen/blood will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal,

state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

This study is being financially supported by funds from the University of Kentucky and the National Institutes of Health.

Signature page

I have read this document/had its contents explained to me. I understand the purpose of this study and what will happen to me in this study. I do freely give my consent to join in this study, as described to me in this document. I understand that I will receive a copy of this document as signed below.

_____ _____

Signature of person agreeing to take part in the study or the legally authorized individual — Date

_____

Printed name of person agreeing to take part in the study or the legally authorized individual

_____

Relationship of the legally authorized individual to the subject

_____ _____

Signature of [authorized] person obtaining informed consent — Date

_____ _____

Printed name of [authorized] person obtaining informed consent — Date

_____

Signature of Investigator