The Impact of Carnosine Loading and Rehabilitation Therapy on Exercise Capacity in Multiple Sclerosis

NCT03418376

Date: 10/02/2017

Model (ICD) for clinical interventional study in adults

Title of the study : The impact of β-alanine supplements on the effects of a home-based (cycling) training program in Multiple Sclerosis and healthy persons.

Client : Hasselt University, Agoralaan, Building D, Diepenbeek

Research institute *:* REVA L - Rehabilitation Research Center, Agoralaan Building A, Diepenbeek

Medical Ethics Committee : Ethical Review Committee Jessa Hospital and Medical Ethics Committee of Hasselt University

Local physician researchers:

1. University Campus, Hasselt University, Building A
   Name local researcher s : Charly Keytsman Prof. Dr. Bert Op't Eijnde
   E-mail address of the local researcher: charly.keytsman@uhasselt.be
2. Jessa hospital, Campus Jessa, Hasselt
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I Necessary information for your decision to participate

preface

You are invited to participate in a clinical e study evaluating email and nutritional supplements and exercise intervention on the exercise capacity and performance capability in multiple sclerosis (MS) . In this research, we want to assess the impact of β-alanine supplementation (a supplement used in the sports world to combat acidification during high-intensity efforts) and a training intervention (consisting of endurance training and short, highly intense intervals, on self-employmentsome basis) in persons with MS compared to healthy persons .

The sponsor and physician researcher hope that this supplement, in combination with physical training, will provide benefits for treating patients affected by the same disease as you. However, there is no guarantee that your participation in this study will benefit you.

Before you decide on your participation in this study , we would like to give you some more information about what this means in organizational terms and what the potential benefits and risks are for you. K as an take a decision based on the right information. This is called "informed consent".

We ask you to read the following pages with information carefully. If you have questions, then k an contact the physician-researcher or his or her representative. This document consists of 3 parts: essential information you need to make your decision, your written consent and attachments that provide more details about certain parts of the basic information.

If you participate in this clinical trial , you should know the following :

·This clinical study will be initiated after evaluation by one or more ethics committee (s).

Your participation is voluntary; there can be no compulsion in any way. Your signed permission is required to participate. Even after you have signed, k an to the physician researcher to know that you want to stop your participation. The decision whether or not (further) part to take up one will not have any negative impact on the jellyfish i capacity of the concerns nor the relationship with the doctor (s).

- ·The data collected in the context of your participation is confidential. Your anonymity is assured when the results are published.
- ·You will not be charged for specific treatments, visits / consultations, examinations in the context of this study .
- ·Insurance has been taken out in the event that you should be harmed as a result of your participation in this clinical trial .
- ·If you require additional information, k an always contact the physician-researcher or a member of his or her team.

Additional information on "Rights of participants in a clinical e study " can be found in Annex 3 .

Objective and description of the study protocol

We invite you to participate in a clinical e study on research into the effect of β-alanine supplementation in combination with a (bicycle) training program at homeon the exercise capacity and performance in persons with MS and healthy persons.

Carnosine is a natural substance (produced by the body himself and feeding back to find is) in the muscle that causes the muscle to contract properly and slowing acidification (during exercise). We have already shown that this concentration in the muscle has decreased in persons with MS. That is why we want to try to increase this via supplements. This can be done via the administration of β-alanine supplements such as often in the sporting world applied becomes. D addition, the amendments we want to see what the impact of a training program (6 months) with alternating low and high intensity workouts, combined with the supplements, the inspa nningscapaciteit and performance in people with MS compared to healthy subjects.

Inclusion criteria for test subjects : MS patients (EDSS <3) + healthy subjects, male / female,> 18 years old, in possession of a signed information and consent document and their own (racing) bicycle .

Exclusion criteria subjects: other chronic conditions besides MS, pregnant, <18 years , taking other supplements that may promote performance .

In d e start of the examination, your exercise capacity (uithoudingstes t on your bike) and the strength of your abdominal and back muscles ge measure . We will also take a scan of your body to see your body composition (fat and muscle mass) . After these measurements you will be assigned to 1 of our 4 training groups. In addition, you will follow a training intervention with combined low and high-intensity cycling training for 6 months , with or without the addition of β-alanine supplements (the ones used in the sports world to improve performance). The groups that do not receive β-alanine supplements will receive placebo supplements, which have the same taste and appearance as the β-alanine. After 6 months the training program ends and we perform all tests again as at the start of the study.

Course of the study

Your participation in the study takes about seven months to complete .

At the start of the study, 20 persons with MS and 20 healthy persons (HC) will be subjected to a number of tests. We measure the exercise capacity (exercise test on your own bicycle) and the body composition . We also measure the strength in your abdominal and back muscles via a strength test. This gives us an impression of your torso stability (important during long cycling workouts). Then the persons with MS and HC are assigned to 1 of our 4 training groups for 6 months . All subjects (MS and HC) independently perform one training program home base, opa personal (race) bicycle. The subjects receive training instructions every week via a heart rate monitor (Polar ®) that is linked to a smartphone.

During the training program will in each case two groups of β-alanine supplements (MS β , n = 10, HC β , n = 1 0) to take and the second groups of placebo supplements ($MS_{placebo}$, n = 10, $HC_{placebo}$, n = 10) with an identical taste and appearance. Both the participant and the researcher will not know what the supplements or placebos are. The training program will consist of cycles of 3 weeks each and will be carried out independently by the participant on a personal (racing) bicycle. At week 1 3 will training sessions can itvoeren of long duration for moderate / severe intensity, w aaronder 2 sessions of 3 hours (70 -80 % maximal harts lag - green zone figure below), and the first session of 1.5h (80 -90 % maximum heart rate - orange zone figure). In week 2 you train 3x short sessions at a high intensity. You do 3 sets of maximum effort / sprint (1.5min - red zone figure) alternated with rest intervals (3min). During week 3 we ensure that there are sufficient recovery moments (important for recovery and training stimuli), where you cycle 1x 1.5h (80-90 % maximum heart rate - orange zone) and 1x perform an interval session (red zone) . The rest will be able to recover in the 3 ◦week. We repeat this cycle for the entire duration of the study and then take the full measurements again to view the effect of our training schedule in combination with the supplements .

β-alanine will increase the carnosine concentration in the muscle, which is done in the sports world to improve muscle contraction and prevent acidification. We make this substance in our body, we find it in food and it is reduced in people with MS (shown by us). These supplements are safe and do not cause side effects at such a dose . Rarely, you may feel slight tingling on the skin. However, this disappears after one hour. If this occurs repeatedly, we ask you to contact us. During the first 12 weeks you take the β-alanine supplements (tablet, 800mg) 4 times a day, preferably during a meal. After 12 weeks, the carnosine concentration in the muscles is sufficiently increased, after which you take a maintenance dose of 2 tablets per day, until the end of the study.

Risks and inconveniences

The research (measurements) is carried out in such a way that it does not pose any threatening risks. You may experience some temporary inconveniences.

- The determination of your exercise capacity and muscle strength of the abdominal and back muscles is done using a maximum test. This means that during this test you will have to go to extremes to see what your maximum values are. We then use these to set up your training schedule and to view your progress over the 6 months of training. It may be possible to feel strain on the back muscles by performing the strength measurement of the back.During this test , however, we warm up enough to avoid discomfort.
- The DEXA Body Composition Device works with a quantityid X-rays which is comparable to the radiation during a flight, therefore no special measures have to be taken and consequently a limited is a risk to general health.
- The supplementation of β-alanine in this dose does not pose any risks. The only discomfort that can occur is that you feel tingling on the skin, but this is transient (1 h). If this continues to occur , we ask you to contact us.
- All participants receive an individual training schedule . However, you may still experience mild muscle stiffness after the first 2 to 3 training sessions. These are a result of an improvement in your condition and are completely harmless.

Benefits

If you decide to participate in this study , β-alanine supplements in combination with rehabilitation training may or may not prove beneficial in treating your condition or reducing its symptoms.

The information obtained through this research may contribute to a better knowledge of the use of this supplement or to new insights into rehabilitation multiple sclerosis in future patients.

We will not pay any financial compensation for your participation in the study. However, we offer you the opportunity to follow a training program during 6 months , free of charge, in which you will be guided by experts. After completing the study, you will receive a full report of the results of the study, including all calculated values and any lifestyle recommendations. These are of course only informative. Moreover, your participation in the research can be seen as a selfless participation in scientific research.

Confidentiality

The research team guarantees that both your personal data and all research results resulting from this study will be treated in a confidential, encrypted manner in accordance with Article 7 and according to the 'Personal Data Protection Act' of December 8, 1992. Your personal research data may, with permission, only be inspected by authorized employees of Hasselt University and the Medical Ethics Committee. The research results of this study will be announced at conferences and published in academic journals, without your identity being revealed. Only meaningful results obtained within 2 years after collection of the material via clinically validated screening tests will be reported to your treating physician.

Termination of participation

Your participation is voluntary. You have the right to stop participating in the study for any reason and without reason. But it may be for physician-researcher and the client be useful to know if retiring because the study limitations of treatment are too heavy (eg too many unpleasant side effects, too many follow-up visits).

It is also possible that the investigator may stop participating in the study because you are pregnant, because he / she believes it is better for your health, or because he / she finds that you are not following the requirements for participation .

Also, it sometimes happens that the competent national or international authorities, the Ethics Committee 's initially approved had the data for the study of the principal study discontinuation

because the information gathered showed that the treatment does not work (the health of the participants does not improve sufficient) or that the treatment under investigation is causing more or more serious side effects than expected or for any other reason such as, for example, the decision to discontinue the study and the development of the drug under study .

The study team may withdraw you from the study without permission and therefore terminate your participation in the following cases:

- You do not adhere to the research protocol (do not follow the training program / do not take supplements correctly)
- You have a serious illness or there is a significant worsening of a disease other than MS
- You participate in another study
- The dose or type of medication you are taking will change significantly during the course of this project
- You become pregnant

If you participate in this study , we ask you to:

- Take full with work for a proper conduct of the study .
- Do not conceal any information about your health, the medicines you are taking or the symptoms you are experiencing .
- Not part to participate in a clinical study with -no matter experimental treatment or a study drug, medical device or procedure betreft- while participating in the current study .

You should also know that:

it is recommended for your safety to inform your general practitioner or other treating physicians involved in your treatment about your participation in this study . We ask you to give your permission for this.

Approval of this study

This study was approved by the Ethics Review Committee of the Jessa Hospital and the Medical Ethics Committee of Hasselt University. After reading this information, you can always contact us for questions and / or more information. When you have had sufficient reflection period, you will be asked to decide whether to participate in this study. If you give permission to participate, you must sign the corresponding permission form. You will receive a copy of this information and the signed consent form if you decide to participate. You can send it to us at the start of the study or you can send it to the following address, but before the start of the study:

Charly Keytsman
REVAL - Rehabilitation Research Center
Agoralaan building A
B-3590 Diepenbeek

Contact

If you need additional information, but also in case of problems or if you are worried, k an can contact the researcher (Charly Keytsman) or an employee of his / her study team on the phone (011/26 93 70 or charly .keytsman @ uhasselt.be).

Title of the study : The influence of β-alanine supplementation and rehabilitation / exercise therapy on exercise capacity and performance in individuals with Multiple Sclerosis and healthy persons.

II Informed Consent

Participant

I declare that I informed 'm on the ground, h et purpose, duration , the potential benefits and risks of the study and I know what is expected of me. I have taken note of the information document and its annexes.

I have had enough time to think and talk to a person I have chosen, such as my doctor or a family member.

I have been able to ask all the questions that came to mind and I have received a clear answer to my questions.

I understand that my participation in this study is voluntary and that I am free to end my participation in this study without affecting my relationship with the therapeutic team responsible for my health.

I understand that during my participation in this study, data will be collected about me and that the investigator and the sponsor ensure the confidentiality of this data in accordance with the relevant Belgian legislation.

I agree to the processing of my personal data according to the modalities described in the section on ensuring confidentiality. I also authorize the transfer to and processing of my encrypted data in countries other than Belgium.

I agree / I do not agree (strike out which is not applicable) that the study data collected for the study listed here will be processed later, provided that this processing is limited to the context of the here listed study for a better understanding of the disease and its treatment.

I agree / I will not agree (which is not delete any) that my family doctor and other specialists involved are my treatment to be informed of my participation in this clinical e study .

I have received a copy of the information to the participant and the informed consent.

Name, first name, date and signature of the participant

Please fill in the information below as completely as possible.

Personal information

in block letters

Name:

Date of birth:

Home address:

Tel / GSM:

Email (if used frequently):

Sex:

Which medication are you currently taking:

Doctor researcher

I, the undersigned Charly Keytsman, researcher , declare that I have provided the necessary information regarding this study orally and that I have provided a copy of the information document to the participant.

I confirm that any pressure on the participant is applied to him / her to do to vote to participate in the study , and I am ready for any possible additional questions to answer.

I confirm that I am working in accordance with the ethical principles as stated in the latest version of the "Declaration of Helsinki", the "Good clinical practice" and the Belgian law of 7 May 2004 on human experiments.

Name, First name, Date and signature of the investigator's representative

Naa m , Name, Date and signature Naa m , Name, Date and signature of the representative of the physician-researcher

from the physician researcher

Title of the study : The influence of β-alanine supplementation and rehabilitation / exercise therapy on exercise capacity and prestatiev Power rating at double ones of Multiple Sclerosis.

III Additional Information

1 : Additional information about the organization of the study

If you decide to participate in the study and meet all the conditions for participation, you will complete the following tests and studies :

Each measurement session will take a maximum of half a day and consists of 3 measurements .

The first measurement session will start in the spring of 2017. After that, the training programs will be started. The training is individually adapted and the participants are supervised by experts. The training sessions are conducted independently by the participants and were described above. After the end of

the training program, the tests, such as during the first measurement, are again performed after 6 months. Finally, a comparison is made between the results before and after the training program between persons with MS and healthy controls .

Measurements

- **Physical endurance test:** your general condition or endurance is tested on the basis of a bicycle test. This is necessary to tailor your training programs to your needs. During the test, the oxygen uptake is checked by means of a mask. This measurement takes about 30 minutes.
- **Body composition:** to determine your body composition we will measure your height and weight in order to calculate your body mass index (BMI). Then we will use a dexa device to calculate the amount of body fat, the fat-free mass and the bone density. The dexa device is a kind of scanner where you are placed on a table and have to lie still for 7 minutes.
- **Strength measurement:** by means of a strength test for abdominal and back muscles, we get an impression of your torso stability (important during long cycling workouts). During this test, stretch and bend the back (while seated) against a resistance. In this way we can measure the strength of these muscles.

Additional information about the risks associated with participating in the study

Apart from the potential risks and inconveniences discussed earlier, this study does not present any other risks.

Risks related to the clinical investigation procedures

The supplements administered are harmless and have no side effects.

3 : Additional information on the protection and rights of participants in a clinical e study [1]

Ethical committees

This study was evaluated by an independent ethics committee, **the Ethics Review Committee after consultation of the Medical Ethics Committee,** which has issued a favorable opinion . The ethics committees have a duty to protect those who participate in clinical studies . They check your rights as a patient and as a participant in a study respected are , or - based on current knowledge - the balance [2] between risks and benefits is beneficial to participants, whether the study is scientifically relevant and ethically sound.

The ethics committees issue an opinion on this in accordance with the Belgian law of 7 May 2004.

Under no circumstances should you consider the positive advice of the Ethics Committees as an incentive to participate in this study .

Voluntary participation

Don't hesitate to ask any questions that come to mind before signing. Take the time to discuss it with a counselor if you wish.

You have the right not to take part in this study or stop the study , without a reason for having to give, even if you have previously agreed to participate in this study. Under no circumstances will your decision affect your relationship with the investigator , nor the quality of your further care.

If you agree to participate in this study, sign the consent form. The investigator will also sign this form and will confirm that he has provided you with the necessary information about this study. You will receive the copy intended for you.

For your safety, it is recommended to notify the investigator if you decide to discontinue your study .

Costs related to your participation

The sponsor has provided to reimburse the hospital for the time that the investigator and his / her team devote to the study , for the consultations that take place specifically in the context of the study and for all examinations that take place in the context of this study. are planned. The costs of the examined treatment (study medication) are also borne by the client.

If you decide to to the them study participate, so this brings no additional costs to you or your insurance company. The visits and procedures that belong to this study and that are mentioned in the description of the course of the study are paid by the client .

Confidentiality guarantee

Your participation in the study means that you agree that the medical researcher collects data about you and that the sponsor of the study uses it for research and in the context of scientific and medical publications.

You have the right to ask the investigator what information he / she has collected about you and what it is used for in the course of the study . This information pertains to your current clinical situation, but also to your medical history and to the results of studies performed to treat your health according to current healthcare standards. You have the right to view this information and to have it corrected if it were incorrect [3] .

The medical examiner is obliged to treat this collected data confidentially.

This means that he / she undertakes to never disclose your name , eg in the context of a publicati email or a conference and he / she will encrypt your data (your identity will be replaced by an identification in the study) before he / she passes them on to the administrator of the database

Throughout the clinical trial, the physician investigator and team will be the only individuals who can link the transferred data to your medical record[4] .

The transferred personal data does not include a combination of elements that allow you to identify yourself[5] .

The administrator of the research data appointed by the client cannot identify you on the basis of the transferred data. This person is responsible for collecting the data collected by all doctors and researchers participating in the study and for processing and protecting that data in accordance with the Belgian law on the protection of privacy.

To monitor the quality of the study , your medical record may be viewed by persons bound by professional secrecy, such as representatives of the ethics committees , the sponsor of the study, or an external audit firm . This can only happen under strict conditions, on the r is the responsibility of the physician-researcher and under his / her supervision (or one of his / her research staff) .

The (coded) research data can be passed on to Belgian or other regulatory authorities , to the relevant ethics committees , to other doctors and / or institutions that collaborate with the client .

They can also be passed on to other sites of the client in Belgium and in other countries where the standards regarding the protection of personal data can be different or less strict[6] . This is always done in coded form as explained above .

Your permission so in this study participate also means that you agree that your encrypted medical data be used for purposes of this information sheet describes standing and they transferred to the abovementioned persons and / or institutions.

The client will use the collected data in the context of the study in which you participate .

If you withdraw your consent to participate in the study , the encrypted data already collected before your withdrawal will be retained . This guarantees the validity of the study. There is no new data to the client will be by passed.

Insurance

Every participation in a study poses a risk, however small . The client is - even if there is no error - liable for the damages that the participant or in case of death his / her beneficiaries , rise and which is directly or indirectly related to its participation in the study . You must do so no error detection. The client has taken out insurance for this liability [7] .

Ethias NV

Prins-Bisschopsingel 73

3500 Hasselt

Policy number: **45,197,381**,

We therefore request that you report any new health problems to the investigator. He / She can provide you with additional information about possible treatments

If the physician-researcher believes that there is a link to the study is possible (there is no connection with the study on damage caused by the natural course of your illness or due ge experienced side effects from your standard treatment), he / they inform the principal of the study who will start the declaration procedure with the insurance. He or she will appoint an expert to assess the link between your new health concerns and the study , if she considers it necessary .

In the event of disagreement with the medical examiner or with the expert appointed by the insurance company , and whenever you deem it necessary , you or your beneficiaries in the event of death may sue the insurer directly in Belgium (name of insurance, policy number, contact details) .

The law provides that the subpoena of the insurer may be brought before either the court of the place where the harmful offenses occurred, or the court of your place of residence, or the court of the seat of the insurer.

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[1]

[2]

[3] These rights are determined by the Law of 8 December 1992 on the protection of privacy with regard to the processing of personal data and by the Law of 22 August 2002 on patient rights.

[4] For clinical studies, the law requires that you maintain a record of your record for 20 years. In the case of a study medicine for an innovative therapy that uses human body material, this period is a minimum of 30 years and a maximum of 50 years in accordance with the Belgian law of 19 December 2008 on the use of human body material and the applicable Royal Decrees . .

[5] The study results database therefore does not relate to elements such as your initials, gender and full date of birth (dd / mm / yyyy).

[6] The client agrees to the terms of the European Directives to and the Belgian legislation on the protection of privacy respected .

[7] In accordance with Article 29 of the Belgian W et on experiments on the human person (May 7, 2004)