ISRCTN37558313 https://doi.org/10.1186/ISRCTN37558313

Creatine supplementation to treat "muscle wasting" in rheumatoid arthritis patients

Submission date
07/01/2013

Recruitment status
No longer recruiting

Registration date
25/03/2013

Overall study status
Completed

Last Edited
06/01/2017

Condition category
Musculoskeletal Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English Summary
Background and aims
Rheumatoid arthritis (RA) patients typically experience a significant loss of muscle. This reduces their ability to complete daily tasks and increases disability, as well as increasing the risk to infection and other illness. Exercise is most effective for increasing muscle size and strength, but it is time consuming, expensive and hard work, meaning uptake and adherence to appropriate exercise is poor. Consequently, widely acceptable alternative treatments are required. This study is looking at a food supplement called creatine. Creatine, most often found in meat and fish, make up an essential part of the systems that provide energy to the muscles for movement and exercise. The creatine supplement will be provided as a fruit flavoured powder that participants will mix with water and drink, much like a fruit squash. In healthy individuals, supplementation with creatine increases muscle size and improves physical function and quality of life. The aim of this study is to investigate whether RA patients supplementing creatine enjoy the same benefits.

Who are the participants?
We aim to test 50 patients with who have stable and controlled RA, are over age 18, and have normal kidney function.

What does the study involve?
50 participants will be given a powdered supplement to take for 12 weeks; this supplement will either be creatine or a placebo (a regular fruit flavoured powder that has no benefits). Participants will be randomly allocated to a group and will not be told which supplement they are taking until the end of the trial. The supplement will be taken as a drink 4 times a day for the first 5 days, and then once a day for the remainder of the 12 weeks. When mixed with water, the creatine and placebo supplements have the same appearance and taste. Since the principal study investigator will not know which groups participants are allocated to, this study by design is double-blinded.
Participants will be asked to attend Bangor University 4 times to have a battery of tests.
The four testing points are:
(1) before they start supplementation
(2) after the 5 days loading
(3) at completion of the 12-weeks of supplementation

(4) 12 weeks following withdrawal of the supplementation.
At all four testing points (1-4) body fat and muscle size (body composition), physical function, and fitness (aerobic capacity of your heart and lungs to transport oxygen to the exercising muscles) will be tested. In addition, quality of life questionnaires will be completed, RA disease activity will be assessed, and blood samples will be taken. Muscle samples (muscle biopsy) will be obtained from those who volunteer to provide them, at baseline and post-treatment (test points 1 and 3).
Body fat and muscle size (body composition) will be assessed using a type of X-ray called dual-energy X-ray absorptiometry (DXA) and by looking at body water levels (Bioelectrical Impedance). DXA allows the research team to estimate the amount of lean tissue (muscle) and fat that is in the body. Both procedures are safe and completely painless.
Physical function will be assessed using the following tests:
1) strength tests the knee extensor muscles (quadriceps) and hand-grip
2) the Up-and-Go Test (UG) - For the UG, participants are required rise from a seated position on a fixed chair, walk forward to a cone placed 8ft (2.44 m) away, and return to the chair and a seated position.
3) the sit-to-stand in 30 sec test (SST-30) - For the SST-30 participants will rise from the same seated position as during the UG as many times as possible in 30 s whilst keeping their arms folded across the chest.
4) 50-ft walk test - During the 50-ft walk test, time taken to complete the walk along a straight line marked by cones is recorded
5) To assess fitness participants will complete a step test. During the test participants are required to step up and down a 10-inch step at a tempo controlled by a metronome for three x three-minute stages or until the target heart rate (65% of predicted maximum heart rate) is achieved. This test will normally last 3 minutes and involves only moderate levels of exertion.

What are the potential benefits and risks of participating?
We expect that taking creatine supplements will increase muscle strength and improve physical function (including the ability to perform daily tasks).
If creatine proves effective in RA patients, the participants in the control group will receive 12weeks supply of creatine at the completion of the study. Participants will also be informed about their body composition and fitness levels and will receive advice on how to improve these. As part of the standard DXA we can look at participants bone density, and this can inform us of a disease in the bone than can increase the risk of fractures (osteoporosis) that they might not know they had. RA significantly increases the risk of having osteoporosis.
A disadvantage of taking part is the time commitment required to participate in the study. Whilst taking the supplement drink will be quick and simple, there are 4 testing sessions which may last 2 hours in which participants must attend at Bangor University. Any travel expenses participants incur for participating in this study will be paid for.
Creatine supplementation will cause some weight gain; in the short-term this is due to water retention by the muscle and in the long-term this is due to an increase in muscle size. Previous research, including research with RA patients, has found no adverse side effects linked to the creatine supplementation. There are anecdotal reports of creatine supplementation causing muscle cramps, stomach and heart problems; however no evidence has ever linked these directly to creatine supplementation.
There is also a slight possibility that the muscle biopsy site could bruise and be sore but this is quite rare and most people report only a short term slight ache following biopsy.
There is also limited exposure to radiation (emission of energy) from the DXA scan; roughly equivalent to the radiation absorbed by standing outside for 48 hours. However, because of this radiation pregnant women are excluded from the study.

Where is the study run from?
The study is being undertaken by the School of Sport, Health and Exercise Sciences (SSHES) at Bangor University, Wales, in association with the Rheumatology Department in North Wales.

When is the study starting and how long is it expected to run for?
The study started in January 2013. We hope to finish the study within an 18 month time frame, with recruiting open for a year or until 50 patients have been found.

Who is funding the study?
The study is being funded by Betsi Cadwalader University Health Board.

Who is the main contact?
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Contact information

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Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Can creatine supplementation improve body composition and physical function in rheumatoid arthritis patients? A randomised controlled pilot trial

Study hypothesis
Rheumatoid arthritis (RA) is an autoimmune disease with no known cause. It typically presents itself in the form of inflamed swollen joints causing tenderness and pain to the patient. Underlying this inflammation lies progressively severe joint destruction, specifically to the bone and cartilage around the synovium. RA can lead to several co-morbidities such as muscle wasting, cardiovascular disease, diabetes, osteoporosis, infection and fatigue.

Rheumatoid arthritis patients are typically muscle wasted and weaker than age- and gender-matched healthy individuals. This muscle loss reduces physical capability and increases disability, as well as increasing vulnerability to infection, morbidity and mortality. High intensity exercise is very effective for increasing muscle mass; however, uptake and adherence to this is poor, so widely acceptable alternatives are required.

In healthy individuals nutritional supplementation with creatine (Cr) increases muscle size and strength and improves physical function. This study will investigate whether RA patients benefit similarly. We hypothesise that Cr will prove efficacious in improving body composition, physical function and quality of life of RA patients; and therefore will provide an easily administered, widely acceptable and inexpensive treatment option that significantly improves muscle mass and physical function, and reduces patient disability and, potentially, morbidity.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. North Wales Research Ethics Committee West, 29/10/2012, trg: 12/WA/0320
2. R&D Internal Review Panel West, 01/11/2012, ref: 110850

Study design
Double blind randomised placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Condition
Rheumatoid Arthritis

Interventions

The intervention will be of a nutritional supplement: creatine. Participants will be randomly assigned to either a Cr or placebo supplementation group.

12 week oral Cr supplementation with a subsequent 12 week follow up.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Creatine

Primary outcome measure
Objectively assessed whole body function - measured via the objective physical functional tests at Baseline, Day 6. Week 12 and Week 24

Secondary outcome measures
1. Body composition - measured via Dual-energy X-ray absorptiometry (DEXA) scan at all time points - Baseline, Day 6. Week 12 and Week 24
2. Muscle strength - measured via the objective physical functional tests at Baseline, Day 6. Week 12 and Week 24
3. Muscle biochemistry - analysed from fasting blood samples taken at Baseline, Week 12 and Week 24. Also analysed from muscle biopsy's (if consented) taken at Baseline and Week 12.

Overall study start date
01/07/2012

Overall study end date
01/03/2015

Eligibility

Participant inclusion criteria
All volunteers have to:
1. Fulfill the American Rheumatism Association 1987 revised criteria for the diagnosis of RA
2. Be functional class I or II
3. Be age 18 years or over, either sex

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex

Both

Target number of participants
50 RA patients

Participant exclusion criteria
All volunteers must not:
1. Be cognitively impaired
2. Have any other cachectic diseases and any condition preventing safe participation in the study
3. Have a glomerular filtration rate above 60mL/min/1.73m2, assessed from medical records, and no other evidence of kidney damage
4. Be taking drugs or other nutritional supplements known to increase muscle mass
5. Be participating in regular and intense physical training program
6. Be pregnant

Recruitment start date
01/02/2013

Recruitment end date
01/02/2014

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Bangor University
School of Sport, Health and Exercise Sciences
George Building
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LL57 2PZ

Sponsor information

Organisation
Bangor University (UK)

Sponsor details
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Sponsor type
University/education

Website
http://www.bangor.ac.uk/

ROR
https://ror.org/006jb1a24

Funder(s)

Funder type
Charity

Funder Name
Organisation BCUHB Small Grants Committee (UK)

Results and Publications

Publication and dissemination plan
Planned publication of results and presentation at the British Society Rheumatology conference.

Intention to publish date
31/12/2016

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Andrew Lemmey (a.lemmey@bangor.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/06/2016		Yes	No