ISRCTN49496801 https://doi.org/10.1186/ISRCTN49496801

Modified citrus pectin as therapy in heart failure

Submission date 28/05/2012	**Recruitment status** Stopped	[X] Prospectively registered [ ] Protocol
Registration date 09/07/2012	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 18/04/2019	**Condition category** Circulatory System	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Chronic heart failure (HF) is a leading cause of death and disability, despite great advances in medical, interventional and device therapies. Patients suffering from heart failure often have raised levels of a substance in their blood known as Galectin-3. Studies have shown that Galectin-3 controls the production of a protein in the body called collagen. Collagen is known to accumulate within tissues, causing cirrhosis and fibrosis (the collection of fibrous deposits), which if severe enough can cause scarring and damage to some of the bodys organs, including the heart. This damage could, if severe enough, lead to the heart not functioning properly. Reducing the levels of Galectin-3 in the body could therefore have an important role in improving the health of patients suffering from heart failure. The harmful effects of Galectin-3 can be blocked by Modified Citrus Pectin (MCP). MCP is available to buy from a variety of retailers (health shops and supermarkets) and is made from the peel and pulp of citrus fruits, such as oranges. The aim of our study is to test if MCP could be helpful as an additional treatment for patients with chronic HF. In order to prove this we need to carry out a study to compare MCP with a placebo (dummy) tablet.

Who can participate?
You should be at least 18 years old, have a clinical diagnosis of heart failure, be attending the Hull and East Yorkshire Hospitals NHS Trusts heart failure service, and have high levels of galectin-3 in your blood (we will do a blood test to find this out).

What does the study involve?
If you are suitable to enter the study following a screening visit, you will be given a prescription to take either MCP or a matched placebo for 18 weeks. Which capsule you take will be decided randomly like tossing a coin. After that period you will take the other capsule for another 18 weeks. It means you will take both the active and placebo in turn during your time in the study. This way, we directly compare the effect of the active capsule and the placebo on your health. During the study, we will use echocardiography to take ultrasound pictures of your heart to look for any physical changes such as structural changes and how efficiently the heart pumps. We will also take some blood samples to look at certain biomarkers (natural substances in your blood associated with the severity of heart failure) and to see if Galectin-3 levels are reduced by the capsules. Some of the blood samples will be analysed by our research partners in Scotland. These samples will be coded so that they cannot be traced to you. We will give you some dietary sheets to fill out each day.

What are the possible benefits and risks of participating?
It is not known whether taking MCP has any direct benefits to your health. This is the purpose of the study, and as such you should assume that there are no direct benefits to you in participating in this study. We hope that the results of this study will help others in the future. MCP contains fibre which may cause transient minor stomach upset, including wind, but has no lasting side-effects. MCP may raise levels of a substance in the body called potassium. We will provide advice about how best to prepare your meals to help with this and we will regularly measure levels of potassium in your blood so that this does not become a problem for you. Providing a blood sample can cause bruising and soreness.

Where is the study run from?
The study is run from the Castle Hill Hospital in Cottingham, East Yorkshire.

When is the study starting and how long is it expected to run for?
The study will start in 2015 and will run for 2 years.

Who is funding the study?
We are applying for funding from the British Heart Foundation (UK).

Who is the main contact?
Kenneth Wong
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Contact information

Type(s)
Scientific

Contact name
Dr Kenneth Wong

Contact details
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Modified citrus pectin as Anti-Galectin-3 therapy In heart Failure Trial (MAGnIFicenT): a pilot randomised study of the effects of modified citrus pectin on biomarkers of collagen turnover and left ventricular function in optimally medicated patients with heart failure

Acronym
MAGnIFicenT

Study objectives
Current hypothesis as of 27/10/2014:
The present study is intended as a pilot and feasibility study of using Modified Citrus Pectin (MCP) as an adjunctive nutritional therapy in heart failure. We aim to investigate the following hypotheses:
1. MCP inhibits galectin-3 mediated adverse remodelling resulting in a reduction of , or smaller increase in, N-terminal prohormone of brain natriuretic peptide (NT-proBNP).
2. MCP reduces collagen turn-over in patients with elevated baseline galectin-3 levels.
3. MCP improves left ventricular systolic and/or diastolic function and reduces left ventricular size and hypertrophy.
4. The effects of MCP on serial measurements of Galectin-3, NT-proBNP, fibrosis biomarkers, and anti-galectin assay are seen early (6 weeks compared with 18 weeks).

Previous hypothesis:
The present study is intended as a pilot and feasibility study of using Modified Citrus Pectin (MCP) as an adjunctive nutritional therapy in heart failure. We aim to investigate the following hypotheses:
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2. MCP reduces collagen turn-over in patients with elevated baseline galectin-3 levels.
3. MCP improves left ventricular systolic and/or diastolic function and reduces left ventricular size and hypertrophy.
4. MCP improves exercise capacity and left ventricular function during exercise.
5. The effects of MCP on serial measurements of Galectin-3, NT-proBNP, fibrosis biomarkers, and anti-galectin assay are seen early (6 weeks compared with 18 weeks).

On 28/10/2014 the following changes were made to the trial record:
1. The study design was changed from 'Controlled randomized single-centre cross-over study with blinded assessment of outcome' to 'Controlled randomized double-blind single-centre cross-over study'.
2. The target number of participants was changed from 50 to 100.
3. The sources of funding field was changed from 'BG Medicine Inc (USA) and University of Hull (UK)' to 'We are applying to the British Heart Foundation for funding'
4. The anticipated start date was changed from 01/09/2012 to 01/01/2015.
5. The anticipated end date was changed from 01/08/2013 to 01/01/2017.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Yorkshire and the Humber Bradford Leeds Research Ethics Committee, 04/09/2014, REC ref: 12 /YH/0105

Study design
Controlled randomized double-blind single-centre cross-over study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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

Health condition(s) or problem(s) studied
Heart failure

Interventions
Current interventions as of 27/10/2014:
MCP (6) capsules three times a day (total daily intake 14.4 g) vs matched placebo. The placebo is a microcrystalline cellulose placebo in matching opaque capsule (vegetable capsule: natural vegetable cellulose, titanium dioxide, and water) with equivalent sodium (2-5%) and potassium (7-11%).

Previous interventions:
MCP (6) capsules three times a day (total daily intake 14.4g) vs placebo (Glucotabs) 1 x 4mg tablet three times per day (total daily intake 12g).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Modified citrus pectin

Primary outcome measure
Current primary outcome measures as of 27/10/2014:
1. Effect of MCP supplementation on NT-proBNP (primary endpoint of the study). Natriuretic peptides such as NT-proBNP increase in response to myocardial stretch
2. Effect of MCP supplementation on collagen turnover and extracellular remodelling (PICP)

Previous primary outcome measures:
1. Effect of MCP supplementation on NT-proBNP (primary endpoint of the study). Natriuretic peptides such as NT-proBNP increase in response to myocardial stretch
2. Effect of MCP supplementation on collagen turnover and extracellular remodeling
3. Global longitudinal strain

Secondary outcome measures
Current secondary outcome measures as of 27/10/2014:
1. Galectin-3, a mediator of heart failure development and progression secondary to myocardial fibrogenesis. Its levels are unaffected by myocardial stretch
2. Effect on microalbuminuria
3. Effect on vascular function and haemodynamics (ENVERDIS with GTN sublingually and NEXFIN)
4. Effect on clinical endpoints will include 6-minute walk distance
5. Effect on ventricular remodelling (with left ventricular end diastolic volume as the main secondary endpoint), and ventricular function with the main secondary endpoint as left ventricular global longitudinal strain, which is thought to be more reproducible (with less potential of measurement error) as well as more sensitive than ejection fraction (Pellicori et al. 2013)
6. Nutritional intake and weight change, this is part of safety monitoring to minimise the risk of undernutrition and cardiac cachexia which will be assessed and early nutrition support will be initiated as required

Previous secondary outcome measures:
1. Procollagen type I N-terminal propeptide (PINP) - main secondary endpoint of fibrosis
2. Procollagen type III N-terminal peptide (PIIINP) - marker of cardiac collagen synthesis
3. Type I collagen telopeptide (ICTP) - marker of cardiac collagen synthesis
4. Matrix metalloproteinase-1 (MMP-1) - marker of cardiac collagen degradation
5. Tissue inhibitor of metallopeptidase 1 (TIMP1) - marker of cardiac collagen degradation
6. Left ventricular end diastolic volume
7. Ejection fraction

Overall study start date
01/01/2015

Completion date
01/01/2017

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Patients diagnosed with heart failure, who had been or are currently on diuretics, substantiated by a raised NT-pro BNP and /or evidence of left ventricular systolic or diastolic dysfunction
2. Plasma galectin-3 level > 17.8 ng/mL
3. Therapy with an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and beta-blocker (BB) (unless documented intolerance) for at least 3 months duration.

4. Aged over 18
5. If female, not of childbearing age or, if of childbearing age and sexually active, willing to use birth control.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
100

Key exclusion criteria
1. Current decompensated heart failure
2. Inability to provide informed consent
3. Use of eplerenone or spironolactone within 30 days of randomization or for more than 7 days within the previous 6 months (because they suppress galectin-3 effects and have potassium sparing effects which could increase the risk of hyperkalemia)
4. Pregnant or breast-feeding women

Date of first enrolment
01/01/2015

Date of final enrolment
01/01/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Department of Cardiology
Cottingham
United Kingdom
HU16 5JQ

Sponsor information

Organisation
Hull and East Yorkshire Hospitals NHS Trust (UK)

Sponsor details
Daisy Building
Castle Hill Hospital
Castle Road
Cottingham
England
United Kingdom
HU16 5JQ

Sponsor type
Hospital/treatment centre

Website
http://www.hey.nhs.uk/

ROR
https://ror.org/01b11x021

Funder(s)

Funder type
Charity

Funder Name
We are applying to the British Heart Foundation (UK) for funding

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration