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The effects of N-acetyl cysteine (NAC) in patients with heart failure

Submission date 30/09/2005	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 30/09/2005	**Overall study status** Completed	
Last Edited 11/07/2016	**Condition category** Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N0084144632

Study information

Scientific Title
The effects of N-acetyl cysteine (NAC) in patients with heart failure: a double-blind, placebo-controlled, randomised cross-over trial

Study objectives
The principle aim of the study is to determine whether the drug N-acetyl cysteine (NAC) is of benefit in patients with known heart failure. Specifically we will be looking for an improvement in the ejection fraction of the left ventricle which is a measure of the heart's ability to contract.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Randomised controlled trial

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 contact details to request a participant information sheet

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

Interventions
We intend to conduct a double blind, placebo-controlled, randomised, cross-over trial comparing NAC (600 mg once daily [od], effervescent tablet Flumicil®) to placebo in patients with persistent major left ventricular systolic dysfunction and symptomatic heart failure despite maximal conventional therapy for heart failure. There will be a two-week run in phase followed by two treatment periods each lasting 12-weeks with a 4-week wash out period between phases.

The cross-over design framework is one that we routinely use within our department. Patients will be selected from our outpatient heart care clinics and will be asked to participate in the trial after a full explanation of the medication to be used and the measurements involved in the trial.

Prior to the run-in phase, patients' symptoms and functional capacity will be assessed using standard departmental symptom and Minnesota quality of life questionnaires, a six minute corridor walk test and a treadmill 'ramp' exercise test with metabolic gas exchange. Peripheral vascular function will be assessed using pulse wave velocity analysis (Vingmed 5 ultrasound machine, Sony, with a GE NFLA 10 megaHertz MedVascular probe) before and after nitrolingual spray. Blood will be taken to assess standard haematology and biochemistry variables including, N terminal pro-BNP, TNF, IL-6, sTNFR1, sTNFR2. Oxidative stress will be assessed by the measurement of 8-iso PGF2. The effects on the myocardial interstitium will be assessed by measuring 3 degradation markers total membrane metalloproteinase 1 (MMP-1), total tissue inhibitor of metalloproteinase 1 (TIMP 1), and the MMP-1/ TIMP 1 complex. As well as 3 extra-cellular matrix serum markers pro-collagen type I carboxy-terminal peptide (P-I-CP), pro-collagen type I amino terminal peptide (P-I-NP), and pro-collagen type III amino terminal peptide (P-III-NP).

At the end of run-in, prior to randomisation, these tests will be repeated but instead of echocardiography, the patients will undergo cardiac cine-magnetic resonance imaging before and after injection of gadolinium with acquisition of late enhancement images. This will allow the myocardial substrate to be characterized as normal, scar or 'viable- but-with-reduced-contraction' using a 16 segment model. The relationship between myocardial substrate and treatment intervention will be analysed on a global and segmental basis. Baseline assessments will be repeated after 12-weeks, at the end of the washout phase (16 weeks) and at the end of study (28 weeks).

Though patients have not been directly involved in the design of the trial we have in our department a long record of patient education with regard to their condition and many of our patients are very keen to undertake such studies when the benefits and possible risks are discussed in a frank and honest manner.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
N-acetyl cysteine (Flumicil®)

Primary outcome measure
Improvement in left ventricular ejection fraction (LVEF), measured by cine-magnetic resonance imaging.

Secondary outcome measures
1. Symptoms
2. Exercise capacity
3. Natriuretic peptides
4. Serum creatinine
5. Vascular function

Overall study start date
01/04/2004

Completion date

01/04/2006

Eligibility

Key inclusion criteria
Blood samples will be taken to measure N-terminal pro-brain natriuretic peptide (NT-proBNP), tumour necrotising factor (TNF), interleukin-6 (IL-6), soluble tumour necrosis factor receptor 1 (sTNFR1), soluble tumour necrosis factor receptor 2 (sTNFR2). Oxidative stress will be assessed by the measurement of 8-epimer of Prostaglandin F2 (8-iso-PGF2). The effects on the myocardial interstitium will be assessed by measuring 3 degradation markers total membrane metalloproteinase 1 (MMP-1), total tissue inhibitor of metalloproteinase 1 (TIMP 1), and the MMP-1/TIMP 1 complex. As well as 3 extra-cellular matrix serum markers pro-collagen type I carboxy-terminal peptide (P-I-CP), pro-collagen type I amino terminal peptide (P-I-NP), and pro-collagen type III amino terminal peptide (P-III-NP).

They will be collected by Dr Windram and members of the nursing staff of the Department of Academic Cardiology Department.

Participant type(s)
Patient

Age group
Not Specified

Sex
Not Specified

Target number of participants
50

Key exclusion criteria
1. Asthma
2. Known intolerance to NAC
3. Serum creatinine greater than 200 mol/L

Date of first enrolment
01/04/2004

Date of final enrolment
01/04/2006

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Hull Royal Infirmary
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Sponsor information

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Funder(s)

Funder type
Government

Funder Name
The North and South Bank Research and Development Consortium (UK)

Funder Name
NHS R&D Support Funding (UK)

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