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The HeartCycle Nitrates Study - to assess the effectiveness of non-invasive devices in measuring responses to hydralazine with and without isosorbide mononitrate in heart failure patients

Submission date 14/03/2013	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol
Registration date 08/05/2013	**Overall study status** Completed	[ ] Statistical analysis plan [ ] Results
Last Edited 13/06/2019	**Condition category** Circulatory System	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims
We intend to investigate how good new non-invasive sensors are at detecting the response of the heart and circulation to single doses of two types of drug that have been in widespread use (nitrates and hydralazine), alone and in combination, for the management of heart failure. The effects of physiological manoeuvres such as standing and leg raising on blood circulation will also be studied. The focus of this study is to assess the ability of non-invasive sensors to detect and track changes in congestion and blood circulation.

Who can participate?
Male and female heart failure patients aged over 18, and a control group of patients with stable coronary artery disease or high blood pressure without heart failure.

What does the study involve?
In the heart failure group, we will investigate the ability of non-invasive sensors to detect changes in congestion and blood circulation in response to changes in two drugs that are recommended for the management of heart failure, although not used routinely. Patients in this group will be studied on four occasions at least 72 hours apart. Each study day lasts up to about eight hours. Patients will be asked to avoid large changes in daily diet in the three days before each study period. On study days patients will be asked to take their usual morning heart failure medications apart from loop diuretics. Patients will be asked to bring their diuretic with them to be given immediately after being weighed. They will then have a 60-minute investigation period using wearable, non-invasive monitoring devices, many of which are already commercially available. Then the following drugs will be administered to the patient in a random order:
1. No extra medication.
2. A tablet of isosorbide mononitrate.
3. A tablet of hydralazine.

4. On the final study day both isosorbide mononitrate and hydralazine, unless the patient had any problems with side effects from these medicines on the previous study days, in which case this study day will be omitted.
The control patients will be studied on a single occasion with their usual daily treatment withheld for 4 hours. Only physiological manoeuvres will be studied and not drug therapy.

What are the possible benefits and risks of participating?
Not provided.

Where is the study run from?
Hull York Medical School, Cottingham, UK.

When is the study starting and how long is it expected to run for?
The study will run from April to September 2013.

Who is funding the study?
European Union 7th Framework Programme (Belgium).

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

Study information

Scientific Title
Assessing the acute haemodynamic effects of hydralazine and nitrates, singly and in combination, in patients with chronic heart failure using novel non-invasive sensor technologies

Acronym
HeartCycle Nitrates Study

Study objectives
The main study objective is to investigate the ability of a variety of noninvasive sensors to detect changes in haemodynamics (e.g. blood pressure, heart rate, cardiac output, vascular resistance and venous pressure) and congestion induced by hydralazine and isosorbide mononitrate, singly and in combination.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee: Yorkshire & The Humber - Leeds West, Approval date: 12 March 2013, Ref: 13 /YH/0059

Study design
Open label randomised study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Screening

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
Chronic heart failure

Interventions
Randomisation will be by blocks using an unequal block size.

Control group 10 patients with hypertension or coronary artery disease but not heart failure. The control group does not receive pharmacological therapies.

There other group is the heart failure group (16). Every patient in this group receives all the therapies in a random sequence (unless if there are side effects).

Comparison being made by administering the therapies in random order is to assess the ability of non-invasive sensors to detect and reliably track cardiovascular physiological changes in response to the administered therapy.

The focus of this study is to assess the ability of these devices to detect more subtle changes in congestion and haemodynamics that might be used to guide therapy and thus aid our ability to improve cardiovascular health maintenance rather than just detect and manage crises.

In the heart failure group (16 patients), we will investigate the ability of non-invasive sensors to detect changes in congestion and haemodynamics in response to changes in two vasodilators that are recommended in therapeutic guidelines for the management of heart failure, although not used routinely. Patients in this group will be studied on four occasions at least 72 hours apart. Each study day lasts up to about eight hours. Patients will be asked to avoid large changes in daily diet in the three days before each study period. As part of the consent process, patients will be introduced to the sensors and manoeuvres required in the study. On study days patients will be asked to take their usual morning heart failure medications apart from loop diuretics. Patients will be asked to bring their diuretic with them to be given immediately after being weighed. They will then have a 60 minute investigation period involving the assessment of haemodynamic variables using novel, wearable, non-invasive monitoring devices, many of which are already commercially available and CE marked. These include devices measuring: real-time central venous pressure and cardiac output (Mespere Venus 1000); blood pressure (Nexfin); lung-congestion (Philips BIM); pulse wave velocity (ENVERDIS) and expiratory nitric oxide (INNOCOR). Then the following pharmacological therapies will be administered to the patient in random order:
1. No extra medication
2. A tablet of isosorbide mononitrate (20mg dose)
3. A tablet of hydralazine (25mg dose)
4. (On the final study day) both isosorbide mononitrate (20mg) and hydralazine (25mg) unless the patient had any problems with side effects from these medicines on the previous study days, in which case this study day will be omitted.

These measurements will be compared to those obtained using physical examination, cardiac ultrasound and plasma concentrations of NT-proBNP.

In addition, 10 control patients with stable coronary artery disease or hypertension without heart failure or gross cardiac dysfunction will be studied on a single occasion with their usual daily treatment withheld for 4 hours. Only physiological manoeuvres will be studied and not pharmacological therapy.

The results will form the basis of a clinical calibration protocol that may become a routine part of home telemonitoring services. The information will also be used to design intelligent algorithms to remotely optimise the patients cardiac status.

Intervention Type
Device

Phase
Not Applicable

Primary outcome measure
No single primary outcome. This is a pilot study to investigate the ability of novel noninvasive sensors to detect and track the acute haemodynamic effects of medication (hydralazine and/or hydralazine or combination) and a series of physiological manoueuvres.

Secondary outcome measures
No secondary outcome measures

Overall study start date
01/04/2013

Completion date
20/09/2013

Eligibility

Key inclusion criteria
1. Male and female, 18 y.o. plus, legally able to provide written informed consent
2. Clinical diagnosis of Heart Failure
3. Objective evidence of cardiac dysfunction
3.1. NTproBNP >200ng/L and at least one of the following:
3.2. Left ventricular ejection fraction (≤45%)
3.3. Left atrial dimension >40mm
4. Treated with at least 40mg/day of furosemide or 1mg/day of bumetanide
5. Receiving other guideline indicated therapy for heart failure
6. Patients should be in sinus rhythm. Atrial fibrillation may reduce accuracy of some signals

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
26 (16 with heart failure; 10 control patients with stable coronary artery disease or controlled hypertension)

Key exclusion criteria
1. Patients with implanted pacemakers or defibrillators
2. Severe aortic or mitral valve disease
3. Breathlessness at rest or on minor exertion

4. Chest pain at rest or on mild or moderate exertion
5. Patients with unstable heart failure or 'brittle' diabetes
6. Patients who are known to be intolerant [including patients using Phosphodiesterase type 5 (PDEV) inhibitors] of nitrates or hydralazine

Date of first enrolment
01/04/2013

Date of final enrolment
20/09/2013

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)

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Sponsor type
Hospital/treatment centre

Website

http://www.hey.nhs.uk

ROR
https://ror.org/01b11x021

Funder(s)

Funder type
Government

Funder Name
Seventh Framework Programme ref: FP7-ICT-2007-1, Proposal No 216695

Alternative Name(s)
EC Seventh Framework Programm, European Commission Seventh Framework Programme, EU Seventh Framework Programme, European Union Seventh Framework Programme, EU 7th Framework Programme, European Union 7th Framework Programme, Siebten Rahmenprogramm, Séptimo Programa Marco, Septième programme-cadre, Settimo programma quadro, 7th Framework Programme, Seventh EU Framework Programme, FP7

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No