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IMPRESS-AF: Improved exercise tolerance in heart failure with preserved ejection fraction by spironolactone on myocardial fibrosis in atrial fibrillation

Submission date
14/01/2015

Recruitment status
No longer recruiting

Registration date
15/01/2015

Overall study status
Completed

Last Edited
17/12/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Atrial fibrillation is a heart rhythm problem (arrhythmia) which causes the heart to beat irregularly and often at an abnormally fast pace. In these cases, the heart is often unable to supply enough blood to the body (a condition called 'heart failure'). In about half of all heart failure patients the heart contracts reasonably well, but it does not relax properly because it is very stiff and so does not fill with sufficient blood between heart beats. These patients have a poor quality of life and a high risk of death, just as those heart failure patients who have hearts that contract poorly. There is a clear need to find beneficial therapies for such patients. The reason why patients with atrial fibrillation tend to have stiff hearts that fill poorly and develop heart failure is not known, but high levels of aldosterone have been suggested to play an important role. Aldosterone is normally produced by the kidney, travels in the blood, and has a wide range of affects throughout the body. We think that raised aldosterone levels may explain the stiffening of the heart and its poor filling in patients with atrial fibrillation and heart failure. The effects of aldosterone can be blunted with the drug spironolactone, and with this clinical trial we want to find out if giving spironolactone to patients with atrial fibrillation improves the way their hearts relax and so increases their ability to perform exercise and improving their quality of life.

Who can participate?
Adults aged 50 or over, with permanent atrial fibrillation and normal levels of the hormone called brain natriuretic peptide.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in group 1 are treated with spironolactone for two years. Those in group 2 are treated with a placebo for two years. We then measure each participants tolerance to exercise, assess their health-related quality of life, assess

the ability of the heart to relax (diastolic function measured by echocardiography) and also look at rates of hospitalisations (regardless of cause) during the trial. Participants are blinded to their group allocation.

What are the possible benefits and risks of participating?
The study treatment aims to improve exercise performance of quality of life of the participants. The study drug benefits from a very well established safety profile with possible side effects (such as increase in blood potassium) being usually mild and disappearing on stopping the drug.

Where is the study run from?
University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
January 2015 to October 2017

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Eduard Shantsila

Contact information

Type(s)
Scientific

Contact name
Dr Eduard Shantsila

Contact details
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Additional identifiers

EudraCT/CTIS number
2014-003702-33

IRAS number

ClinicalTrials.gov number
NCT02673463

Secondary identifying numbers
18080

Study information

Scientific Title
IMPRESS-AF: IMproved exercise tolerance in heart failure with PReserved Ejection fraction by Spironolactone on myocardial fibrosiS in Atrial Fibrillation - an open randomised double-blind parallel-group trial

Acronym
IMPRESS-AF

Study objectives
It is hypothesised that in symptomatic patients with permanent AF with normal BNP levels treatment with spironolactone will improve exercise tolerance as a surrogate for cardiovascular mortality/morbidity (primary outcome), and will improve quality of life and diastolic function, as well as reduce the rate of all-cause hospital admissions, and increase rate of spontaneous cardioversion to sinus rhythm (secondary outcomes).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Coventry and Warwickshire Research Ethics Committee, 07/01/2015, ref: 14/WM/1211

Study design
Two-year open randomised double-blind parallel-group single-site

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 patient information sheet

Health condition(s) or problem(s) studied
Treatment of symptomatic patients with atrial fibrillation with preserved ejection fraction

Interventions
The study patients will be randomised to receive spironolactone or placebo (i.e., two-arm study). Study patients and researchers will be blinded to treatment allocation. Placebo and spironolactone will be identical in appearance and packaging and manufactured as 25-mg tablets in accordance with national and international standards. Patients will be instructed to take the study drug at one capsule once daily after randomisation. There is no up-titration planned.

In the case of an increase in potassium level to 5.1-5.5 mmol/L or in the presence of other non-life-threatening side effects (such as gynaecomastia) the trial drug will be down-titrated to 25 mg each second day. In such cases, the investigators are advised to re-up-titrate the trial medication if the reason for down-titration has resolved. Routine laboratory surveillance of serum potassium, sodium, full blood count with hematocrit, and renal function will be done by protocol at each visit and within 1 week of any dose adjustment.

Drug toxicity will be defined as an increase in potassium level to >5.5 mmol/L. In the case of toxicity or suspected toxicity, the trial medication will be stopped for the duration of the trial, but the patient will be requested to attend the remaining follow-up visits.

The trial treatment will be administered during 2 years with no further follow-up planned.

The protocol calls for current optimised management of AF and any background cardiac pathology as per current guidelines.

Intervention Type
Drug

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

Primary outcome measure
Exercise tolerance (peak VO2 on cardio-pulmonary exercise testing); Timepoint(s): 2 years of treatment

Secondary outcome measures
1. Diastolic function measured by echocardiography; Timepoint(s): After 2 years of treatment
2. Exercise tolerance measured by 6-minute walking test; Timepoint(s): 2 years of treatment
3. Health-related quality of life (assessed using the validated questionnaires); Timepoint(s): After 2 years of treatment
4. Rates of all-cause hospitalisations; Timepoint(s): After 2 years of treatment
5. Sinus rhythm; Timepoint(s): After 2 years of treatment

Overall study start date
01/01/2015

Completion date
30/09/2017

Eligibility

Key inclusion criteria
1. Age 50 years old or over
2. Permanent AF as defined by the European Society of Cardiology (ESC) criteria
3. Normal BNP levels (<100 pg/mL)
4. Ability to understand and complete questionnaires (with or without use of a translator/translated materials)

Participant type(s)

Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 250; UK Sample Size: 250

Total final enrolment
250

Key exclusion criteria
1. Severe systemic illness with life expectancy of less than 2 years from screening
2. Left ventricular ejection fraction (LVEF) <50% (echocardiography)
3. Severe chronic obstructive pulmonary disease (COPD) (e.g., requiring home oxygen or chronic oral steroid therapy)
4. Severe mitral/aortal valve stenosis/regurgitation
5. Significant renal dysfunction (serum creatinine 220 µmol/L or above), anuria, active renal insufficiency, rapidly progressing or sever impairment of renal function, confirmed or suspected renal insufficiency in diabetic patients/ diabetic nephropathy
6. Increase in potassium level to > 5mmol/L)
7. Recent coronary artery bypass graft surgery (within 3 months)
8. Use of aldosterone antagonist within 14 days before randomisation
9. Use of or potassium sparing diuretic within 14 days before randomisation
10. Systolic blood pressure >160 mm Hg
11. Addison’s disease
12. Hypersensitivity to spironolactone or any of the ingredients in the product
13. Any participant characteristic that may interfere with adherence to the trial protocol

Date of first enrolment
01/01/2015

Date of final enrolment
31/12/2015

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University of Birmingham
Department of Cardiovascular Medicine
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Sponsor information

Organisation
University of Birmingham

Sponsor details
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

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?
Results article	results	01/07/2020	17/12/2020	Yes	No
HRA research summary			28/06/2023	No	No