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Rate control therapy evaluation in atrial fibrillation

Submission date 28/11/2016	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 29/11/2016	**Overall study status** Completed	
Last Edited 25/01/2021	**Condition category** Circulatory System	

Plain English summary of protocol

Background and study aims
Atrial fibrillation (AF) is a common heart condition that around 1 in 4 adults are at risk of developing. It is caused by a fault in the electrical control centre in the heart which is found in the upper right chamber (right atrium), causing it to fire erratically. These uncoordinated signals cause the heart to beat irregularly and often very fast (arrhythmia). Sufferers are typically elderly and often have a number of other medical conditions, including high blood pressure and heart failure. In addition, AF is a common cause of stroke, hospital admissions and early death, and leads to reduced quality of life. An important part of AF treatment is the control of heart rate however evidence as to which medication is the best for rate-control is and whether it can improve quality of life or heart function is currently lacking. The aim of this study is to find out which, of two treatments (digoxin or bisoprolol), improves quality of life and heart function.

Who can participate?
Adults aged 60 and over who have AF, symptoms of breathlessness, and ability to provide written, informed consent.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are treated with digoxin through a drip once a day for 12 months. Those in the second group are treated with bisoprolol through a drip once a day for 12 months. In both groups, the dosage will vary depending on each participant's clinical need. At the start of the study and then after 6 and 12 months, participants in both groups complete a number of questionnaires to assess their quality of life, heart monitoring to assess their heart function and blood testing to see how well their bodies are responding to treatment.

What are the possible benefits and risks of participating?
Although there may be no direct benefit to those participating, it is hoped that this study will benefit all future patients with atrial fibrillation. Patient will benefit from being seen more regularly than normal because they are taking part in a study and will have access to the expert study team. There is a small risk that having to take part in the questionnaires, tests and visits to the hospital might be an inconvenience. There is also a small risk of bruising or discomfort during blood tests.

Where is the study run from?
The study is run from Queen Elizabeth Hospital, Sandwell and West Midlands Hospital and Heartlands Hospital and takes place at general practitioners' practices in the Birmingham area (UK)

When is the study starting and how long is it expected to run for?
March 2016 to December 2019

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

Who is the main contact?
Dr Dipak Kotecha
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Study website
www.birmingham.ac.uk/rate-af

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2015-005043-13

IRAS number

ClinicalTrials.gov number
NCT02391337

Secondary identifying numbers
32563

Study information

Scientific Title
Evaluating different rate control therapies in permanent atrial fibrillation: a prospective, randomised, open-label, blinded endpoint study comparing digoxin and beta-blockers as initial rate control therapy. RAte control Therapy Evaluation in permanent Atrial Fibrialltion (RATE-AF)

Acronym
RATE-AF

Study objectives
The aim of this study is to compare two strategies of rate-control in patients with atrial fibrillation (AF), based either on initial treatment with digoxin or beta-blockers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands - Derby Research Ethics Committee, 18/07/2016, ref: 16/EM/0178

Study design
Randomised; Interventional; Design type: Treatment, Process of Care, Drug

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 to request a patient information sheet

Health condition(s) or problem(s) studied
Specialty: Cardiovascular disease, Primary sub-specialty: Other; UKCRC code/ Disease: Cardiovascular/ Other forms of heart disease

Interventions
Participants are be randomised to one of two groups in a 1:1 ratio by a computer generated and stratified minimisation algorithm:
Group 1: Participants receive Digoxin 62.5 – 250 micrograms once daily uptitrated according to

response and symptoms.
Group 2: Participants receive Bisoprolol 1.25 – 15 mg once daily uptitrated according to response and symptoms.
Patients in both groups will remain on treatment for 12 months as part of the trial.

The trial is testing the initial randomisation to either a digoxin or beta-blocker strategy. In both groups, additional therapy will likely be needed over the course of the trial.

Follow-up takes place at 6 and 12 months, and involves quality of life measurement, heart ultrasound (echocardiography), blood tests and assessment of function (questionnaires and a walking test).
Most patients will continue their treatment after the trial, according to their needs.

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Patient-reported quality of life is measured using the SF-36 physical component summary score at baseline and 6 months

Secondary outcome measures
1. Patient-reported quality of life is measured using SF-36 global and domain-specific scores, EQ-5D-5L summary index and visual analogue scale and AFEQT overall score at baseline, 6 and 12 months
2. Cardiac function is assessed by measuring echocardiographic left ventricular ejection fraction and diastolic function (E/e' and composite of diastolic indices) at baseline and 12 months
3. Six-minute walking distance is measured at baseline, 6 and 12 months
4. European Heart Rhythm Association (EHRA) functional class information is checked at baseline, 6 and 12 months
5. B-type natriuretic peptide (BNP) levels and other biomarkers of treatment response are measured using blood testing at baseline, 6 and 12 months
6. Heart rate control is measured using 24-hour ambulatory ECG at approximately 3 months

Overall study start date
23/03/2016

Completion date
31/12/2019

Eligibility

Key inclusion criteria
1. Adult patients aged 60 years or older
2. Permanent AF, characterised (at time of randomisation) as a physician decision for rate-control with no plans for cardioversion, anti-arrhythmic medication, or ablation therapy
3. Symptoms of breathlessness (New York Heart Association Class II or more)
4. Able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Planned Sample Size: 160; UK Sample Size: 160

Total final enrolment
160

Key exclusion criteria
Current exclusion criteria as of 22/06/2018:
1. Established clinical indication for beta-blocker therapy, e.g. myocardial infarction in the last 6 months
2. Known contraindications for therapy with beta-blockers or digoxin, e.g. a history of severe bronchospasm that would preclude use of beta-blockers, or known intolerance to these medications
3. Baseline heart rate history of atrioventricular node ablation
4. History of second or third-degree heart block
5. Supraventricular arrhythmias associated with accessory conducting pathways (e.g. Wolff-Parkinson-White syndrome) or a history of ventricular tachycardia or fibrillation
6. Decompensated heart failure (evidenced by need for intravenous inotropes, vasodilators or diuretics) within 14 days prior to randomisation
7. A current diagnosis of obstructive hypertrophic cardiomyopathy, myocarditis or constrictive pericarditis
8. Received or on waiting list for heart transplantation
9. Receiving renal replacement therapy
10. Major surgery, including thoracic or cardiac surgery, within 3 months of randomisation
11. Severe, concomitant non-cardiovascular disease (including malignancy) that is expected to reduce life expectancy

Previous exclusion criteria:
1. Established clinical indication for beta-blocker therapy, e.g. myocardial infarction in the last 6 months
2. Known contraindications for therapy with beta-blockers or digoxin, e.g. a history of severe bronchospasm that would preclude use of beta-blockers, or known intolerance to these medications
3. Baseline heart rate history of atrioventricular node ablation
4. Decompensated heart failure (evidenced by need for intravenous inotropes, vasodilators or diuretics) within 14 days prior to randomisation
5. A current diagnosis of obstructive hypertrophic cardiomyopathy, myocarditis or constrictive pericarditis
6. Received or on waiting list for heart transplantation
7. Receiving renal replacement therapy

8. Major surgery, including thoracic or cardiac surgery, within 3 months of randomisation
9. Severe, concomitant non-cardiovascular disease (including malignancy) that is expected to reduce life expectancy

Date of first enrolment
05/12/2016

Date of final enrolment
02/10/2018

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Queen Elizabeth Hospital
University Hospital Birmingham NHS Trust
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
City Hospital
Sandwell and West Birmingham Hospitals NHS Trust
Dudley Road
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B18 7QH

Study participating centre
Sandwell General Hospital
Sandwell and West Birmingham Hospitals
Lyndon
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B71 4HJ

Study participating centre

Birmingham Heartlands Hospital
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Sponsor information

Organisation
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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
The Chief Investigator will coordinate dissemination of data from this trial (likely publication mid-2019). All publications and presentations, including abstracts, relating to the main trial will be authorised by the RATE-AF Trial Management Group. The results of the analysis will be published in the name of the RATE-AF Collaborative Group in a peer reviewed journal (provided that this does not conflict with the journal's policy). Named authors must satisfy the International Committee of Medical Journal Editors (ICMJE) criteria for authorship (contribute to drafting of the article or revision for important intellectual content), provide timely approval of the final version to be published and supply detailed statements on any potential conflict of interest or financial relationship (http://www.icmje.org/). Members of the group who do not fulfil ICMJE criteria for authorship will be listed in the article appendix. Trial participants will be sent a lay summary of the final results of the trial, which will contain a reference to the full paper.

Intention to publish date
31/12/2020

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	20/07/2017		Yes	No
Results article	results	02/12/2020	25/01/2021	Yes	No
HRA research summary			28/06/2023	No	No