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Does allopurinol reduce thickening of the left ventricle of the heart in patients with treated hypertension?

Submission date
10/09/2014

Recruitment status
No longer recruiting

Registration date
03/10/2014

Overall study status
Completed

Last Edited
22/07/2019

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
People with high blood pressure are at increased risk of heart complications. One of the biggest problems is that the muscle wall of the heart thickens. The medical term for this is left ventricular hypertrophy (LVH). LVH makes the heart work less well less well and patients with LVH are at a 10 times greater risk of heart complications than those without it. A goal of treating high blood pressure is to reduce the strain on the heart and to try to decrease this thickening of the heart wall. However, even when blood pressure is treated and is under control, LVH can persist, and as there are no symptoms some people dont know they have it. Currently the only way to reduce LVH would be to lower blood pressure (BP) even further. This can cause side-effects from low BP such as dizziness and nausea. However, a drug, allopurinol used to treat gout, has been shown to reduce this thickening of the heart wall in patients who had kidney disease or diabetes. We now want to see if patients with high blood pressure and LVH may also benefit from treatment with allopurinol. If LVH can be reduced using allopurinol, this might be a new way to reduce cardiac risk in these patients without needing to lower BP even further.

Who can participate?
People over 18 with high blood pressure and LVH.

What does the study involve?
Participants are first screened for LVH by doing an ultrasound scan of the heart. This diagnosis is confirmed with a Magnetic Resonance Imaging (MRI) scan. This is a special scan of the heart using an MRI machine to measure the extent of thickening of the heart muscle before they start the trial. Participants are then randomly allocated into one of two groups. Those in group 1 are treated with allopurinol for a year. Those in group 2 are given a placebo (dummy pill) for the same time period. All the patients currently prescribed medication for their high blood pressure continue as normal on that. After the years treatment is complete, a second MRI scan of the heart is then done to compare the effects of the allopurinol with that of the placebo.

What are the possible benefits and risks of participating?
Participants are monitored closely during the study and seen by a doctor with a special interest

in cardiology at each study visit and their medication will be reviewed on a regular basis. The tests provide information about the function of the heart, kidneys and blood circulation. If any of these investigations, including information from the MRI scan of the heart reveal any new abnormality, this is discussed with the participants hospital consultant to refer them specialist clinic. If the results of the study are positive, it may change how patients with controlled high blood pressure and LVH are managed and it potentially will have a great impact on other such patients in the future. Side effects from taking allopurinol are very rare (less than 1 in 10,000 people) but include headache, stomach upset, drowsiness and anaemia. Having blood tests taken can cause some mild bruising. The flow mediated dilatation may cause temporary numbness. MRI scanning is very safe and does not use radiation but some may feel a bit closed in. The scanner is a bit noisy but participants are given ear protection which also plays music.

Where is the study run from?
Ninewells Hospital & Medical School, Dundee (UK)

When is the study starting and how long is it expected to run for?
September 2014 to July 2017

Who is funding the study?
British Heart Foundation (UK)

Who is the main contact?
Dr Christopher Gingles
c.r.gingles@dundee.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Jacob George

Contact details
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Additional identifiers

EudraCT/CTIS number
2014-002083-33

IRAS number

ClinicalTrials.gov number
NCT02237339

Secondary identifying numbers
2012CV15

Study information

Scientific Title
Does allopurinol regress left ventricular hypertrophy in patients with treated essential hypertension?

Acronym
ALLAY

Study objectives
Does allpourinol causes regression of left ventricular hypertrophy in patients with essential hypertension?

Ethics approval required
Old ethics approval format

Ethics approval(s)
East of Scotland Research Ethics Service, 27/06/2014, ref. 14/ES/0073

Study design
Randomised double-blinded placebo-controlled single-centre study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet: c.r.gingles@dundee.ac.uk

Health condition(s) or problem(s) studied
Essential hypertensives with left ventricular hypertrophy

Interventions
Treatment arm: Allopurinol 300mg daily for one month then 300mg twice daily for eleven months.
Placebo arm: Microcrystalline cellulose one tablet daily for one month then twice daily for eleven months.

Intervention Type
Drug

Phase
Not Applicable

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

Primary outcome measure
The change LV mass index with allopurinol versus placebo
Timescale: 12 months
Description: Baseline and repeat CMRI examinations at baseline (day 0) and after the final (12 month visit) on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of left ventricular mass. This single observer will analyse all the scans. The reproducibility of the left ventricular mass assessment using MRI will be derived for this observer. The change LV mass index in participants treated with allopurinol will be compared with placebo.

Secondary outcome measures
1. % change in brachial artery diameter and change in augmentation index with allopurinol versus placebo. Timescale: 12 months. Description: Flow mediated dilatation (FMD) of the brachial artery will be performed on two visits (baseline(day 0 and month 12) according to the guide-lines set by the International Brachial Artery Reactivity Task Force. FMD will be expressed as percent change in diameter relative to the baseline diameter at rest. Analysis of all FMDs will be performed on Brachial Analyser software by a single trained investigator. This investigator will be blind to allocated treatments. PWA and PWV will be determined in the arm by recording the radial waveforms and radial-carotid waveforms, respectively, at two visits (baseline and month 12) using the Sphygmocor system. The central augmentation index (AIx) will be corrected to a heart rate of 75 beats/min. A single trained investigator who is blind to the allocated treatment will perform the PWA and PWV.
2. Change in average 24 hour BP control with allopurinol versus placebo. Timescale: 12 months. Description: Patient will undergo 24 hour ambulatory BP monitoring after the screening and final visit (12 months) to assess the difference in blood pressure control with allopurinol versus placebo.
3. The change in C reactive protein (CRP), brain naturetic peptide (BNP), troponin I (TnI), oxidized lactate dehydrogenase (oxidized LDH) and Procollagen carboxyl end peptide (PICP) with allopurinol versus placebo. Timescale: 12 months. Description: Research bloods will be taken at vist 2 (day 0) and visit 7 (12months) and will compare changes between groups.
4. Measure a change in left ventricular (LV) mass, LV end systolic volume, LV end diastolic volume or LV ejection fraction.
Timescale: 12 months. Description: Baseline and repeat CMRI examinations at baseline (+/- 2 weeks) and after the final 12 month (+/- 2 weeks) visit will be performed on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of ventricular volumes (EDV, ESV, stroke volume), EF, and left ventricular mass. This single observer will analyse all the scans. The reproducibility of the left ventricular mass assessment using MRI will be derived for this observer. We will assess left ventricular (LV) mass, LV end systolic volume, LV end diastolic volume and LV ejection fraction in participants treated with allopurinol versus placebo.

5. The change in LV mass after subtracting the volume of scar with allopurinol versus placebo.
Timescale: 12 months
Description: Baseline and repeat CMRI examinations at baseline (+/- 2 weeks) and after the final 12 month (+/- 2 weeks) visit will be performed on a 3T Magnetom scanners (Siemens, Erlangen, Germany) using dedicated phase array cardiac coils. Analysis will be performed offline (Argus Software, Siemens) by a single blinded observer for the assessment of left ventricular mass and scar volume

Overall study start date
09/09/2014

Completion date
31/07/2017

Eligibility

Key inclusion criteria
1. Aged over 18 years
2. Previously diagnosed with essential hypertension
3. Been on stable antihypertensive therapy for at least 3 months prior to study screening
4. Have screening ABPM (or home based BP monitoring if ABPM not tolerated) with daytime average systolic <135mmHg or 24-hour average systolic ≤ 130mmHg
5. Have screening echocardiography based diagnosis of LVH based on ASE criteria (males >115g /m2, females >95g/m2)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
66

Total final enrolment
72

Key exclusion criteria
1. Documented intolerance to allopurinol
2. Left ventricular ejection fraction <45% on echocardiography screening
3. Severe aortic stenosis on echocardiography screening
4. Already had gout or currently on allopurinol
5. Severe hepatic disease
6. Renal disease; CKD class 3B or worse

7. On azathioprine, 6 mercaptopurine, or theophylline
8. Malignancy (receiving active treatment) or other life threatening diseases
9. Pregnant or lactating women
10. Any contraindication to MRI (claustrophobia, metal implants, penetrative eye injury or exposure to metal fragments in eye requiring medical attention)
11. Patients who have participated in any other clinical trial of an investigational medicinal product within the previous 30 days will be excluded
12. Patients who are unable to give informed consent
13. Any other considered by a study physician to be inappropriate for inclusion

Date of first enrolment
30/09/2014

Date of final enrolment
31/07/2017

Locations

Countries of recruitment
Scotland

United Kingdom

Study participating centre
Department of Clinical Pharmacology
Dundee
United Kingdom
DD1 9SY

Sponsor information

Organisation
The University of Dundee and NHS Tayside (UK)

Sponsor details
c/o Catrina Forde
Tayside Medical Sciences Manager
Ninewells Hospital & Medical School
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation 2012CV15 (UK)

Alternative Name(s)
the_bhf, The British Heart Foundation, BHF

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

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
The datasets generated during and/or analysed during the current study are/will be available upon request from Prof. Jacob George.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2019	22/07/2019	Yes	No
HRA research summary			28/06/2023	No	No