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Evaluation of blood pressure TREATment stratified according to Central Aortic Systolic Pressure (CASP) in young hypertensive patients: The TREAT CASP study

Submission date
08/11/2013

Recruitment status
No longer recruiting

Registration date
08/11/2013

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
Blood pressure (BP) is usually measured using a cuff inflated over the upper arm. BP exceeding a threshold value is indicative of hypertension (high blood pressure). However, the decision whether to treat hypertension is based on an additional assessment of future risk of heart disease, indicated by presence of existing heart or kidney disease, evidence of damage caused by BP, prediction based on cardiovascular (CV) risk calculators. Despite this, uncertainty remains about whether to treat young people with moderately elevated BP (stage 1 hypertension; BP 140-159/90-99mmHg). This is because young people are unlikely to have developed pressure-mediated damage and because risk factor calculators have little validity in young people. This uncertainty is recognised in the UK national treatment guidelines (NICE) which currently recommend leaving these people untreated but acknowledges that simple tools to better assess which younger people with stage 1 hypertension should receive treatment are required. This study aims to address this issue by looking at whether the way in which we measure blood pressure could be refined. Usual BP measurement assumes that pressure measured in the arm is uniform throughout the body. However, we know from previous studies that there is an increase of pressure with increasing distance moving away from the heart towards the periphery (i.e. towards the arm). Importantly, this amplification varies markedly between people, particularly between young people. This means that despite having the same moderately elevated BP measured over the arm, some young people may have elevated blood pressure near their heart, whilst others may have a near normal BP near their heart. Moreover, some studies have shown that BP measured near the heart is more relevant to CV risk than BP measured over the arm. Blood pressure near the heart can now be measured routinely using a modified blood pressure monitor. We wish to test whether BP near the heart can be used to identify young people with moderately elevated BP who are at increased CV risk and who should receive treatment.

Who can participate?
Men aged 18-54 years with stage 1 hypertension (BP 140-159/90-99mmHg) not receiving BP lowering therapy and with no other cardiovascular disease (diabetes, kidney disease) or BP-

related disease (changes to the blood vessels in the eye, left ventricular hypertrophy) can participate in the study.

What does the study involve?
Participating in this study will involve attending the research centre to undergo a number of clinical measurements. These include measurements of blood pressure over the arm, blood pressure near the heart (CASP), height, weight, body fat, electrical activity in your heart i.e. an electrocardiogram (EKG), documenting a medical and lifestyle history, standard clinical blood tests (for blood components including cells, iron, cholesterol, sugar, markers of liver and kidney function), standard clinical urine tests (diabetes, kidney function). When we have collected this data in 500 men with stage 1 hypertension, we will identify those with the highest and lowest CASP values (130 each). They will then be invited to undergo a detailed scan of their heart and arteries using MRI imaging. The remaining people in the middle groups for CASP will have completed the study. The men with the highest CASP values who underwent MRI scanning will then be asked to participate in a clinical study for twelve months. This study will compare blood pressure lowering (using standard BP lowering drugs) with usual clinical care (no treatment). Participants will be randomly allocated to blood pressure lowering or usual care. Participants will be asked to attend the research centre at regular occasions over the course of the year so we can check and record their BP and issue further medication where appropriate. At the same time, the men with the lowest CASP values who underwent MRI scanning will be asked to enter an observational follow-up study (one year) and will remain untreated for BP lowering. These people will be asked to attend the research centre on a number of occasions over the course of the year so we can check and record their BP. For the men in both groups, at the end of the one-year follow-up period we will repeat the MRI scan. This will allow us to find out whether BP lowering has a beneficial effect in changing the structure of the heart and arteries back towards the level seen in people with the lowest CASP values.

What are the possible benefits and risks of participating?
All participants will receive the results of their health check and cardiac MRI scan. The overall study results could help improve the future management of people with this condition. By taking part participants may be required to attend the research centre on a number of occasions over one year. Some people find MRI scanning an uncomfortable experience. Occasionally taking losartan (for blood pressure lowering) may be associated with changes to the chemical composition of blood (potassium) or with increased incidence of dizziness.

Where is the study run from?
This study will be run from the Clinical Research Facility at University College Hospital, London, UK.

When is the study starting and how long is it expected to run for?
November 2013 to December 2017

Who is funding the study?
This study is funded by the National Institute for Health Research (NIHR), UK.

Who is the main contact?
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Type(s)
Scientific

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Protocol serial number
14991

Study information

Scientific Title
Comparing standard blood pressure lowering therapy with usual care on left ventricular mass index by cardiac MRI in young men with stage 1 hypertension stratified by central aortic systolic blood pressure

Acronym
TREAT CASP

Study objectives
High blood pressure (BP) is a leading cause of heart disease and strokes and is a common chronic condition treated in primary care. National (NICE) guidance recommends treatment where BP exceeds 160/100mmHg (stage II hypertension). Treatment is also recommended for people with lower pressures (140-159/90-99mmHg, i.e. stage Ihypertension) but only in those with pre-existing cardiovascular disease (CVD) or at high risk of CVD. Importantly, there is uncertainty in treating younger people (aged <55 (changed from "<40 years" on 14/10/2016) with stage I hypertension. Indeed NICE has identified this group (~1 million people) as a key priority for research. Our study will investigate and test a mechanism to better identify those younger people with stage 1 hypertension who might most benefit from treatment. Using simple, non-invasive clinical methods, we have shown that BP measured conventionally in the arm does not accurately reflect the pressure near the heart known as the central aortic systolic pressure, (CASP), especially in younger people. Moreover, we have shown that CASP is a better predictor of stress on the heart and may better predict stroke and CVD compared to BP measured in the arm. Our study will apply this technology to young men (aged 18-54 years) with stage I hypertension. We will identify those men with stage 1 hypertension who have high CASP and distinguish them from men with stage 1 hypertension and low CASP. We hypothesise that those with high CASP will have early evidence of strain on the heart and will benefit from treatment. We will test this hypothesis using high resolution imaging (MRI) and by investigating the effects

of treatment for 1 year to see whether lowering CASP improves early heart and artery damage versus no treatment. Findings from this study may provide evidence for a better way to stratify younger people with early hypertension who would benefit most from treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London Bloomsbury NRES Committee, 03/06/2013, ref: 13/LO/0563

Study design
Both; Interventional and Observational; Design type: Not specified, Cross-sectional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Primary Care Research Network for England, Cardiovascular; Subtopic: Not Assigned, Cardiovascular (all Subtopics); Disease: All Diseases, Heart Failure

Interventions
130 participants identified from the screening cohort will take part in the clinical trial. These people will have the highest central aortic systolic blood pressure (CASP) values from the screening cohort and will have increased left ventricular mass index by cardiac MRI relative to those with the lowest CASP values. These people will be assigned to blood pressure lowering or usual care (no treatment) for 12 months follow-up. Simple randomisation will be used to assign participants to the treatment or usual care arms of the clinical trial via a computer-based assignment system.

The blood pressure lowering arm will use treatments recommended by national (NICE) guidance and licensed for use in this age group. Treatment will constitute an angiotensin receptor blocker (losartan 50mg once daily) for all ethnic groups other than for younger black men of African or Caribbean descent for whom a calcium antagonist (amlodipine 5mg once daily) will be used. Treatment will be titrated according to the CASP value rather than brachial BP values to achieve a CASP value of less than 120mmHg and/or at least a 5mmHg reduction in CASP from baseline. Treatment may be up-titrated (losartan 100mg once daily) or combination therapy (i.e. angiotensin receptor blocker plus calcium antagonist) may be used in order to achieve blood pressure target.

Participants in the clinical trial will be followed up over 12 months. During follow-up participants will return to the research centre on six occasions to allow for medication titration and to collect prescriptions for their study medication.

At the end of the 12 month follow-up period, participants will undergo a repeat cardiac MR scan.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
Left ventricular mass index; Timepoint(s): Baseline and study end (1 year treatment)

Key secondary outcome(s))
Not provided at time of registration

Completion date
13/12/2017

Eligibility

Key inclusion criteria
1. Men aged 18-54 years (changed from "18 - 40 years" on 14/10/2016)
2. A diagnosis of stage 1 hypertension using conventional brachial BP measurements confirming a seated blood pressure of 140-159/90-99
3. No current treatment for hypertension (if previously treated with antihypertensives, patients will have received no treatment for >3 months)
4. Willing and capable of giving informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
54 years

Sex
Male

Total final enrolment
162

Key exclusion criteria
1. Women.
2. Men who have stage 2 hypertension, i.e. brachial blood pressure >=160/100
3. Men with secondary hypertension, e.g. renal artery stenosis, Conns adenoma, pheochromocytoma, aortic coarctation
4. Men who have stage 1 hypertension and on routine clinical testing have clinical evidence of overt target organ damage (e.g. ECG Left Ventricular hypertrophy LVH, renal impairment,

proteinuria)
5. Cardiovascular disease (e.g. stroke, Transient Ischaemic Attack TIA, cardiac or peripheral vascular disease)
6. Diabetes mellitus i.e. risk factors that would indicate that the stage 1 hypertension should be treated according to current guidance (ref NICE guideline)
7. Men who are unable or unwilling to give written informed consent to participate in the study
8. Men in whom it is not possible to measure conventional brachial blood pressure
9. Men with atrial fibrillation or any other significant pulse rhythm irregularity in whom blood pressure measurement is difficult and unreliable
10. Regular consumption of an average of more than 28 units of alcohol per week, or use of recreational drugs
11. Men with chronic inflammatory diseases requiring concomitant medications with steroids and /or non steroidal antiinflammatory drugs
12. Men with concurrent nonspecific malignancy
13. Men unwilling to undergo MRI studies

Date of first enrolment
01/08/2013

Date of final enrolment
31/12/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Institute of Cardiovascular Science
London
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Sponsor information

Organisation
University College London (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
NIHR Efficacy and Mechanism Evaluation; Grant Codes: 10/90/22

Results and Publications

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	01/12/2019	17/12/2020	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes