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Antihypertensives to reduce blood pressure variability after stroke

Submission date
23/10/2017

Recruitment status
No longer recruiting

Registration date
24/10/2017

Overall study status
Completed

Last Edited
11/03/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
Hypertension (high blood pressure) is an important modifiable risk factor in primary and secondary stroke prevention. Blood pressure (BP) control has been shown to reduce recurrence after stroke or transient ischaemic attack (TIA) (mini stroke). However, recent work has suggested BP variability (BPV) over short periods (minutes) as well as variation over days and weeks may be as important a risk factor as mean BP levels for stroke recurrence. Furthermore, studies looking at the effect of different classes of antihypertensive medications on BPV have shown that not all drug classes affect BPV equally. This differential effect on BPV may explain the differences in stroke risk reduction between different drug classes where the reduction in mean BP is similar. Strategies to treat BPV as well as mean BP levels after a stroke or TIA may therefore be useful, but data relating to this are limited. The aims of this study are to assess the feasibility of recruiting from this patient group, and concordance rates with treatment and follow-up measurements. This information will help design a larger randomised controlled trial to investigate the effect of treatment strategies for BPV on stroke outcome.

Who can participate?
Adult patients aged 18 and older who have had a stroke.

What does the study involve?
Participants provide baseline data. Standard routine investigations including baseline ECG, blood tests, and imaging investigations are also be recorded. Baseline blood pressure measurements using a standard validated monitor are taken. In addition, blood pressure variability measures is taken including 30 minutes of beat-to-beat measurements using a Finometer and daytime ambulatory blood pressure monitoring over a 12 hour period. Finally participants undergo routine cognitive screening. Participants are then randomly allocated to one of two groups to determine what type of blood pressure medication they receive. Those in the first group receive a calcium channel blocker and those in the second group receive an angiotensin converting enzyme inhibitor/angiotensin receptor blocker. Participants are re-assessed at three weeks and three months for their blood pressure and blood pressure variability and for their treatment compliance and adverse events. At the three week visit if participants blood pressure has not reached the recommended target for secondary prevention (defined as 130/80mmHg) then medication is adjusted according to an agreed treatment plan.

What are the possible benefits and risks of participating?
Participants may benefit from lowering their blood pressure helps to prevent future strokes and so we hope that the treatment you get will reduce your chances of having another stroke or mini-stroke. We hope that the results of the study will help to design further research projects and will improve stroke care in the future.

Where is the study run from?
1. University Hospitals of Leicester NHS Trust (UK)
2. Norfolk and Norwich University Hospital NHS Foundation Trust (UK)
3. John Radcliffe Hospital (UK)

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

Who is funding the study?
1. British Heart Foundation (BHF) (UK)
2. Stroke Association (UK)

Who is the main contact?
Professor Thompson Robinson
tgr2@leicester.ac.uk

Contact information

Type(s)
Public

Contact name
Prof Thompson Robinson

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Additional identifiers

Clinical Trials Information System (CTIS)
2017-002560-41

Protocol serial number
35639

Study information

Scientific Title
A Calcium channel or Angiotensin converting enzyme inhibitor/Angiotensin receptor blocker Regimen to reduce Blood pressure variability in acute ischaemic Stroke (CAARBS): A Feasibility Trial

Acronym
CAARBS

Study objectives
Reducing blood pressure variability after ischaemic stroke or transient ischaemic attack will improve outcomes. Furthermore, Calcium channel blockers will be more effective at reducing blood pressure variability than drugs which act on the renin-angiotensin system.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London – Central Research Ethics Committee, 05/09/2017, ref: 17/LO/1427

Study design
Randomised; Interventional; Design type: Treatment, Drug

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Specialty: Stroke, Primary sub-specialty: Prevention; UKCRC code/ Disease: Stroke/ Cerebrovascular diseases, Cardiovascular/ Other and unspecified disorders of the circulatory system

Interventions
All patients who consent to be involved in the study have baseline data recorded including demographics, baseline modified Rankin score, NIHSS score, and stroke classification. Standard routine investigations including baseline ECG, blood tests, and imaging investigations are also be recorded.

Baseline blood pressure measurements using a standard validated monitor are taken. In addition, blood pressure variability measures is taken including 30 minutes of beat-to-beat measurements using a Finometer and daytime ambulatory blood pressure monitoring over a 12 hour period.

Finally participants undergo routine cognitive screening using the Montreal Cognitive Assessment, Albert’s line test and MiND-B questionnaire, and a short mood assessment called the Geriatric Depression Scale.

Participants are then randomised by a computer based randomisation system to one of the two treatment groups (a calcium channel blocker or an angiotensin converting enzyme inhibitor /angiotensin receptor blocker). The treating clinician has the discretion to choose a specific medication from the relevant class.

Participants are re-assessed at three weeks and three months post-randomisation. These assessments include repetition of blood pressure and blood pressure variability measurements and an assessment of treatment compliance and adverse events. At the three week visit if participants blood pressure has not reached the recommended target for secondary prevention (defined as 130/80mmHg) then medication is adjusted according to an agreed treatment plan.

Intervention Type
Drug

Phase
Phase IV

Primary outcome(s)
1. Feasibility and acceptability of study is measured using recruitment rates and reasons for non-eligibility at the end of the study
2. The proposed primary outcome for the future study is the stroke outcome as assessed using the modified Rankin Score at 90 days

Key secondary outcome(s))
Secondary feasibility outcome measures:
1. Systolic and diastolic blood pressure variability is assessed with beat-to-beat blood pressure measurement and daytime ambulatory blood pressure measurement from baseline to three weeks and three months
2. Treatment compliance assessed using a self-reported questionnaire and pill count at three weeks and three months
3. Serious adverse events associated with either intervention is measured using patient self-report of any new symptoms at three weeks and three months

Proposed secondary outcome measures for any future study:
1. Stroke outcomes are assessed by modified Rankin score at three weeks and then the change in the National Institutes of Health Stroke Scale (NIHSS) at baseline to three weeks.
2. Mean blood pressure are assessed by clinic blood pressure measurement at three weeks and three months
3. Systolic and diastolic blood pressure variability are assessed by beat-to-beat and daytime ambulatory blood pressure measurement at three weeks and three months
4. Cognitive outcome assessed by the Montreal Cognitive Assessment at three months

Completion date
31/07/2019

Eligibility

Key inclusion criteria
Participant inclusion criteria as of 24/09/2018:
1. Adult patients (male and female) aged over 18
2. First episode TIA or mild to moderate ischaemic stroke (NIHSS <10)

3. Blood pressure >130/80mmHg
4. Within 7 days of symptom onset
5. Willing to comply with randomly assigned blood pressure treatment and blood pressure measurements
6. Able to understand verbal and written English
7. Able to provide informed consent
8. Willing for their GP to be notified of their involvement in the study

Previous participant inclusion criteria:
1. Adult patients (male and female) aged over 18
2. First episode TIA or mild to moderate ischaemic stroke (NIHSS <10)
3. Blood pressure >130/80mmHg
4. Within 72 hours of symptom onset
5. Willing to comply with randomly assigned blood pressure treatment and blood pressure measurements
6. Able to understand verbal and written English
7. Able to provide informed consent
8. Willing for their GP to be notified of their involvement in the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
14

Key exclusion criteria
1. Known definite contra-indication to BP-lowering regime or therapeutic agents
2. Swallowing difficulties which would preclude the taking of oral medication
3. Definite indication for beta blocker, calcium channel blocker, angiotensin converting enzyme inhibitor, or angiotensin receptor blocker therapy
4. Significant pre-stroke dependency (modified Rankin Score >3)
5. Co-existing life-threatening condition with life expectancy <3 months
6. Previous participation in this trial or current participation in another investigational drug trial
7. Atrial fibrillation
8. Female participants who are pregnant, lactating or planning pregnancy during the course of the study
9. Participants who intend to donate blood during the study
10. Unable to understand verbal and written English
11. Cannot give informed consent

Date of first enrolment
01/12/2017

Date of final enrolment
31/12/2018

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals of Leicester NHS Trust
Gwendolen House
Gwendolen Road
Leicestershire
Leicester
United Kingdom
LE5 4QF

Study participating centre
Norfolk and Norwich University Hospital NHS Foundation Trust
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
John Radcliffe Hospital
Oxford University Hospitals NHS Foundation Trust
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation

University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Charity

Funder Name
British Heart Foundation (BHF)

Funder Name
Stroke Association

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository. Non-identifiable patient data will be stored in encrypted format on secure computers at the University of Leicester. Data will be stored for 15 years following the completion of the study in line with standard procedure for a CTIMP. Professor Robinson will act as the data custodian.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/06/2020	11/03/2020	Yes	No
Protocol article	protocol	19/02/2019	11/03/2020	Yes	No
HRA research summary			26/07/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version V1.1	11/09/2017	15/02/2018	No	No
Protocol file	version V2.0	20/07/2018	24/09/2018	No	No