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How intensively should we treat blood PRESsure in established cERebral small VEssel disease?

Submission date
25/01/2012

Recruitment status
No longer recruiting

Registration date
25/01/2012

Overall study status
Completed

Last Edited
01/06/2021

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Disease of the small blood vessels in the brain, which is called cerebral small vessel disease (SVD), causes a fifth of all strokes and is the major cause of dementia. High blood pressure (hypertension) is the major risk factor for this disease but we do not know how intensively we should treat blood pressure in people who have already developed the disease. Reducing the blood pressure to lower levels may delay progression of the disease; on the other hand leaving blood pressure slightly higher may increase blood flow to the brain and improve cognition. We are carrying out this study to find out how best to treat blood pressure in patients with this disease. In the study we will compare whether lowering blood pressure more than we usually do results in less people suffering cognitive problems over a two year period. At some sites, we are also carrying out an MRI study in which we are using MRI to assess the amount of brain damage and blood flow to the brain and seeing whether one of the two treatments is better at reducing brain damage and increasing blood flow to the brain.

Who can participate?
We are recruiting participants with cerebral small vessel disease and hypertension.

What does the study involve?
Participants are randomised to one of two groups: one group will have blood pressure reduced to normal levels (standard therapy). The other will have blood pressure reduced further to slightly lower levels (intensive therapy). The study involves several hospital visits, at the beginning of the study and again after 1, 3, 6, 12, 18 and 24 months. Participants will have a review of medication and blood pressure at each visit and cognitive assessments (memory type tests) at some visits. When participants enter the study, they will have a blood sample taken. Participants involved in the MRI sub study will have an MRI scan at the beginning and at 24 months. In addition, people in the blood flow additional study will have a further MRI scan at 3 months.

What are the possible benefits and risks of participating?
This study will be useful in informing future research.

Where is the study run from?
Stroke and Dementia Research Centre at St. Georges University of London, UK.

When is study starting and how long is it expected to run for?
It is currently open to recruitment and is expected to run until 2016.

Who is funding the study?
The Stroke Association (UK)

Who is the main contact?
Stroke and Dementia Research Centre at St. Georges University of London, UK
preserve@sgul.ac.uk

Study website
http://www.preserve.sgul.ac.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
10962

Study information

Scientific Title
Blood pressure treatment in small vessel disease

Acronym
PRESERVE

Study objectives
Cerebral small vessel disease (SVD) accounts for about 20% of all stroke and is the major cause of vascular cognitive impairment and dementia. The major risk factor is hypertension but in patients with severe disease (with radiological changes of extensive white matter damage, which is called leukoaraiosis) we do not know how intensively we should treat blood pressure. In this clinical trial we will determine whether intensive, versus standard, treatment of blood pressure in hypertensive patients with SVD and radiological leukoaraiosis is associated with reduced cognitive decline.

In nested substudies we will:
1. Investigate if the type of treatment is associated with brain changes detectable on MRI imaging
2. Investigate if a treatment effect is seen in a reduced rate of white matter damage and/or an increase in blood flow in the brain seen in specific MRI techniques. In addition, we will use this substudy to compare the sensitivity of different types of MRI imaging in identifying white matter damage in the brain and also the relationship between white matter damage and cognitive decline.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North London REC 3, 01/07/2011 ref: 11/LO/0458

Study design
Randomised interventional treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
http://www.preserve.sgul.ac.uk/study-documents

Health condition(s) or problem(s) studied
Dementias and Neurodegenerative Diseases

Interventions
Participants are randomised to either Intensive or Standard blood pressure treatment. The intensive blood pressure lowering arm aims for a systolic blood pressure of less than 125mmHg.

The standard blood pressure lowering arm aims for a systolic blood pressure of 130 to 140mmHg, as recommended by current guidelines. The trial is comparing 2 strategies for lowering blood pressure and not looking at specific blood pressure drugs.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Main study:
Composite cognitive score, which is an overall score for the cognitive tests carried out at baseline, 12 months & 24 months.

Structural DTI MRI sub-study:
DTI white matter ultrastructure measured by MD and FA.
All outcome measures for this sub-study are measured at baseline and 24 months

Perfusion MRI sub-study:
Cerebral blood flow, measured at baseline, 3 months and 24 months.

Secondary outcome measures
Main study:
1. Results of specific cognitive tests
2. Disability measures
3. Quality of life questionnaires
4. Blood pressure readings (taken at all visits)
5. Record of adverse events (taken at all visits)
Measured at baseline, 12 months & 24 months

Structural DTI MRI sub-study:
Brain atrophy and White matter lesion volume measured on T2/FLAIR.
All outcome measures for this sub-study are measured at baseline and 24 months

Overall study start date
14/10/2011

Completion date
01/07/2016

Eligibility

Key inclusion criteria
1. Clinical evidence of cerebral small vessel disease with MRI evidence of lacunar infarcts(s) (<=1.5cm maximum diameter) and confluent leukoaraiosis (defined on Fazekas scale as >=grade 2)
2. Clinical evidence of cerebral small vessel disease is defined as:

a. Lacunar stroke syndrome with symptoms lasting >24 hours

3. Transient ischaemic attack lasting < 24 hours with limb weakness, hemisensory loss or dysarthria AND with MR DWI imaging performed acutely showing lacunar infarction, or if MRI is not performed acutely (>2 weeks after TIA) with a lacunar infarction in an anatomically appropriate position on MRI

4. Vascular cognitive impairment with MRI shoing no evidence of hippocampal atrophy
5. Systolic BP > 140 mmHg
6. Taking no more than two BP lowering drugs at assessed for study participation.
7. Aged 40 years or over
8. Not diagnosed with dementia and Minimental state examination (MMSE) 21
9. Able and willing to consen
10. Expected life expectancy > 2 years
11. Able to perform study cognitive assessment

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
UK Sample Size: 422

Key exclusion criteria
1. Unable or unwilling to conset
2. Women of childbearingage
3. Minimental state examination (MMSE) <21 or diagnosis of dementia on Diagnostic and Statistical Manual of Mental Disorders (DSM IV) criteria
4. Life expectancy less than 2 years
5. Symptomatic postural hypotension
6. Known single gene disorder causing small vessel disease (eg CADASI)
7. Cortical infarction (>2 cm maximum diamete)
8. Symptomatic carotid stenosis or vertebral stenosis >70% as measured on NASCET criteria

Date of first enrolment
14/10/2011

Date of final enrolment
01/07/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Stroke and Dementia Research Centre
London
United Kingdom
SW17 0RE

Sponsor information

Organisation
St George's University of London (UK)

Sponsor details
Joint Research and Enterprise Office
Cranmer Terrace
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United Kingdom
SW17 0RE

Sponsor type
University/education

Website
http://www.sgul.ac.uk/

ROR
https://ror.org/040f08y74

Funder(s)

Funder type
Charity

Funder Name
The Stroke Association (UK)

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	01/06/2018		Yes	No
Results article		01/08/2021	01/06/2021	Yes	No