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Observational study assessing early markers of high blood pressure mediated brain damage and the impact of single-pill treatment with Perindopril/Indapamide

Submission date
30/01/2020

Recruitment status
No longer recruiting

Registration date
06/02/2020

Overall study status
Completed

Last Edited
08/10/2020

Condition category
Circulatory System

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

Plain English summary of protocol

Background and study aims
High blood pressure (hypertension) is a risk factor for mild deterioration in mental abilities and brain damage. The state of the brain structure can be assessed using a special form of MRI known as diffusion tensor imaging and blood flow in the brain can be assessed using functional MRI.
This study aims to identify the effect on brain structure and bloodflow of anti-hypertensive medication in hypertensive patients and healthy volunteers.

Who can participate?
Patients aged 40 - 59 years with hypertension-mediated organ damage can participate in the hypertension group. People aged 40 - 59 years who do not have hypertension will be included in the control group.

What does the study involve?
Participants will visit the test centre for MRI scanning and then be asked to wear a blood pressure monitor at home for 24 hours. Hypertensive patients will then be provided with blood pressure lowering medication to take once daily. Patients will have their blood pressure checked after two and four weeks to see if the medication is having any effect. After 12 weeks the assessments will be repeated.

What are the possible benefits and risks of participating?
Possible benifits of participating: additional diagnostic methods used in the present study can help your physician to improve and personalise your treatment strategy.
Possible risks of participating: all procedures are non-invasive, but require additional time. Patients recieving antihypertensive medications may expirience side-effects of the drug.

Where is the study run from?
A.Y. Kozhevnikov Clinic of Nervous Diseases (Russia)

When is the study starting and how long is it expected to run for?
December 2016 to December 2018

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
protocol №11-16

Study information

Scientific Title
Observational study to assess cognitive functions, white matter hyperintensities, cerebral blood flow and fractional anisotropy in treatment-naive middle-aged hypertensive patients compared

to normotensive controls and to assess the impact of 12-weeks single pill Perindopril /Indapamide treatment on those domains to improve personalized antihypertensive therapy

Study objectives
1. Treatment-naive middle-aged hypertensive patients have worse executive functions, more white matter hyperintensities, lower cerebral blood flow and fractional anisotropy compared to normotensive controls
2. 12-weeks single pill Perindopril/Indapamide treatment improves blood pressure level, cognitive status and potentially has an impact on cerebral blood flow and fractional anisotropy

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/12/2016, Ethics committee of I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (8-2 Trubetskaya st., Moscow, 119991, Russia; +7 495 609-14-00; iec@sechenov.ru), ref: 11-16

Study design
Single-centre observational study

Primary study design
Observational

Secondary study design
In parallel groups

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Arterial hypertension

Interventions
All participants undergo a baseline assessment as follows:
1. Neuropsychological assessment (MoCA, verbal fluency test, TMT (parts A and B), 10-words list learning task, Stroop Color and Word Test)
2. 24-hour ambulatory blood pressure monitoring (BPLab monitoring system BP2005-01.04.00.2540, “Petr Telegin”, Russia): following SBP, DBP and pulse pressure (PP) data were provided: 24-h mean values and variability, daytime (07:00–23:00) mean values and variability, night time (23:00–07:00) mean values and variability
3. Brain magnetic resonance imaging (MAGNETOM Skyra 3.0 T, Siemens AG, Germany): T1,

MPRAGE, T2 FLAIR, PASL, TOF 2D, DTI to evaluate white matter hyperintensities (Fazekas scale), cerebral blood flow in the cortical plates of frontal lobes and fractional anisotropy in 28 regions of interest

Non-hypertensive patients end participation at this point.

Hypertensive patients are prescribed with perindopril (5 mg) / indapamide (1.25 mg) single-pill combination, given once daily in the morning. If after 2 weeks of treatment office BP level is >140/90 mm Hg, Perindopril/Indapamide will be up-titrated to Perindopril (10 mg) / Indapamide (2.5 mg). If after 2 weeks of treatment the patient's office BP level is still >140/90 mm Hg, the patient is excluded from the study. The follow-up period after reaching the target BP level was 12 weeks.

At follow-up the assessments are repeated.

Intervention Type
Mixed

Primary outcome measure
At baseline and follow-up
1. Blood pressure measured using sphygmomanometer
2. Cognitive function measured using MoCA, verbal fluency test, TMT (parts A and B), 10-words list learning task, Stroop Color and Word Test
3. Cerebral blood flow measured using fMRI

Secondary outcome measures
Fractional anisotropy measured using fMRI at baseline and follow-up

Overall study start date
01/09/2016

Completion date
15/12/2018

Eligibility

Key inclusion criteria
Hypertension group:
1. Age 40-59 years
2. Office SBP – 140–179 mmHg and/or DBP – 90–109 mmHg
3. Presence of at least one hypertension-mediated organ damage (heart – left ventricular hypertrophy assessed by echocardiogram, blood vessels – atherosclerotic plaques assessed by triplex scanning of the brachiocephalic arteries, kidneys – microalbuminuria and/or glomerular filtration rate according to CKD-EPI between 30-60 ml/min/1.73 m^2)
4. Lack of antihypertensive treatment

Control group
1. Healthy men and women
2. Age 40-59 years
3. Absence of hypertension

Participant type(s)
Mixed

Age group
Adult

Sex
Both

Target number of participants
140

Total final enrolment
64

Key exclusion criteria
1. Body mass index ≥ 40 kg/m²
2. Pregnancy, lactation
3. Clinically significant heart disease (myocardial infarction, 2nd and 3rd degree atrio-ventricular block without artificial pacemaker, sinoatrial block, sick sinus syndrome, hypertrophic cardiomyopathy, aortic and mitral stenosis, chronic heart failure, angina pectoris)
4. Clinically significant liver disease
5. Clinically significant kidney disease (GFR according to CKD-EPI <30 ml/min / 1.73 m², hemodialysis, anuria)
6. Clinically significant respiratory organ disease (including bronchial asthma and chronic obstructive pulmonary disease)
7. Clinically significant immunological disease
8. Clinically significant endocrine disease (including diabetes mellitus)
9. Secondary hypertension
10. Gout
11. Mental illness and disorders, dementia, drug and alcohol abuse
12. Severe peripheral vascular diseases (including Raynaud's syndrome)
13. Metabolic acidosis
14. Refractory hypokalemia
15. Clinically significant neurological diseases (including stroke and transient ischemic attack)
16. Surgical operation in the previous 3 months (excluding dental or plastic surgery)
17. Use of any medication (including regular intake of antihypertensive treatment) that could have affected the results of the study for 12 weeks before enrollment, at the time of enrollment and until the end of the study

Date of first enrolment
15/12/2016

Date of final enrolment
30/11/2017

Locations

Countries of recruitment
Russian Federation

Study participating centre
A.Y. Kozhevnikov Clinic of Nervous Diseases
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Sponsor information

Organisation
Sechenov University

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Sponsor type
University/education

Website
https://www.sechenov.ru/eng/

ROR
https://ror.org/02yqqv993

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
15/12/2020

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2020	08/10/2020	Yes	No