

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	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 06/02/2020	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 08/10/2020	Condition category Circulatory System	<input type="checkbox"/> 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 benefits 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 receiving antihypertensive medications may experience 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

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
protocol №11-16

Study information

Scientific Title
Observational study to assess cognitive functions, white matter hyperintensities, cerebral blood flow and fractional anisotropy in treatment-naïve 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-naïve 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

Study type(s)

Prevention

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(s)

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

Key secondary outcome(s)

Fractional anisotropy measured using fMRI at baseline and follow-up

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 m²)
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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

Total final enrolment

64

Key exclusion criteria

1. Body mass index $\geq 40 \text{ kg/m}^2$
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 $<30 \text{ ml/min} / 1.73 \text{ m}^2$, 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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Moscow

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Sponsor information

Organisation

Sechenov University

ROR

<https://ror.org/02yqqv993>

Funder(s)

Funder type

Other

Funder Name

Investigator initiated and funded

Results and Publications

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
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes