Medication induced blood pressure reduction; assessment of cerebral perfusion and cognition in hypertensive elderly

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To demonstrate that after a reduction in systolic blood pressure between 20 and 80mmHg within 3 months to reach a target of 140 mmHg, cerebral blood flow is not lower than prior to the start of treatment.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON33986

Source
ToetsingOnline

Brief title
MBRACE

Condition

- Central nervous system vascular disorders
- Vascular hypertensive disorders

Synonym
high blood pressure, hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W,Nederlandse Hartstichting

Intervention

Keyword: aging, blood pressure, cerebrovascular circulation, hypertension

Outcome measures

Primary outcome

Total cerebral blood flow as measured by MRI. Difference between baseline measurement and end measurements after reaching systolic blood pressure target of 140mmHg.

Secondary outcome

1. Additional cerebral hemodynamics:

a. Cerebral blood flow velocity in the middle cerebral artery as measured by transcranial Doppler sonography (TCD)

b. Cerebral autoregulation

c. Vasomotor reactivity

2. Cognition: Executive function, attention and memory as measured with CANTAB

3. The incidence of orthostatic hypotension

4. Blood pressure profile as measured by 24h ABPM

a. Change in nocturnal dipping of BP

b. Change in postprandial hypotension, in combination with food diary

5. Change in quality of life

6. Changes on structural MRI (white matter lesions, lacunar stroke, global and hippocampal atrophy) and functional MRI (fractional anisotropy (DTI), resting state connectivity, neurovascular coupling).

Study description

Background summary

Hypertension affects as much as 77% of the elderly population, over age 70. The majority (approximately 60%) of these hypertensive patients have isolated systolic hypertension. Hypertension is an important risk factor for cardiovascular disease. Study shows that the benefits of antihypertensive treatment clearly extend to elderly subjects age over 70. Despite the benefits of treatment, blood pressure control is inadequate in the majority of patients. Contributing to these low treatment rates is the widespread concern about the negative effects of blood pressure lowering on morbidity and quality of life. Specifically it is feared that lowering of blood pressure to the targets proposed by recent guidelines (ESH/ESC 2007, JNC-7) may cause cerebral hypoperfusion, resulting in ischemia, cognitive decline and/or falls. At present, no data are available to deal adequately with the concerns that many clinicians have when deciding if and how to treat elderly subjects with hypertension. This study will demonstrate whether older patients maintain a stable cerebral perfusion when their blood pressure is adequately reduced to meet blood pressure targets set by current guidelines

Study objective

To demonstrate that after a reduction in systolic blood pressure between 20 and 80mmHg within 3 months to reach a target of 140 mmHg, cerebral blood flow is not lower than prior to the start of treatment.

Study design

Prospective, open-label design with blinded end-points. Anti-hypertensive treatment will be open-label as this therapy is aimed at reaching a specific target BP. During analysis of the endpoints, the researcher will be blinded for patient identity and if the data concerns baseline or end measurement.

Methods:
Run-in phase
To obtain an actual BP status, eligible patients will receive standardized blood pressure measurements during two home visits. If BP-level is according to inclusion criteria (systolic pressure 160mmHg), patients will visit the GP*s office once for diagnostic evaluation which is essentially identical to what is considered *guideline care* in the evaluation and treatment of hypertension in general practice. Specifically, patients will receive a thorough work-up of hypertension, including assessment of cardiovascular risk factors, exclusion of secondary causes, and evaluation of targetorgan damage and cardiovascular disease.

Treatment phase
Subjects will receive hypertensive treatment to lower blood pressure (<=140mmHg). The researcher, supervised by project group members, will be responsible for titration of treatment and will perform BP measurements and clinical evaluation during two-weekly house calls. In order to reach target BP of systolic BP <=140mmHg within 8-12 weeks, medication will be uptitrated if the decline in BP is less than 20mmHg per 2 weeks and clinical evaluation does not contraindicate an increase of medication.

Measurements
There are 3 measurement sessions: 1 after the run-in phase and 2 sessions after the treatment phase. Each measurement session consist of 2 parts on different days. Part 1 during a house call, consists of neuropsychological testing and fitting of the 24h-ABPM device. For part 2 subjects will visit the RUNMC. Effects of blood pressure lowering on cerebral hemodynamics will be measured here using state-of-the-art techniques in this field: MRI, transcranial Doppler sonography, Near-Infrared-Spectroscopy and Finapres.

Study burden and risks

The patients will be subjected to diagnostic evaluation and treatment which is essentially identical to what is considered *routine care* in the evaluation and treatment of hypertension in general practice. Hypertensive treatment will lower blood pressure to the level set by current guidelines (ESH/ESC 2007, JNC-7). The selected hypertensive agents proposed by these guidelines have proven their effectiveness and safety in extensive clinical use. A gradual blood pressure reduction will be accomplished, starting with a low dose combination therapy and gradual uptitration, based on blood pressure level and clinical evaluation.
The tests performed for research purposes: MRI, TCD, NIRS and Finapres are non-invasive and save. However, these tests and the repeated visits are time-consuming and therefore place a considerable burden on participating patients and their caregivers. The requirement to lie still for a period of one hour during MRI scanning can be seen as a burden for elderly patients. The principal investigator has had previous experience with elderly patients,

including Alzheimer patients undergoing the proposed non-invasive methods.
These patients tolerated these investigations very well.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Systolic hypertension grade II-III (Systolic BP >=160mmHg) as measured according to JNC-7 protocol

Exclusion criteria

•Systolic blood pressure >220mmHg

•Indication for urgent treatment of HT
•Contra-indication for MRI including claustrophobia
•Contra-indication for anti-hypertensive medication used (Chlorthalidone, Amlodipine, Valsartan)
•Dementia
•Renal failure requiring dialysis
•Atrial fibrillation
•A life expectancy of less than a year
•Disabling stroke
•Impairment by any cause prohibiting participation as mentioned by the general practitioner
•Diabetes Mellitus

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-08-2009
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	07-04-2009
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL26149.091.09