Effects of temporary discontinuation of antihypertensive treatment in older patients with cognitive impairment: a randomised controlled trial.
The DANTE Study Leiden, Discontinuation of ANtihypertensive Treatment in the Elderly

Published: 17-12-2010
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To assess whether temporary discontinuation of antihypertensive therapy in mildly cognitively impaired older patients on antihypertensive treatment improves cognitive and psychological functioning.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON37958

Source
ToetsingOnline

Brief title
DANTE study Leiden.

Condition

- Other condition
- Central nervous system vascular disorders
- Dementia and amnestic conditions

Synonym
Blood pressure and cognition

Health condition

depressie, apathie, dagelijks functioneren en kwaliteit van leven

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,This research is funded by ZonMw;Program Priority Medicines for the Elderly;dossier number 40-41600-98-9014

Intervention

Keyword: Blood pressure increase, Cognitive impairment, Discontinuation of antihypertensive treatment, Elderly, Gerandomiseerd klinisch onderzoek, Psychiatric symptoms.

Outcome measures

Primary outcome

Primary outcome is the change in the compound cognitive score between baseline

and follow-up at 4 months after randomisation.

Secondary outcome

Secondary outcomes are the changes in the four separate cognitive domains

(executive functioning, cognitive speed, immediate memory, and delayed memory);

depressive symptoms, apathy, daily functioning, and quality of life between

baseline and follow-up, 4 months after randomisation; and change in cerebral

perfusion at MRI scan.

Study description

Background summary

A high blood pressure at middle age is deleterious and may lead to cardiovascular disease, dementia and depression and apathy at old age. Therefore, many people use antihypertensives. However, the usefulness of antihypertensive treatment at old age had not been convincingly demonstrated and increasing evidence suggests that at old age a low blood pressure is deleterious for mental health. Low blood pressure at old age may compromise cerebral perfusion, which may increase the risk of cognitive impairment, depressive symptoms, and apathy. Cerebral imaging studies have shown that cerebral blood flow is reduced in areas of small vessel disease and that the degree of hypoperfusion correlates with disease severity. Hence, blood pressure reduction in older people may lead to hypoperfusion, especially in patients with cerebral small vessel disease, resulting in increased mental health problems like cognitive impairment, depression, and apathy.

Study objective

To assess whether temporary discontinuation of antihypertensive therapy in mildly cognitively impaired older patients on antihypertensive treatment improves cognitive and psychological functioning.

Study design

Randomized non-blinded controlled clinical trial.

Intervention

Patients will be randomized to either continuation (n=200) or discontinuation (n=200) of antihypertensive treatment. Discontinuation of antihypertensive medication by patients* own general practitioner may vary from abrupt and complete discontinuation to gradual and partial discontinuation, with a 20 mmgHg increase in systolic blood pressure as target and 180 mmHg as maximum systolic blood pressure. For the various antihypertensive drugs commonly used by older people a discontinuation algorithm will be used. Discontinuation will be executed and completed within four weeks from randomization by the GP for a period of three months thereafter.

Study burden and risks

Patients have to come to the LUMC for a MRI-scan. Assessments of cognitive functioning and mental wellbeing (2x2 hours) will be done at the patients* home. The patients will receive blood pressure measurements every 2 weeks

during the first 4 weeks by their GP. Thereafter, in order to make both treatment arms as similar as possible the blood pressure of all patients, both in the discontinuation arm and the stop arm, will be monitored monthly during the entire study period by the research personnel and patients in the discontinuation arm will be put on their original antihypertensive medication when systolic blood pressure exceeds 200 mmHg or diastolic blood pressure exceeds 110 mmHg. Moreover, all cardiovascular events during the study will be closely monitored to prevent an increase in cardiovascular events in the discontinuation group. A Data Safety and Monitoring Board (DSMB) will be installed for monitoring of the safety data (cardio- and cerebrovascular events). The DSMB will check progression of the study and adverse events after the first 50 participants, and afterwards after every 100 participants. A charter has been written detailing the exact procedures.

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

(1) age >= 75 years,
(2) current antihypertensive treatment with a calcium antagonist, beta-blocker, diuretic, ACE-inhibitor, or angiotensin-II-receptor blocker prescribed by their general practitioner for hypertension,
(3) a last systolic blood pressure as reported in the chart of the general practitioner <= 160 mmHg(4) Mini-Mental State Examination (MMSE) score 21t/m 27.

Exclusion criteria

A history of myocardial infarction and/or coronary reperfusion procedures (CABG/PCI) < 3 years, stroke, or heart failure requiring antihypertensive medication and/or a clinical diagnosis of dementia.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2011
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO

Date:	17-12-2010

Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	11-06-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL34418.058.10