Induced hypertension for treatment of delayed cerebral ischaemia after aneurysmal subarachnoid haemorrhage.

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To investigate the outcome after induced hypertension versus no induced hypertension in patients with DCI after aneurysmal SAH.

Ethical review	-
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON38214

Source
ToetsingOnline

Brief title
Induced hypertension for DCI after SAH.

Condition

- Central nervous system vascular disorders

Synonym
"brain haemorrhage", "intracerebral haemorrhage"

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: DCI, Hypertension, SAH

Outcome measures

Primary outcome

The primary outcome parameter will be the proportion of SAH patients with DCI with poor outcome three months after the SAH, defined as a modified Rankin Scale score of 3 or more.

Secondary outcome

Secondary study parameters are related to treatment failure, functional outcome, adverse events and to the influence on cerebral haemodynamics.
Related to treatment failure: proportion of patients in the induced hypertension group in which induced hypertension did not give clinical improvement of symptoms of DCI within 24 hours.
Related to the functional condition: case fatality 30 days after SAH, Activities of daily living (ADL), three months after the SAH assessed with the Barthel Index, Quality of life, three months after the SAH, estimated with the Stroke Specific Quality of Life Scale (SSQoL-12-NL). Anxiety and depression, three months after the SAH, assessed with the Hospital Anxiety and Depression Scale (HADS). Cognitive functioning, three months after the SAH, evaluated by the Cognitive Failures Questionnaire (CFQ). Functional outcome twelve months after the SAH, assessed with the modified Rankin Scale.
Related to adverse effects: Complications related to insertion of a central venous catheter or intra-arterial catheter (including local haemorrhage and pneumothorax). Intracranial complications related to induced hypertension (such

as exacerbation of cerebral oedema, hemorrhagic infarction and bleeding of an asymptomatic aneurysm). Systemic complications related to induced hypertension (including cardiac rhythm disorders, low cardiac output state and cardiac ischemia).

Related to the influence on cerebral haemodynamics: The difference in CBF, CBV, TTP and MTT between the intervention and the control groups 24-36 hours after the start of the study (i.e. CTP-2). The difference in CBF, CBV, TTP and MTT between the perfusion CT-scan (at baseline, the moment of deterioration, i.e. CTP-1) and the second perfusion CT-scan (CTP-2) within the same patients.

Study description

Background summary

Delayed cerebral ischaemia (DCI) is a major complication after aneurysmal subarachnoid hemorrhage (SAH). The proportion of SAH patients who develop DCI is around 30%. DCI is associated with a 1.5-3 fold higher mortality rate. Many centers around the world use induced hypertension, alone or in combination with haemodilution and hypervolaemia, so called Triple-H, as standard therapy in the treatment of DCI, but the efficacy of induced hypertension in reducing DCI is based on case series only, and not on a randomized clinical trial.

Study objective

To investigate the outcome after induced hypertension versus no induced hypertension in patients with DCI after aneurysmal SAH.

Study design

Multi-centre, randomized, single blind, controlled clinical trial

Intervention

Group1. No induced hypertension: patients will not be treated with induced hypertension when DCI develops. Hypotension (mean arterial pressure (MAP) below 80 mmHg) will be prevented. In order to achieve this, vasopression will be

applied according to the protocol of the participating centre.

Group 2. Induced hypertension group: increasing the blood pressure with vasopressors as described in the protocol of the participating centre until clinical improvement is observed. The maximum MAP in these patients will be 130 mmHg and the maximum systolic blood pressure 230 mmHg. If there is no clinical improvement observed within 24 hours after reaching one of the above mentioned maximum values the administration of vasopressors will be tapered (according to the protocol of the participating centre). If clinical improvement is seen within 24 hours after the start of induced hypertension, induced hypertension will be continued for 48 hours, after which attempt will be made to lower the vasopression slowly. The vasopression will be restarted when, at such a point, clinical worsering happens.

Study burden and risks

Patients will be randomised into two groups. The induced hypertension group will undergo induced hypertension. The medical and nursing staff has large experience with induced hypertension and the patient will be monitored continuously at the ICU or Medium Care Unit. Patients in the no induced hypertensiongroup will not have their blood pressure highered.

In selected centres, where a substudy will be performed on the influence of induced hypertension on cerebral haemodynamics by means of CT perfusion scan, the risk excists of allergic reaction to CT contrast when this was not known priorly. Furthermore, patients are submitted to radiation.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Admission to the hospital 2. Age 18 years or over 3. Aneurysmal SAH, demonstrated on CT-angiography or cerebral angiograph 4. DCI (decrease of at least one point on the GSC sumscore, unless the decrease doesn*t reflect DCI as evaluated by the treating physician, and/or all new neurological focal deficits), diagnosed by a neurologist, neurosurgeon or intensivist, 5. Informed consent

Exclusion criteria

0. Evidence of DCI after the SAH at time of asking for informed consent, unless symptoms of DCI started within 3 hours 1. Co-existing severe head injury. 2. A perimesencephalic haemorrhage. 3. A history of a ventricular cardiac rhythm disorder, necessitating medical treatment. 4. A history of left ventricular heart failure, necessitating medical treatment. 5. Pregnancy. 6. Transferral to another hospital, 7. moribund, 8. Other cause for neurological deterioration (see page 19 of the study protocol for the differential diagnosis) 9. Symptomatic cerebral aneurysm not yet treated by coiling or clipping, 10. Severe hypertension, defined as a spontaneous MAP of 120 mmHg or more at the moment of evaluation for trial participation, 11. Any contraindication for induced hypertension (such as a cardiac complication necessitating medical treatment) as evaluated by the treating physician. And furthermore, in selected centres where the sub study with CT perfusion will be performed: 12. known allergy for CT-contrast agents. 13. renal failure, defined as a serum creatinine > 150 µmol/l, because of the risk of contrast nephropathy. 14. diabetes mellitus.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2011
Enrollment:	240
Type:	Actual

Ethics review

Approved WMO Date:	10-08-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-02-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
ClinicalTrials.gov	NCT01613235
CCMO	NL32978.018.10