Organ protection by noble gases - helium therapy in acute ischemic stroke

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The primary objective is to investigate the feasibility and the safety of heliox administration, a gaseous mixture of 79% helium en 21% oxygen, for 8 hours in acute ischemic stroke.

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

Summary

ID

NL-OMON33571

Source
ToetsingOnline

Brief title
Helium in ischemic stroke

Condition

- Central nervous system vascular disorders

Synonym
cerebral infarct, ischemic stroke

Research involving
Human

Sponsors and support

Primary sponsor: Gooi-Noord Ziekenhuis
Source(s) of monetary or material Support: wetenschapsfonds Tergooiziekenhuizen

Intervention

Keyword: helium, ischemic stroke, neuroprotection, penumbra

Outcome measures

Primary outcome

Main clinical outcome is the change in neurological deficits between subjects and controls quantified by the National Institute of Health Stroke Scale (NIHSS) at 4 hours. Improvement is defined as a decrease of 4 or more points on the NIHSS.

For safety analysis, clinical deterioration - defined as a decrease on the Glasgow Coma Scale of more than 2 points and/or a increase of 4 or more points on NIHSS - is primary outcome.

Secondary outcome

Secondary clinical measures are NIHSS scores at 24 hours, 1 week and 3 months and level physical function measured by modified Rankin Scale (mRS) at 3 months. Independency (mRS <= 2) is considered as good outcome, whereas dependency (mRs 3 -5) as bad.

Secondary safety outcomes are death by any cause and total and specific serious adverse events. One defined specific serous adverse event is the occurrence of symptomatic intracerebral haemorrhage. This event is regarded as symptomatic when a decline in clinical performance in opinion to the clinical investigator is related to the presence of these findings on a subsequently performed CT-scan.

The final infarct size on CT-scan at 1 week related to the total amount of tissue at risk volume on baseline CT-Perfusion scan is an outcome measure considered as a signal of efficacy. Other secondary outcomes are the occurrence of hemorrhagic transformation of infarcted tissue and final infarct size demonstrated on the 1 week non-enhanced CT. Experienced discomfort from the face mask and/or Helontix Vent is another secondary outcome.

Study description

Background summary

In acute stroke therapy treatment with rt-PA thrombolysis within 3 hours showed a favourable outcome. Because of its small time window only a minority of stroke patients is eligible for this treatment. Therefore, strategies that arrest the transition from the hypoperfused but still viable penumbra to infarction are necessary. Numerous experimental studies and clinical trials assessing neuroprotective effects in ischemic stroke have been performed, but failed to show convincing results.
One hypothesis of this failure is that in absence of oxygen neuronal cells take up nitrogen in the mitochondria. As reperfusion - by thrombolysis or spontaneous recanalization - occurs, an intracellular *nitrogen lock* prevents oxygen to be taken up in the penumbra and ischemia will turn out into infarction. By replacing nitrogen with another gas in the air inhaled this intracellular nitrogen can be washed out before reperfusion. Partly due to methodological shortcomings, 100% oxygen therapy studies have never conclusive positive results. Helium, an inert gas, has a lower density and diffuses more rapidly in comparison with oxygen. These properties could be of interest in egressing nitrogen from the mitochondria and secondly, helium might serve as a tissue oxygen facilitator. An in vivo experiment tested the nitrogen washout hypothesis in ischemic stroke and showed promising results with 100% oxygen and even better results with helium. In cardio protection studies noble gas xenon has inhibitory effects on the adhesive properties of the endothelium. As helium lacks side effects and can be administered easily, it is a possible neuroprotective option which should be further investigated as a first-step treatment in acute ischemic stroke. Supported by experimental data on the use of helium in acute ischemic stroke, we want to investigate the safety and feasability of helium as a neuroprotective agent in acute ischemic stroke.

Study objective

The primary objective is to investigate the feasibility and the safety of heliox administration, a gaseous mixture of 79% helium en 21% oxygen, for 8 hours in acute ischemic stroke.

Study design

Monocenter, prospective, randomized controlled safety and feasability study

Intervention

Eligible patients with ischemic stroke are randomized to receive either heliox for 8 hours via a tight sealed face mask upon regular stroke care or regular stroke care alone. Clinical outcome will be evaluated at baseline, at 4 hours, 24 hours at 1 week and at 3 months follow up.

Study burden and risks

As helium lacks relevant side effects no risks are associated with the application and there is a possibility of neuroprotection. Study subjects are wearing a face mask for 4 hours. Study subjects and controls will undergo a brain CT-Perfusion scan at baseline and at 4 hours and a non-enhanced brain CT scan at 1 week. Study-related radiation exposure is a negligible risk due to the low dose exposure.
An outpatient department visit at 3 months makes an appeal to a subject*s willingness.

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

age >= 18 years;
clinical anterior circulation ischemic stroke;
< 12 hours of witnessed symptom onset
National Institutes of Health Stroke Scale (NIHSS) score >= 4;
pre-admission modified Rankin scale (mRS, dutch version) <= 1;
Visual estimation of penumbra/infarct ratio > 20%

Exclusion criteria

eligible for rt-PA thrombolysis;
inability to obtain written informed consent;
legal incapacity
medically instable (blood pressure >230/120 or <100/60 mmHg, pulse > 120 bpm, mechanical ventilation needed, body temperature above 39*C)
intracerebral hemorrhage on admission non-enhanced CT;
rapidly improving neurological deficits;
pregnancy;
impaired renal function (serum creatinin levels > 130 µmol/l)
allergic to contrast agent;
use of anticoagulation drugs or coagulopathy (PTT > 1.5 times control)
use following nephrotoxic medications: aminoglycosids, amfoterecine B or cisplatin
contra-indication or intolerance to any used substance;

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2011
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Heliox
Generic name:	Helium
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	23-12-2008
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	29-01-2009
Application type:	First submission
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)
Approved WMO Date:	06-04-2010

Application type:	Amendment
Review commission:	IRB Amsterdam: Independent Review Board Amsterdam (Amsterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 25537
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2008-001737-10-NL
CCMO	NL21743.003.08
OMON	NL-OMON25537