Neuroprotection in Aneurysmal Subarachnoid Hemorrhage - from Laboratory to Clinical Practice

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Delayed cerebral ischemia (DCI) is an important cause of death and dependence after SAH. Vasospasm plays an important role in the pathogenesis of DCI, because many patients have constricted arteries during the period of DCI, but vasospasm is not a...

Ethical review	Not approved
Status	Will not start
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON29768

Source
ToetsingOnline

Brief title
Neuroprotection in SAH - from Laboratory to Clinical Practice

Condition

- Central nervous system vascular disorders

Synonym
subarachnoid hemorrhage

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Hersenstichting Nederland

Intervention

Keyword: cerebral ischemia, interferon-beta, neuroprotection, subarachnoid hemorrhage

Outcome measures

Primary outcome

- relatie between studymedicatie and complicatiions

Secondary outcome

- serum TNF alfa

- the occurrence of DCI within three months after onset of SAH and poor outcome

after three months. DCI is defined as the occurrence of a new spontaneous

hypodense lesion as revealed by a CT scan compatible with clinical features of

DCI

(gradually developed focal deficits, decreased level of consciousness, or

both). Three months after the SAH we assess functional outcome with the

modified Rankin scale, a 6-point handicap scale that focuses on restrictions in

lifestyle, by means of a telephone interview.

Study description

Background summary

The project is part of a long standing line of research on subarachnoid hemorrhage (SAH) of neurologists and neurosurgeons in the UMC Utrecht. This research includes epidemiology, pathogenesis, treatment and prevention of SAH. The principal investigators have published more than 100 articles on this subject in the recent years. In this program, clinical and experimental research is carried out on cerebrovascular disorders with the aim to characterize pathogenesis, pathophysiology, and therapeutic intervention strategies. Our project is aimed at improving pharmacological treatment for SAH and will additionally contribute to a better understanding of pathophysiological mechanisms of cerebral ischemia and SAH. Studies will be

carried out at the Image Sciences Institute for Biomedical Imaging and the Rudolf Magnus Institute for Neuroscience. These groups have a joint research program on cerebral ischemia. MR imaging of cerebral ischemia has been a key topic of research for many years. The strong link between these groups enables optimal integration of tools and expertise, thereby allowing direct bridging of experimental findings to the clinic.

Study objective

Delayed cerebral ischemia (DCI) is an important cause of death and dependence after SAH. Vasospasm plays an important role in the pathogenesis of DCI, because many patients have constricted arteries during the period of DCI, but vasospasm is not a sufficient factor to explain the occurrence because not all patients with vasospasm develop DCI. Moreover, treatments aiming to reduce vasospasm have hardly been successful in improving outcome after SAH. Although promising drugs have been presented from laboratories all over the world, only a few have made it to the stage of testing the clinical application, and apart from nimodipine, none proved to be effective. The main reason probably is that most of these drugs were developed to reduce vasospasm only.
Our objectives for the clinical part of the study is to prepare the entree in clinical practice of drugs that proved to be effective in the experimental setting.

Study design

We aim to measure serum concentration of TNF daily in 50 consecutive patients with SAH to provide more evidence for the relation between serum concentrations with the occurrence of DCI and subsequent poor outcome. Serum TNF will be measured at admission and every 2 days up to 21 days after the event, or until discharge if this occurred within the first 3 weeks.
We will relate the occurrence of DCI to increased TNF before, and during the DCI onset period (Days 4-21 after SAH) by means of the Cox proportional hazards model, which yields a crude hazard ratio (HR). HRs will be considered statistically significant if the 95% confidence interval (CI) did not include 1. We will relate poor
outcome after 3 months to increased TNF before, and during the DCI onset period by means of the nonparametric Kruskal-Wallis test. This group will be used as controls in the IFN-β safety study.

Safety study for IFN-β in SAH:

TNF production is inhibited by IFN-β. Consequently, TNF may serve as a parameter for cerbral damage after SAH and IFN-β action. Three months after the SAH we assessed functional outcome with the modified Rankin scale, a 6-point handicap scale that focuses on restrictions in lifestyle, by means of a

telephone interview.

Data analysis and statistics:

The effects of IFN-β treatment will be assessed by comparison of various outcome measures (e.g., headache, TNF, neurological status, DCI and outcome) between IFN-β and non-treated group. Statistical comparisons will be performed using Logistic regression and Cox proportional hazard modelling.

Intervention

Betaferon 250 microgram (8.0 million IU), contained in 1 ml of the reconstituted solution, to be injected subcutaneously every other day for 14 days.

Study burden and risks

Moderate to severe side effects are uncommon and mostly related to extended administration of study medication. The more common side effects are mild and exists mainly of flu-like complaints and inflammation or pain at the site of the injections.

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

aneurysmal subarachnoid hemorrhage

Exclusion criteria

- non-aneurysmal causes of subarachnoid hemorrhage
- pregnancy
- use of interferon
- a history of hypersensitivity to natural or recombinant interferon
- severe depression and/or suicidal ideation
- decompensated liver disease.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-09-2007
Enrollment:	100
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Betaferon
Generic name:	interferon beta-1b
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	24-10-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
EudraCT	EUCTR2006-002878-21-NL

Register	ID
CCMO	NL12902.041.06