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Cooling in INtraCerebral Haemorrhage (CINCH) trial

Submission date	Recruitment status	[ ] Prospectively registered
04/01/2011	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
18/02/2011	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
18/02/2011	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Cooling in INtraCerebral Haemorrhage (CINCH) trial: a multicentre, controlled, prospective, randomised, blinded endpoint assessment

Acronym
CINCH

Study objectives
Cooling in INtraCerebral Haemorrhage (CINCH) trial has been designed to determine whether therapeutic hypothermia over a period of 8 day plus rewarming reduces perihaemorrhagic oedema and improves survival rates after large intracerebral haemorrhage (ICH).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethik-Kommission der Universtiät Erlangen-Nürnberg, Germany, approved on the 17th November 2010 (ref: 4303)

Study design
Multicentre controlled prospective randomised blinded endpoint assessment trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet (German only)

Health condition(s) or problem(s) studied
Intracerebral haemorrhage

Interventions
Treatment
All patients in both study groups receive standard neurointensive care, following the recommendations of current guidelines and the agreements from a consensus meeting of the steering board. Only patients in the TH-group receive additional cooling by endovascular catheters as outlined in detail below.
Standard neurointensive care

1. ICP-measurement: All patients will be monitored by invasive ICP-measurement. The monitoring device can be selected by the treating study center. We recommend measuring in hemisphere ipsilaterally to the ICH or an EVD, respectively. The EVD should be positioned to 15 cm above the level of the foramen Monroi to avoid overdrainage and subsequent complications.
2. Osmotherapy: Hyperosmolaric therapy will be initiated in case of an ICP-crisis. An ICP-crisis is defined by plausible increase of the ICP above 20 mmHg for a period of 15 min or more. Hyperosmolar therapy includes mannitol (e.g. Osmofundinâ 100 ml 15%-solution, initial dose 4 per day) or glycerol (e.g. Glycerosterilâ 250 ml 10%-solution, initial dose 4 per day). Further dosing will be adjusted to at least daily measured serum osmolality (target value: 315 to 320 mOsm). If this treatment does not lead to a sufficient improvement of clinical signs of hernation and/or ICP-reduction below 20 mmHg, hypertonic saline is given in a dose of 50 ml 5- to 7.5%. In case of ICP-crisis, hypertonic saline can be given repeatedly until a serum level of 158mmol/l. Other ICP-reducing approaches such as barbiturate use and/or hyperventilation are not recommended.
3. Intubation and mechanical ventilation: Mechanical ventilation will be initiated at a Glasgow-Coma-Scale (GCS) Score of 8 or less, during global respiratory insufficiency (pO_2<60 mmHg, pCO_2>48 mmHg) or/and in case of mechanical respiratory problems, Target parameters in mechanically ventilated patients are: pO_2>75mmHg, pCO_2 36-44 mmHg. In case of ICP-crisis a pO_2>100mmHg should be reached.
4. Patients with additional intraventricular hemorrhage (IVH) can be included into the study, if there is a local protocol for intracventricular lysis and lumbar drainage. Centers lacking the described protocol cannot include patients which additional IVH.
5. Sedation: The medication for sedation can be selected by the local PI.
6. Blood pressure management (BPM): BPM will be done according to the recent guidelines. The upper limit of systolic blood pressure is 140 to 170 mmHg. The antihypertensive medication can be selected by the local PI.
7. Body temperature: Body core temperature will be measured in the urinary bladder. Increase of body temperature above 37.5°C will be treated by antipyretics (AHA guidelines), cold infusions or/and surface cooling. These methods should not lower the body core temperature below 36.5°C.
8. The hemoglobin concentration should be above 9.0 g/dl. Lower values should be treated by erythrocyte transfusions.
9. Patients should receive subcutaneously low molecular weight heparin for prophylaxis of deep venous thrombosis within 24 hours after ICH after exclusion of hemorhage growth in the 24-h control CT.
10. A recent study has shown, that patients with large ICH require cranial CT at least 4-5 times during NICU-stay, since the value of the neurological examination in mechanically ventilated, sedated patients is limited and the course of ICH is often not predictable and can be very dynamic (re-bleeding, increase of PHE, occlusion hydrocephalus). Patients of the CINCH-study will have cranial CTs within the following defined time periods after ICH to enable later comparison of cCTs between the groups: on admission, 24±3 hours after admission, 36-72 after ICH and at day 8+0,5 and 11+0,5 after ICH symptom onset. Patients can be monitored by additional transcranial ultrasound.

Intervention: Therapeutic hypothermia
Patients randomised to TH are treated with an endovascular catheter-based cooling system positioned in the femoral vein as described previously (15). The target temperature is set to 35.0° C. The body core temperature is measured by a urinary bladder catheter. As soon as body core temperature drops below 36.0°C, patients are covered by a warming blanket to avoid shivering. 8 days (192 hours) after initiation of TH, patients receive slowly, controlled rewarmed by 0.05°C per hour (approximately within 40 hours). The catheter will be changed at least once during the treatment period, preferably on day 4±0.5 after ICH, or if clinically indicated. All patients will be

screened for deep venous thrombosis at least twice (day 0 to 5 first ultrasound, day 6 to 9 second ultrasound). Blood testing for coagulation will be performed before, during and after cooling.

Total follow-up is 6 months.

Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
1. Mortality on day 30 after ICH
2. Total lesion volume (volume of ICH and PHE) on day 8±0.5 and day 11±0.5 after ICH

Secondary outcome measures
1. Mortality during treatment in the study centre ("in-hospital-mortality")
2. Mortality on day 90 and 180 after ICH
3. Dichotomised modified Rankin Scale (mRS): for 0 - 3 versus 4 - 6 and 0 - 2 versus 3 - 6 after 3 and 6 months
4. Barthel Index 3 and 6 months after ICH
5. Complications attributed to hypothermia, and hypothermia associated procedures (e.g. bleeding or infection due to endovascular catheter)

Overall study start date
15/01/2011

Completion date
15/07/2012

Eligibility

Key inclusion criteria
1. Aged 18 to 65 years
2. Diagnosis of large acute primary ICH
3. ICH located at the level of the basal ganglia or thalamus
4. Large ICH is defined by between 25 and 64 ml on the initial cranial computertomography (cCT). Since cranial magnetic resonance imaging (MRI) techniques overestimate intracerebral haematoma size, patients with a haematoma size of 35 to 74 ml can be included if the initial tomography of the brain is an MRI.
5. Glasgow Coma Scale (GCS) of less than 8 before intubation or worsening of clinical symptoms defined by a decrease of 2 points on the GCS

Patients who are randomised should be treated earliest 6 hours and up to 18 hours after symptom onset. Before randomisation, patients do not have to show clinical signs of herniation such as bilateral signs of the pyramidal tract or pupillomotory defects. Informed consent has to be given before randomisation by the patients or the legal entity.

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Key exclusion criteria
1. ICH is located in the posterior cranial fossa or extends to the brainstem
2. Patients with additional intraventricular haemorrhage (IHV) and the need for external ventricular drainage (EVD) due to an occlusive hydrocephalus, as IVH is an independent prognostic factor for poor outcome. However, if the local clinical guidelines of the investigator address treatment of IVH by EVD, intraventricular clot lysis and use of lumbar drainage, also patients with additional IVH can be included.
3. Patients with suspected secondary cause of ICH such as vascular malformation, brain tumour, metastasis, impaired coagulation (International Normalised Ratio [INR] greater than 1.5) and a thrombocyte count of below 70,000/ul
4. Patients with a body weight of over 130 kg, severe known heart disease such as severe dilatative cardiomyopathy or severe valve disease, known haematological disease (especially cryoglobulinaemia), vasospastic disease, paramyotonia congenital, severe liver or kidney disease and myocardial infarct within the last 3 weeks
5. Patients with severe comorbidity defined by a Modified Rankin Scale (mRS) of greater than 3 and severe infection defined by leukocytosis of over 20,000/ul
6. Female patients with an age below 45 will have to have a negative urinary test for pregnancy

Date of first enrolment
15/01/2011

Date of final enrolment
15/07/2012

Locations

Countries of recruitment
Austria

Germany

Study participating centre

University Hospital Erlangen
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Sponsor information

Organisation
University Hospital Erlangen (Germany)

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Sponsor type
University/education

Website
http://www.uk-erlangen.de/

ROR
https://ror.org/0030f2a11

Funder(s)

Funder type
University/education

Funder Name
University of Erlangen-Nürnberg (Germany)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration