COOLing for Ischaemic Stroke Trial.

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1. Cooling to 34, 34.5 or 35°C by means of a surface cooling device, started within 4.5 hours after the onset of acute ischaemic stroke and maintained for 24 hours in awake patients on a stroke unit is safe; 2. In awake patients with ischaemic...

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21707

Bron
NTR

Verkorte titel
COOLIST

Aandoening

acute ischaemic stroke

Ondersteuning

Primaire sponsor: University Medical Center Utrecht
Overige ondersteuning: Netherlands Heart Foundation 2010B239

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Feasibility, defined as the number of patients that has successfully completed the treatment strategy they had been assigned to.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:

Cooling to 32 - 34°C improves outcome in patients with post-anoxic encephalopathy after cardiac arrest. Animal studies strongly suggest that cooling also improves outcome after ischaemic stroke. In these studies, cooling was efficacious at temperatures of 35°C or below, with lower temperatures associated with a greater benefit. In clinical practice however, each °C decrease in temperature may be tolerated less well by awake patients on a stroke unit. In contrast to endovascular cooling, surface cooling can probably be combined with concurrent thrombolysis. The feasibility of surface cooling to temperatures of 35°C or below in patients with acute ischaemic stroke has not been evaluated systematically in clinical studies.

Hypotheses:

1. Cooling to 34, 34.5 or 35°C by means of a surface cooling device, started within 4.5 hours after the onset of acute ischaemic stroke and maintained for 24 hours in awake patients on a stroke unit is safe.

2. In awake patients with ischaemic stroke, the feasibility of cooling decreases with each °C temperature reduction.

Aim:

To compare the feasibility and safety of surface cooling to 34, 34.5 and 35°C, started within 4.5 hours after the onset of acute ischaemic stroke and maintained for 24 hours, in awake patients on a stroke unit.

Methods:

This is a randomised, open, multi-centre, phase II clinical trial with masked outcome assessment, comparing three different surface cooling strategies with standard treatment in 48 awake adult patients with acute ischaemic stroke and a score on the NIH Stroke Scale > 6, admitted to a stroke unit. Intravenous or intra-arterial thrombolysis or thrombectomy are not exclusion criteria. Patients will be randomised to conventional treatment (n = 12) or to surface cooling to 34, 34.5, or 35°C maintained for 24 hours (n = 12 in each group). In all patients randomised to hypothermia, cooling will be started within 4.5 hours after the onset

of symptoms by means of intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 to 60 minutes, followed by surface cooling. Shivering and discomfort will be prevented and treated with intravenous pethidine and with oral buspirone. The primary outcome measure is feasibility, defined as the number of patients that has successfully completed the treatment strategy they had been assigned to. Secondary outcome measures include the time to target temperature, stability at target, complications, and the score on the modified Rankin scale at three months.

Sample size:

Based on an alpha of 0.05 and a power of 80%, we will need 12 patients per group to detect a difference in feasibility of 40%.

Study monitoring:

Unblinded outcome and safety data will be forwarded to an international data safety monitoring committee (DSMC) after final follow-up of the first 12, 24 and 36 patients, after which the DMSC will advise the steering committee with regard to the continuation of the study.

Expected results:

This study will provide adequate information on the feasibility and safety of different surface cooling strategies on a stroke unit. A validation study, in which the two most promising treatment strategies will be assessed again, is anticipated. The results of the present trial and those of the validation trial will inform the design of a conclusive phase III trial of surface cooling for acute ischaemic stroke. As cooling is probably more effective with lower temperatures, cooling to 34°C will be preferred if shown feasible and safe.

Doel van het onderzoek

1. Cooling to 34, 34.5 or 35°C by means of a surface cooling device, started within 4.5 hours after the onset of acute ischaemic stroke and maintained for 24 hours in awake patients on a stroke unit is safe;

2. In awake patients with ischaemic stroke, the feasibility of cooling decreases with each °C temperature reduction.

Onderzoeksopzet

Feasibility: 24 hours;

Complications: 3 months;

Modified Rankin scale: 3 months.

Onderzoeksproduct en/of interventie

Patients will be randomised to conventional treatment (n = 12) or to surface cooling to 34, 34.5 or 35°C maintained for 24 hours (n = 12 in each group). In all patients randomised to hypothermia, cooling will be started within 4.5 hours after the onset of symptoms by means of intravenous infusion of 20 ml/kg cooled normal saline (4°C) over 30 to 60 minutes, followed by surface cooling. Shivering and discomfort will be prevented and treated with intravenous pethidine and with oral buspirone.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. A clinical diagnosis of acute ischaemic stroke;

2. A possibility to initiate cooling within 4.5 hours of stroke onset. Onset time for patients who awoke with symptoms is defined as the last time the patient was awake without symptoms of stroke;

3. Score on the National Institutes of Health Stroke Scale (NIHSS) > 6;

4. Age > 18 years;

5. Written informed consent by the patient or a legal representative.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Evidence from a CT or MRI scan or from other pre-randomisation investigations of an intracranial haemorrhage, a brain tumour, encephalitis, or any diagnosis other than acute ischaemic stroke likely to be the cause of the symptoms. Haemorrhagic transformation of the infarct is not an exclusion criterion, except when there is a parenchymal haematoma covering more than 30% of the infarcted area, with significant space-occupying effect, or when there is a bleeding remote from the infarcted area (PH2 on Fiorelli's scale);

2. Conditions that may be complicated by hypothermia, such as haematological dyscrasias (including oral anticoagulant treatment with INR > 1.7 or a platelet count < 100.109/L), severe pulmonary disease, severe heart failure (defined as a NYHA score of III or IV), myocardial infarction within the previous 3 months, angina pectoris in the previous three months, severe infection with a CRP > 50 mg/L, or a clinical diagnosis of sepsis;

3. Blood oxygen saturation below 92% without use of oxygen therapy or below 94 % with a maximum of 2 L/min oxygen delivered nasally;

4. Bradycardia (<40 beats/min);

5. Body weight > 120 kg;

6. Pre-stroke score on the modified Rankin Scale (mRS) > 2;

7. Allergy to pethidine, buspirone, or ondansetron, use of a monoamine oxidase inhibitor in the previous 14 days, hepatic or severe renal dysfunction, or asthma. Severe hepatic dysfunction is defined as liver enzymes increased above two times above the upper limit of normal, and severe renal dysfunction as a glomerular filtration rate < 30 ml/min.;

8. Pregnancy. Women of childbearing potential are excluded unless a negative test for pregnancy has been obtained prior to randomization;

9. Other serious illness that may confound treatment assessment or increase the risks of cooling;

10. Previous participation in this trial.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-02-2011
Aantal proefpersonen:	48
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2499
NTR-old	NTR2616
Ander register	Netherlands Heart Foundation : NHS 2010B239
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A