Paracetamol (Acetaminophen) in Stroke 2 (PAIS 2): A randomized clinical trial to investigate the effect of high-dose paracetamol in patients with acute stroke and a body temperature of 36,5°C or above.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24724

Source
Nationaal Trial Register

Brief title
PAIS 2

Health condition

acute stroke, cerebral infarction, intracraniel hemorrhage, acetaminophen, body temperature, inflammation, functional outcome

herseninfarct, hersenbloeding, paracetamol, lichaamstemperatuur, inflammatie, functionele uitkomst

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: Erasmus MC

Intervention

Outcome measures

Primary outcome

A favorable outcome defined as improvement on the modified Rankin Scale (mRS) at 3 months from stroke onset.

Secondary outcome

1. Poor outcome defined as mRS>2 at 3 months;

2. Barthel index score as an indicator of functional status (ranging from 0-20, 20 indicating no disability and 0 indicating complete dependence) and European Quality of Life-5 dimensions (EQ5D)25 score at 3 months;

3. Body temperature 12-36 hours after start of treatment;

4. Inflammatory markers and genetic variation thereof.

Study description

Background summary

In the Paracetamol (Acetaminophen) in Stroke (PAIS) trial, a double-blind, placebo-controlled randomized clinical trial of 1400 patients with acute stroke, the paracetamol-treated patients (6 g daily, 3 days) showed more improvement on the modified Rankin scale (mRS) at 3 months, yet the difference was not statistically significant. In the 661 patients with a baseline body temperature of 36,5°C or above, treatment with paracetamol led to a larger decrease in temperature (0.30°C; 95% CI: 0.20-0.40), increased the odds of improvement (OR 1.43; 95% CI: 1.02-1.97) and was associated with a 7% (95% CI: 0-15%, p=0.06) absolute decrease in the risk of poor outcome. These findings need further study.

Study objective

We hypothesize that treatment of patients with acute ischemic or hemorrhagic stroke and a body temperature of 36,5°C or above with paracetamol in a daily dose of 6 g for three consecutive days, leads to improved functional outcome.

At least 50% of patients with acute stroke have a body temperature over 36,5°C. Increased

body temperature is related to poor functional outcome. The risk of poor outcome may double with each degree Celsius increase in body temperature.

Study design

1. Oktober 2010: first inclusion;

2. Juli 2014: final inclusion;

3. Oktober 2014: end of follow-up.

Intervention

Paracetamol or matching placebo will be administered 6 times daily for three consecutive days; the first 24 hours as suppositories of 1 g, or as 2 tablets of 500 mg per dosage (after swallowing difficulties have been excluded), from 24-72 hours as 2 tablets of 500 mg per dosage.

Contacts

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Eligibility criteria

Inclusion criteria

1. Clinical diagnosis of ischemic stroke or intracerebral hemorrhage, confirmed by CT or MRI scan within 24 hours after inclusion in the study;

2. A measurable deficit on the National Institutes of Health Stroke Scale (NIHSS);

3. The possibility to start treatment within 12 hours of symptom onset (for patients who noticed symptoms when awaking from sleep, the time last seen well is taken as the time of onset of symptoms);

4. A body temperature of 36,5°C or higher;

5. Age of 18 years or older;

6. Signed informed consent.

Exclusion criteria

1. A body temperature lower than 36.5°C;

2. A history of liver disease or alcohol abuse;

3. Liver enzymes (ASAT, ALAT, AP or gamma-GT) increased above twice the upper limit of normal values;

4. Allergy to paracetamol;

5. Death appearing imminent at the time of inclusion;

6. Any pre-stroke impairment that has led to dependency (modified Rankin scale (mRS)>2) and therefore interferes with the assessment of functional outcome.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	01-10-2010
Enrollment:	1500
Type:	Anticipated

Ethics review

Positive opinion Date:	14-06-2010
Application type:	First submission

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
NTR-new	NL2239
NTR-old	NTR2365
Other	WHO UTN : U1111-1124-9185
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
Den Hertog HM et al. The Paracetamol (Acetaminophen) In Stroke trial: a multicentre, randomised, placebo-controlled, phase III trial. Lancet Neurol. 2009 May;8(5):434-40.