ISRCTN99503308 https://doi.org/10.1186/ISRCTN99503308

Acute stroke treatment in the ambulance with a nitroglycerin patch

Submission date
31/10/2017

Recruitment status
No longer recruiting

Registration date
02/01/2018

Overall study status
Completed

Last Edited
13/02/2024

Condition category
Nervous System Diseases

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Stroke is a life-threatening medical condition, caused by a disorder in the blood supply to the brain. There are two main types of stroke: ischaemic, caused by a reduction in blood flow, or haemorrhagic, caused by a rupture of an artery in the brain. Within minutes, brain cells die. Symptoms can vary from limb weakness, drooping of the face or speech difficulties. Prompt treatment is crucial and early action can reduce brain damage and complications. This study investigates the treatment of stroke with an adhesive patch containing the medicine nitroglycerin. Nitroglycerin is a medication that is commonly administered as heart medication but it could help if applied quickly after a stroke as it can help lower blood pressure and open up blood vessels. This patch will be given in the ambulance by the paramedic to patients with suspected stroke (brain infarct or bleeding). Recent research suggests a beneficial effect of the treatment with this drug in patients with acute stroke, if given within the first few hours. The aim of this study is to find out if treatment with a nitroglycerin patch will lead to better functional outcome at 90 days.

Who can participate?
Adult patients with suspected stroke with symptom onset within 3 hours and a systolic blood pressure of 140 and higher can participate.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group receive the standard care. Those in the second group receive a transdermal nitroglycerin patch with a dosage of 5 mg/24 hours to wear plus standard care. The patch is applied by a paramedic in the pre-hospital setting and continued during hospital admission for a total of 24 hours. During hospital admission, no extra tests or investigations will be performed. At 90 days, participants receive a phone call to assess the outcomes of the patch.

What are the possible benefits and risks of participating?
The possible benefit of this treatment is a better functional outcome. This will be measured during a telephone follow-up after 3 months. The possible risks of participating are the side

effects of the medication. Nitroglycerin has been used for decades in heart disease and is most often well tolerated. The most common side effects are headache, nausea and low blood pressure.

Where is the study run from?
This study is run from the University Medical Center Utrecht (Netherlands) and the Academic Medical Center in Amsterdam (Netherlands).

When is the study starting and how long is it expected to run for?
May 2017 to June 2021

Who is funding the study?
Dutch Heart Foundation (Netherlands)

Who is the main contact?
Miss Sophie van den Berg

Contact information

Type(s)
Scientific

Contact name
Miss Sophie van den Berg

Contact details
Academisch Medisch Centrum
Meiberglaan 9
Amsterdam
Netherlands
1105AZ

Additional identifiers

Clinical Trials Information System (CTIS)
2016-005086-31

Protocol serial number
60258

Study information

Scientific Title
Multicentre Randomised trial of Acute Stroke treatment in the Ambulance with a nitroglycerin Patch

Acronym
MR ASAP

Study objectives

Prehospital treatment with a transdermal nitroglycerin patch, applied within 3 hours after stroke onset, improves functional outcome at 90 days in patients with acute ischaemic stroke or intracerebral haemorrhage.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional review board of the Erasmus Medical Center, 19/10/2017, ref: MEC-2017-369

Primary study design
Interventional

Study design
Multicentre prospective randomized open-label clinical trial with blinded endpoint assessment (PROBE design)

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute ischaemic stroke and intracerebral haemorrhage

Interventions
Participants are randomly assigned in a 1:1 ratio by a web-based randomisation to one of two groups. Those in the first group receive the standard care. Those in the second group receive a transdermal nitroglycerin patch with a dosage of 5 mg/24 hours to wear plus standard care. The patch is applied by a paramedic in the prehospital setting and continued during hospital admission for a total of 24 hours. During hospital admission, no extra tests or investigations will be performed. At 90 days, a telephone interview is performed by a blinded outcome assessor to assess the outcomes of the patch.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Glyceryl trinitrate

Primary outcome(s)
Functional outcome is assessed using the modified Rankin Scale (mRS) at 90 days.

Key secondary outcome(s)
1. At hospital admission:
1.1. Vital signs (blood pressure and heart rate)
1.2. Collateral circulation assessed with CT-angiography
2. At 24 hours:
2.1. Treatment with intravenous thrombolysis and/or endovascular treatment
2.2. Vital signs (blood pressure and heart rate)

2.3. Neurological deficit assessed using the National Institutes of Health Stroke Scale (NIHSS)
3. At 90 days, assessed during a blinded telephone interview:
3.1. Death
3.2. Dichotomised mRS (0-1 vs. 2-6; 0-2 vs. 3-6; 0-3 vs. 4-6)
3.3. Disability assessed with the score on the Barthel Index
3.4. Quality of life assessed with the EuroQol-5D-5L
3.5. Home time and patient location over the first 90 days

Completion date
24/06/2021

Eligibility

Key inclusion criteria
1. Age 18 years or older
2. Probable diagnosis of acute stroke, as assessed by the paramedic in the prehospital setting
3. Score of 2 or 3 on the Face Arm Speech Test (FAST)
4. Systolic blood pressure ≥ 140 mm Hg
5. Possibility to start the trial treatment within 3 hours of symptom onset
6. Intention to transport the patient to one of the participating hospitals
7. Written informed consent (deferred)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
325

Key exclusion criteria
1. Considerable pre-stroke dependency in activities of daily living, defined as staying in a chronic nursing home or rehabilitation centre
2. Known pregnancy or lactation
3. Indication for acute treatment with nitroglycerin or known use of nitroglycerin in the previous 12 hours
4. Indication for acute reduction of blood pressure
5. Known hypersensitivity to GTN, nitrates in general, or the adhesives used in the patch
6. Glasgow Coma Scale < 8
7. Known with any of the following heart disorders: myocardial insufficiency due to obstruction;

aortic or mitral valve stenosis; constrictive pericarditis; hypertrophic obstructive cardiomyopathy; cardiac tamponade
8. Known marked anaemia, defined as haemoglobin < 5 mmol/L
9. Known closed angle glaucoma
10. Known concomitant use of phosphodiesterase type-5 inhibitors, (e.g. sildenafil, tadalafil, vardenafil)

Date of first enrolment
04/04/2018

Date of final enrolment
31/10/2021

Locations

Countries of recruitment
Netherlands

Study participating centre
Academic Medical Center
Amsterdam
Netherlands
1105AZ

Study participating centre
University Medical Center (lead centre)
Utrecht
Netherlands
-

Study participating centre
Isala, Zwolle
Netherlands
-

Study participating centre
VU University Medical Center
Amsterdam
Netherlands
-

Study participating centre
OLVG-West
Amsterdam
Netherlands
-

Study participating centre
MC Slotervaart
Amsterdam
Netherlands
-

Study participating centre
Waterland Hospital
Purmerend
Netherlands
-

Study participating centre
St. Antonius Hospital
Nieuwegein
Netherlands
-

Study participating centre
Meander Medical Center
Amersfoort
Netherlands
-

Study participating centre
Diakonessenhuis
Utrecht
Netherlands
-

Sponsor information

Organisation
University Medical Center Utrecht

ROR
https://ror.org/0575yy874

Funder(s)

Funder type
Charity

Funder Name
Dutch Heart Foundation

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2022	05/09/2022	Yes	No
Protocol article	protocol	26/06/2019	28/06/2019	Yes	No
Abstract results		22/05/2019	13/02/2024	No	No
Abstract results		01/09/2021	13/02/2024	No	No
Abstract results		03/05/2022	13/02/2024	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes