Groningen Intervention study for the Preservation of cardiac function with sodium thiosulfate after ST-segment elevation myocardial infarction

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To evaluate the efficacy and safety of STS compared to placebo treatment on myocardial infarct size in patients presenting with STEMI and treated with PCI and in adjunction to optimal reperfusion therapy.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Myocardial disorders
Study type	Interventional

Summary

ID

NL-OMON47742

Source
ToetsingOnline

Brief title
GIPS-IV

Condition

- Myocardial disorders

Synonym
myoacardial infarction; heart attack

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Fonds Cardiologie

Intervention

Keyword: cardiac magnetic resonance imaging, Infarct size, Sodium thiosulfate, STEMI

Outcome measures

Primary outcome

Primary endpoint is infarct size as measured with cardiac magnetic resonance imaging (CMR-imaging) 4 months after randomization.

Secondary outcome

Secondary CMR-imaging efficacy measures include left ventricular ejection fraction (LVEF) and myocardial perfusion reserve (MPR) at 4 month follow up. Furthermore, N-terminal fragment brain natriuretic peptide (NT-proBNP) will be assessed 4 months after randomisation. Other secondary efficacy endpoint measures will be obtained from non-mandatory CMR-imaging during hospitalization to study myocardial haemorrhage, microvascular obstruction (MVO) and myocardial salvage index (MSI). Clinical safety endpoints include all-cause mortality and combined incidence of cardiovascular events: cardiovascular death, re-infarction, re-intervention and stroke. As additional safety endpoints we will evaluate the incidence of internal cardiac defibrillator (ICD) implantation and hospitalization for heart failure or chest pain. Finally, enzymatic infarct size as assessed by peak creatine kinase, muscle-brain isoenzymes (CK)-MB) during hospitalization will be used as very early safety parameter.

Study description

Background summary

Timely and effective reperfusion by primary percutaneous coronary intervention (PPCI) is currently the most effective treatment of ST-segment elevation myocardial infarction (STEMI). However, permanent myocardial injury related to the ischemia and subsequent reperfusion is observed in the vast majority (88%) of patients and harbours a risk of heart failure development. Administration of hydrogen sulfide (H2S) has been shown to protect the heart from *ischemia reperfusion injury* in various experimental models. Data in humans suggests that the H2S-releasing agent sodium thiosulfate (STS) can be administered safely.

Study objective

To evaluate the efficacy and safety of STS compared to placebo treatment on myocardial infarct size in patients presenting with STEMI and treated with PCI and in adjunction to optimal reperfusion therapy.

Study design

This is a single-center, prospective, stratified, randomized double blind study. In total, 380 patients with a first acute MI will be included. Before PCI, all patients will be randomly assigned to receive either optimal standard medical care or receive sodium thiosulfate on top of standard medical care. The study will take place at the University Medical Center of Groningen, a center with experience in primary PCI of patients with acute MI and with access to emergency cardiac surgery. Four months after PCI, a period in which the remodeling of the heart has completed, CMR-imaging is performed to determine the infarct size. CMR is a well-recognized, validated, and highly reproducible technique.

Intervention

Patients are randomised in an 1:1 ratio to be treated with STS 12.5g intravenously (i.v.) or matched placebo immediately after arrival at the catheterization laboratory (cath-lab) and a repeated dose administered 6 hours after the first dose, on top of standard treatment.

Study burden and risks

Adverse effects on sodium thiosulfate: Reported side effects include nausea and vomiting and can be controlled by anti-emetics. A less common side effect metabolic acidosis appeared only in end-stage renal disease patients.

Hypernatraemia can occur after STS infusion, but was reported mild and transient.

Adverse effects on intravenous contrast used during the MRI-scan (gadolinium)

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

1. Age * 18 years;, 2. The diagnosis STEMI defined by (1) chest pain suggestive for myocardial ischemia for at least 30 minutes, the time from onset of the symptoms less than 12 hours before hospital admission, and (2) an electrocardiogram recording with ST- segment elevation of more than 0.1 mV in 2 or more contiguous leads or presence of new left bundle branch block;;, 3. Symptoms and/or ST-segment deviation should be present (persisting) at time of

arrival in the catheterization laboratory;, 4. Primary percutaneous intervention is being considered as treatment;, 5. Patient is willing to cooperate with follow-up during 2 years.

Exclusion criteria

1. Prior myocardial infarction, unless maximum troponin T< 50 ng/L (STEMI/non-STEMI/acute coronary syndrome);
2. Known permanent atrial fibrillation;
3. Prior CABG;
4. Prior PCI, complicated by periprocedural infarction, unless maximum troponin T < 50ng/L;
5. Known cardiomyopathy;
6. Previous hospitalization for heart failure
7. Active malignancy (requiring chemotherapy, radiation or surgery at the time of randomization), except for adequately treated non-melanoma skin cancer or other noninvasive or in situ neoplasm (e.g., cervical cancer in situ);
8. History of chemotherapy;
9. History of radiotherapy in chest region;
10. Relieve of symptoms and complete ST-segment resolution prior to arrival at the catheterization laboratory;
11. Presentation with cardiogenic shock (systolic blood pressure < 90 mmHg);
12. Severe hypertension (systolic blood pressure > 220 mmHg);
13. Sedated and/or intubated patients;
14. The existence of a condition with a life expectancy of less than 1 year;
15. Contraindication for 3 Tesla (T) CMR-imaging (e.g. body weight >;150kg; known claustrophobia; 3T MRI incompatible ferromagnetic objects in the body, end-stage renal disease);
16. Pregnancy or breastfeeding women; women of childbearing potential with clinical suspicion of possible pregnancy;
17. A condition which, according to the clinical judgment of the investigator and/or treating physician, does not allow the patient to successfully participate in the study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-07-2018
Enrollment:	380
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	sodium thiosulfate pentahydrate
Generic name:	sodium thiosulfate pentahydrate

Ethics review

Approved WMO Date:	26-07-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-10-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-07-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	16-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-03-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2015-001006-34-NL
ClinicalTrials.gov	NCT02899364
CCMO	NL57899.042.16