Safety and tolerability of sodium thiosulfate in patients presenting with an acute coronary syndrome undergoing coronary angiography via radial approach: a dose-escalation study.

Published: 06-04-2017
Last updated: 12-04-2024

to evaluate the safety and maximum tolerable dose of sodium thiosulfate in patients presenting with acute coronary syndrome undergoing coronary angiography via transradial approach, when given in combination with concomitant vasodilator drugs.

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

Summary

ID

NL-OMON45347

Source
ToetsingOnline

Brief title
safe acs

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: acute coronary syndrome, hemodynamic instability, maximum tolerable dose, Sodium thiosulfate

Outcome measures

Primary outcome

Primary endpoint is the development of DLT:

All-cause mortality OR hemodynamic instability developed during STS

administration, in combination with vasodilators used in radial approach and/or

during second infusion after 6 hours. Hemodynamic instability of significant

clinical impact is defined as :

- Systolic blood pressure <90mmHg for >30 min and/or

- Catecholamines required to maintain pressure >90 mmHg during systole and

- Signs of pulmonary congestion or elevated left-ventricular filling pressures,

and

- Signs of impaired organ perfusion with *1 of the following criteria:

o Confusion;

o Cool, clammy skin;

o Oliguria (urine output <30 ml/h);

o Serum-lactate >2.0 mmol/l.

- Shock of other causes (hypovolemia, sepsis, bradycardia) are ruled out.

Secondary outcome

The effect of STS on:

- the development of anaphylaxis;

- Nausea/vomiting;

- Oxidative stress markers

Study description

Background summary

timely and effective reperfusion by primary percutaneous coronary intervention (PPCI) is currently the most effective treatment of acute coronary syndrome (ACS). However, permanent myocardial injury related to the ischemia and subsequent reperfusion is observed in most 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. A dose of 25 gram/day can be safely applied in other patient groups (haemodialysis patients, paediatric cancer patients treated with chemotherapy). However, the safety and tolerability of H2S have never been tested in ACS patients. These patients are given blood pressure lowering and vasodilating drugs which can potentially interact with H2S. Data regarding the dose-limiting toxicity (DLT) and maximum tolerable dose (MTD) of H2S in the clinical setting of ACS is needed before H2S can be tested in a randomized clinical trial.

Study objective

to evaluate the safety and maximum tolerable dose of sodium thiosulfate in patients presenting with acute coronary syndrome undergoing coronary angiography via transradial approach, when given in combination with concomitant vasodilator drugs.

Study design

a single centre, open label dose-escalation study with a 3+3 design with fixed dosing endpoint.

Intervention

the patients will receive STS i.v. in different doses (0, 2.5, 5, and 10 g, 12.5 and 15g; 3 patients per dose cohort). STS is administered immediately after arrival at the catheterization laboratory (cath-lab). If hemodynamic stable, a second gift of STS is administered 6 hours after the first dose at the coronary care unit (CCU). When no DLT is observed in any of the patients

after two gifts we will enrol 3 additional subjects into the next higher dose cohort. If 1 out of 3 patient suffers hemodynamic instability for 30 minutes at a specific dose, an additional 3 subjects are enrolled into the same dose cohort. When more than 1 out of 6 patients develop DLT this implies that the MTD has been exceeded and the trial is terminated.
Blood samples will be taken at presentation and 3 hours after each injection to evaluate the effect of STS on various oxidative stress markers.

Study burden and risks

The burden for the patient is low. Patients are usually admitted at the hospital during the first 48 hours. All patients receive an extra intravenous catheter at the catheterization lab, upon which they receive STS treatment. Blood samples will be taken from a different catheter for the measurement of oxidative stress markers. The anticipated risks for the patients are possible refractory hypotension, severe hypersensitivity reaction, sever renal dysfunction, and bleeding complications.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age * 18 years;
-The diagnosis ACS defined by: chest pain suggestive for myocardial ischemia for at least 30 minutes, the time from onset of the symptoms less than 24 hours before hospital admission, with (STEMI) or without (nSTEMI/iAP) an electrocardiogram (ECG) recording with ST- segment elevation of more than 0.1 mV in 2 or more contiguous leads;
-cardiac catheterization via radial approach is being considered;
- Patient is willing to cooperate with the trial during hospitalization.

Exclusion criteria

- Known cardiomyopathy or LVEF < 35%;
- History of a malignancy treated with chemo- and/or radiotherapy < 1 year;
- Systolic blood pressure under 100mmHg or over 180mmHg at presentation;
- Cardiogenic shock at presentation? (def: SHOCK II)
- Sedated and/or intubated patients;
- The existence of a condition with a life expectancy of less than 1 year;
- pregnant or breastfeeding at time of presentation;
- 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 type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-10-2017
Enrollment:	36
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	06-04-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-11-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-01-2018
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	EUCTR2017-000203-25-NL
ClinicalTrials.gov	NCT03017963
CCMO	NL60193.042.17

Study results

Date completed: 24-03-2018

Actual enrolment: 18

Summary results
Trial is onging in other countries