HEBE III: A prospective, randomised, clinical study to examine the effects of a single bolus erythropoietin on left ventricular function in patients with an acute myocardial infarction

Published: 11-07-2006
Last updated: 20-05-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON30616

Source
ToetsingOnline

Brief title
HEBE III

Condition

- Coronary artery disorders

Synonym
heart attack, myocardial infarction

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Interuniversitair Cardiologisch Instituut Nederland,Janssen-Cilag

Intervention

Keyword: acute myocardial infarction, erythropoietin, left ventricular function, PCI

Outcome measures

Primary outcome

The main endpoint of the study is left ventricular ejection fraction, measured

with planar radionuclide ventriculography at 6 weeks after onset of the acute

myocardial infarction

Secondary outcome

Not applicable

Study description

Background summary

Erythropoetin (EPO) is commonly known as an effective treatment for anemia, (partly) caused by an inadequate production of endogenous EPO (e.g., renal failure). However, we and others suggested several important extra-hematopoeitic effects of EPO, which might be beneficial in the setting of an acute myocardial infarction. Recent animal studies provided very consistent evidence for a reduced infarct size and improved left ventricular function caused by EPO administration. In addition, we and others have mainly explained the beneficial effects of EPO by non-hematopoietic effects, such as reduction of apoptosis and stimulation of neovascularisation.
Clinical studies with EPO in non-anemic patients are scarce. Ehrenreich et al recently conducted an efficacy and safety study of recombinant human Erythropoietin (rh-EPO) therapy in men suffering from stroke. They found that high dose of EPO administered the first three days after stroke (total dose 100.000 IU), was well tolerated and associated with a marked reduction in cerebral infarct size, and an improvement in clinical outcome. We performed a safety study in our department on the effects of a single bolus of EPO (60.000

IU) in patients with an acute myocardial infarction. Serum EPO levels increased a 200-fold, but no significant effects on hematopoiesis were seen. In addition, EPO administration was not associated with hypertension, nor with an increase in thrombocytes or thrombotic events.
In conclusion, experimental data clearly showed that a single bolus of EPO after the onset of an acute myocardial infarction reduced myocardial infarct size, and improved left ventricular function. In our safety study, EPO administration in patients with an acute myocardial infarction was safe and well tolerated.

Study objective

The primary objective of this study is to establish the effects of a single bolus EPO administered just before a primary PCI for a first acute myocardial infarction, on left ventricular ejection fraction after 6 weeks, measured with planar radionuclide ventriculography.
The secondary objective of this study is to establish the effects of a single bolus EPO on safety, myocardial infarct size, and cardiovascular events in patients after a first acute myocardial infarction.

Study design

Prospective, Randomised, Open label study with Blinded Endpoint analysis (PROBE).

Intervention

In one group one bolus of EPO (Eprex, about 60.000 IU) will be administered intravenously in 30 minutes, within 3 hours after the primary PCI procedure and the other group will receive standard therapy.

Study burden and risks

Blood will be sampled 7 times during the whole study period of 6 weeks according to routine clinical practice. Planar radionuclide ventriculography will be performed at 6 weeks follow up. A previous safety study showed no adverse events after administration of EPO. Therefore, we expect that the risks are negligible and do not expand the possible benefits.

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

Successful primary PCI (TIMI 2/3) for a first acute myocardial infarction, diagnosed by:
a. chest pain suggestive for acute myocardial infarction
b. symptom onset < 12 hour before hospital admission, or < 24 hour in case ongoing ischemia
c. ECG with ST-T segment elevation > 1 mV in 2 or more leads
d. TIMI flow 0/1 before primary PCI on diagnostic coronary angiography;

Exclusion criteria

a. Hemoglobin levels > 10.6 mmol/L;
b. Anticipated additional revascularisation within 6 weeks;
c. Cardiogenic shock;
d. Presence of other serious medical conditions
e. Pregnancy/breast feeding
f. Malignant hypertension
g. End stage renal failure (kreatinin > 220 micromol/l)
h. Previous treatment with rh-EPO

i. Blood transfusion <12 weeks prior to randomisation
j. Allergy against rh-EPO
k. Polycytemia verae
l. Previous acute myocardial infarction
m. Concomitant inflammatory or malignant disease
n. Recent trauma or major surgery
o. Unwilling to sign informed consent
p. Atrium fibrillation

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-02-2007
Enrollment:	466
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Eprex
Generic name:	Epoetin alfa
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-07-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-10-2006
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-06-2007
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-08-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-10-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Not approved Date:	05-03-2019
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	EUCTR2006-002940-28-NL
ISRCTN	ISRCTN46528154
CCMO	NL12758.042.06