The role of inflammation in myocardial infarction in young patients without risk factors: * the unhappy few* - A pilot study -

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To investigate the innate pro-inflammatory response in young patients (

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Observational non invasive

Summary

ID

NL-OMON40814

Source
ToetsingOnline

Brief title
The Unhappy Few

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Myocardial infarction; Heartattack

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: voorlopig worden de kosten betaald uit de

financiele reserves van de afdeling cardiologie; ondertussen wordt sponsoring en/of subsidie aangevraagd

Intervention

Keyword: Acute myocardial infarction, Inflammation, Trained immunity

Outcome measures

Primary outcome

The primary endpoint is H3K4 trimethylation in the promoter region of

inflammatory cytokines and the genetic search for the exonic variant, which can

be correlated to the exaggerated pro-inflammatory response.

Secondary outcome

Secondary endpoints are the cytokine release by monocytes in response to

stimulation with Toll-like Receptor(TLR)-agonists and the transformation of

monocytes in foam cells. Also the specific blood platelet function in these

patients will be examined.

Study description

Background summary

A number of patients suffers from a myocardial infarction (MI) despite the absence of the *classical* risk factors for atherosclerosis; we consider them to be *the unhappy few*. Numerous studies have shown that atherosclerosis is a chronic inflammatory disease and we hypothesize that these *unhappy few* have an (epi-)genetic predisposition of an exaggerated innate pro-inflammatory response, which accelerates the process of atherosclerosis.

Study objective

To investigate the innate pro-inflammatory response in young patients (<50 years of age), who suffer from a myocardial infarction. The pro-inflammatory response will be examined by the search for *trained immunity* especially in the monocytes of peripheral blood, which leads to a more vigorous reaction and

to more production of pro-inflammatory cytokines. At the same time the function of platelets in peripheral blood will be examined, as platelets form part of the inflammatory response. Furthermore, the bacteria present in the acute ruptured plaque within the culprit-coronary will be compared by DNA-analysis with the bacterial spectrum, present in the intestinal microbiota. Examining the specific pro-inflammatory response in young patients without classical risk factors may also lead to discover those genetic traits, which determine the inflammatory role in atherosclerosis. The presence of these genetic traits is probably difficult to find in the usual MI patients with classical risk factors but might become more visible in these young *unhappy few*.

Study design

Single-center, prospective, observational study

Study burden and risks

In the patients 10 tubes of peripheral blood (4x10 cc, 2x3 cc, 1x3cc, 1x5 cc, 1x2 cc en 1x2,5 cc) will be taken in the prehospital phase, 12 hours after hospitalization and after 1 month during their out-patient visit. On the second or third day also 2x10 cc peripheral blood will be taken for genetic analysis. Also faeces and saliva will be collected within the first 48 hours of hospitalization. From the first degree relatives of each patient only once 4 tubes of peripheral blood will be taken as well as once collection of faeces and saliva. Also in the 20 matched healthy volunteers, who are not related to patients who suffered from a myocardial infarction. 4 tubes of peripheral blood and once a portion of faeces will be taken. The examination of the siblings might reveal increased risk for atherosclerotic events, from which they might benefit by getting early preventive treatment.

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

Cases:
Twenty patients aged between 18 and 50 year, who present with an acute ST-elevation myocardial infarction eligible for primary percutaneous coronary intervention. ;Family members:
Forty of their first degree healthy family members of the patients presenting with the acute myocardial infarction (two family members per patient).;Controls:
20 healthy controls aged 18 years or above. Controls will be matched with the cases for age, gender and cardiovascular risk factors.

Exclusion criteria

Cases:
- If the index patient (suffering from the acute myocardial infarction) has one or more of the following factors present:
o Age below 18 years
o Diagnosis of vascular disease (e.g. previous myocardial infarction, CVA, etc)
o Use of statins, anti-inflammatory agents or thrombocyte aggregation inhibitors (these drugs modulate epigenetic changes in in vitro studies)
o Auto-immune diseases (e.g. rheumatoid arthritis)
o Coagulation disorder
o No living first degree family members aged 18 years or above
o Presence of two or more of the following risk factors:
§ Hypertension
§ Hypercholesterolemia
§ Diabetes mellitus
§ Active smoking or an active smoking history within the last 10 years;Family members:
- If the first degree relative (i.e. the participant) has one or more of the following factors

present:
o Age below 18 years
o History of vascular disease (e.g. previous myocardial infarction, CVA, etc)
o Use of statins, anti-inflammatory agents or thrombocyte aggregation inhibitors (these drugs modulate epigenetic changes in in vitro studies)
o Signs or symptoms of a current infection (fever, chills)
o Auto-immune diseases (e.g. rheumatoid arthritis)
o Coagulation disorder
Controls:
- If the control has one or more of the following factors present:
o Age below 18 years
o History of vascular disease (e.g. previous myocardial infarction, CVA, etc)
o A first degree family member with vascular disease (e.g. previous myocardial infarction, CVA, etc)
o Family relationship with the cases
o Use of statins, anti-inflammatory agents or thrombocyte aggregation inhibitors (these drugs modulate epigenetic changes in in vitro studies)
o Signs or symptoms of a current infection (fever, chills)
o Auto-immune diseases (e.g. rheumatoid arthritis)
o Coagulation disorder

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-06-2015
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	27-11-2014
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL49740.091.14