Association of inflammation and coagulation markers with levels of C-reactive proteine in healthy volunteers

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To evaluate whether an increase in inflammatory- and coagulation parameters can be found in healthy volunteers with elevated hsCRP levels compared to age and BMI matched healthy volunteers with normal hsCRP levels

Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Observational invasive

Summary

ID

NL-OMON30501

Source
ToetsingOnline

Brief title
CRP in healthy

Condition

- Cardiac disorders, signs and symptoms NEC
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
atherosclerosis, occlusive heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cardiovascular disease, C-reactive protein, Healthy volunteers, Inflammation

Outcome measures

Primary outcome

- hsCRP

- coagulation

- thrombin generation: F1+2

- fibrinolytic system: D-dimers, PAI-1, tPA

- endothelial cell activation: vWF

- inflammation

- monocytic expression of CD11b, CD18, TF, CD62L

- cytokines: IL-6, IL-8, TNFalpha (receptor)

- chemokines: MCP-1, E-selectin

- sunendothelium: MMP-9, MPO

Secondary outcome

-

Study description

Background summary

It has been demonstrated that C-reactive protein (CRP) is a strong predictive value for cardiovascular (CV) events in asymptomatic subjects with CAD risk and in stable angina. Moreover, CRP levels are highly predictive for intercurrent complications or outcome in unstable angina and after acute myocardial infarction. To date, CRP predominantly has been considered a nonspecific marker of inflammation rather than a participant in the development and progression of atherosclerotic lesions including plaque vulnerability.
Accumulating in vitro evidence indicates that CRP elicits direct proatherogenic

effects in endothelial cells, involving upregulation of adhesion molecules and chemoattractant chemokines, reduction of nitric oxide (NO) synthesis, and enhancement of plasminogen activator inhibitor (PAI)-1 expression and activity. Likewise, CRP in monocytes stimulates the release of proinflammatory cytokines and tissue factor (TF) through binding of the FcgRIIa receptor. The clinical relevance of these findings has been underscored by in vivo animal studies, showing that human CRP results in worsened outcome in experimental myocardial infarction and increased thrombosis in response to arterial injury.
Recently, in a proof-of-principle study we evaluated the effect of human recombinant CRP (hrCRP) infusion study on endothelial function, inflammation and coagulation in 7 healthy volunteers using hrCRP (Biospacific). Briefly, we measured endothelium-derived vasomotor function using venous occlusion plethysmography at baseline, and 1h and 6h post infusion. Furthermore, blood was drawn at baseline, and 1, 4, 8 and 24 hours after hrCRP infusion to assess parameters of coagulation/ fibrinolysis, peripheral leukocyte phenotype, inflammation and complement activation. The data indicate that a single bolus of human recombinant CRP induced endothelial cell activation, a proinflammatory response illustrated by IL-6 and IL-8 levels within 4 hours of time, and activation of the TF-dependent coagulation pathway. Accordingly a second peak of endogenous CRP release was noted after 24 hours. Notably, no adverse events were recorded throughout the protocol.
Although infusion of hrCRP demonstrated an increase in inflammatory markers, and coagulation markers, the question remains whether a difference can be found in inflammation and coagulation parameters in healthy volunteers with elevated CRP (2-10 mg/L) levels versus healthy volunteers with normal CRP levels (<2 mg/L).

Study objective

To evaluate whether an increase in inflammatory- and coagulation parameters can be found in healthy volunteers with elevated hsCRP levels compared to age and BMI matched healthy volunteers with normal hsCRP levels

Study design

This study will be a single centre observational study. Volunteers will be recruited by telephone from the database of our own Department of Vascular Medicine, which contains volunteers who have indicated to be willing to participate in future research. Volunteers will be asked to visit our center for venapunction. Age and sex matched controls with normal CRP levels will be recruited from the same database.

Study burden and risks

- Obtainment of subject informed consent
- Screening for inclusion

- Physical examination
- Venapunction for blood samples (small risk of hematoma at puncture site; some subjects develop a vasovagal reaction)

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

Male sex, or postmenopausal female, age 50 years or older

Exclusion criteria

Other disease

Medication use
(Other) cardiovascular risk factors

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	100
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL15062.018.06