The role of SNARE protein genes in the regulation of Von Willebrand Factor concentration and other coagulation factors

Published: 30-11-2010
Last updated: 04-05-2024

To define the role of genetic variations in SNARE protein genes in the regulation of VWF plasma concentrations and their effect on other substances secreted by WPBs and alpha-granules and coagulation parameters under physiological circumstances.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON36387

Source
ToetsingOnline

Brief title
SNARE proteins and VWF

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
increased inclination to clotting, thrombofilia

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Trombosestichting Nederland

Intervention

Keyword: Exercise, Genetics, SNARE proteins, Von Willebrand Factor

Outcome measures

Primary outcome

The VWF plasma concentration will change after heavy exercise and this change will differ among genotypes. We expect a 60% increase of VWF plasma levels after heavy exercise and approximately 30% difference between genotypes.

Secondary outcome

Other coagulation parameters and substances secreted by WPBs.

To what extent does variation in skin-autofluorescence as a non-invasive marker for accumulation of advanced glycation endproducts and atherosclerotic processes explain the variance in the regulation of VWF concentration?

Study description

Background summary

High VWF levels have been associated with an increased risk of CVD. However, factors which are involved in the regulation of VWF plasma concentrations are largely unknown. Recently, a meta-analysis of genome-wide association studies of the CHARGE consortium revealed two novel genes, STXBP5 and STX2, which are highly associated with VWF levels. These genes encode proteins, which are involved in the regulation of numerous secretory events, such as Weibel Palade Body (WPB) exocytosis. WPBs and alpha-granules release large amounts of VWF upon endothelial cell activation, as in atherosclerosis and subsequent arterial thrombosis. In addition, these storage granules do not only secrete VWF molecules, but also other pro-inflammatory factors and pro-thrombotic factors. It is yet unknown how SNARE proteins exactly regulate VWF plasma concentration and how SNARE proteins contribute possibly to the occurrence of arterial thrombosis.

Study objective

To define the role of genetic variations in SNARE protein genes in the regulation of VWF plasma concentrations and their effect on other substances secreted by WPBs and alpha-granules and coagulation parameters under physiological circumstances.

Study design

We will perform an observational study among 100 healthy volunteers, males and females, aged 18-35 years. During an inclusion period of 8 months we will recruit healthy volunteers (student and employees of the Erasmus MC) via advertisements in the Erasmus University Medical Center building and in the local Erasmus magazine.
During the clinic visit a short interview will be taken, as well as a physical examination, including blood pressure, height, and weight measurements. Blood will be drawn before and after the cycle ergometer test. Study participants will perform a cycle ergometer test during approximately 20 minutes. The subject will start with a warming-up of 4 minutes. Every 6 seconds the cycling resistance will increase by 2 watt until exhaustion. Subsequently, resistance will decrease again and the participant can cool down for five minutes. During the cycle ergometer test the heart rhythm will be monitored continuously with ECG and VO2 will be measured.
Fore-arm skin autofluorescence will be measured using the AGE-reader®.15 The measurement is completely automated and is obtained by placing the forearm on the device. The measurement takes aproximately 1 min to complete.

Study burden and risks

Participants will visit the once. A short interview will consist of health related questions. The physical examination includes blood pressure, height, and weight measurements. At two different time points a total of 45 mL. blood will be collected from each participant. The blood sampling may cause a haematoma or minor bleeding. Participants will perform considerable physical exercise during 20 minutes. By selecting only healthy volunteers and by continuously monitoring heart rhythm with ECG and measuring the VO2, there are no risks associated with this intervention.
There are now risks associated with the AGE-reader measurement.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230, kamer L-435
3015 CE Rotterdam
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

's Gravendijkwal 230, kamer L-435
3015 CE Rotterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Males and females
- 18 - 35 years
- Caucasians

Exclusion criteria

- Known cardiovascular risk factors, such as hypertension, diabetes, hypercholesterolemia, obesity (BMI > 30 kg/m2), and a positive family history of CVD.
- Smoking
- Use of medication known to influence VWF levels, such as statins, beta-blockers etc. (oral contraceptive use is allowed).
- Known malignancies, liver dysfunction or renal dysfunction.
- Pregnancy
- If the participant wishes not to be informed about clinically relevant abnormalities that could be detected during the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-03-2011
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	30-11-2010
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	03-11-2011
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL32877.078.10