The influence of Annexin A2 SNP (rs17845226) on von Willebrand factor secretion by endothelial cells

Published: 25-05-2016
Last updated: 16-04-2024

The aim of this research is to study the effect of Annexin A2 SNP rs17845226 on vWF secretion by endothelial cells of controls carrying different Annexin A2 SNP rs17845226 genotypes (WT, homozygous, heterozygous). By testing several endothelial cell...

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

Summary

ID

NL-OMON42870

Source
ToetsingOnline

Brief title
VWF secretion Annexin A2 (rs17845226)

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
von Willebrand disease, VWD

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Annexin A2, endothelial cells, SNP, von Willebrand factor

Outcome measures

Primary outcome

This study is a laboratory driven study. The main study endpoint is the

elucidation of the Annexin A2 dependent VWF secretion pathway.

Secondary outcome

N.A.

Study description

Background summary

Von Willebrand factor (vWF) is an adhesive protein essential for the arrest of bleeding after vascular injury. vWF mediates the primary hemostatic response by promoting platelet adhesion and platelet aggregation ultimately leading to the formation of a primary hemostatic plug. Besides this, vWF also serves as a carrier protein for the procoagulant clotting factor VIII and protects FVIII from proteolysis. A deficiency of vWF results in the most common inherited bleeding disorder named Von Willebrand disease (VWD).

Endothelial cells store vWF in Weibel Palade Bodies (WPB) and secrete vWF by exocytosis of the WPB. The phospholipid binding protein Annexin A2 is involved in the exocytosis of WPB in endothelial cells and thus the secretion of vWF. Annexin A2 resides in a tight complex with the S1000A10 protein. Upon Ca^{2*} binding, WPB exocytosis in endothelial cells is stimulated. Recently the Annexin A2 SNP rs17845226 (c.346G>T) is shown to be involved in lowering the plasma vWF levels in controls. The effect of the Annexin A2 SNP rs17845226 on vWF secretion by endothelial cells and the pathway involved is still unclear.

Study objective

The aim of this research is to study the effect of Annexin A2 SNP rs17845226 on vWF secretion by endothelial cells of controls carrying different Annexin A2 SNP rs17845226 genotypes (WT, homozygous, heterozygous). By testing several endothelial cell activation pathways the Annexin A2 dependent activation

pathway can be determined.

Study design

This design of our study is cross-sectional with a single collection of blood samples and serves to find out whether the Annexin A2 SNP rs17845226 (c.346G>T) has an influence on the vWF secretion by endothelial cells. We will obtain max. 36 ml of citrated blood from participants of a former Nijmegen Biomedical Study (NBS), which are selected based on their Annexin A2 SNP rs17845226 (c.346G>T) genotype (3 to 5 heterozygous participants, 3 to 5 homozygous participants, and 3-5 wild type (WT) participants.

Study burden and risks

The subjects will be asked to donate blood. A single blood collection of 36 ml will be performed, for which the subjects will be specifically invited. The patients will not be challenged by any other intervention. Therefore, we anticipate that risks are negligible and the burden minimal in this study.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein Zuid 8
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Participant of the Nijmegen Biomedical Study (NBS) with informed consent to be contacted for further research.
- Homozygous or heterozygous for the Annexin A2 SNP rs17845226 (c.346G>T), or WT.

Exclusion criteria

- No written informed consent for study participation obtained from the subject.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-10-2016
Enrollment:	0
Type:	Actual

Ethics review

Approved WMO

Date:	25-05-2016
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	NL57314.091.16