STIMULATE study: Statins influence on Minrin upregulation of von Willebrand factor and factor VIII

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON32666

Source
ToetsingOnline

Brief title
STIMULATE

Condition

- Other condition

Synonym
Hemophilia A, Von Willebrand Disease

Health condition

Bloedstollingsstoornissen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Desmopressin, Factor VIII, Statin, von Willebrand factor

Outcome measures

Primary outcome

* vWF antigen, vWF activity and vWF propeptide plasma levels after DDAVP

stimulation, during statin therapy.

* FVIII activity and F VIII antigen plasma levels after DDAVP stimulation,

during statin therapy.

Secondary outcome

* vWF multimers, ADAMTS13 and tPA plasmalevels after DDAVP stimulation during

statin therapy.

Study description

Background summary

Currently, in Hemophilia A and Von Willebrand patients treatment with DDAVP is the most feasible and patient friendly method of treatment. In patients with a limited response to DDAVP or individuals with inhibitors to F VIII, optimalisation of DDAVP treatment is all the more important. There is evidence that statin therapy might upregulate transcription factor Kruppel-like factor 2 (KLF2) and thereby enhance WPB exocytosis. Although statin therapy has many pleitropic effects next to its lipid lowering effects, the exact mechanism by which statin therapy might influence the endothelium remains unclear. Literature on this topic is scarce and conflicting. A better insight in the influence of statin therapy on DDAVP-mediated VWF and F VIII release might open ways to improve DDAVP treatment in these patient groups.

Study objective

The aim of this study is to investigate the influence of statin therapy on DDAVP mediated release of VWF and F VIII. We aim to investigate this by measuring F VIII and VWF levels by means of a prolonged DDAVP test prior and after 6 weeks of statin therapy.

Study design

The total duration of the study is 6 weeks, in this period a DDAVP test will be performed on two time points. The first DDAVP test will take place prior to starting statin therapy and the second test will be performed after 6 weeks of statin therapy. During both tests blood samples will be taken until 32 hours after DDAVP infusion (in total 7 times per test), in each bloodsample e.g. vWF activity and F VIII activity will be determined.

Intervention

The subjects in the study will undergo two DDAVP tests. The first DDAVP test will take place prior to starting statin therapy and the second test will be performed after 6 weeks of statin therapy. During both tests blood samples will be taken until 32 hours after DDAVP infusion (in total 7 times per test). After the first DDAVP test subjects receive 40 mg simvastatin for 6 weeks. After 6 weeks simvastatin the second DDAVP test will be performed.

Study burden and risks

There are no direct benefits for the study participants related to this study. However, the results of the study may be relevant and beneficial to the patients and their families as well as their treating physicians. If DDVAP response improves after statin use, participants will be able to benefit from optimized treatment.
Risks of study participation:
- Venipunctures: hematomas
- Statin therapy: adverse events of statin use: see studyprotocol Appendix D
- DDAVP: adverse events of DDAVP use: see study protocol Appendix E

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

1. Mild hemophilia A: defined as a F VIII deficiency with a F VIII plasma concentration of 10-40 IU mL-1, confirmed on at least two occasions.
2. or Von Willebrand disease type 1: defined as a VWF deficiency with a VWF plasma concentration of 10-40 IU mL-1, confirmed on at least two occasions.
3. DDAVP response has been tested at least once before, VWF activity and VWF antigen after DDAVP should not exceed > 200 %.
4. Age: 18 * 60 years
5. Male

Exclusion criteria

1. Moderate/Severe hemophilia A: defined as a F VIII deficiency with a F VIII:C plasma concentration of * 2 IU mL-1, confirmed at at least two occasions.
2. Von Willebrand disease type 2 or 3
3. Clinical history of any other hemostatic or thrombotic disorder.
4. Clinical history of any disorder specified in Appendix C of the study protocol
5. Use of any medications specified in Appendix C of the study protocol
6. Medical indication for statin therapy.
7. Co-enrolment other clinical study
8. DDAVP response has not previously been tested or vWF antigen and vWF activity increase after previous DDAVP exposure was less than two fold.

9. First relative (brother/sister) participating in this study

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2010
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Minrin
Generic name:	Desmopressin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Simvastatin
Generic name:	Simvastatin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	16-11-2009
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
EudraCT	EUCTR2009-017060-17-NL
CCMO	NL30422.018.09