Response to DDAVP In mild Hemophilia A patients, in Search for dEterminants

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The aim of this project is to investigate the association between clinical and genetic factors and DDAVP response in MHA patients and to determine their relative contributions to the DDAVP response.

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

Summary

ID

NL-OMON43824

Source
ToetsingOnline

Brief title
RISE

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
bleeding disorder, hemophilia A

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Access to insight research fund

Intervention

Keyword: DDAVP, Hemophilia A, Mild/moderate, Response

Outcome measures

Primary outcome

The main study parameters are:

- Clinical factors that determine DDAVP response

- Genetic factors that determine DDAVP response

The main study endpoint is the response to DDAVP, which is defined as complete

(1h after DDVP FVIII: C >0.50 IE/ml), partial (1h after DDVP FVIII: C 0.30-0.50

IE/ml), or none (1h after DDVP FVIII: C < 0.30 IE/ml). Therapeutic response

will also be evaluated.

Secondary outcome

N.a.

Study description

Background summary

Mild Hemophilia A (MHA) usually presents as a mild to moderate bleeding disorder that occurs in one in 10 000 men and is a hereditary disease. MHA is caused by a deficiency of clotting factor VIII. More personalised, safer and cheaper treatment strategies for MHA are needed. In most MHA patients, FVIII: C levels increase to a hemostatic range after DDAVP administration, a synthetic analogue of vasopressin. This decreases the need for FVIII concentrates, and thereby reduces the associated risk of inhibitor development and cost of treatment. However, a yet undetermined proportion of patients partially or completely fail to respond to DDAVP. Single center studies have demonstrated an association between DDAVP response and clinical and genetic determinants. However, their relative contribution remains unknown.
Understanding the clinical and genetic determinants for the DDAVP response may enable better prediction and optimal clinical use of DDAVP. Furthermore, identifying genetic predictors of DDAVP response will help to understand

biological mechanisms associated with the release of vWF and rise in FVIII: C.

Study objective

The aim of this project is to investigate the association between clinical and genetic factors and DDAVP response in MHA patients and to determine their relative contributions to the DDAVP response.

Study design

The RISE is an international multicenter cohort study that analyses the response of MHA patients to DDAVP. The cohort will include all MHA patients who have received DDAVP from the participating Hemophilia Treatment Centers (HTCs) between 1980 and 2013.

Study burden and risks

N.a.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Moderate/mild hemophilia: defined as a FVIII deficiency with a FVIII:C plasma concentration of 2-40 IU/DL.
Treated or tested with DDAVP (between 1980 and 2013), and documented FVIII and VWF plasma levels prior to DDAVP administration and at least for 1 time point after DDAVP administration.

Exclusion criteria

Severe hemophilia A patients (factor VIII <1 IU/DL) will be excluded from the study population.
The patient has other bleeding disorders, especially von Willebrand Disease (documented vWF plasma levels are available)
Type 2N von Willebrand Disease, or highly likely that patient has this disease since there are female bleeding patients in the pedigree
First DDAVP test is not taken at current hemophilia treatment center

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-02-2013
Enrollment:	281
Type:	Actual

Ethics review

Approved WMO Date:	20-02-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-09-2013
Application type:	Amendment
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	NL42418.018.12