National study of moderate and severe von Willebrand disease in the Netherlands

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON53028

Source
ToetsingOnline

Brief title
WiN study (Willebrand disease in the Netherlands)

Condition

- Other condition

Synonym
von Willebrand disease, vWD

Health condition

bloed- en lymfestelsel aandoeningen: stollingsstoornissen en bloedingsdiathesen

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,CSL Behring, Leuven (unrestricted grant),Stichting Haemophilia

Intervention

Keyword: bleeding disorder, national study, quality of life, von Willebrand disease, von Willebrand factor

Outcome measures

Primary outcome

See study design

Secondary outcome

See study design

Study description

Background summary

In the Netherlands the population with hemophilia is well known, and several studies (Hemophilia in the Netherlands, HIN1-5 studies) have been performed to obtain insight in the disease, treatment and complications of treatment. This does not apply for patients with von Willebrand disease. The incidence of von Willebrand disease in the Netherlands is unknown, but the occurrence of all types of von Willebrand disease together is estimated at 1:100-1:200 individuals. Most patients have mild von Willebrand disease, mostly type 1.
For the more severe forms of von Willebrand disease the incidence in unclear, but the expectation is, that there are at least 500-1500 patients. In the Netherlands, an unique situation exists for the treatment of patients with hemophilia and related coagulation disorders.
In 2000 a hemophilia management policy was set up by the Ministry of Health, which stated that the care for these patients should be concentrated in 13 Hemophilia Treatment Centers (HTC). The representatives of the attending centers, the hemophilia specialists, have been organized in the NVHB, the Dutch society of Hemophilia treaters. In the hemophilia management policy is stated that all patients with a coagulation disorder dependent of replacement products must be treated in a HTC or under responsibility of a HTC. These patients will be followed and seen in a HTC at least once a year and all patients have a

maintenance program.

Because all moderate and severe von Willebrand patients in the Netherlands are known in HTC, it is possible for this study to register this population. This is imperative to the research of von Willebrand disease. Because the moderate and severe forms of von Willebrand disease are rare, it is impossible for an individual center to perform research of moderate severe and severe von Willebrand disease. Therefore a national approach is necessary. A similar national study done for hemophilia patients (HIN-study), resulted in important information about diagnosis, treatment, related diseases and social consequences. The HIN-study facilitated national research, in which hemophilia patients participate. For this WIN-study, expertise of the HIN-study can be used.

For optimal care of patients with the moderate and severe form of von Willebrand disease a better understanding of symptoms, diagnostics, treatment and complications of treatment is necessary. The present study aims to register and investigate all patients in the Netherlands with moderate and severe von Willebrand disease.

Study objective

The objective of this study is to assess the clinical presentation, the treatment and the complications of treatment in moderate and severe von Willebrand disease. Another goal is to investigate the influence of von Willebrand disease on quality of life.

Study design

To perform this study a number of study topics are formulated:

1. Clinical presentation
a. What is the frequency and severity of bleeding symptoms in patients with von
Willebrand disease, measured with the Bleeding Score of Tosetto et al. completed with hematuria and bleedings in children
b. Which proportion of women with von Willebrand disease has menorrhagia. Do they have iron deficiency anemia, do they need treatment with drugs or surgical interventions
c. Which proportion of patients with von Willebrand disease has joint bleedings.
What is the frequency of joints bleedings. Which proportion of patients with
von Willebrand disease has arthropathy. Which joints are damaged
d. Which proportion of patients with von Willebrand disease has irreversible

damage of organs because of the bleedings and the treatment bleedings (for instance: arthropathy, brain damage, fertility problems due to hysterectomy).
What is the nature of organ damage. What are the risk factors of irreversible
organ damage (vWF levels, age, treatment et cetera)

2. Treatment
a. Which drugs (DDAVP, antifibrinolytics or coagulation factor concentrates) has
been used as treatment of von Willebrand
disease and based on which indication
b. Have patients been treated prophylactic with coagulation factor concentrates

3. Complications of treatment
a. Which proportion of patients has inhibitors against vWF due to treatment with
coagulation factor concentrates
b. Which proportion of patients has had an allergic reaction after treatment with
coagulation factor concentrates
c. Which proportion of patients has had venous thromboembolism or pulmonary embolism during treatment with coagulation factor concentrates
d. Which proportion of patients is tested for hepatitis B, C or HIV. Which proportion of patients is infected with hepatitis B, C or HIV. Are they treated
because of this transmission
3. Which risk factors can be identified

4. Heart and blood vessel disease
a. Which proportion of patients has had arterial thrombotic complications such as
cerebral ischemia, myocardial infarction or peripheral arterial disease

5. Social implications of von Willebrand disease
a. What is de influence of von Willebrand disease on quality of life, measured with
the RAND-36 questionnaire in patients older than 11 years. In children the Haemo-QoL questionnaire is used
b. What are the effects of von Willebrand disease on social participation (education, work, sports, family planning)
c. Which factors have an influence on quality of life in von Willebrand disease patients (for instance: amount of bleeding episodes, irreversible organ damage
due to bleedings, age, living with a partner)

6. Mutation analysis
a. Which mutations in the von Willebrand-gene are responsible for von Willebrand disease
b. What is the correlation between the different mutations of the von Willebrand-gene and the Bleeding Score

To answer these questions a questionnaire is developed, which will be sent to the study population. Blood will be taken and result in a plasma and DNA bank.

Amendment Unravellingen von Willebrand disease: a new genetic bleeding disorder: The aim is to gain more knowledge on the genetic background of von Willebrand disease. Mutations in von Willebrand-factor gene are not always found in patients, and different family members with the same mutations an have different phenotypes. We will perform mutation analysis in both the von Willebrand factor gene and other genes in patients already included and family members with mild disease and unaffected family members and compare their phenotype.

Study burden and risks

The study population will be sent a questionnaire, it will take approximately 50 minutes to fill in this questionnaire. Furthermore a venapunction will take place once, four blood tubes (18ml) will be obtained in adults. In children this will be two blood tubes (9 ml).

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80 Wytemaweg 80
Rotterdam 3015 CN
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80 Wytemaweg 80
Rotterdam 3015 CN
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

1) haemorrhagic symptoms or
a family history of von Willebrand disease
2) vWF antigen <= 30%, lowest measurement counts and/or
vWF activity (vWF:RCo of vWF:CB) <= 30%, lowest measurement counts and/or
FVIII:C <= 40 %, lowest measurement counts
3) being known in a hemophilia treatment center or
if only the diagnose is made in a hemophilia treatment center this must be
done
after 1987

Exclusion criteria

Hemophilia A
Carriership of hemophilia A
No informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-06-2007
Enrollment:	1000
Type:	Actual

Ethics review

Approved WMO Date:	26-04-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2012
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-02-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2022
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	NL14986.078.07