Whole clotting assessment as predictor of clinical phenotype in aged patients with haemophilia A

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The aim of this study is to investigate if there is a correlation between the clinical phenotype (defined as age of first bleeding) of patients with haemophilia A and the results of the whole clotting assessment (TMETP + T-TAS).The results will...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON37558

Source
ToetsingOnline

Brief title
HAEMOTYPE-AGING study

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

Synonym
haemophilia

Research involving
Human

Sponsors and support

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

Intervention

Keyword: bleeding pattern, haemophilia, thrombin generation, T-TAS

Outcome measures

Primary outcome

Clinical parameters:

- age of first bleeding,

- extent of arthropathy

Laboratory parameters:

- result ETP/TM-ETP (lag time, peak thrombin, area under the curve)

- result T-TAS (time to occlusion, occlusion time, occlusion speed, area under

the curve)

Secondary outcome

n.v.t.

Study description

Background summary

Haemophilia A is a congenital coagulation disorder, caused by a decreased level of clotting factor VIII (FVIII > 0.01 IU/mL, known as mild/moderate haemophilia A) or a complete absence of FVIII (FVIII < 0.01 IU/mL, known as severe haemophilia A). Patients with severe haemophilia suffer from recurrent haemarthroses, resulting in haemophiliac arthropathy, muscle bleeds and life threatening bleeding, causing a decreased life expectancy.
Although all these patients have no FVIII plasma level, a heterogeneity in clinical phenotype (age of first joint bleeding and/or bleeding frequency) is observed.

Patients with severe haemophilia are treated with FVIII replacement therapy on a prophylactic schedule, i.e. three times a week 25-40 IU/kg in order to

minimize the amount of joint bleeds. In general, these treatment regimens are fixed regimens. If a patient on prophylaxis has no joint bleeds, it can be caused by adequate treatment or by over-treatment. Since haemophilia treatment is very costly (about 100,000-200,000 ¤/year), cost awareness and measurements to reduce costs are important. Proper predictions of the clinical phenotype will make it possible to individualize the haemophilia treatment and hopefully to reduce the cost. Furthermore, the risk of over-treatment (e.g. induction FVIII inhibiting antibodies) may be reduced. Since the residual FVIII level is not able to predict the clinical phenotype accurately, other haemostatic tests are needed, to serve as a more reliable base for treatment regimens. Assessment of the whole clotting system, by using a modified thrombin generation test (TM-ETP) in combination with the total thrombus-formation analyzing system (T-TAS), is a promising candidate as it provides information about different aspects of the haemostatic system. It is hypothesized that assessment of the whole clotting system will have the ability to predict the clinical severity more accurately, since more determinants of the phenotype are included in the assessment.

Currently, a study is performed to find a correlation between the results of these coagulation tests and bleedingsfenotype in young patients with servere hemophilia (the Haemotype study). In older (>60 years) hemophiliacs it seems there is a reduced bleedingsfenotype. In this study, we assess whether the new clotting tests change with age.

As a result of the severity of the disease, there are very few aged haemophilia patients with the severe form. As a result, this study, in contrast to the Haemotype study, does not consist of patients with severe haemophilia

The results of the older patients (> 60 years) and younger patients (20-30 years) may be correlated with age. This can lead to new insights into the coagulation system in older age and can possibly lead to improved patient-oriented treatment.

Study objective

The aim of this study is to investigate if there is a correlation between the clinical phenotype (defined as age of first bleeding) of patients with haemophilia A and the results of the whole clotting assessment (TMETP + T-TAS).

The results will contribute to a better understanding of the interplay between the coagulation system and the clinical severity, more accurate predictions of the course of haemophilia and a more reliable base for prophylactic treatment of haemophilia A.

Study design

A retrospective study of 12 patients, of which 6 are aged between 20-30 years, and 6 are aged older than 60 years. It concerns patients with a mild form of haemophilia A.

The whole clotting assessments will be compared between both patient populations, so a correlation can be made with age.

Study burden and risks

Patients with severe haemophilia visit the outpatient clinic every 8 to 12 months and refrain prophylactic administration of FVIII concentrate for at least 3 days prior to the visit in order to test their nadir FVIII level and to perform inhibitor testing. During this outpatient visit, extra blood (3 tubes of 5 mL) for the whole clotting assessment will be drawn during the same venapuncture used for regular blood testing. The total amount of drawn blood will be less than 2.5 percent of the total circulating volume.

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

- male;
- patients aged > 60 years with haemophilia A;
- patients aged between 20-30 years with haemophialia A;
- patients known at the Haemophilia Center of the Academic Medical Center;
- patients who visit the Haemophilia Center for routine blood testing (inhibitor testing);
- patients whose age of first bleeding and bleeding frequency have been recorded;
- only if written informed consent from patient is given.

Exclusion criteria

- patients with an inhibitor in the past;
- administration FVIII concentrate < 72 hours prior to blood sampling;
- acquired coagulation disorders by hepatic dysfunction;
- usage of ASA or NSAID.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12
Type:	Anticipated

Ethics review

Approved WMO Date:	15-05-2012
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
CCMO	NL39742.018.12