Association between HMOX1 and HP polymorphisms and joint damage in haemophiliacs

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Joint disorders
Study type	Observational invasive

Summary

ID

NL-OMON34673

Source
ToetsingOnline

Brief title
HMOX1 and HP polymorphisms in haemophiliacs

Condition

- Joint disorders

Synonym
clotting factor VIII/IX deficiency

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cartilage, Haemophilia, Haem-oxygenase, Haptoglobin

Outcome measures

Primary outcome

The main parameters that are measured are the length of the (GT)n-repeat in the promoter region of the HMOX1 gene; divided in two groups: n < 25 and n >= 25, and the phenotype of Hp; Hp 1-1, Hp 1-2, and Hp 2-2 in relation to radiographic joint damage.

Secondary outcome

The number of joint bleedings per year as recorded by patients in daily practice and the age of the patients have an effect on joint damage progression and might confound the relation of the length of the (GT)n-repeat or Hp phenotype and joint damage.

Study description

Background summary

Haemophilia is an X-chromosome linked, recessive bleeding disorder due to a deficiency or functional defect of coagulation factor VIII or IX. Due to recurrent joint bleeds (haemarthroses) specific changes occur in synovium and cartilage in the joint.
Our group showed that haemoglobin-derived iron is one of the major contributors of blood-induced cartilage damage. Possible mechanisms of protection against haem-induced oxidative and inflammatory stress are haem-oxygenase (HO-1) that breaks down haem, and the haemoglobin-scavenging molecule haptoglobin (Hp). The length of a guanine-thymidine (GT)n-repeat polymorphism in the promoter region of the HMOX1 gene determines the level of HO-1 induction. In RA patients a long (GT)n-repeat (n >= 25; less HO-1 expression) is associated with joint damage, but not with disease activity. The Hp gene codes for three phenotypes, Hp 1-1, Hp 1-2, and Hp 2-2. Hp 1-1 is characterized by a higher haemoglobin binding ability, suggesting that haemophilia patients with this phenotype will

be better protected against blood-induced joint damage.
Unless prophylactic treatment of haemophiliacs with clotting factors, patients still have the tendency to bleed and to develop joint damage. Until now, there are no indications which patients will develop more severe joint damage after bleedings. Even with a similar bleeding pattern, the amount of radiological joint damage differs between patients.

Study objective

With this study we want to get more insight in genetic characteristics that are able to predict the susceptibility to joint damage in haemophilia patients. Therefore we want to determine the association between the (GT)n-repeat length within the HMOX1 promoter region and radiographic joint damage in haemophilia patients, and the association between the HP phenotype and radiographic joint damage.

Study design

This study is designed as a cross-sectional study: at one time point in the disease process, biomaterials will be collected and evaluated. No intervention is performed. Severe haemophilia patients visit the Van Creveld Clinic on a regular base, two or three times a year, and a moderate patient once a year. During these visits blood will be taken to perform routine tests, like determination of antibodies against factor VIII or IX. When blood is drawn for routine tests, we will ask the patient to give an additional 2x10 ml blood for our study once.

Study burden and risks

There are no considerable risks or benefits for the patients. X-rays to determine radiological damage are made every 5 years by the Van Creveld Clinic and the number of bleedings is kept in daily practice by the patients. During a visit at the Van Creveld Clinic we will draw an additional 2x10 ml while blood is taken routinely by a nurse.

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

Severe (factor VIII/IX activity < 1%) and moderate (factor VIII/IX activity of 1-5%) haemophilia patients of 18 years or older who are treated according to the Van Creveld protocol.

Exclusion criteria

Patients with known HIV positivity.

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:	284
Type:	Anticipated

Ethics review

Approved WMO Date:	27-04-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL31822.041.10