Influence of factor VIII concentrate infusion on platelet activation, inflammatory parameters and endothelial parameters; a pilot study

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Inflammatory and endothelial parametersTo investigate the influence of factor VIII concentrate infusion on inflammatory and endothelial parameters in patients with severe hemophilia A.Platelet activity and responsivenessTo investigate the influence...

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

Summary

ID

NL-OMON33269

Source
ToetsingOnline

Brief title
Influence of factor VIII concentrate infusion

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
bleeding disorder, Hemophilia

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: factor VIII concentrate, hemophilia, inflammatory and endothelial parameters, platelet activity

Outcome measures

Primary outcome

Inflammatory and endothelial parameters

- Inflammation: hs-CRP, IL-1, -6, -8, TNFα

- Endothelial activation : sVCAM-1, sICAM-1, MCP-1

Platelet activity and responsiveness

- Platelet activity markers

- Platelet responsiveness to ADP and XL-CRP stimulation, and to Iloprost and

SNAP inhibition

Secondary outcome

Not applicable.

Study description

Background summary

Inflammatory and endothelial parameters:
Nowadays, life expectancy of hemophilia patients approaches that of the general male population. Consequently, aging hemophilia patients are increasingly confronted with age-related co-morbidity, including ischemic cardiovascular disease. Although the incidence and prevalence of ischemic cardiovascular disease appear to be increasing in hemophilia patients, several cohort studies

reported a reduced mortality caused by ischemic heart disease in hemophilia patients as compared to the general male population. Not much is known about the causes or mechanisms behind the reduced mortality due to ischemic heart disease. One hypothesis is that hemophilia patients develop less atherosclerosis than persons without hemophilia.
The majority of patients with severe hemophilia A are using prophylactic treatment with clotting factor concentrate. This continuous partial correction may dilute the possible protective effect of FVIII deficiency on atherosclerosis. In this pilot study, we will investigate whether infusion of FVIII concentrate influences levels of inflammatory and endothelial parameters, important in the development of atherosclerosis, in patients with severe hemophilia A.

Platelet activity and responsiveness
There is a great diversity of bleeding patterns within the group of patients with severe hemophilia. This indicates that the bleeding pattern is influenced by other factors than the residual FVIII concentration. An element of the coagulation system, which to our knowledge has not yet been studied in the context of bleeding pattern variability in hemophilia A, is the functioning of blood platelets.
In a future study, we will determine the role of platelet functioning in the bleeding pattern of patients with severe hemophilia A, by comparing the degree of platelet activation and platelet responsiveness of patients with a mild bleeding pattern to those of patients with a severe bleeding pattern. In this pilot study, we want to observe if FVIII concentrate infusion, which is used on a regular basis by many haemophilia patients, influences platelet activation and responsiveness. If factor VIII concentrate infusion influences platelet activation and responsiveness, this must be incorporated into future study protocols.

Study objective

Inflammatory and endothelial parameters
To investigate the influence of factor VIII concentrate infusion on inflammatory and endothelial parameters in patients with severe hemophilia A.

Platelet activity and responsiveness
To investigate the influence of factor VIII concentrate infusion on platelet activation and responsiveness in patients with severe hemophilia A.

Study design

The study population will consist of patients with severe hemophilia A, scheduled for an elective operation.
It is a standard pre-operative procedure to administer a high dose of FVIII concentrate several hours before the operation to increase FVIII activity.

Before and 15 minutes after FVIII concentrate infusion, blood is collected to measure FVIII activity. In this pilot study, we will collect extra blood before and 15 minutes after FVIII concentrate infusion. An extra venapunture is needed to collect blood 1 hour after FVIII infusion.

Study burden and risks

By using patients with severe hemophilia A, scheduled for an elective operation, we only need to collect extra blood on 2 occasions and perform 1 extra venapuncture. Patients do not have to come to the hospital especially for this study, because they are already here for their operation. Pre-operative factor VIII infusion is part of the standard procedure. We can conclude that both risk and burden for the patient is low.
The results of this study will not be directly beneficial for the participating patients. This study will contribute to the knowledge about the effects of treatment with factor VIII concentrate, which is necessary for the interpretation of future studies on the development of atherosclerosis in hemophilia patients and on assessment of bleeding phenotype in patients with severe hemophilia.

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 hemophilia A
18 years and older
Scheduled for an elective operation

Exclusion criteria

Hemophilia patients with symptomatic cardiovascular disease
Hemophilia patients with HIV and/or HCV

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-07-2009
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	21-04-2009
Application type:	First submission
Review commission:	METC NedMec

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	NL27071.041.09