Desmopressin and FVIII concentrate combination treatment in non-severe hemophilia A patients undergoing minor interventions

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To show a reduction in FVIII-concentrate consumption with perioperative desmopressin and FVIII concentrate combination treatment compared to FVIII concentrate monotherapy, without decreasing the effectivity of treatment.

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

Summary

ID

NL-OMON47789

Source
ToetsingOnline

Brief title
Little-DAVID

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Blood and lymphatic system disorders congenital

Synonym
Hemophilia A; coagulation disorder

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,Innovatiefonds Zorgverzekeraars

Intervention

Keyword: Desmopressin, Hemophilia A, Minor (surgical) interventions, Pharmacokinetic modeling

Outcome measures

Primary outcome

The average deviation of the measured FVIII level before the minor intervention

to the predicted peak FVIII values in IU/mL and the FVIII-concentrate

consumptionfor the first 24 hours around the minor intervention.

Secondary outcome

- Treatment costs in both arms

- Number and nature of bleeding during the first 14 days after the minor

intervention (appendix VI)

- Other adverse events during the first 14 days after the minor intervention

- The proportion of patients with FVIII plasma levels within set target levels

after the minor intervention

- Experienced quality of care in participating patients

- Discrepancies between one-stage and chromogenic FVIII-measurements before and

after desmopressin administration

- Inhibitor measurements 4-6 weeks after the minor intervention

Study description

Background summary

Hemophilia A (HA) is a rare bleeding disorder, caused by factor VIII deficiency. In non-severe HA patients, minor interventions, such as dental surgery and endoscopies, are an important treatment indication. Two treatment options are currently available: FVIII concentrate and desmopressin. Unfortunately, perioperative treatment is not optimal, as bleeding rates after dental surgery, the most important type of minor interventions, of 12% and 25% were found in two recent studies. Moreover, a previous evaluation of FVIII concentrate treatment from our centre shows a high rate of dosing above FVIII target levels (79%) and a low rate of dosing below FVIII target levels of 8%. Both may lead to complications. Moreover, FVIII concentrate is expensive. Pharmacokinetic (PK) guided dosing, a patient tailored dosing method, can improve dosing accuracy.
Desmopressin, the second treatment option, releases endogenous FVIII and von Willebrand factor, improving haemostasis. Desmopressin is not ideal due to several barriers. Amongst others, most patients do not reach sufficient FVIII levels to undergo minor interventions. An increase in the use of desmopressin instead of FVIII concentrate would be highly beneficial, as desmopressin is cheaper and more widely available. Desmopressin and FVIII concentrate combination treatment may be an innovative treatment option.

Study objective

To show a reduction in FVIII-concentrate consumption with perioperative desmopressin and FVIII concentrate combination treatment compared to FVIII concentrate monotherapy, without decreasing the effectivity of treatment.

Study design

Randomized controlled trial

Intervention

The first group receives standard treatment consisting of FVIII concentrate monotherapy. The intervention group receives desmopressin and FVIII concentrate combination treatment.

Study burden and risks

This study aims to assess desmopressin and FVIII concentrate combination treatment in non-severe hemophilia A patients undergoing a minor intervention. During combination treatment, we will monitor FVIII plasma levels to guarantee

safety.
Preoperative desmopressin-testing in each individual will be performed according to the desmopressin-testing protocol in each participating centre. During this procedure, a standard dose of desmopressin is infused and FVIII response is evaluated by measuring FVIII levels before and after desmopressin administration. Patients who have undergone a desmopressin-test in the past with admissible test results, will not have to undergo an additional desmopressin-test.

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)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible for this study, a subject must meet all of the following criteria:, - Non-severe hemophilia A patients (FVIII 0.01-0.40 IU/mL), - In need of a minor surgical intervention, - Age minimally 12 and maximally 70 years at study inclusion date, - Need for perioperative FVIII concentrates for a maximum of 48 hours, - Having admissible results of a desmopressin test (see paragraph 3.1), - Absolute increase in FVIII 1 hour after desmopressin administration * 0.2 IU/mL after a previous (test) dose, - Male gender, - (Parental) informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:, - Patients with other congenital or acquired hemostatic abnormalities, - Clinically relevant FVIII inhibiting antibodies (>0.5 BU) preoperatively, unless successfully treated with immunotolerance therapy, - Needed treatment duration with FVIII concentrates longer than 48 hours, - Contraindications for desmopressin, e.g. cardiovascular disease , - Use of co-medication that has an interaction with desmopressin , - Intolerance to previous desmopressin administrations

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	27-01-2018
Enrollment:	75
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Minrin
Generic name:	Desmopressin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	19-12-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-03-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-07-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2019
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

ID: 26618
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
Other	6036
EudraCT	EUCTR2016-001875-57-NL
CCMO	NL57682.078.16
OMON	NL-OMON26618