DDAVP treatment combined with FVIII clotting factor concentrates in patients with mild hemophilia A

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23569

Source
NTR

Brief title
DAVID

Health condition

hemophilia A; hemofilie A
desmopressin; desmopressine
surgery; chirurgie
pharmacokinetics; farmacokinetiek

Sponsors and support

Primary sponsor: Erasmus Medical Center Rotterdam
Source(s) of monetary or material Support: ZonMw
Ferring b.v.

Intervention

Outcome measures

Primary outcome

The main endpoint will be the proportion of patients within FVIII target levels with DDAVP and FVIII concentrate combination treatment in the first 72 hours after surgery, without adding off-protocol FVIII concentrates

Secondary outcome

- A population based pharmacokinetic model

- Number and nature of adverse events during combined treatment

- Incidence & severity of bleeding

- Incidence of thrombosis

- Incidence and extent of tachyphylaxis

- Economical evaluation

- Experienced quality of care

Study description

Background summary

Summary

Rationale: Hemophilia A is a rare X-linked hereditary bleeding disorder in which the secondary hemostasis is affected by a deficiency in clotting factor VIII (FVIII). As a consequence, patients may suffer from excessive bleeding in response to minor (surgical) trauma or injury. In all hemophilia A patients, perioperative factor concentrate replacement therapy is required, aiming for physiological FVIII plasma levels during up to 6 weeks. In mild hemophilia A patients, surgical procedures are the main reason for intensive treatment with FVIII concentrates. Treatment with FVIII concentrates is effective, but highly expensive. On average, treatment with FVIII concentrates costs €17,520 per mild hemophilia A patient, per surgical procedure. Moreover, exposure to exogenous FVIII may cause the development of FVIII neutralizing antibodies. Recent studies have shown this incidence is higher than realized previously. Neutralizing antibodies are a major challenge in hemophilia A patients, as they lead to ineffectiveness of administered FVIII concentrates and cause subsequent bleeding complications with an increased mortality. Sometimes, these neutralizing antibodies inhibit patients' endogenous FVIII, reducing endogenous FVIII levels below 0.01 IU/ml and a concomitant phenotype of severe hemophilia. Therefore, it is of utmost importance to reduce administration of FVIII concentrates when not strictly indicated and when potential

alternatives are available. More specifically, the release of endogenous FVIII, present in mild hemophilia A patients, can be stimulated by the on-market drug desmopressin (DDAVP). These endogenous FVIII plasma levels, temporarily increased by DDAVP, can be supplemented with FVIII concentrate in order to reach perioperative FVIII target levels, as prescribed by National Consensus.

Objective: The primary objective is to assess the proportion of patients within FVIII target levels with DDAVP and FVIII concentrate combination treatment in mild hemophilia A patients in the first 72 hours postoperatively. Secondary objectives are to acquire data to improve a population based pharmacokinetic (PK) model and to perform an economical evaluation to quantify potential cost reduction.

Study design: A multicenter non-randomized clinical trial in the Netherlands

Study population: Fifty mild hemophilia A patients (FVIII >0.05 IU/mL), between 12-70 years of age, undergoing a surgical procedure and requiring perioperative FVIII replacement therapy for at least 48 hours.

Intervention: Included patients will receive DDAVP and FVIII concentrate combination treatment in the perioperative setting. The FVIII concentrate dose required to reach perioperative FVIII target levels after DDAVP infusion, will be calculated based on a PK population model, constructed by Bayesian analysis using NON-MEM® statistical software prior to the observational trial.

Main study parameters/endpoints: Primary endpoint is the proportion of patients that reach the set FVIII target levels during the first 72 hours postoperatively when treated with DDAVP and FVIII concentrate combination treatment.

Study objective

DDAVP and FVIII concentrate combination treatment will be able to be implemented as standard care for mild hemophilia A patients in the perioperative setting

Study design

preoperatively

postoperatively 0-72 hours

postoperatively 72-144 hours

postoperatively > 144 hours - 90 days

Intervention

DDAVP and FVIII concentrate combination treatment

Contacts

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Eligibility criteria

Inclusion criteria

- Non-severe hemophilia A patients (FVIII ≥ 0.01 IU/mL)
- In need of surgery or suffering from bleeding
- Age minimally 12 and maximally 70 years at study inclusion date
- Need for clotting factor concentrates
- Treatment duration with FVIII-concentrates of at least 48 hours
- Results of FVIII levels after a DDAVP test dose, or if test results are not available, willingness to undergo a DDAVP test
- Male gender

- (Parental) informed consent

Exclusion criteria

- Patients with other congenital or acquired hemostatic abnormalities
- Very low response to DDAVP after 1 hour – absolute increase in FVIII < 0.2 IU/mL
- Clinically relevant FVIII inhibiting antibodies (>0.5 BU) preoperatively, unless successfully treated with immunotolerance therapy
- Contraindications for DDAVP, e.g. cardiovascular disease (see appendix IV)
- Use of co-medication that has an interaction with DDAVP (see appendix IV)
- Intolerance to previous DDAVP administrations
- DDAVP not advisable due to type of surgery or bleeding according to the hematologist and/or surgeon
- Start of FVIII-concentrate treatments >24 hours ago

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2016
Enrollment:	50
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion
Date: 27-08-2015
Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 47474
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL5267
NTR-old	NTR5383
CCMO	NL53686.078.15
OMON	NL-OMON47474

Study results