The DRAIHA study: Data Registry of AutoImmune Hemolytic Anemia, to improve diagnostic testing for the development of personalized treatment protocols in AIHA patients

Published: 01-02-2019
Last updated: 04-01-2025

Primary objective1. The primary aim of the study is to answer the question whether specification of a positive direct antiglobulin test and/or red blood cell autoantibody specification is correlated with the clinical course in patients with AIHA. We…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haemolyses and related conditions
Study type	Observational invasive

Summary

ID

NL-OMON54572

Source
ToetsingOnline

Brief title
The DRAIHA study: Data Registry of AutoImmune Hemolytic Anemia

Condition

- Haemolyses and related conditions
- Autoimmune disorders

Synonym
antibody mediated destruction of red bloodcells, auto-immune hemolytic anemia

Research involving
Human

Sponsors and support

Primary sponsor: Sanquin Bloedbank
Source(s) of monetary or material Support: Sanquin Research

Intervention

Keyword: Anemia, Antibody, Autoimmune, Hemolysis

Outcome measures

Primary outcome

The main study parameter is to determine the causal contribution of the pathogenic characteristics of the autoantibody in relation to the clinical course of AIHA. We will study the autoantibody characteristics such as 1) isotype (IgG, sometimes IgM and rarely IgA class), 2) the ability to activate the complement system, 3) the optimal temperature for reactivity of the RBC autoantibodies, associated with so called *warm AIHA* or *cold AIHA*, 4) the nature of the antigen recognized and the interaction of IgG-Fc receptor, 5) the glycoprofile of the IgG-Fc fragment, and 6) other features of the autoantibodies which are related to the antibody-mediated effects, hence to the course of disease and response to therapy.
Main study parameters obtained from the referring laboratories are hemoglobin levels and hemolysis parameters (LDH, haptoglobin, bilirubin).
Main study parameters obtained from the questionnaire after 1-1,5 year are 1) number of red cell transfusions, 2) number and type of therapy, 3) response of hemoglobin level after each therapy.

Secondary outcome

Study parameters for the secondary objectives of safe and efficient transfusion

in AIHA patients are: development of alloantibodies; development of hyperhemolysis after transfusion; aggravation of hemolysis, based on hemolysis parameters after transfusion; aggravation of autoantibody reactivity after transfusion.

Study description

Background summary

In autoimmune hemolytic anemia (AIHA) auto-antibodies directed against red blood cells (RBCs) lead to increased RBC clearance (hemolysis). This can result in a potentially life-threatening anemia. AIHA is a rare disease with an incidence of 1-3 per 100,000 individuals. An unsolved difficulty in diagnosis of AIHA is the laboratory test accuracy. The current *golden standard* for AIHA is the direct antiglobulin test (DAT). The DAT detects autoantibody- and/or complement-opsonized RBCs. The DAT has insufficient test characteristics since it remains falsely negative in approximate 5-10% of patients with AIHA, whereas a falsely positive DAT can be found in 8% of hospitalized individuals. Also apparently healthy blood donors can have a positive DAT. The consequences of DAT positivity are not well known and may point to early, asymptomatic disease, or to another disease associated with formation of RBC autoantibodies, such as a malignancy or (systemic) autoimmune disease. Currently, there are no guidlines to follow-up DAT positive donors.
A second unsolved difficulty is the choice of treatment in AIHA. Hemolysis can be stopped or at least attenuated with corticosteroids, aiming to inhibit autoantibody production and/or RBC destruction. Many patients do not respond adequately to corticosteroid treatment or develop severe side effects.
Currently, it is advised to avoid RBC transfusions since these may lead to aggravation of hemolysis and RBC alloantibody formation. But in case symptomatic anemia occurs, RBC transfusions need to be given. An evidence-based transfusion strategy for AIHA patients is needed to warrant safe transfusion in this complex patient group.
To design optimal diagnostic testing and (supportive) treatment algorithms, we aim to study a group well-characterized patients with AIHA and blood donors without AIHA, via a prospective centralized clinical data collection and evaluation of new laboratory tests. With this data we want to improve the knowledge of the AIHA pathophysiology and to evaluate diagnostic testing in correlation with clinical features and treatment outcome.

Study objective

Primary objective
1. The primary aim of the study is to answer the question whether specification of a positive direct antiglobulin test and/or red blood cell autoantibody specification is correlated with the clinical course in patients with AIHA. We will set up a registry and databank for DAT positive persons to achieve a centralized collection of clinical data in combination with laboratory data of AIHA patients and DAT positive donors. This data will be analyzed to quantify the potential risk factors for the cause of AIHA. We also aim to determine the causal contribution of standard laboratory and experimental test results to predict the clinical course of AIHA.

Secondary objectives
1. Determine diagnostic predictors for safe and efficient blood transfusion in AIHA patients.
2. Determine the clinical consequences of DAT-positivity in blood donors to develop a clinical guideline for follow up and counseling.

Study design

An observational cohort study:

Intervention: Patients, from the age of 16 with a positive DAT, a positive eluate and signs of hemolysis and patients with a positive DAT for complement only, with a negative eluate and signs of hemolysis, and blood donors with a positive DAT and a positive eluate and/or clinically relevant cold autoantibodies, will be informed about the DRAIHA study and requested to participate by their (donor) physician.
Around diagnosis and concomitantly with a standard blood test performed in the hospital or at Sanquin, 35-50 ml* of blood will be additionally collected for experimental diagnostic testing. No extra venipuncture has to be done.
Physician and blood donor need to fill in a questionnaire about their history, health, medication and diagnostic test results.
After 1-1,5 year the participant will be requested to once again donate an additional amount of 35-50 ml* of blood at time of a standard blood test to perform the same experimental diagnostic tests. At that time point clinical data will also be collected by a structured report form for donor and (donor)physician.
In the patients from the age of 3 months until 16 years, no extra blood will be collected. They will be registered in the databank and experimental diagnostic testing will be performed on residual blood obtained from routine diagnostic testing.

* Depending on the available blood tubes in each participating center.

Study burden and risks

1. AIHA patients and blood donors:
After informed consent, an additional blood will be collected for experimental diagnostic testing. No additional (medical) procedures will be performed, and all blood samples for experimental testing will be collected during routine diagnostic testing of patient and/or donor at time of inclusion and after 1-1,5 years of follow up.

2. AIHA patients from 3 months - 16 years of age:
After informed consent, no additional blood collection will be performed. All clinical and routine laboratory results will be registered in the databank. Experimental diagnostic testing will only be performed on residual blood obtained from routine diagnostic testing.

Venipuncture for blood collection is seen as a minimal risk procedure, however, there is a possibility of complications. The main risks are discomfort and bruising at the site of the venipuncture, and in rare cases this site may become infected. Since nerves are very close to veins and arteries, there is a small risk a nerve is hit by the needle. This is a rare out-come of venipuncture which may lead to, an almost often transient, pain or numbness sensation.

Participation in the study does not result in individual benefits. Nor the patient/blood donor, nor the physician will be informed about the results of the experimental testing. Thus no additional information can be used to change the current standard care of the patient/blood donor.

Contacts

Public
Sanquin Bloedbank

Plesmanlaan 125
Amsterdam 1066 CX
NL
Scientific
Sanquin Bloedbank

Plesmanlaan 125
Amsterdam 1066 CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients with a positive DAT, a positive eluate and signs of hemolysis
Patients with a positive DAT with complement only, negative eluate and sings of hemolysis
Blood donors with a positive direct antiglobulin test and a positive eluate and/or clinically relevant cold auto-antibodies.

Exclusion criteria

No informed consent
Insufficient comprehension of the Dutch language

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-07-2019
Enrollment:	800
Type:	Actual

Ethics review

Approved WMO

Date:	01-02-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-06-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	05-08-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	09-01-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-05-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-07-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL60533.058.17

Study results

Results posted:	17-06-2021
Actual enrolment:	155

First publication
17-06-2021