Clinical sequelae and pathophysiology of rare congenital hemolytic anemias

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1.To create insight in current disease burden by creating a descriptive cohort of patients, diagnosed with rare congenital hemolytic anemia. Points of interest are:- Prevalence and incidence of disease- Quality of life- Prevalence and incidence of...

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

Summary

ID

NL-OMON42799

Source
ToetsingOnline

Brief title
ZEbRA-study

Condition

- Haemolyses and related conditions
- Blood and lymphatic system disorders congenital

Synonym
congenital anemia, hereditary anemia

Research involving
Human

Sponsors and support

Primary sponsor: Van Creveldkliniek UMC Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: congenital hemolytic anemia, hereditary hemolytic anemia, pathophysiology

Outcome measures

Primary outcome

To create insight in current disease burden by creating a descriptive cohort of patients, diagnosed with rare congenital hemolytic anemia. Study parameters are:

- Prevalence and incidence of disease, based on chart review

- Quality of life, based on questionnaires EuroQol-5D-5L and FACT-An

- Prevalence and incidence of iron overload, based on chart review

- Prevalence and incidence of comorbidities and related silent organ damage, based on chart review

- Prevalence and incidence of splenectomy and complications, based on chart review

Secondary outcome

To further analyze the disease process of congenital hemolytic anemia by a case control study.

Parameters:

To determine:

- the tolerability of low hemoglobin levels in rare congenital hemolytic anemia patients based on a 6 minute walking test. This will be compared to the standard model, but will also be compared in between group, to determine possible patterns in tolerability.

- laboratory parameters: pro-inflammatory profile, Red blood cell characteristics, microparticle analysis, and markers of coagulation activation,

by blood sample analysis and chart review. This will be compared to results of healthy control blood by use of the mini donor service. Also, the results will be compared in between group, to determine possible patterns in parameters.
- RNA seq parameters for peripheral blood mononuclear cell transcriptome mapping using blood sample analysis and then compare and relate outcome to other results of the study., Here we will look at the expression of certain gene markers for the clinical symptoms as defined above. For instance,we will analyse the expression of the gene markers for iron regulation and compare this with healthy controls and in between group.

Study description

Background summary

Hemolytic anemia is defined as anemia due to a shortened survival of circulating red blood cells. In congenital or hereditary hemolytic anemia patients suffer of inherited membrane, enzyme or hemoglobin disorders.

Due to the rarity of the diagnoses, to date little is known about the natural history, epidemiology and comorbidities of the different rare hereditary hemolytic anemias.
With the treatment approach for symptomatic hemolysis being mainly supportive, including blood transfusions and long term monitoring, the importance of better understanding of this complex disorder cannot be overstated, in the context of developing future monitoring and treatment regimens for both patients and asymptomatic carriers.

Due to impaired red cell survival, intravascular hemolysis and frequent blood transfusion, excessive iron accumulation can occur, necessitating chelation therapy.
Previous research suggested a link between high intracellular iron exposure and increased inflammation and mortality in patients with sickle cell anemia, a relatively more prevalent form of congenital hemolytic anemia.
In some patients, in order to reduce the blood transfusion burden, splenectomy is performed as a last resort to improve anemia. However, splenectomy is not a curative intervention and earlier findings suggest that some patients develop a

hypercoagulative state resulting in a higher risk of thrombosis. This might be due to a high level of red blood cell derived microvesicles with presentation of phosphatidylserine on the outer membrane, causing a strong procoagulant effect.

For rare diseases, an up to date registry of patients is the only way to provide prompt eligibility data. To our knowledge, an observational cohort study like this is not yet performed. This study will substantially increase the understanding of the pathophysiology of rare hereditary hemolytic anemia.

Study objective

1.To create insight in current disease burden by creating a descriptive cohort of patients, diagnosed with rare congenital hemolytic anemia. Points of interest are:
- Prevalence and incidence of disease
- Quality of life
- Prevalence and incidence of iron overload
- Prevalence and incidence of comorbidities and related silent organ damage
- Prevalence and incidence of splenectomy and complications

2: To further analyze the pathophysiology of congenital hemolytic anemia: to perform a case control study comparing patient parameters and healthy control parameters.
Points of interest are:
To determine:
- the tolerability of low hemoglobin levels in rare congenital hemolytic anemia patients.
- Patterns in laboratory parameters: pro-inflammatory profile, Red blood cell characteristics, microparticle analysis, and markers of coagulation activation,
- RNA seq parameters for peripheral blood mononuclear cell transcriptome mapping using blood sample analysis and then compare and relate outcome to other results of the study.

Study design

The proposed study is a longitudinal retrospective and prospective cohort study, coordinated from the Van Creveldkliniek of the University Medical Hospital of Utrecht. Secondary: a case-control study in which blood parameters and the results of the 6 minute walking test will be compared to results of the healthy populations. For this existing references will be used where possible. For remaining results blood samples of ten healthy controles will be obtained form the Mini Donor Service.

Study burden and risks

Patients are asked to yearly fill out two short questionnaires about quality of life.

Patient participation comprises the donation of a limited amount of blood. Physical discomfort is limited but may include bruising.

Patients also undergo a 6 minute walking test.
Patients choose their own intensity of exercise and are allowed to stop and rest during the test. .
The test, has been performed in thousands of older persons and thousands of patients with heart failure or cardiomyopathy, without serious adverse events .

The burden and risk associated with participation are minimal.

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

Adult patients, 18 years or older with biochemically or genetically diagnosed rare congenital hemolytic anemia

Exclusion criteria

Inability to give informed consent

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):	25-01-2016
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	11-09-2015
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	22-12-2015
Application type:	Amendment

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

ID: 22083
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL53609.041.15
Other	NTR: 22518
OMON	NL-OMON22083