Investigating red blood cell deformability of sickle cell patients who started therapy.

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Investigating red blood cell deformability changes, during treatment, measured with hyperoxia-hypoxia ektacytometry in sickle cell anemia patients, patients with HbSC disease and patients with HbS-beta-thalassemia.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Haemoglobinopathies
Study type	Observational invasive

Summary

ID

NL-OMON54704

Source
ToetsingOnline

Brief title
Sicklecellscreen

Condition

- Haemoglobinopathies
- Blood and lymphatic system disorders congenital

Synonym
hereditary hemoglobinopathy, sickle cell disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Agios Pharmaceuticals,RR Mechatronics,RR

Mechatronics;Agios Pharmaceuticals

Intervention

Keyword: deformability, ektacytometry, Red blood cell, Sickle cell anemia

Outcome measures

Primary outcome

Investigating changes in red blood cell deformability, before and during treatment with hydroxyurea, or before and after blood transfusion, or during the first 9 months of life, as measured with the hyperoxia-hypoxia Lorrca module in SCD patients, patients with SCD and HbC disease, and patients with SCD and thalassemia.

Secondary outcome

1. To assess changes in RBC deformability measured with other Lorrca modules during 6 months of HU treatment, or just before and after blood transfusion, before and after HSCT or gene therapy, or during the first 9 months of life.

2. To explore the association between ektacytometry measurements at different time points with clinical symptoms and signs, haematological parameters and oxidative stress markers.

Study description

Background summary

Sickle cell disease (SCD) is a hemoglobinopathy in which a single nucleotide mutation in the beta-globin chain causes the formation of the abnormal hemoglobin S (HbS). When HbS becomes deoxygenated it polymerises, resulting in sickling of red blood cells (RBCs). These sickled RBCs have strongly reduced deformability, leading to vaso-occlusive crises, multi organ failure and chronic hemolytic anemia.

Hydroxyurea is the only approved drug for the treatment of sickle cell disease. It increases the production of fetal hemoglobin (HbF), thereby lowering HbS levels and, consequently, decreases sickling events. There is however no accurate measurement of a dose-and-effect relation, other than the next life-threatening crisis.
Altered red blood cell (RBC) deformability is a feature of many RBC disorders, including SDC. It can be measured using the Lorrca (Laser-assisted Optical Rotational Red Cell Analyzer) under varying circumstances. For instance, the hypoxia-hyperoxia ektacytometry module of the Lorrca enables the measurement of RBC deformability in response to changes in oxygen tension. This is particularly relevant in the field of SCD. Variables known to be of influence for sickling (e.g. HbF levels, presence of transfusion blood) can be studied by using one single fully automated, operator independent test. We hypothesize that this single test can determine an individual*s status and/or susceptibility to sickling, and measure the effect of hydroxyurea therapy and blood transfusion.
Besides this whole blood of newborns with SCD will be investigated to see if there is a correlation between HbF (which decreases during the first 9 months of life) and RBC deformability.

Study objective

Investigating red blood cell deformability changes, during treatment, measured with hyperoxia-hypoxia ektacytometry in sickle cell anemia patients, patients with HbSC disease and patients with HbS-beta-thalassemia.

Study design

This study is a longitudinal observational study in which Lorrca measurements and other blood tests will be performed at 4 different time points: before (1 time point) and during treatment (3 time points). Extra blood will be drawn at baseline when therapy is started, at 1 month, 3 months and 6 months.
In case of neonates, timepoints will depend on regularly visits at the outpatient clinic.

In case of blood transfusion there will be only 1 timepoint as this treatment has an direct effect on Lorrca measurements.

In case of the baseline cohort there will be only 1 time point.

In case of patients receiveing a allogeneic HSCT of gene therapy before the treatment, after 3 months and after 6 months blood will be drawn.

Study burden and risks

Generally, most SCD patients start hydroxyurea therapy already in childhood,

rarely in adult life. Therefore, the study group will mainly consist of children who are currently not on hydroxyurea therapy, but are about to start. Adults can also participate but will be scarce as they are already on hydroxyurea therapy. The venipuncture will be combined with a routine visit and routine venipuncture. The subjects will not directly benefit from this study. However, this study may lead in the future to a better way to assess therapy efficacy.

Physical discomfort is limited but may include bruising.

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)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

• No blood transfusion within the past 2 months (only in case of hydrea therapy and newborns)
• Diagnosed with sickle cell disease by electrophoresis or HPLC.
• Starting with Hydrea therapy or getting blood transfusion or HSCT or gene therapy, or newborn with SCD, or in steady state with treatment or without treatment. When included in baseline cohort: no treatment, or on chronic blood transfusion or steady state under hydroxyurea.
• Adults patients or parents/legal guardians (and child depending on age) must give informed consent

Exclusion criteria

• Blood transfusion within past 2 months (not a criteria in patients who are treated with blood transfusion)
• Body weight below 10 kg (not a criteria in newborns)
• Age <1 year (not a criteria in newborns)

Study design

Design

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

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-11-2017
Enrollment:	344
Type:	Actual

Ethics review

Approved WMO Date:	14-09-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-02-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	20-09-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-11-2018
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	06-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023

Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-05-2024
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: 24314
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL62011.041.17
OMON	NL-OMON24314