Cerebrovascular reserve and white matter disease in patients with chronic anemia

No registrations found.

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

Summary

ID

NL-OMON27211

Source
Nationaal Trial Register

Brief title
IMPROVE

Health condition

Sickle Cell Disease, Thalassemia

Sponsors and support

Primary sponsor: AMC
Source(s) of monetary or material Support: No funding

Intervention

Outcome measures

Primary outcome

relationship between CVR, CB, and vascular/inflammatory markers
Co-localization of white matter damage and regions of low CVR
Global and regional rsponse of CVR to simple trnasfusions, exchange transfusions and

hydroxyurea.

Secondary outcome

Relationship between neurcognitive performance and white matter damage
Sex differences in baseline CVR and response to interventions
Relationship between haemoglobin genotype and CVR

Study description

Background summary

Low haemoglobin levels raise resting cerebral blood flow (CBF) and leave patients with inadequate cerebrovascular reserve (CVR). As a result , impaired CVR represents the strongest risk factor for white matter injury, volume loss, and stroke. The main goal of this project is to identify CVR predictors including CBF, age, sex and vascular stressors in anaemic and control subject using several MRI techniques. While anaemia is correlated with other cerebrovascular risk factors in the general population (hypertension, kidney disease, chronic inflammation, heart failure), we assume that anaemia, by decreasing CVR, created and increased vulnerability to white matter damage in patients with Sickle Cell Disease (SCD). Through the use of simple and exchange transfusions in selected patients with SCD and thalassemia, we will study the relative importance of haemoglobin S% and total haemoglobin level on regional CVR. We will identify other modifiable risk factors (iron overload, vascular inflammation) that may impair CVR. By comparing CVR and white matter damage across a broad spectrum of SCD and thalassemia syndromes, we will be able to separate the damaging effects of haemolytic anaemias in general froom damage specifi to sickle haemoglobin.

Study objective

relationship between CVR, CB, and vascular/inflammatory markers
Co-localization of white matter damage and regions of low CVR
Global and regional rsponse of CVR to simple trnasfusions, exchange transfusions and hydroxyurea.

Study design

2 MRIs

Intervention

Blood draw, Neurocognitive tests, infusion placed. ECG leads or pulse unit placed, 15 minutes structural MRI, 15 min Functional MRI pre-ACZ, administration of ACZ, 15 min ASL assesses

time course, 15 min functional MRI post ACZ.

Contacts

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Eligibility criteria

Inclusion criteria

Patient group:
Sickle cell disease,
Thalassemia major, thalassemia intermedia, and HbH disease
18 years of age or older
Informed consent

Control Group:
Either AS or AA haemogobin
18 years of age or older
Informed consent

Exclusion criteria

Patient group:
Hospitalization in the past month for any reason
Inability of the patient to provide informed consent
Contraindications for MRI, such as claustrophobia or the presence of metal in the body
Sickle cell crisis at the moment of participation up to one month prior to participation
History of cerebral pathology that comprimized measeurements, such as cerebral palsy, brain tumour, meningitis, overt infrarct

Brain surgery performed in the last 3 months

ACZ contraindications
Severe liver, heart of renal dysfunction (clearance <10 mL/min)
Allgergy to sulphonamide
Pregnant or breastfeeding
Use of phenytoin, procaïne or acetylsacylic acid
Risk of hypokalaemia
Addison's disease
Severe asthma or emphysema

Control Group:
Any known chronic illness that may compromise subject safety or data integrity.
Vascular risk factors
Hypercholesterolemia
Contraindications for MRI
Contraindications for ACZ
Developmental delay, stroke, seizure disorder, or neurological conditions other than simple migraine
inability to cooperate with MRI examinations
Diabetes
Uncontrolled hypertension or history of hypertension

Study design

Design

Study type:	Interventional
Intervention model:	Factorial
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-08-2018
Enrollment:	140
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	20-03-2019
Application type:	First submission

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
NTR-new	NL7620
Other	METC AMC : METC 2018_215

Study results