Cerebrovascular Reserve measUrements In Sickle cell diseasE, a MRI-based study

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

Summary

ID

NL-OMON46956

Source
ToetsingOnline

Brief title
Cerebrovascular Reserve measUrements In Sickle cell diseasE/CRUISE

Condition

- Haemolyses and related conditions

Synonym
hereditary blood disease, sickle cell disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: NutsOhra

Intervention

Keyword: arterial spin labeling, cerebral autoregulation, magnetic resonance angiography, sickle cell disease

Outcome measures

Primary outcome

cerebral blood flow (CBF) measured by ASL; velocity in the MCA measured by 3D TOF MRA; volume and count of semi-automatically delineated cerebral vessels on 3D TOF MRA; volume and count of SCI on 3D fluid attenuated inverse recovery (FLAIR) and T2-weighted MRI scans; wall shear stress measurements

Secondary outcome

count and volume of SCI on previous scans, if available; hematological whole blood parameters including Hb, reticulocytes, free Hb, HbF, Hct, leukocytes, neutraphil count, platelet count, creatinine, total/direct bilirubine, LDH, ferritine; hematological inflammatory parameters including hsCRP, pentraxine-3, AGEs (pentosidine and N*-(carboxy-methyl) lysine, CML), ADMA, von Willebrand factor antigen, sP-selectine, sE-selectine, VCAM-1, ICAM-1, VEGF and nucleosomes; heartbeat frequency; complication frequency.

Study description

Background summary

Impairment of the cerebrovascular reserve (CVR) is a suggested cause for cerebrovascular pathology in sickle cell disease (SCD). It can be evaluated by vasodilatation induction by acetazolamide (ACZ), which has previously shown good results. However, previous imaging modalities did not supply a direct quantification of CVR parameters. Newer imaging modalities, such as arterial spin labeling (ASL), 3-dimensional time-of-flight magnetic resonance angiography (3D TOF MRA) and 3D-flow allow a more concise quantification of CVR

parameters. Furthermore, they allow evaluating their time course during vasodilatation induction. These modalities may clarify the pathophysiological process leading from disturbed autoregulation to cerebrovascular pathology in SCD.

Study objective

The current study aims to evaluate magnetic resonance imaging (MRI)-based CVR measurements with ACZ in SCD. It*s primary objective is to assess whether there is a correlation between CVR with silent cerebral infarcts (SCI) (i.e. the cerebrovascular biomarker). The secondary objectives are to investigate whether 1) CVR are correlated with clinical or vascular biomarkers; 2) 3D TOF MRA in cooperation with ASL can display compensatory collateral circulation in SCD and 3) whole brain averaged vessel diameter is more sensitive than velocity measurement in the medial cerebral artery (MCA). Patients will be compared with healthy controls to estimate the level of disease severity in relation to the heatlhy population.

Study design

The current study will be a single center observational cross-sectional cohort study with intervention and with maximal duration of four years. It consists of one single MRI-examination consisting of four parts of 15 minutes: 1) anatomical imaging; 2) functional imaging before vasodilatation induction; 3) functional imaging during vasodilatation induction; 4) functional imaging after vasodilatation induction. In order to study the CVR, 16 mg/kg ACZ (Diamox®), with a maximum of 1400 mg, will be administrated to induce vasodilatation.

Study burden and risks

MRI is harmless, the ACZ injection has been declared safe and venapunction is routine in patients with SCD.
Parameters obtained by blood drawn in this study will be used clinically as well. Presumably, participation is associated with minimal burden and risks.
As cranial MRI is not routinely performed in adults with SCD, coincidental findings are potentially beneficial. The studied population represents the group of patients with the highest disease severity, and is, thus, representable.

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

- sickle cell disease (HbSS or HbS0)
- 18 years of age or older
- informed consent

Exclusion criteria

* inability of the patient to provide informed consent or legally incompetent/incapacitated to do so
* contraindications for MRI, such as pregnancy, claustrophobia or the presence of metal in the body
* sickle cell crisis at the moment of participation
* history of cerebral pathology that compromises measurements, such as cerebral palsy, brain tumor, meningitis, overt infarct
* brain surgery performed in the last 3 months
* severe liver, heart or renal dysfunction (clearance < 10 mL/min)
* allergy to sulfonamide
* breastfeeding

* use of phenytoin, procain, acetylsacylic acid (*Ascal/aspirine*)
* risk of hypokalemia (use of diuretics, primary hyperaldosteronism)
* Addison*s Disease
* severe asthma or emphysema

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-08-2014
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO Date:	12-03-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL37995.018.11