Sickle Red blood Cell Survival: explaining heterogeneity

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To examine the determinants of survival of donor RBCs in SCD patientsTo look into the effect of transfusion on the innate immune system of sickle cell patients, in particular, the phenotype of the neutrophils.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Red blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON51617

Source
ToetsingOnline

Brief title
SURVIVE

Condition

- Red blood cell disorders
- Blood and lymphatic system disorders congenital

Synonym
Sickle Cell Anemia, Sickle Cell Disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Determinants, Erythrocyt transfusion, Sickle cell disease, Survival

Outcome measures

Primary outcome

- Survival of donor RBCs in top up and exchange transfusions in SCD patients 4 weeks post-transfusion

- Effects of patient-derived factors (genotype, HbS%, hemolysis, endothelial activation (proVWF/VWF ratio), inflammation, neutrophil activity/phenotype) on donor RBC survival

Secondary outcome

- Phenotypic changes in endogenous and donor RBCs after transfusion in SCD patients (1 hour, 24 hours, 1 week, 2 weeks, 3 and 4 weeks post-transfusion) as compared to pre-transfusion

- Oxidative stress in endogenous/donor RBCs after transfusion in SCD patients as expressed by intracellular metabolomics (1 hour, 24 hours, 1 week, 2 weeks, 3 weeks and 4 weeks post-transfusion)

- Immediate and late effects of transfusion on neutrophil activity and phenotype in SCD patients (1 hour, 24 hours, 1 week and 2 weeks post-transfusion) as compared to pre-transfusion values

- Survival of endogenous RBCs 1, 2 and 4 weeks after transfusion measured by the ratio of glycine-15N and glycine 14N in heme

Study description

Background summary

Red blood cell (RBC) transfusions are currently one of the most important therapeutic options for patients with sickle cell disease. Widespread variability in survival of transfused RBCs has been described in literature, both between different patients and within a patient over time. The mechanisms causing this variability in donor RBC survival in SCD patients are largely unknown. Possible factors influencing donor RBC survival in SCD patients are oxidative stress, chronic inflammation with exacerbations during VOCs, neutrophil activity/phenotype and endothelial activation. It is important improve our understanding of these inter- and intra-individual differences in donor RBC survival and the mechanisms behind them, as it might provide novel targets for therapeutic strategies to improve the survival of transfused RBCs.

Study objective

To examine the determinants of survival of donor RBCs in SCD patients
To look into the effect of transfusion on the innate immune system of sickle cell patients, in particular, the phenotype of the neutrophils.

Study design

Longitudinal observational cohort study. At seven different time points (before transfusion, 1 hr, 1 day, 1 week, 2 weeks, 3 weeks and 4 weeks after transfusion), data and blood samples will be collected. Furthermore patients of >=12 years old will be asked to take 2 grams of 15N-glycine, dissolved in 30 mL of water orally just before the transfusion.

Study burden and risks

Very little is known about the mechanisms causing variability in donor RBC survival in SCD patients. Increased knowledge on this subject might provide novel targets for therapeutic strategies to improve the survival of transfused RBCs. Therefore a study in this population is essential. Risk of participation is considered to be very small, as it will only consist of approximately five additional blood drawings (maximum three additional blood drawings for children). Blood drawings will be combined as much as possible with sample collection for diagnostic purposes. Furthermore, patients of 12 years or older are asked to take the stable isotope 15N-glycine (non-investigational product) once. Stable isotopes have been used safely for research purposes in adults and children for years. Since stable isotopes have the same atomic number, but differ in mass number, they can be used to safely label erythrocytes.

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)
Elderly (65 years and older)

Inclusion criteria

Sickle Cell Disease
>=6 years old
Clinical need for an erythrocyte transfusion

Exclusion criteria

- No informed consent
- Pregnancy, self-reported

- Active cancer
- Chronic of acute HIV infection
- Comorbid autoimmune/inflammatory disease
- Pre-operative incidental transfusion

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-03-2023
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	05-07-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	11-08-2022
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	NL80752.018.22