RBC clearance

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25526

Source
NTR

Brief title
Storage lesion

Health condition

Problem studied:
To try and identify the so called 'removal signals' on donor erythrocytes after transfusion to ensure a longer RBC survival and higher quality of the transfused erythrocytes due to removal of those cells prior to a blood transfusion.

Het identificeren van "verwijdersignalen" op donor erytrocyten zodat in de toekomst de kwaliteit/overlevingsduur van de erytrocyten wordt vergroot na depletie van deze cellen voorafgaand aan een bloedtransfusie.

Keywords:
Storage lesion
RBC clearance
Removal signals

Trefwoorden:
Bewaarinvloeden
Erytrocyten afbraak
Verwijdersignalen

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum (LUMC)
Albinusdreef 2,
2333 ZA Leiden
071 526 9111
Source(s) of monetary or material Support: Sanquin Blood Bank
Plesmanlaan 125
1066 CX Amsterdam
Tel: 020-5123000

Intervention

Outcome measures

Primary outcome

Changes in all possible “removal signals” on the outer layer of the RBC membrane compared to short versus long stored RBC, like upregulation of phosphatidylserine (PS), conformation of CD47, and auto-antibody binding. We would also like to study the binding of PS-bridging proteins such as lactadherin, Von Willebrand Factor (vWF) and Protein S, as well as the CD47-binding protein thrombospondin-1.

Secondary outcome

Standard of care parameters:

Hemoglobin, platelets, WBC and differentiation, ferritin, CRP

Additional measured parameters for study:

Other parameters on infection (CRP), iron status (Fe, hemopexin, hepcidin, NTBI), cytokines (TNFa, IL-1/IL-6, IL8), complement (C3 and C4) and antigens in complement biology (CD35, CD55, CD59, and factor H), antigens for adhesive capacities: CD44, CD147, ICAM-4, L-selectin for activation of monocyte, sICAM-1/sVCAM1 for endothelial activation and monocyte markers (CD14, CD11b), will also be studied.

Study description

Background summary

Rationale: The molecular mechanisms by which red blood cells (RBCs) are cleared in vivo are still elusive. Identification of the routes that lead to RBCs clearance are in particular important for transfusion practice, since 10-25% of the donor RBCs are cleared within 24 hrs after transfusion. This phenomenon will not only decrease the efficacy of transfusions but moreover, may be associated with serious side-effects in the recipient. While, in the normal life span of erythrocytes, RBCs are probably cleared by gradual acquisition of “eat me” signals that regulate progressive phagocytosis by macrophages predominantly in the spleen and liver. However, these normal mechanisms seem dysregulated for allogeneic transfused RBCs while additionally monocytes in the blood stream and endothelial cells seem to participate in their clearance.

In the Netherlands donor erythrocytes are stored for a maximum of 35 days. Storage induces several changes in the erythrocytes that are collectively defined as the “storage lesion”. The exact nature of these changes is unclear. We hypothesize that storage of RBCs is associated with an increased number or change of removal signals on the RBCs and, therefore, with a faster clearance after transfusion.

Objective: To determine the critical ‘removal mechanisms’ for donor RBCs by comparing clearance characteristics of both short and longer stored donor RBCs within patients and correlating these to “removal signals” on the membrane of the donor RBCs as well as their rheologic, adhesive, metabolic, complement activating and proteomic characteristics.

Study design: Prospective, randomized, double blinded, cross-over trial.

Study population: 20 myelodysplastic syndrome (MDS) patients with low WPSS (WHO classification-based prognostic scoring system 0-1) with transfusion requirement who are not eligible for intensive treatment or clinical trials (i.e. elderly MDS patients).

Main study endpoints: Primarily to determine the difference in percentage of clearance for and between short and longer stored donor RBCs within patients and secondary the possible determinants for this clearance.

Intervention arms: Patients will be randomized to either first receive a transfusion of one unit of RBCs stored for < 10 days and subsequently one unit of RBCs stored for > 25 days or vice versa.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The 2 to study RBC transfusions are part of standard patient care. Standard processed RBC units will be transfused although they are selected for storage time and are of a special blood group typing to facilitate detection of these RBCs from patients own and previous transfused circulating RBCs. From all MDS patients 5 times 5 ml blood will be collected along each of the 2 studied RBC transfusions of 350 ml, equalling 50 ml of additional blood collections in total. Of these, 2 will be done via the infusion system that is standard needed for the transfusion but 3 collections will require an additional vena puncture. At every sampling moment there is a minimal risk of a puncture hematoma and

infection. In addition, patients are asked to answer detailed questionnaires to asses the Quality of Life.

Study objective

RBC clearance is caused by "removal signals".

Study design

For each transfusion given (in total 2)

T0: blood sample prior to blood transfusion (includes blood typing and matching);

Randomization takes place with short (<10 days) vs. long (>25 days) stored erythrocytes;

T1h: blood sample taken 1 hour after blood transfusion;

T24h: blood sample taken 24 hours after blood transfusion;

T7d: blood sample taken 7 days after blood transfusion;

T14d: blood sample taken 14 days after blood transfusion;

During the course of this study all patients will receive one short and one long stored blood transfusion (including a wash-out period of 120 days between transfusions).

In addition, standardized questionnaires will be used to assess the quality of life at two different time points: pre-transfusion (baseline) and 14 days post-transfusion.

Intervention

Venipuncture

Contacts

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Scientific

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Eligibility criteria

Inclusion criteria

- A low WPSS 0-1 with transfusion requirement who are not eligible for intensive treatment or Clinical trials (i.e. elderly MDS patients);

- A life expectancy of a minimum of 6 months;

- Age > 18 years;

- Full knowledge of the Dutch language.

Exclusion criteria

- If no minor antigen mismatch can be made;

- No informed consent (IC);

- Patients under the age of eighteen;

- Patients that have a medical history with an autoimmune haemolytic anemia (AIHA) or patients that will develop an AIHA during the study;

- Patients with an enlarged spleen;

- Pregnancy;

- Patients with intensive MDS treatment.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2014
Enrollment:	20
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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	NL4631
NTR-old	NTR4783

Register	ID
Other	NLRBCC0813 : ABR nummer: 44711

Study results