RBC clearance

Gepubliceerd: 11-09-2014 Laatst bijgewerkt: 18-08-2022

RBC clearance is caused by "removal signals".

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25526

Bron
NTR

Verkorte titel
Storage lesion

Aandoening

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

Ondersteuning

Primaire sponsor: Leids Universitair Medisch Centrum (LUMC)
Albinusdreef 2,
2333 ZA Leiden
071 526 9111
Overige ondersteuning: Sanquin Blood Bank
Plesmanlaan 125
1066 CX Amsterdam
Tel: 020-5123000

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

RBC clearance is caused by "removal signals".

Onderzoeksopzet

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.

Onderzoeksproduct en/of interventie

Venipuncture

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- 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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-12-2014
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Ethische beoordeling

Niet van toepassing

Soort:	Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4631
NTR-old	NTR4783
Ander register	NLRBCC0813 : ABR nummer: 44711

Resultaten