Effect of storage time and additive solution on posttransfusion clearance and metabolic recovery

Gepubliceerd: 28-03-2017 Laatst bijgewerkt: 15-05-2024

Fresh red blood cells (RBC) and RBCs stored in PAGGGM will recover more extensively and faster compared to stored RBCs in SAGM respectively.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24366

Bron
NTR

Verkorte titel
Chimera

Aandoening

storage leasion red blood cells, metabolic recovery red blood cells, additive solution red blood cells

Ondersteuning

Primaire sponsor: Academisch Medisch Centrum, Amsterdam, The Netherlands
Overige ondersteuning: Sanquin Blood Supply Foundation, Amsterdam, The Netherlands

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1) Compare posttransfusion RBC clearance of fresh and stored RBCs and investigate whether glycolytic enzyme function, glycolysis, pentose phosphate pathway function and related metabolic pathways recover after transfusion of a 35 day stored RBC product in humans.

Toelichting onderzoek

Achtergrond van het onderzoek

Red blood cell (RBCs) transfusions are frequently administered to patients that require an increase in circulating blood oxygen delivery capacity to improve tissue oxygenation. In most countries, the shelflife of RBCs has been maximized to 35 - 42 days as blood products undergo changes referred to as the ¡°storage lesion¡± during aging. The ¡°storage lesion¡± is characterized by RBC vesiculation, membrane loss and lysis, changes in their metabolic activity and increased oxidation of cellular lipids and proteins. These processes induce a storage dependent decrease in pH and an increase of extracellular potassium.
Multiple strategies have been tried to reduce the ¡°storage lesion¡± and increase the quality of stored red cell concentrates. However the clinical relevance of the ¡°storage lesion¡± remains unclear. A recent study showed that RBCs stored in the new additive solution PAGGGM maintain higher levels of ATP and 2,3 diphosphoglycerate during storage, which shows that RBC stored in this medium are metabolically more active than standard stored RBC, which may result in a higher recovery after transfusion.

In this randomized intervention trial, healthy volunteers will be transfused with autologous fresh RBCs (2days old) and stored RBCs (35 days old) to compare differences in clearance and metabolic recovery between RBC stored in the standard additive solution, SAGM, and RBC stored in the new additive solution, PAGGGM. Fresh and stored RBCs will be labeled with different densities of biotin, which allows their identification and isolation. The different RBC populations will be sorted by flow cytometry and analyzed by mass spectrometry to study metabolic recovery.

Doel van het onderzoek

Fresh red blood cells (RBC) and RBCs stored in PAGGGM will recover more extensively and faster compared to stored RBCs in SAGM respectively.

Onderzoeksopzet

1)Before study day:

- Screening twice, at the AMC and at Sanquin

- Donating blood 2 days and 35 days prior to study day

2)Study day

- Subjects will be admitted for one day at the AMC

3)Follow up

- One, two, seven, 30 and 90 days after transfusion a venous blood sample will be collected

Onderzoeksproduct en/of interventie

Screening:

all subjects will be screened at the AMC and Sanquin. Investigation of the medical history, a physical examination, ECG and blood and urine examination will be performed to determine volunteer eligibility to participate in the study.

Study

All included healthy volunteers (n=20) will donate 1 unit of whole blood at Sanquin Blood Bank which will be processed into 1 unit of RBCs (approximately 300ml) 35 days before the experiment. Processing and storage will be according to Sanquin Blood Bank protocol and products will be stored in either SAGM or PAGGGM. Every week, a sample will be collected from these products with a sterile coupler. Two days before the experiment healthy volunteers will donate a second smaller blood product (approximately 200 ml; miniature whole blood donation processed with a
whole blood leukodepletion filter; validated Sanquin product) which will be processed into a small RBC concentrate. Both donations will be labelled with biotin, using two densities of biotin according to previously published protocols. To exclude any effect of biotin label concentration half of each group will receive fresh RBCs labelled with a low biotin concentration and stored RBCs labelled with a high concentration.
The other half will receive fresh RBCs labelled with a high concentration biotin and stored RBCs labelled with a low concentration of biotin.

Two days after the second smaller donation subjects will be admitted to the hospital where they first will receive indocyanine green to calculate circulating volume, followed by the autologous biotinylated RBCs stored for 2D and 35D. At the study day, blood samples will be drawn from an indwelling venous canula prior to indocyanine green infusion, 5, 10 and 20 min
after infusion, prior to the transfusion and 10 minutes, 0.5, 1, 2, 4, 6 and 8 hours after transfusions. During the experiment subjects will be monitored for heart rate and blood pressure by noninvasive continuous monitoring.

Volunteers will return to the AMC 24 hours, 2, 7, 30 and 90 days after transfusion for follow-

up samples. These samples will be used to detect and sort the two populations of transfused RBCs by flow cytometry.

The metabolism of the two sorted BioRBC populations and samples of stored blood products will be investigated. These analyses will be combined with direct enzymatic measurements (spectrophotometry and cytofluorometry) of selected enzymes in these samples, for example glucose-6-phosphate dehydrogenase (G6PD). Thus we will be able to investigate the effect of storage on enzyme activity in the stored RBC and metabolic recovery of the stored RBC after transfusion.

1, 2, 7, 30 and 90 days after transfusion a venous blood sample (12 ml) will be collected to monitor RBC clearance and to monitor the development of anti-biotin antibodies. These data will be used to monitor antibody prevalence after exposure to biotin. Antibodies will be tested using an IgG gel card test (Ortho Clinical Diagnostics, MTS¢â Anti IgG Card).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1) Healthy volunteer

2) Age ¡Ã 18 years <35 years

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1) No informed consent

2) Any abnormal test result during the screening prior to inclusion of the study (medical history, physical examination, ECG, blood and urine examination)

3) History of drugs or alcohol abuse

4) Any present medication use on prescription

5) Smoking < 6 months

6) Blood loss of more 500 ml < 3 months, including blood donation

7) Previously transfused

8) Participation in any other intervention study during the course of this study

9) Allergy or hypersensitivity for iodine

10) Active thyroid disease

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland
Status: Werving nog niet gestart

(Verwachte) startdatum:	01-04-2017
Aantal proefpersonen:	20
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	28-03-2017
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 47236
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL6317
NTR-old	NTR6492
CCMO	NL59816.018.16
OMON	NL-OMON47236

Resultaten