Development of a ¡°two hit¡± in vivo autologous platelet transfusion model in healthy volunteers

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON26852

Source
Nationaal Trial Register

Brief title
DIVA

Health condition

Transfusion related acute lung injury (TRALI), Metabolic recovery of transfused thrombocytes after storage

Sponsors and support

Primary sponsor: Academisch Medisch Centrum, Amsterdam, The Netherlands
Source(s) of monetary or material Support: Sanquin Blood Supply Foundation, Amsterdam The Netherlands

Intervention

Outcome measures

Primary outcome

Test the hypothesis that in the presence of a ¡°first hit¡± an aged apheresis platelet

transfusion is able to induce a mild form of ALI.

Secondary outcome

1)unravel several hypothesized inflammatory processes in the lungs of patients that develop TRALI (i.e., production of inflammatory mediators, neutrophil activation, complement activation, disturbed alveolar fibrin turnover).

2)assess the usefulness of several potential biomarkers of lung injury in TRALI (in particular recently proposed potential biomarkers, such as surfactant proteins, Clara cell protein, sRAGE and KL-6).

3)identify phenotypic changes of the transfused platelets and their interaction with other cell types in the receiver¡¯s circulation and their potential contribution to the development of lung injury.

4)Metabolic recovery of transfused thrombocytes after storage

Study description

Background summary

Transfusion related acute long injury (TRALI) is the leading cause of transfusion related morbidity and mortality. TRALI is thought to be a ¡°two hit¡± event. The first event is the underlying condition of the patient, often sepsis or an infection, resulting in priming of neutrophils. The second event is the transfusion of a blood product. Additional research is needed to determine whether the use of fresh cell-containing blood products may be an additional measure to reduce TRALI.

The aim of this study is to develop a TRALI model in healthy volunteers. Subjects are extensively screened at the AMC and Sanquin (including medical history, physical examination, ECG, laboratory testing, spirometry and DLCO, X-thorax). If the subjects are enrolled in the study, they are randomized for the first hit in two groups, one receiving LPS 2ng/kg, the other group will receive saline. For the second hit the subjects are randomized between autologous fresh platelets (2 days old) and autologous stored platelets (7 days old). A small portion of the platelets will be biotinylated to identify the transfused platelets from the circulating population. 6 h after the transfusion spirometry, DLCO and X-thorax will be repeated and a broncho alveolar lavage will be performed to test whether the subjects did develop TRALI.

After transfusion multiple blood samples will be drawn to measure markers of inflammation, neutrophil activation and coagulation activation are measured to confirm whether we have developed a model of TRALI. Furthermore, biotinylated platelets will be isolated by flow cytometry to test metabolic recovery using liquid chromatography and mass spectrometry.

Study objective

In the presence of a ¡°first hit¡± an aged apheresis platelet transfusion is able to induce a mild form of ALI

Study design

1)Prior to experiment:

- Screening twice, at AMC and Sanquin

- Donating 1 unit of platelets 2or 7 days prior to experiment

2)Experiment day: subject will be admitted for one day at the intensive care

3)Follow up

- 2 days, 4 days and 3 months after experiment day

Intervention

All subjects will be screened (medical history, physical examination, ECG, blood examination, spirometry, DLCO, chest x-ray) by the research physician of our hospital and of Sanquin Blood Bank prior to involvement in the experiment. All included healthy volunteers (n=36) will donate 1 unit of apheresis PLTs (approximately 150 - 400 ml). Processing and storage will be according to Sanquin Blood Bank protocol. Prior to transfusion, stored PLTs will be biotinylated to allow their identification by flow cytometry. In short, stored PLTs will be labelled with Sulfo-NHS biotine (5¦Ìg/ml). Subsequently on the study day healthy volunteers will receive a ¡°first hit¡± of either E. coli lipopolysaccharide (LPS) 2 ng/kg i.v. (n=18) or NaCl 0.9% 10 ml intraveneously (n=18). Two hours after the ¡°first hit¡± the volunteers will receive an autologous transfusion of 1 unit of fresh (2 day storage) biotinylated PLTs or an autologous transfusion of 1 unit aged biotinylated (7 days of storage) PLTs or an equivalent volume of saline 0.9% infusion. The transfusion itself will be performed in 30-60 minutes. During the experiment subjects will be monitored for blood pressure and arterial oxygenation using an indwelling arterial line. Blood samples will be drawn from an indwelling artery line prior to the ¡°first hit¡±, prior to the transfusion, 10 minutes, 0,5, 1, 2, 4 and 6 hours after transfusion. Furthermore, 6 hours after transfusion spirometry and DLCO measurement will be repeated. A chest x-ray and a directed bronchoalveolar lavage (BAL) will be performed 6 hours after transfusion. In the BAL-fluid and plasma samples markers of inflammation, neutrophil activation and coagulation activation are measured to confirm whether we have developed a model of TRALI. Two days,four days and three months after the study day a venous sample of 4 ml will be collected to monitor platelet kinetics and to measure prevalence of biotin antibodies.

Contacts

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Eligibility criteria

Inclusion criteria

1)Healthy male volunteer

2)Age ¡Ý 18 years <35 years

Exclusion criteria

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, spirometry, DLCO measurement, chest x-ray).

3)History of drugs or alcohol abuse

4)Any present medication use on prescription

5)Smoking < 6 months

6)History of blood donation < 3 months

7)Blood loss of more 500 ml < 3 months

8)Previously transfused

9)Participation in any other medical drug study < 3 months

10)Participation in previous volunteer studies using LPS

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2017
Enrollment:	36
Type:	Anticipated

Ethics review

Positive opinion

Date:	28-03-2017
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 55634
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL6318
NTR-old	NTR6493
CCMO	NL50117.018.14
OMON	NL-OMON55634

Study results