Transfusion related acute lung injury (TRALI) in cardiac surgery patients: incidence, risk factors and underlying pathophysiology

Published: 10-11-2006
Last updated: 20-05-2024

(i.) to determine the incidence of and risk factors for TRALI in a prospective cohort of cardiac surgery patients (ii.) to test the hypotheses of TRALI in this patient group(iii.) to study local inflammatory responses during TRALI(iv.) to determine...

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON30078

Source
ToetsingOnline

Brief title
TRALI in cardiac surgery patients

Condition

- Other condition

Synonym
Transfusion Reaction

Health condition

Bloedtransfusie reacties

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: blood transfusion, cardiac surgery, Intensive Care, TRALI

Outcome measures

Primary outcome

Riskfactors for TRALI (Type of operation, medical history, intoxications etc.)

Incidence of TRALI in this cohort group

Donors: Anti HLA/HNA antibodies in the donor blood

Pro-inflammatory cytokines (TNF-x, IL-1, IL-6, IL-8) and bio acrive lipids in

the transfusions.

Patients: Biomarkers (CC10, SP-D, SP-A en KL-6), Pro-inflammatory cytokines,

complement concentration, activity of the coagulation and fibrinolysis (TF,

Factor VIIa, TATc, PAI-1, t-PA).

Surfactant protein A and D, Clara cell protein and KL-6.

Secondary outcome

none

Study description

Background summary

With the reduction of clerical errors transfusion-related acute lung injury (TRALI) has currently surpassed hemolytic reactions as the leading cause of transfusion-related morbidity and mortality. Generally considered to be rare, TRALI is almost certainly underdiagnosed and underreported. At this moment we have a consensus about the definition of TRALI, the patient needs to confirm the definition of acute lung injury (ALI) and in the past 6 hours given a transfusion and no other riskfactor for ALI may be present. However, clinical diagnosis of TRALI stays difficult by the absence of specific markers of this disease. As a consequence, most cases of TRALI remain unnoticed, misdiagnosed as fluid overload or ALI of other etiology. Two distinct mechanisms of TRALI have been suggested: the traditional theory proposes an antibody-mediated reaction between recipient leukocytes and anti-leukocyte antibodies from donors who were sensitized during pregnancy (multiparous women) or by previous transfusion. Recently, an alternative mechanism has been put forward implicating pro-inflammatory molecules that accumulate during blood storage. In either case, TRALI is considered to be a *double hit* entity, in which the condition of the patient at the time of transfusion (e.g., surgery, shock, mechanical ventilation) predisposes to priming and adherence of neutrophils in the lung vasculature.
Cardiac surgery patients may form a group of patients at high risk for TRALI: first, during the intra-thoracic surgical procedure the lungs are usually left deflated and non-ventilated for several hours. This procedure may cause injury to the lung vasculature (the *primary hit* in the *double hit* theory). Second, these patients often receive transfusion of numerous blood products, in particular red blood cells and furthermore fresh frozen plasma and platelets. The basis for the proposed study follows from our preliminary data that oxygenation of post-cardiac surgery patients in 1 in 15 patients rapidly declines without any obvious reason. Indeed, these patients are confronted with oxygenation problems, which do not seem to be caused by simple fluid overload or pulmonary atelectasis. The majority of these patients received a transfusion during or after cardiac surgery, from which we suggest that these patients may have had TRALI.

Study objective

(i.) to determine the incidence of and risk factors for TRALI in a prospective cohort of cardiac surgery patients

(ii.) to test the hypotheses of TRALI in this patient group

(iii.) to study local inflammatory responses during TRALI

(iv.) to determine the role of old and new biomarkers of lung injury in the diagnosis of TRALI.

Study design

In a observational cohort study of cardiac surgery patients we expect to recruit a total of 100 TRALI-patients from approximately 1500 patients after cardiac surgery with transfusion. Patients receiving bloodproducts without developing TRALI and patients developing ALI without receiving bloodproducts, a total of maximum 400, will be included in the control groups by using a matched case control design. Assuming this incidence of ALI after blood transfusion of approximately 6,6% and a standard deviation of 15% and an alpha of 0.05, we will have > 80% power to detect modest independent increase in risk for development of TRALI. Since not all cardiopulmonary surgery patients will receive blood product transfusions, we expect 2* years to be needed to recruit enough patients in the study. The whole project is performed in 3 years.

Study burden and risks

Bloodsampling will be done during standard clinical rounds. Lung lavage is a standard procedure in intubated and mechanically ventilated patients (normally the obtained fluid is discarded)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Cardiac surgery patient with post operative ICU admittance
Informed consent
>18 years

Exclusion criteria

Immunosupressive drugs

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2006
Enrollment:	1500
Type:	Anticipated

Ethics review

Approved WMO
Application type: First submission

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	NL12952.018.06