Comparison of a single dose fibrinogen with placebo and the number of blood transfusions after ascending aorta surgery (FIBTEG study)

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Interventional

Summary

ID

NL-OMON41387

Source
ToetsingOnline

Brief title
Bloodtranfusions after aortic surgery

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Cardiac valve disorders
- Aneurysms and artery dissections

Synonym
loss of functionality of the thoracic aorta, postoperative coagulopathy

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: aortic, bloodtransfusion, fibrinogen, reconstruction surgery

Outcome measures

Primary outcome

Number of transfused allogenic blood products, up to 24 hours after surgery.

Secondary outcome

Postoperative blood loss (= thoracic drainage volume) up to 24 hours after

surgery.

* Re-operation during postoperative hospitalization.

* Admission time in Intensive Care Unit (ICU) and hospital.

* Hospital mortality

Study description

Background summary

Cardiothoracic surgery (CTC) is associated with blood loss and an increased risk for impaired coagulation by the use of a CBP. Coagulation is a process of primary hemostasis by adhesion of trombocytes and aggregation, followed by secondary coagulation and fibrin formation. During CTC fibrinogen is the first coagulation factor which reaches critical concentration necessary for clotting. Point of Care clotting assay with thromboelastography (TEG) provides qualitative information on coagulation factors and clot strength. Specific coagulation factor correction of impaired clotting improves clot strength and may reduces the number of perioperative allogeneic blood transfusions, resulting in possible reduction of postoperative blood loss and reduction of the risk of re-operation in the short and long term.
The hypothesis of this study is that a single dose fibrinogen concentrate immediately after CTC leads to a decrease in the number of allogenic blood

transfusions in patients with clinically impaired clotting, verified by TEG.

Study objective

The purpose of this study is to answer the following question: Leads a primary coagulation corrected with a single dose of fibrinogen concentrate after ascending aorta-arc reconstruction to a decrease in the number of allogenic blood transfusions, compared to placebo?

Study design

Mono Center, prospective, double-blind, randomized, placebo-controlled study

Intervention

During the operation, clotting is measured with point of care with TEG, and the usual intra-operative hemostasis protocol was followed (transfusion of blood products in the form of blood plasma (FFP), thrombocytes (5ET) and erythrocytes (PRBC) based on TEG and laboratory results. After disconnection of the HLM patients receive a single dose of fibrinogen concentrate (FC) or placebo intravenously and they will be assigned randomly to FC (4,6 or 8 grams, depending on weight) dissolved in water or an equivalent volume of 0.9% NaCl.

Study burden and risks

General anesthesia and monitoring
Elective ascending aorta-arch reconstruction is done under general anesthesia. Prior to induction, a patient routinely receives a venous cannula in the hand and an arterial cannula in the a right radial. After induction, an endotracheal tube is placed in the arterial cannula in the left radial, a central venous line in the right jugular vein and esophageal ultrasound probe. The anesthesia policy for a study patient does not differ from a patient who does not participate in the study.

TEG
During surgery the TEG will monitor clotting, executed by the anesthesiologist. Per patient, 20 ml of blood spread over 4 times, 6 ml routine bloodsample and 14 ml extra bloodsample for this study. Blood samples will be taken from the arterial cannula or from the circuit of the HLM. There is no additional venipuncture or arterial puncture site. TEG measurements have been established in the intraoperative hemostaseprotocol and are identical for all patients. This protocol is the basis of the study protocol. Transfusion products are ordered (or 5ET FFP). Based on TEG measurements. A study patient receives a dose study medication immediately after disconnenction of the CPB. Three blood samples are taken during surgery for the TEG determiniation and also for determination of plasma fibrinogen concentration at the same time for all study

patients.

Study Medication
After discontinuation of the CBP a study patient receives a single dose of FC (4,6 or 8 grams, depending on weight) administered, or the same volume of 0.9% NaCl. Fibrinogen Concentrate (brand name; Haemocomplettan P) is a normal constituent of human plasma and acts like endogenous fibrinogen. It is since registration in 1997 used for therapy and prophylaxis of hemorrhagic diathesis. In the Netherlands it is used to include major perioperative bleeding and has a permanent place in transfusion protocols to massive blood loss. Administration of fibrinogen has a low allergy risk and low risk of thrombotic complications. This is supported by the registrations in the farmacosurveillance program Haemocomplettan P, which mentioned only 9 reports of thrombotic side effects in 250,000 doses of 4 grams in 21 countries.
The study group who receive fibrinogen after discontinuation of the CBP will expected to require less blood products have improved coagulation. This may lead to a more favorable postoperative situation.

Intensive Care and postoperative phase
The postoperative care in the ICU takes routine bloodsamples for measurements. In the context of the study 24 hours after the gift FC / placebo a 3ml of blood was taken for the determination of plasma fibrinogen concentration. The blood sampling was taken from the artery of the patient. There is no additional venipuncture or arterial puncture necessary. Twenty-four hours after the operation, the total number of transfused blood products and total blood loss was monitored in study patients. For this, a researcher will visit the patient.
In an uneventful course patients stay after elective ascending aorta-arch reconstruction normally for 48 hours in the ICU. After that the patient will be resigned to another department. During the hospitalization patients are monitored remotely. The required postoperative data is collected by the researchers from the electronic patient file and Meta Vision (OK and IC patient data management system). The study is terminated after discharge from the hospital. Patients will be after discharge not approached again by the researchers, in any form whatsoever.

Substudies.
Three substudies involve comparative and observational research.
(1) Routine TEG and FF-TEG are compared at the end of the study with the von Clauss fibrinogen test, the gold standard .
(2) Fibrinogen is the first coagulation factor in need of supplementation. This together with thrombin generation is essential in the clotting cascade. This substudy investigates the height of the trombinepeak after discontinuation of HLM. Therefore it compares the TEG and FF-TEG data with the thrombin level and coagulation factor assays (preoperatively , t = 0 , t = 10 , postoperative and in case of allogeneic blood transfusion also t = 15) . This includes a total of 36 ml (4x 9 mL) of blood samples which are processed and stored until all measurements are performed.

(3) Erythrocytes supply in addition to platelets and coagulation factors also contribute to thrombus formation because they are incorporated into the clot . To understand the relationship between clot strength and the effect of hematocrit (Ht) this is measured at two timepoints. At induction and after discontinuation of the HLM are Hb , Ht and platelets measured (2x3 ml) , this are routine assays to which timing is specified for the study. The study will show the impact of reduced Ht and platelet number on the clot strength after discontinuation of HLM.

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

* > 18 years
* Competent

* Scheduled for ascending aorta replacement using CPB
* Signed informed consent

Exclusion criteria

* Presence thrombosis or previous myocardial infarction
* Severe recorded atherosclerosis
* Hypersensitivity to any component of FC
* Congenital or acquired impaired clotting
* Hypofibrinogenemia (<1 g / l)
* The use of vitamin K antagonists, direct thrombin inhibitors, antiplatelet or in the last 5 days before surgery
* Previous cardiothoracic surgery
* Perioperative exclusion; CPB time <90 minutes

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-08-2014
Enrollment:	82
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Haemocomplettan
Generic name:	Fibrinogen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	22-04-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-07-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
EudraCT	EUCTR2013-002820-18-NL
CCMO	NL45370.100.14