The effect of haemoadsorption in relation to the cytokine concentration during cardiothoracic surgery procedures while using extracorporeal circulation.

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The aim of the study is, to analyze the effect of the haemoadsorption device Cytosorb in relation to the inflammatory parameters IL-6, IL-8, IL-10,TNF-* and CRP at six different time points during conventional CABG procedures.We assess whether the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON45517

Source
ToetsingOnline

Brief title
CS-Study (Cytosorb study)

Condition

- Other condition
- Coronary artery disorders

Synonym
Cytokine production, Inflammatory reactions

Health condition

Produktie van cytokine door het lichaam tijdens open hartchirurgie.

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cytokine concentration, Cytokine reduction, Extracorporeal circulation, Haemoadsorption

Outcome measures

Primary outcome

To analyze of the haemoadsorption device Ctosorb.

We will evaluate whether the elevated cytokine levels (IL-6, IL-8, IL-10 and

TNF-alpha) as a result of surgery can be reduced to the initial value. This

will be done during elective CABG procedures with the use of ECC.

Secondary outcome

None.

Study description

Background summary

Many attempts have been made to reduce the inflammatory activation during coronary bypass surgery (CABG procedure) using extracorporeal circulation (ECC), however without much success.
The inflammatory activation process takes place, both locally in the organs, as in the systemic circulation. Surgical trauma and the contact of blood with non-endothelial surfaces such as the heart-lung machine disposables, activates the cellular and humoral defense mechanism.
In addition, aberrant organ perfusion during ECC, the duration of the ECC and the restore of normal organ perfusion (ischemia/reperfusion =) after ECC leads to activation of the humoral and cellular defense mechanism with numerus pathways. These pathways consist of activation/generation or expression of

thrombin, complement, cytokines, adhesion molecules, mast cells and neutrophils, different inflammatory mediatore.
Some patients have to deal with organ dysfunction and hemodynamic instability after ECC.
Inflammatory processes and ischemic-reperfusion injury also triggers the development of vascular dysfunctions and activation of the complementsystem. As result pro-and anti-inflammatory mediators (cytokines) wil be released in the circulation. In the worst case systemic inflammatory syndrome (SIRS) wil be developed, by initiation of the inflammatory cascades and profound amplification. The duration of ECC is considered as a risk, but it is not necessary to develop SIRS.
Complement activation with increased cytokine release in cardio surgery may also be caused by the following factors:
chronic immune activation (it is associated with atherogenesis and/or progression of atherosclerosis) whith the inflammatory activation already activated before the surgical procedure. Patients older (> 65 Jr.) have a higher complement concentration at the decline of the aortic clamp, by an increased IL-6 production.
So far one tried a number of methods/techniques to decrease the excessive release of cytokines related to ECC, namely:
* Cardio surgery procedures without the use of heart-lung machine, but this also leads to increased release of cytokines and other mediators.
* ECC without cardioplegic arrest.
* Leukocyte filter.
* Administration of corticosteroids.
* Hemofiltatrion strategys such as: Balanced ultrafiltration, high volume Hemofiltration (HVHF), high cut-off (HCO) Hemofiltration and other ultrafiltration (UF) techniques related to extracorporeal circulation.

In the fight against excessive cytokine production is the CytoSorb * haemoadsorber developed. The operation of this haemoadsorber is based on adsorption of particles with a low molecular weight (5-60 kDa).
Previous study(s) with CytoSorb (at non-homogeneous groups) are promising, other(s) showed no clinical relevance and the literature does not provide a consistant start value for the cytokines during ECC. We want to analyze the effect of the Cytosorb during CABG-surgery and describe the effect on cytokine level in this pilot study. A pilot study is necessary because it is still unclear what initial cytokine concentration we may expect.
Depending on the results, the Cytosorb may be used in the future by indication during heart surgery.

Study objective

The aim of the study is, to analyze the effect of the haemoadsorption device Cytosorb in relation to the inflammatory parameters IL-6, IL-8, IL-10,TNF-* and CRP at six different time points during conventional CABG procedures.
We assess whether the haemoadsorption device Cytosorb can relevantly reduce

cytokine levels to the normal start concentration.

Study design

In this single (patient) blind randomized pilot study 30 patients planned for elective CABG surgery with ECC support will be asked/informed, they will be included after signing the informed consent.
The subjects are randomized into 2 groups.
* Group 1: CABG group without the haemoadsorber in the ECC circuit: control group (CECC).
* Group 2: CABG group with the haemoadsorber in the ECC circuit: intervention group (HECC).

The intervention consists of leading blood through the Cytosorb adsorber the ECC.
Extend of the research: on arrival at the operating room up to 4 hours post surgically.
Subject inclusion starts as soon as RTPO approval issued is received. The end of the study is achieved when data of all 30 subjects is analyzed.

In the intervention group, the haemoadsorber in the extra cannon system behind the oxygenator. The blood flow over the adsorber is 350-400 ml/min.

During this survey, bloodsamples will be collected according to the schedule below.
T0: pré anaesthesiological induction
T1: 5 min after start ECC
T2: at 60 min ECC and or slightly before the end of the ECC.
T3: on ICU arrival (aproximately 30 min after surgery)
T4:2 hours after ICU arrival.
T5:4 hours after ICU arrival.

T3, T4 and T5: will be collected according to: the sample protocol at the ICU.

Intervention

The intervention consists of the leading blood through the Cytosorb adsorber during CABG-surgery.

Study burden and risks

The only load for the patient consists of filling the informed consent, this covers about 15 minutes.
There is no risk of burden with the participation, the entire CABG-procedure will be performed as normal. The cytokines will not be completely removed but they will be reduced.

During the investigation bloodsamples will be collected at six times from the test subjects, this total is less than 60 ml. The bloodsample collection is chosen simultaneously with the regular blood collection associated with the surgery. The blood will be collected from a already placed infusion line.
This haemoadsorber adsorbs possibly certain types of antibiotics as with dialysis or haemofiltration. These are not the antibiotics which are administered to the test subjects during the standard heart surgery.
There is a possibility of hypersensitivity to (polystyrene / divinylbenzene, polycarbonate, polypropylene, silicone and polyester). With known hypersensitivity to these substances, the test subjects will not be included.

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

Elective CABG
Signed informed consend
age >18 years, <75 years

Exclusion criteria

Emergency surgery
Combined surgical intervention
Coagulation disorders
Low platelet count <100*109/l
Hb:< 7,5 mmol/l, calculated Ht <20 % after hemodilution
Serum creatinine of more than 2x reference value (110 µmol/l)
Severe COPD
Long-term therapy with corticosteroids or Immunosuppressive therapy
Participation in another clinical intervention trial
CRP >5 mg/l
Patients that are Heparin Induced Thrombocytopenia (HIT) positive and citrate regional anticoagulation is unavailable as an alternative anticoagulation method.
Hypersensitive / allergic reaction to: polystyreen/divinylbenzeen, polycarbonaat, polypropyleen, siliconen en polyester

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-06-2017

Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Cytosorb;haemoadsortion device
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	15-03-2017
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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	NL59687.099.16