MANNOSE-BINDING LECTIN AND L-FICOLIN POLYMORPHISM IN PATIENTS WITH STAPHYLOCOCCAL BACTEREMIA

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To determine the frequency of MBL and FCN SNPs in patients with a history of a proven gram-positive bacteremia, compared to patients without such history. A secondary objective is to determine whether extracorporeal circuits, used in cardiothoracic...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON39711

Source
ToetsingOnline

Brief title
The MANDOLINS project

Condition

- Immunodeficiency syndromes
- Bacterial infectious disorders

Synonym
bloodstream infection, sepsis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: complement, L-ficolin, mannose-binding lectin, staphylococcus

Outcome measures

Primary outcome

The primarily studied endpoint is the difference between the frequency of MBL

and FCN SNPs in patients with and without a history of gram-positive

bacteremia.

Secondary outcome

Secondary endpoints are the change in MBL en FCN circulating levels before and

after cardiothoracic surgery and before and after high dose chemotherapy.

Study description

Background summary

Blood stream infections with gram-positive bacteria, especially Staphylococcus Aureus (S. aureus), are associated with significant morbidity and mortality, resulting in considerable health care costs. Gram-positive bacteremia is relatively common in patients with mediastinitis following cardiothoracic surgery, in patients with endocarditis and in neutropenic patients who received high dose chemotherapy.
Mannose-binding lectin (MBL) and L-ficolin (FCN) are activators of the lectin pathway of complement and are crucial components of the innate immune defence against infection. Single-nucleotide polymorphisms (SNPs) in the MBL and FCN genes, which are common in the general population, influence the functionality of these pathways. Recent data from the research group in the Medical Microbiology & Immunology (MMI) laboratory has indicated that both MBL and FCN are capable of binding directly to gram-positive bacteria.
In a joined project of the departments of MMI, Internal Medicine and Pulmonology the role of MBL and FCN in patients with community acquired pneumonia (CAP) has been investigated. We showed that MBL can act as a acute phase protein and that this acute phase responsiveness is highly dependent upon the MBL genotype. In addition we recently showed that CAPD (continuous ambulatory peritoneal dialysis) patients with FCN genotypes coding for FCN deficient staphylococcal binding, had an increased risk of developing

peritonitis with gram positive bacteria. We were able to show genetic differences in a study of 40 cases and 60 controls. The relatively low number of cases needed to show genetic differences points at the major role of FCN in the defence against CAPD related peritonitis caused by gram-positive micro-organisms.
We hypothesize that polymorphisms in the genes encoding for MBL and FCN also increase the risk of gram-positive bacteremia in patients following cardiothoracic surgery, in patients with endocarditis and in neutropenic patients who received high dose chemotherapy.
Furthermore we want to study whether extracorporeal circuits, used in cardiothoracic surgery, and high dose chemotherapy influence the circulating levels of MBL and FCN, thereby potentially increasing the risk of infection.

Study objective

To determine the frequency of MBL and FCN SNPs in patients with a history of a proven gram-positive bacteremia, compared to patients without such history. A secondary objective is to determine whether extracorporeal circuits, used in cardiothoracic surgery, and high dose chemotherapy influence circulating levels of MBL and FCN.

Study design

The main study consists of three separate case-control studies. These studies are observational, mono-centre, retrospective studies.
In the sub-study the primary goal is to study the effect of extracorporeal circuits and high dose chemotherapy on the circulating levels of MBL and FCN. This is a small, observational, prospective cohort study.

Study burden and risks

From all patients who agree to participate, one or two (only in the sub-study) blood samples will be drawn. When patients are admitted (as will be the case for all sub-study patients), this will be combined with regular diagnostic blood sampling, so no extra venipuncture is necessary for these patients. Alternatively, a blood sample can be obtained when patients visit the outpatient department for regular check-up and blood sampling. If patients are deceased or when they don*t visit the hospital regularly, sampled tissue or stored blood serum is often available and can be used to measure MBL and FCN polymorphisms. Therefore, the risks associated with participation can be considered negligible and the burden can be considered minimal.

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

Main study:
-Age > 18 years.
-At least one proven episode of mediastinitis/endocarditis/neutropenic bacteremia.
-Proven mediastinitis/endocarditis/neutropenic bacteremia according to predefined criteria.
-To avoid population stratification only patients with a Caucasian background can be included.;Controls:
-Age > 18.
-Previous high dose chemotherapy or cardiothoracic surgery,
-No infections with gram-positive micro-organisms.
-To avoid population stratification only patients with a Caucasian background can be included.;Sub-study:
-Age > 18 years.

-High dose chemotherapy as a treatment for acute leukemia or prior to an autologous stem cell transplantation OR cardiothoracic surgery with a median sternotomy, in which an extracorporeal circuit is used.
-To avoid population stratification only patients with a Caucasian background can be included.

Exclusion criteria

Main study:
-Previous thoracic radiotherapy.
-Emergency cardiothoracic surgery.
-Re-thoracotomy.;Sub-study:
-Active infection at the time of or within two weeks before blood sampling.
-Current use of antibiotics or antibiotic use within two weeks before blood sampling.
-MBL and/or FCN deficient genotype.
-Neutropenia at the time of blood sampling, defined as an absolute neutrophil count <500 cells/µL.

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:	Recruiting
Start date (anticipated):	02-07-2014
Enrollment:	378
Type:	Actual

Ethics review

Approved WMO Date:	04-02-2013
Application type:	First submission
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
CCMO	NL42421.100.12