Influence of Mannose-Binding Lectin Polymorphisms on Infectious Complications in Trauma Patients

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Skin and subcutaneous tissue disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON30944

Source
ToetsingOnline

Brief title
MBL Polymorphisms in Trauma Patients

Condition

- Skin and subcutaneous tissue disorders NEC

Synonym
MBL-deficiency, suboptimal immune status

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Infection, Mannose-Binding Lectin, Polymorphism, Trauma

Outcome measures

Primary outcome

Bacteremia (BSI)

Pneumonia

Systemic Inflammatory Response Syndrome (SIRS)

Sepsis

Septic shock

Secondary outcome

Death within 3 months

Surgical site infection

Osteitis after osteosynthesis of fractures

Study description

Background summary

Infection and sepsis are serious complications that occur in up to 10% of trauma patients. Sepsis, bacteremia, (ventilator-associated) pneumonia and surgical site infections seriously hamper recovery, and may eventually lead to death. Resistance to infection is determined by the innate and the acquired immune systems. The innate immune system is the first line of defense against invading microorganisms. The complement system is part of the innate immune system and consists of three pathways: the classic, alternative and the lectin pathway. These are activated through different mechanisms but eventually all lead to activation of the C3 molecule. The central molecule in the lectin pathway is Mannose-Binding Lectin (MBL), a C-type serum lectin that is primarily produced by the liver. Binding of MBL to carbohydrates present on pathogens activates the lectin pathway of complement activation, resulting in opsonization and anti-microbial protection. Three frequently occurring single nucleotide polymorphisms (SNPs) are described in exon 1 of MBL-2 that are

associated with abnormal polymerization of the MBL molecule, decreased serum concentrations, and strongly impaired function. Clinical studies have shown that single nucleotide polymorphisms (SNPs) in the MBL2 gene are associated with increased susceptibility to infections, especially in immune-compromised persons. In addition, SNPs in the promoter region and the 5* untranslated region of the MBL-2 gene reduce the promoter activity and, hence, result in reduced protein levels.
Clinical studies indicate that SNPs in MBL-2 are a predisposing factor for infection: for example they (1) increase the chance of infection with Mycoplasma in patients with Primary Antibody Deficiency, (2) increase the risk of developing SARS, (3) enhance the chance of infectious complication in neutropenic oncology patients, and (4) increase the incidence of infection in patients with hematologic malignancy. These and other studies revealed that studying MBL variant alleles is of considerable clinical interest. During treatment, the immune system of trauma patients is often challenged, therefore on optimal immune status is important.
Extrapolating from other studies resulted in the following study hypothesis: MBL-deficiency as a result of SNPs in the MBL-2 gene confers a major risk for the development of and mortality from (serious) infectious complications in trauma patients.

Study objective

The aim of this study is to determine to what extent MBL-2 polymorphisms influence the outcome of polytraumapatients. Serious (systemic) infections and local infections are the main outcome parameters. The MBL-status will be measured by determining the MBL2 genotype, serum-MBL concentration, and the serum-MBL activity.

Study design

Prospective, observational study.

Study burden and risks

The risk for the patients is limited to a single withdrawal of 2 tubes of blood (10 ml each). This will preferably be done at the time of routine blood sampling. If that is not possible, one venipuncture will be performed. The risk of this venipuncture is slight, and the total duration of the examination will take 10 minutes at the most.

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

Trauma patients with an ISS of 16 or higher
Age between 18 and 70 years
Compos mentis
Informed consent

Exclusion criteria

ISS<16
Age <18 or >70 years
Death within 24 hours after the trauma
No informed consent
Patients with a known immune disorder
Use of immunosuppressive drugs

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-12-2007
Enrollment:	450
Type:	Actual

Ethics review

Approved WMO

Date:	12-11-2007
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 27107
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL17368.078.07
OMON	NL-OMON27107