Invloed van Mannose-Binding Lectin Polymorfismen op Infectieuze Complicaties bij Traumapatiënten.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON27107

Source
Nationaal Trial Register

Brief title
N/A

Health condition

Polytrauma; trauma with injury severity score > 15 points

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: OTC Foundation

Intervention

Outcome measures

Primary outcome

1. Bacteremia (BSI);

2. Pneumonia;

3. Systemic Inflammatory Response Syndrome (SIRS);

4. Sepsis;

5. Septic shock.

Secondary outcome

1. Death within 3 months;

2. Surgical site infection;

3. Osteitis after osteosynthesis of fractures.

Study description

Background summary

Background of the study:

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.

Objective of the study:

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

Study design:

Prospective, observational study.

Study population:

All trauma patients (ISS>15) between 18 and 70 years of age.

Primary study parameters/outcome of the study:

1. Bacteremia (BSI);

2. Pneumonia;

3. Systemic Inflammatory Response Syndrome (SIRS);

4. Sepsis;

5. Septic shock.

Secundary study parameters/outcome of the study (if applicable):

1. Death within 3 months;

2. Surgical site infection;

3. Osteitis after osteosynthesis of fractures.

Study objective

De studiehypothesen zijn:

1. Traumapatiënten (ISS>15) met MBL-deficiëntie als gevolg van een variant MBL2 haplotype hebben een hogere gevoeligheid voor het ontwikkelen van ernstige (infectieuze) systemische complicaties;

2. Traumapatiënten (ISS>15) met MBL-deficiëntie als gevolg van een variant MBL2 haplotype hebben een hogere kans op overlijden als gevolg van (infectieuze) complicaties tijdens een langdurige opname op de Intensive Care Unit.

Study design

Not applicable; single venipuncture.

Intervention

None (observational study).

Contacts

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Eligibility criteria

Inclusion criteria

1. Trauma patients with an ISS of 16 or higher:

2. Age between 18 and 70 years;

3. Compos mentis;

4. Informed consent.

Exclusion criteria

1. ISS<16;

2. Age <18 or >70 years;

3. Death within 24 hours after the trauma;

4. No informed consent;

5. Patients with a known immune disorder;

6. Use of immunosuppressive drugs.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

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

Ethics review

Positive opinion

Date:	12-01-2009
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 30944
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL687
NTR-old	NTR1625
CCMO	NL17368.078.07
ISRCTN	ISRCTN wordt niet meer aangevraagd
OMON	NL-OMON30944

Study results

Summary results

Bronkhorst MWGA, Boyé NDA, Lomax MAZ, Vossen RHAM, Bakker J, Patka P, Van Lieshout EMM. Single Nucleotide Polymorphisms in the Toll-Like Receptor Pathway increase Susceptibility to Infections in Severely Injured Trauma Patients. J Trauma Acute Care Surg 2013 Mar;74(3):862-870.

Bronkhorst MWGA, Lomax MAZ, Vossen RHAM, Bakker J, Patka P, Van Lieshout EMM. Risk of infection and sepsis in severely injured patients related to single nucleotide polymorphisms in the lectin pathway. Br J Surg. 2013 Dec;100(13):1818-26.