Post-traumatic dysfunction of the innate and adaptive immune system and its relationship with the development of infectious complications in severely injured patients (POSEIDON study)

Published: 14-02-2014
Last updated: 23-04-2024

We expect to provide evidence for our hypothesis stating that patients who develop infectious complications after trauma are characterized by a specific subset of circulating neutrophils displaying a reduced capacity to eradicate bacteria....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	White blood cell disorders
Study type	Observational invasive

Summary

ID

NL-OMON53029

Source
ToetsingOnline

Brief title
POSEIDON-study

Condition

- White blood cell disorders
- Immune disorders NEC
- Bacterial infectious disorders

Synonym
blood poisoning, sepsis

Research involving

Human

Sponsors and support

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

Intervention

Keyword: immune system, neutrophil, sepsis, trauma

Outcome measures

Primary outcome

The difference in (anti-bacterial) characteristics of circulating neutrophils between trauma patients who develop sepsis and non-septic patients.

Secondary outcome

- The difference in (anti-bacterial) characteristics of circulating neutrophils between trauma patients who develop infectious complications other than sepsis (e.g. pneumonia, meningitis, urinary tract infections, pericarditis, abdominal abscesses, wound infections and fracture related infections) and non-infectious patients.
- The difference in (anti-bacterial) characteristics of circulating neutrophils between trauma patients who develop pro-inflammatory complications (e.g. SIRS) and patients who don't develop these complications.
- The difference in (inducible) activation status of neutrophils between patients with and without infectious or inflammatory complications

Study description

Background summary

Severely injured patients are prone to suffer from infectious complications and even sepsis. Despite tremendous efforts, the etiology of this increased susceptibility to infectious complications of trauma patients is not fully understood. Clinical signs and symptoms aswell as current diagnostic clinical tests (WBC, CRP, cytokines, interleukines) lack sensitivity or specifity for adequate prediction of the development of infectious complications or sepsis.

Neutrophil granulocytes, cells of the innate immune system, play an important role in the defence against invading (bacterial) pathogens and are crucial in preventing fulminant infections. For succesfull eradication of a pathogen, neutrophils need to exert specific functions: e.g. chemotaxis, migration, phagocytosis, degranulation and production of radical oxygen species. Previous research on the altered bactericidal functions of neutrophils shows inconclusive results. For adequate determination of the neutrophil's capicity to eradicate bacteria we developed a novel in-vitro assay in which neutrohpils are accurately tested for their capability to kill bacteria. This assay allows us to identify dysfunctional neutrophils (or neutrophils subsets) adequately.

The main focus of this study is the determination of the (antibacterial) functionality of specific neutrophils circulating in the peripheral blood of severly injured patients following trauma.

Study objective

We expect to provide evidence for our hypothesis stating that patients who develop infectious complications after trauma are characterized by a specific subset of circulating neutrophils displaying a reduced capacity to eradicate bacteria. Furthermore we hypothesize that this deterioration in function will occur days before the actual development of clinical symptoms due to an infection. For that matter we will make use of our novel in-vitro techniques.

Establishing the correlation between an acquired dysfunctional innate immune system and the development of infectious complications would have great implications for future trauma patients and their treatment. This might lead to early identification of patients at risk for infectious complications. Thereby providing physicians clinical guidelines for either agressive pharmaceutical preventive therapy or postponement of surgical treatments to avoid these infectious and/or inflammatory complications.

Study design

A prospective cohort trial. A maximum of 8 milliliters blood will be obtained within 12 hours of arrival at the Emergency Department. Succeeding samples will be drawn at day 3, 6, 10 and 15 days after admission (9 milliliters per timepoint). These samples will enable us to study the (bactericidal)

characteristics of neutrophils throughout time, making use of isolated neutrophils.

Study burden and risks

A total of max. 44 milliliter will be sampled from the patient over a period of 15 days. Sampling of this amount of blood will (insignificantly) diminish the total volume of circulating blood in the vasculature of these patients temporarily. The daily average volume of bloodsampling sampling of patients on the ICU is 53.2 milliliters. Even if this sampling volume would increase with 18 milliliter every day during 15 days, the additional risk for clinical signs and symptoms due to anemia is not significant (citation: Andrew W Lyon and others, *Simulation of Repetitive Diagnostic Blood Loss and Onset of Iatrogenic Anemia in Critical Care Patients with a Mathematical Model.*, Computers in biology and medicine, 1 (2012), 1-7).

Blood sampling from the arterial line during the patient's stay on the IMCU/ICU or venapunctures on the surgical ward will be combined with regular sampling performed for clinical diagnostic tests. The placement of this arterial catheter is standard care in this group of trauma patients and sampling from this line will not result in any form of discomfort for the patient. If the arterial line is removed, the blood will be drawn through vena puncture. This will be combined with clinical blood withdraw as much as possible. We expect a patient to require 1 additional venapuncture during the study period on average.

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
Utrecht 3508 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Severely injured trauma patients based on the following criteria:
- Severe injury (e.g. AIS > 3) in at least 2 body regions
- Physiological disturbances on hospital admission based on:
* Heart rate > 100 beats/min, and/or
* Systolic blood pressure < 100 mmHg, and/or
* Base excess < -6 mmol/L, and/or
* pH < 7,20, and/or
* Hb < 5,5
2. Admission to the IMCU or ICU of the UMCU with an expected stay of at least 48 hours.
3. Age: 18 - 80 years
4. Informed consent (when proxy consent is obtained and the patient leaves the IMCU/ICU in good mental health, personal informed consent is additionally necessary)

Exclusion criteria

- Immunosuppressive medication
- Known HIV positive status and related diseases

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):	27-06-2014
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	14-02-2014
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	29-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-09-2022
Application type:	Amendment
Review commission:	METC NedMec

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
Other	43279
CCMO	NL43279.041.13