KIRS-study: expression of inhibitory receptors on polymorphonuclear neutrophils during sepsis in children

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Primary Objective: To compare the expression of inhibitory receptors SIRL-1 and LAIR-1 on blood neutrophils of patients under age 12 admitted with sepsis to the paediatric intensive care with healthy controls and intensive care patients without...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON41281

Source
ToetsingOnline

Brief title
KIRS

Condition

- Hepatobiliary neoplasms malignant and unspecified

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, LAIR-1, Sepsis, SIRL-1

Outcome measures

Primary outcome

Inhibitory receptor (SIRL-1 and LAIR-1)expression on blood neutrophils

Disease severity as determined by the PRISM-III score, PELOD-2 score and

Inotropic score

Secondary outcome

none

Study description

Background summary

Sepsis is a potentially life threatening systemic inflammatory reaction of the body to an infection. The immune system engages in an extreme inflammatory cascade in an attempt to eradicate the infection. However, most of the pathology associated with sepsis is not caused by the pathogen, but by the extreme intensity of the immune response. Despite the development of international treatment guidelines, sepsis is a leading cause of death worldwide in both children and adults. Unfortunately, recent attempts at finding a new therapeutic target for sepsis have thus far failed. To find a proper treatment, the balance between clearing the infection without damaging the body*s own cells must be restored.
Paediatric sepsis is not the same as adult sepsis, children have different comorbidities and their bodies respond to sepsis in a completely different way. There are significant differences in the immune response, especially inflammation plays a larger role in sepsis pathophysiology in children than in adults. This indicates that especially children suffering from sepsis could profit from attenuating the immune system.
Inhibitory receptors function as downregulators of the immune response. Identifying the specific inhibitory receptors that are expressed during sepsis could be the first step towards a new therapeutic target. Signal Inhibitory Receptor on Leukocytes-1 (SIRL-1) and Leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1) are tyrosine-based inhibitory motif (ITIM)-bearing immune receptors expressed on human monocytes and neutrophils. Neutrophils play a

central role in sepsis pathology. Therefore, modulating the immune response of neutrophils by means of inhibitory receptors could decrease sepsis related morbidity and mortality.
We hypothesize that a decreased expression of inhibitory receptors plays a central role in the pathophysiology of disproportional inflammation as seen in sepsis. This is a relevant hypothesis, as immune inhibitory receptors could be a potential new therapeutic target.

Study objective

Primary Objective: To compare the expression of inhibitory receptors SIRL-1 and LAIR-1 on blood neutrophils of patients under age 12 admitted with sepsis to the paediatric intensive care with healthy controls and intensive care patients without sepsis.

Secondary Objective: To determine the relationship between inhibitory receptor expression and sepsis disease severity during the course of disease in children under age 12.

Study design

This will be a single-centre observational study. Inclusion will be performed from 01-08-2013 until 01-07-2017. Patients under age 12 admitted to the intensive care department of the Wilhelmina Children*s Hospital (Wilhelmina Kinderziekenhuis) in Utrecht, diagnosed with severe paediatric sepsis or paediatric septic shock, may be included. Control groups will consist of patients under age 12 admitted to the ICU for non-infectious pathology and patients under age 12 that will undergo elective heart catheterisation (healthy controls).
After informed consent has been obtained, a blood sample will be collected as soon as possible. If possible, this will be combined with a regular diagnostic blood draw or taken from a central venous or arterial line. Additional blood samples will be obtained after approximately six hours, one day, two days, and three days. However, these subsequent blood samples will only be taken when blood is already being drawn for diagnostic or monitoring purposes, or if the patient has a central venous or arterial line.
Disease severity will be monitored according to the PRISM-III score, PELOD-2 score and Inotropic score. Physiologic variables, age, and biochemical findings of each patient that are necessary to calculate the disease severity scores are part of normal care for sepsis patients and will be extracted from medical records or requested from the attending physician.

Study burden and risks

A maximum of one blood sample will be taken separately from diagnostic procedures (if possible this sample will also be combined with a diagnostic

blood draw). Any additional samples will only be taken as part of the normal diagnostic process upon which an additional 0.5 mL of blood will be extracted. Alternatively, these samples will be drawn from a central arterial or venous catheter when the patient has one. Drawing venous blood by venepuncture is moderately painful. The amount of blood was carefully determined according to WHO guidelines and the patient will be monitored to keep risk to a minimum. Due to the type of study, observational, with no additional invasive procedures on top of routine diagnostics, no study related adverse events, serious adverse events, or suspected unexpected serious adverse reactions are to be expected.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Sepsis patients: under age 12, diagnosed with severe paediatric sepsis or paediatric septic shock

Control group 1: patients under age 12, admitted to the ICU for a non-infectious, non-inflammatory illness
Control group 2: patients under age 12, undergoing elective cardiac catheterization.

Exclusion criteria

Patients with any type of chronic infectious, inflammatory or autoimmune diseases
Patients after hematopoietic or solid organ transplantation
Patients receiving long term treatment with steroids or other immunosuppressive agents
Patients with an immunodeficiency
For control group 2: cyanotic heart disease

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:	Recruitment stopped
Start date (anticipated):	23-09-2013
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	19-03-2013
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-12-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-07-2015
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL42065.041.12