Effect of C1-esterase inhibitor on systemic inflammation in trauma patients with a femur or pelvic fracture.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON39485

Source
ToetsingOnline

Brief title
CAESAR Study

Condition

- Immune disorders NEC
- Ancillary infectious topics

Synonym
activated immuun system, Systemic inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Sanquin, divisie plasmaproducten. Postbus

9190, 1006 AD, Amsterdam, The Netherlands,Sanquin;divisie plasmaproducten. Postbus 9190;1006 AD;Amsterdam;The Netherlands

Intervention

Keyword: C1-esterase inhibitor, Cytokines, Systemic inflammation, Trauma

Outcome measures

Primary outcome

Delta interleukine-6 after surgical repair of a femur or pelvic fracture in

trauma patients in the absence of presence of C1-esterase inhibitor.

Secondary outcome

- Cytokines, cellulair markers, complement

- Leukocyt count, CRP, base deficit/excess and lactate

- Development of inflammatoiry complications (Acute Respiratory Distress

Syndrome, MODS, sepsis, septic shock)

- Severity of illness

Study description

Background summary

Systemic inflammation in response to femur or pelvic fracture and fixation is associated with complications, such as acute respiratory distress syndrome (ARDS) and multiple organ dysfunction syndrome (MODS). The injury itself, but also the additional fixation procedure give a release of pro-inflammatory cytokines, in particular interleukin (IL)-6. This results in an aggravation of the initial systemic inflammatory response, and will cause in some patients an increased risk on the development of inflammatory complications, like ARDS and MODS. Which can lead to higher morbidity, mortality and prolonged hospital stay.
Various strategies, such as damage control orthopedics, have been proposed to prevent these complications. Another strategy is to decrease the inflammatory reaction caused by the surgical procedure, and by interventions focused on inhibition of the innate inflammatory response. This will lower the risk of

complications.
A promising candidate is the endogenously produced serum protein C1-esterase inhibitor (C1-INH). This protein is an acute phase protein, produced by the liver in response to inflammatory conditions. C1-INH is a major inactivator of the complement system, but important additional anti-inflammatory properties have been demonstrated. A previous study of from our laboratory showed that administration of the drug C1-INH significantly reduced the concentration of circulating pro-inflammatory cytokines such as IL-6, during human experimental endotoxemia. Treatment with C1-INH has been proven to be safe in treatment with humans, even in high dosages and in pregnant patients with C1-INH deficiency.

Study objective

A previous study of from our laboratory showed that administration of the drug C1-INH (100E/kg) significantly reduced the concentration of circulating pro-inflammatory cytokines, such as IL-6, in healthy male volunteers during human experimental endotoxemia.

The aim of this study is to demonstrate that administration of C1-INH, in trauma patients with a femur fracture, reduces the release of early pro-inflammatory cytokines and, therefore, will attenuate the humane inflammatory response. Consequently, administration of C1-INH may attenuate the onset of SIRS and the occurrence of organ failure and can, therefore, be a potential drug for the prevention of late inflammatory complications in injured patients.

Study design

A prospective double-blind randomized placebo-controlled trial in trauma-patients, between 18 and 80 years old, admitted to the shock room of our trauma centre with a femur or pelvic fracture and an injury severity score of >=18.

A first blood sample will be taken within 12 hours after trauma, this blood sample serves as a reference for the degree of inflammation. A second blood sample will be drawn pre-procedural just before the femoral fixation, when the patient is anaesthetized. Then the patient is randomized and C1-INH or placebo is administrated intravenously. The third blood sample is taken 2 hours after the first (femoral or pelvic fixation-procedure) skin incision and the fourth withdrawal will take place 6 hours after the procedure. Teh remaining samples will be taken 24, 48 hours, 7 and 12 days after surgery.
As long as the patient is admitted on the Intensive Care Unit, blood samples can be taken from the arterial catheter. When the patients leave the ICU, they will be asked if he/she will provide us an additional sample.

Intervention

Subjects will receive once a single dose of 200E/kg C1-INH intravenously or placebo (saline 0.9%).

Study burden and risks

C1-INH is a normal compnent of the humane blood. No side effects are described by administration of C1-INH.
Patients could, theoretically, develop an allergic reaction after admission of C1-INH, manifesting as urticaria or anaphylatic shock, this has never been described.

The blood is drawn from the arterial line, if possible. The patient does not experience any discomfort of this procedure. The placement of an arterial line is standard care in this groiup of trauma patients. If the arterial line is removed, the blood will be drawn through vena puncture. This will be combined with clinical blood withdrawl.

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

Multi trauma patients
Femur fracture and/or pelvic fracture
Injury Severity Score (ISS) >= 18
Age 18-80 yrs

Exclusion criteria

Congenital C1-inhibitor deficiency
Use of immune suppressants
Pregnancy
Known hypersensitivity for blood products
Fixation of femur fracture with external fixation or osteosynthesis
Fixation of the pelvic fracture with external fixation

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-04-2012
Enrollment:	70

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cetor
Generic name:	C1-esterase inhibitor
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-01-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-07-2011
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	20-04-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	28-03-2013
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
EudraCT	EUCTR2010-024327-24-NL
ClinicalTrials.gov	NCT01275976
CCMO	NL34932.041.11