Randomized Controlled Trial Investigating the Efficacy and Safety of Nebulized Heparin versus Placebo in Burn Patients with Inhalation Trauma

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

Summary

ID

NL-OMON39556

Source
ToetsingOnline

Brief title
The Hepburn*study

Condition

- Respiratory disorders NEC

Synonym
acute lung injury, inhalationtrauma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: Nederlandse Brandwonden Stichting

Intervention

Keyword: coagulopathy, heparin, inhalationtrauma, nebulization

Outcome measures

Primary outcome

Number of ventilator-free days during the first 28 days after inclusion.

Secondary outcome

- clinical outcome parameters such as Lung Injury Score (LIS), ICU length-of-stay (LOS), 28- and 90-day mortality, incidence of pneumonia (CDC criteria) and number of bronchoscopies performed to remove foreign particles and accumulated secretions

- pulmonary coagulation and fibrinolysis as reflected by tissue factor (TF), activated factor VII (FVIIa) antithrombin (AT), thrombin-antithrombin complexes (TATc) and activated protein C (APC), plasminogen activator activity (PAA), tissue plasminogen activator (tPA), urokinase plasminogen activator (uPA) and plasminogen activator inhibitor 1 (PAI*1), and FDP in BALF

- pulmonary inflammation as reflected by IL*1 beta, IL*6, IL-8, IL-10, TNF-alpha, VEGF and TGF-beta

- safety of nebulized heparin, as reflected by activated partial thromboplastin (aPTT) time, prothrombin time (PT) and blood thrombocyte count

Study description

Background summary

Inhalation trauma is a major cause of morbidity and mortality in burn patients, but the underlying pathophysiological mechanisms of inhalation trauma are poorly understood. Thermal injury and inhaled toxins are thought to destroy the airway mucosa, subsequently leading to an inflammatory response, vascular leakage, pulmonary edema and impaired gas exchange. We have previously shown that the inflammatory response in burn patients with inhalation trauma is associated with severe pulmonary coagulopathy as compared to non-injured lungs. Since local administration of heparin has been shown to increase ventilator-free days in acute lung injury patients, we hypothesize that burn injury patients with inhalation trauma will have an improved outcome upon treatment with nebulized heparin.

Study objective

The aim of this project is to address whether nebulized heparin:
1) increases the number of ventilator*free days during 28*days in burn patients with inhalation trauma
2) improves lung injury scores in burn patients with inhalation trauma
3) reduces pulmonary coagulopathy in burn patients with inhalation trauma
4) impacts pulmonary inflammation in burn patients with inhalation trauma
5) is safe in burn patients with inhalation trauma

Study design

We will perform a multi-center double-blind placebo-controlled trial to investigate the impact of nebulized heparin on inhalation injury in the lungs of burn patients. We will include adult burn patients with bronchoscopic confirmed inhalation trauma.

It will be conducted in three burn centers in the Netherlands (Rode Kruis Ziekenhuis in Beverwijk, Martini Ziekenhuis in Groningen and Maasstad Ziekenhuis in Rotterdam) and three burn centers in Belgium (Universitair Ziekenhuis Leuven, Universitair Ziekenhuis Gent, Ziekenhuis Netwerk Antwerpen (ZNA) Stuivenberg).

Intervention

Nebulized heparin (25,000 IU) every 4 hrs every 24 hrs for the maximum duration of 14 days versus placebo (NaCl 0.9%)

Study burden and risks

The burden to the patient is considered to be low. The collection of general data from hospital charts and (electronic) medical records does not affect the patients. Blood sampling is combined with routine sampling for standard care of burn patients. Non-directed bronchial lavage is often used to remove soot from the bronchial tree and can be considered a safe procedure. At present, nebulisation of unfractionated heparin is occasionally used in burn patients with inhalation trauma and has been shown to be safe in a cohort of critically ill patients. We hypothesize that nebulized heparin accelerates weaning from mechanical ventilation, which may be a benefit for this treatment arm. This study may improve standard care for burn patients with inhalation trauma.

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

- informed consent
- age > 18 years
- need for intubation and mechanical ventilation
- clinical diagnosis of inhalation trauma confirmed by bronchoscopy

Exclusion criteria

- > 36 hours after trauma
- Receiving invasive ventilation > 24 hours
- Expected duration of mechanical ventilation < 24 hours
- Chronic obstructive pulmonary disease GOLD stage III and IV
- Any history of pulmonary hemorrhage in the past 3 months
- Any history of significant bleeding disorder
- Known allergy to heparin, including heparin*induced thrombocytopenia
- Pregnancy or breast feeding
- Unlikely to survive for > 72 hours
- Total body surface area (TBSA) > 60%
- Witnessed or proven aspiration (i.e., confirmed by bronchoscopy)

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:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2014

Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	unfractionated heparin
Generic name:	heparin natrium
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	04-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-07-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2012-003289-42-NL
CCMO	NL41399.018.12