# The effect of inhaled heparin on pulmonary coagulation activation and vascular permeability in mechanically ventilated patients with acute lung injury / acute respiratory disress syndrome

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Objectives1. to determine whether nebulization of heparin decreases coagulation activation in the pulmonary compartment (i.e. BAL fluid)2. to determine whether nebulization of heparin decreases pulmonary vascular permeability

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|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Respiratory disorders NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON31496

**Source**
ToetsingOnline

**Brief title**
HEPALI study

### Condition

- Respiratory disorders NEC

**Synonym**
acute lung injury, pneumonia

**Research involving**
Human

## Sponsors and support

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

## Intervention

**Keyword:** ALI/ARDS, coagulation, heparin, inhalation therapy

## Outcome measures

### Primary outcome

TATc in BAL fluid

PLI

### Secondary outcome

• LIS

• In blood: TF, TFPI activity, TFPI antigen, Factor VII/VIIa, protein C / activated protein C, prothrombin fragment 1.2, TATc, endogenous thrombin potential, fibrin monomers, soluble thrombomodulin, PAPc, PAI.

• In BAL fluid: TF, TFPI activity, TFPI antigen, Factor VII/VIIa, protein C / activated protein C, prothrombin fragment 1.2, TATc, endogenous thrombin potential, fibrin monomers, soluble thrombomodulin, PAPc, PAI.

• Occurrence and severity of bleeding events

# Study description

### Background summary

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are potentially lethal conditions, responsible for a considerable amount of admissions to the Intensive Care Unit (ICU) and for which, at present, only supportive care is available.

Pulmonary edema, as a result of increased pulmonary vascular permeability caused by proinflammatory changes, together with pulmonary coagulopathy, resulting in alveolar fibrin deposition and disturbed fibrin turnover, are the hallmarks of ALI/ARDS. The alveolar fibrin deposition is in part comparable to the intravascular deposition of fibrin in patients with sepsis and disseminated intravascular coagulation and may be aggravated by mechanical ventilation. Based on a substantial body of evidence, both in vitro and in vivo, there is rationale to intervene in the pulmonary coagulopathy with anticoagulants in general, and with heparin in particular, in order to attenuate lung injury. Delivering heparin directly into the pulmonary compartment may attenuate fibrin depositions more effectively than systemic administration of heparin, while reducing the risk of bleeding as a result of systemic anticoagulant effects. In sheep, nebulization of heparin has been found to be beneficial. Furthermore, the nebulization of heparin to the lower respiratory tract is feasible and safe. In pediatric patients with inhalation injuries, heparin nebulization significantly reduced mortality.

With a bedside radionuclide method the pulmonary leak index (PLI) can be obtained as a measure of vascular leakage. The PLI is an ideal instrument to measure effects of therapy on pulmonary vascular leakage, since serial measurements can be performed.

Hence, nebulization of heparin may have a beneficial effect on pulmonary coagulopathy and may subsequently decrease pulmonary vascular permeability.

## Study objective

Objectives
1. to determine whether nebulization of heparin decreases coagulation activation in the pulmonary compartment (i.e. BAL fluid)
2. to determine whether nebulization of heparin decreases pulmonary vascular permeability

## Study design

This study will be an open label, placebo controlled, randomized, clinical trial in which patients will be treated with either unfractionated heparin, or placebo (i.e. sodium chloride 0.9%). It will be conducted in the medical-surgical intensive care units of two academic hospitals.

## Intervention

Patients will receive 4 nebulizations of either 4 mL unfractionated heparin (ie 100,000 IU) or 4 mL placebo (ie 0.9% NaCl) depending on randomisation, in a timeframe of 24 hours.

**Study burden and risks**

Both bronchoscopies will be performed when the patients is sedated. In a well monitored environment such as an Intensive Care Unit, the risk is considered to be very low.
The radiation from the isotopes used in the radionuclide-techique to obtain the PLI is well within all safetylimits.
Bloodsampling will be performed with an intra-arterial catheter that is already in situ in Intensive Care patients. Venous punctures will not be necessary.

# 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

All patients who are intubated and mechanically ventilated in the ICU, who meet the International Consensus Criteria of ALI/ARDS
Inclusion Criteria:
-Informed consent
-Age 18-80 years
-Recent onset of ALI/ARDS (i.e. <48 hrs)

### Exclusion criteria

Exclusion criteria
-Acute bleeding at any site
-Increased risk of bleeding:
•Platelets< 50 * 109 / L
•PT > 20 sec
•APTT > 60 sec
•Within 24 hours after major surgery
-Proven of clinically suspected heparin induced thrombocytopenia
-Hemorrhagic diathesis
-Heparin allergy
-Pregnancy or breast feeding

## Study design

### Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Placebo |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-02-2007 |
| Enrollment: | 26 |

| | |
|---|---|
| Type: | Anticipated |

### Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Unfractionated Heparin |
| Generic name: | Unfractionated Heparin |
| Registration: | Yes - NL outside intended use |

## Ethics review

Approved WMO

| | |
|---|---|
| Application type: | First submission |
| 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 | EUCTR2006-006801-99-NL |
| CCMO | NL15626.018.07 |