Respiratory, hemodynamic and inflammatory effects of induced HypothermiA using NoVAtherm with extra corporeal membrane ventilator iLA-Activve in patients with acute respiratory distress syndrome (ARDS)

Published: 06-12-2012
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Primary Objective: Does induced hypothermia using NovathermTM combined with the iLA-Activve MinilungTm result in a reduction in minute volume ventilation and work of breathing by reducing positive peak inspiratory pressure levels in patients with...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Interventional

Summary

ID

NL-OMON39735

Source
ToetsingOnline

Brief title
HAVAnA study

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
ARDS; acute lung injury

Research involving

Human

Sponsors and support

Primary sponsor: ICU volwassen / L.E.I.C.A.
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: ARDS, Hypothermia, Novatherm

Outcome measures

Primary outcome

Minute volume ventilation

Secondary outcome

Hemodynamic parameters: intra-arterial systolic and diastolic pressure, cardiac output, right and left ventricular contractile function, parameters of pre-load and after-load and pulmonary arterial pressures

Ventilatory parameters: Pmax, CVD, ScvO2, PaO2, PvO2, (A-a) difference, PCO2, etCO2, tidal volumes, respiratory rate, PEEP level, pressure volume curves, compliance, work of breathing, lung injury score.

Outcome: duration of mechanical ventilation, time to ventilation-free days, length of ICU and hospital stay and 28 day mortality.

Inflammatory parameters: BALF/plasma albumin ratio, BALF and plasma levels of IL-8, TNF, IL-1, IL-6, IL-10, EA complexes, D-dimers, thrombin-antithrombin complex, PAI-1, PAA% (by ELISA).

Metabolic parameters: VO2, VCO2, EE, mitochondrial respiration, mitochondrial

enzymes and mitochondrial DNA (isolated from circulating platelets).

Study description

Background summary

Acute respiratory distress syndrome (ARDS) develops in 30-60% of critically ill patients admitted to the Intensive Care. ARDS is characterized by an inflammatory response, often requiring mechanical ventilation with high pressures, causing additional damage. Also, right ventricular dysfunction is a common finding in ARDS, contributing to mortality. Reduction in pulmonary compliance during ARDS may require application of high pressure levels to maintain adequate ventilation, which can reduce cardiac output or even result in the development of obstructive shock.

The iLA-Activve MinilungTM (artificial lung) is a veno-venous support system that can effectively eliminate CO2. To a lesser extend, it can also oxygenate blood. Induced hypothermia reduces metabolic rate with a concomitant lower CO2 production, allowing for lower minute volume ventilation for adequate decarboxylation. In combination, this device has a strong potential to reduce minute volume ventilation while maintaining adequate gas exchange in ARDS, thereby reducing peak pressures, with subsequent reduction in lung injury. Also, use of iLAartifical lung may favour hemodynamic parameters

Study objective

Primary Objective:
Does induced hypothermia using NovathermTM combined with the iLA-Activve MinilungTm result in a reduction in minute volume ventilation and work of breathing by reducing positive peak inspiratory pressure levels in patients with ARDS?

Secondary Objectives:
1) Does induced hypothermia using NovathermTM with iLA-Activve MinilungTM increase cardiac output and mean arterial pressure (or reduce vasopressor need) by improving loading conditions in patients with ARDS?
2) Does induced hypothermia using NovathermTM with iLA-Activve MinilungTM attenuate lung injury in patients with ARDS?

Study design

Randomized controlled open label trial in mechanically ventilated patients,

admitted at the Intensive Care Unit with ARDS. Patients will be randomized to one of the following groups:
1) Use of iLA-Activve MinilungTM in combination with NovathermTM with cooling to 32-34 ºC during 12 hours;
2) Use of iLA-Activve MinilungTM while maintaining normotemperature during 12 hours;
3) Standard care.

Intervention

Randomized controlled open label trial in mechanically ventilated patients, admitted at the Intensive Care Unit with ARDS. Patients will be randomized to one of the following groups:
1) Use of iLA-Activve MinilungTM in combination with NovathermTM with cooling to 32-34 ºC during 12 hours;
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3) Standard care.

Study burden and risks

To connect the iLA-Activve Minilung device, a double lumen cannula of 18 French Gauge will be inserted in the jugular or femoral vein under ultrasound guidance. Participants will undergo an echocardiography (3x) and SDF (3x). These investigations are non-invasive. Participants will donate a total of 30 ml of blood, drawn from a catheter already in place. Patients will undergo a minilunglavage, which is a minimal burden and is also done as part of routine airway management on our ICU.

Risks related to the artificial lung:
Thrombus/Embolus
bleeding with possible blood transfusion
ischemia of the cannulated leg
These complications occur in < 2%

Risks related to hypothermia:
electrolyte disturbances
bradycardia
These complications are wellknown, anticipated, checked and treated.

Risks related to this study are justified because of their low incidence. Interventions are part of the routine care on the ICU (hypothermia, catherisation en anticoagulation).
Included patients may experience a possibly therapeutic effect, because the artifical lung will allow for lowering of ventilation pressures, thereby possibly lowering lung injury. Also the right ventricle may experience a

beneficial effect.

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

1) Suffering of a clinical condition associated with ARDS
2) ARDS according to the Berlin definition (P/F < 200 with PEEP > 5 cmH2O; bilateral pulmonary opacities at chest X-ray; respiratory failure not fully explained by cardiac failure or volume overload)
3) Mechanical ventilation with maximum inspiratory pressure levels (Pmax) of > 30 cm H2O, while maintaining tidal volume ventilation of 6-8 ml/kg ideal body weight and permissive hypercapnia with an arterial pH < 7.25.

Exclusion criteria

1) Contra-indication for (low dose of) heparin
2) Severe shock, requiring norepinephrin dose of > 2 mg/hour
3) Severe hypoxia, requiring referral for extra corporeal membrane oxygenation

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-07-2013
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Artifical lung iLA-Activve MinilungTM
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	06-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-07-2014

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

ID: 26548
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL42038.018.12
OMON	NL-OMON26548