Effects of Induced Hypothermia on Respiratory parameters and Immunological function

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Observational part on respiratory parametersThe primary objective of this study is to study the effect of hypothermia and rewarming on P/F ratio as a measure of oxygenation and on end tidal CO2 as a measure of ventilation during mechanical...

Ethical review	-
Status	Recruitment stopped
Health condition type	Body temperature conditions
Study type	Observational invasive

Summary

ID

NL-OMON34602

Source
ToetsingOnline

Brief title
REIM study

Condition

- Body temperature conditions
- Immune disorders NEC
- Respiratory disorders NEC

Synonym
Hypothermia; Artificial induced low body temperature

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Hypothermia, Immunology, Respiration

Outcome measures

Primary outcome

The main endpoint of this study is P/F ratio as a measure of oxygenation and

end tidal CO2 as a measure of ventilation.

Secondary outcome

Respiratory:

oxygenation index, lung injury score, static compliance, dead space

ventilation, oxygen consumption.

Immunological:

levels of pro-inflammatory chemokines and cytokines (TNF-alpha, Il-1beta, and

IL-6, IL-2, IFN-g, IL-8), whole blood stimulation, HLA-DR expression.

Study description

Background summary

Induced hypothermia is increasingly applied as a therapeutic intervention in Intensive Care Units. Despite this increase in use of induced hypothermia in critically ill patients, clinical observations on the effect of hypothermia on lung mechanics and gas exchange during mechanical ventilation are limited. Animal experiments suggest a reduction in metabolism with subsequent reduction of CO2 production. Low tidal volume ventilation is protective in acute lung injury. It is very well possible that hypothermia may allow for even further reduction of minute ventilation while maintaining gas exchange, thereby decreasing mechanical stress caused by mechanical ventilation. Also, hypothermia protects from ventilator induced lung injury (VILI) by reduction of

leukocyte influx and attenuation of cytokine responses in experimental murine models. Therefore, hypothermia may be a new therapy for patients with acute lung injury.
Although a persistent increase in infectious complications have not been reported, application of hypothermia may hamper immunologic responses. Increasing the knowledge on the effects of hypothermia on host response will result in the safe application of hypothermia.

Study objective

Observational part on respiratory parameters

The primary objective of this study is to study the effect of hypothermia and rewarming on P/F ratio as a measure of oxygenation and on end tidal CO2 as a measure of ventilation during mechanical ventilation.

Secondary objectives of this study are to study the effect of hypothermia and rewarming on:
- static lung compliance
- dead space ventilation
- oxygen consumption (cardiac output x (CaO2-CvO2))
- lung injury score
- oxygenation index ((FiO2 * mean airway pressure) / PaO2)

Case control part on immunologic function

Secondary objectives are to study the effect of hypothermia on immunologic parameters by comparison with normothermic critically ill patients and healthy controls, including the effect on:
- The response of blood leucocytes to stimulation with Toll like receptor ligands (lipopolysaccharide, lipoteicoic acid),
- Toll-like receptor expression profile (mRNA and protein),
- Levels of pro-inflammatory cytokines (IL1β/IL6/TNFα/IFNγ), chemokines (IL8) and neutrophil degranulation product elastase,
- Expression of monocyte HLA-DR.
- Leukocyte differentiation

Study design

A prospective, observational cohort study in the Academic Medical Centre, in which we will include 50 patients in whom hypothermia is induced after cardiac arrest and who are admitted to the ICU.
Mechanical ventilation will be adjusted according to arterial blood gas results, the same way as is done as part of standard care.

All 50 patients included in the study will receive induced hypothermia for 24

hours plus the standard post-resuscitation care. Blood will be drawn from catheters, which are already in place as part of the standard patient care. The following data will be collected from the patient data monitoring system: previous history, age, gender, weight, length, APACHE II, SAPS II. The following data will be derived from the ventilator at reaching target temperature (32-34 °C), after 24 hours of hypothermia and at every centigrade increase in temperature: tidal volume, minute volume, respiratory rate, FiO2, level of PEEP, peak inspiratory pressure, plateau pressure, compliance, end tidal CO2. At these same time points, blood gas analysis will be performed (extra blood donation of 4 ml).

For the immunological parameters in the case-control part of the study, we will draw 12 ml of blood from 25 patients in whom hypothermia is induced (derived from the 50 included patients) at three time points: at reaching target temperature (32-34 °C), after 24 hours of hypothermia and after rewarming to 37 °C (extra blood donation of 36 ml total). In two control groups (25 critically ill mechanically ventilated normothermic patients and 10 healthy controls), a one time blood sample of 12 ml will be drawn.

Study burden and risks

Outside of standard patient care blood will be drawn from a catheter that is already in place (a total of maximal 50ml). All ventilator and hemodynamic parameters can be read from the ventilation equipment or monitor or will be collected from the electronic patient data monitoring system.
A participating patient will not benefit directly from this observational study. As knowledge of the effect of hypothermia on the respiratory system en immunological parameters will increase, future patients in whom hypothermia will be induced may benefit.

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

For the observational part of the study:
- Admission to the ICU after cardio pulmonary resuscitation
- Treatment with induced mild hypothermia according to protocol, as part of standard patient care
For the case-control part of the study, 2 additional groups will be included:
- Mechanically ventilated normothermic, non-infectious patients
- Healthy volunteers

Exclusion criteria

Exclusion cirteria are:
- No informed consent
- Inability to complete 24 hours of hypothermia
- Presence of pulmonary fibrosis

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-03-2011
Enrollment:	60
Type:	Actual

Ethics review

Not available

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	NL32522.018.10