Impact of Age on the Pulmonary Renin-Angiotensin System in Acute Respiratory Distress Syndrome

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ancillary infectious topics
Study type	Observational invasive

Summary

ID

NL-OMON41340

Source
ToetsingOnline

Brief title
Age and ARDS

Condition

- Ancillary infectious topics
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
acute respiratory distress syndrome (ARDS); acute lung injury

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Acute respiratory distress syndrome, Aging, Inflammation, Renin-Angiotensin System

Outcome measures

Primary outcome

The main study parameters are the different RAS components measured in

bronchoalveolare lavage fluid (BALF) and blood at different time points.

Secondary outcome

- Effector molecules of the pulmonary RAS (including cytokines, compoments of

coagulation and fibrotic components)

- Oxygenation index (OI); alveolar-arterial oxygen difference (DD(A-a)O2);

PaO2/FIO2 ratio

- Score for Neonatal Acute Physiology II (SNAPII) or pediatric risk of

mortality score (PRISM).

- Ventilator-free days (VFDs)

- Bronchopulmonary dysplasia (BPD)

- Mortality: within 60 days after study enrolment

Study description

Background summary

Children have a lower incidence and mortality from acute respiratory distress syndrome (ARDS) than adults. In addition, experimental models of ARDS show that adult animals are more susceptible to lung injury than newborn or young animals. The age dependent mechanisms by which injury responses in the lungs are acquired are unknown. Age dependent changes in the pulmonary renin-angiotensin system (RAS) might offer an explanation for the differences in susceptibility to and outcome of ARDS between children and adults. The two

key enzymes of the RAS, Angiotensin Converting Enzyme (ACE) and ACE2, have opposite actions. ACE functions as a lung injury-promoting factor via production of its effector peptide Angiotensin (Ang) II. In contrast, ACE2 functions as a lung protective factor by degradation of Ang II and generating Ang-(1-7). Recently, an imbalance between ACE and ACE2 was shown in experimental ARDS models. Moreover, experimental data indicate that aging is associated with increased ACE and decreased ACE2 production in several tissues, including the lung.

Study objective

With this study we aim to provide insight in the role of pulmonary RAS in the pathogenesis of ARDS in neonates and children. This study is performed in the context of a comparative study assessing the impact of age on the pulmonary RAS in ARDS. We hypothesize that neonates and children have a relatively more active pulmonary ACE2 pathway at the expense of the ACE pathway compared to elderly patients, which affects the susceptibility and course of ARDS.

Study design

An investigator-initiated observational study at the neonatal intensive care unit (NICU) or pediatric intensive care unit (PICU). Mechanically ventilated neonates and children at risk for ARDS are subjected to serial bronchoalveolar lavages (BAL) (as previous described in the research protocol (METC 98/099 and METC 06/165), approved by the METC of the AMC) and blood collection, aiming to determine the levels of the different RAS components. An identical study protocols will be applied at the adult intensive care unit in order to determine whether there are differences between the different age groups.

Study burden and risks

The BAL procedure has found to be a safe procedure in neonates and children. It is previously used in the research protocol (METC 98/099 or METC 06/165), approved by the METC of the AMC after a pilot was performed assessing the potential complications of this procedure. Blood sample volumes will be limited to 1 ml and collection will be performed within the daily routine collections using an indwelling arterial catheter. Therefore the risks and burden associated with this study protocol can be considered as minimal.
Patients included in the study do not have a direct benefit from the study. The purpose of this study is to investigate the role of pulmonary RAS during ARDS at all ages. We aim to identify biological distinctions in RAS response during ARDS between different age groups, which may influence the course and outcome of the disease. Insight into the role of maturation and aging in the context of ARDS can lead to novel targets for age directed therapeutic options.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

•Signed informed consent by the parents or legal caretakers.
•Admitted to the neonatal intensive care unit (NICU) or pediatric intensive care unit (PICU) of the Emma Children*s Hospital, Academic Medical Center of Amsterdam, the Netherlands.
•Intubated and mechanically ventilated, with an anticipated duration of mechanical ventilation of at least 48 hours at enrolment (as judged by the investigator or the neonatologist on duty).
•Enrolment within 24 hours after the start of mechanical ventilation.
•Body weight of 1 kg or more at the time of enrolment.
•Two or more of the following criteria at the time of enrolment:
o Hypothermia (< 36 °C), fever (> 38.0 °C), or body temperature instability.
o Bradycardia or tachycardia, according to age, or a prolonged capillary refill time.

o Leukopenia or leucocytosis, according to age, or more than 10 % banded neutrophils.
o Tachypneu or apneu*s, according to age, or cyanosis

Exclusion criteria

•Neonates with a postconceptual age less than 32 weeks within 1 week post partum.
•Immune compromised; chronic respiratory failure, neuromuscular diseases, cyanotic congenital heart disease or signs of cardiogenic pulmonary edema, severe congenital pulmonary abnormalities.
•(Previous) use of medication which intervene with the RAS
•Previous mechanical ventilation, surfactant or NO-therapy within 1 week before eligibility for enrolment into the study.
•Longer than 48 hours antibiotics previous to IC-admission.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-05-2013
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO

Date:	18-12-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	17-04-2013
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
CCMO	NL42386.018.12