Neutrophil extracellular trap induced changes in (RSV-infected) pediatric human airway epithelial (HAE) cultures.

Published: 27-03-2020
Last updated: 10-04-2024

1) to determine NETs-induced changes in ex vivo (RSV-infected) pediatric HAE (e.g. mucus hypersecretion and cell death) and 2) to explore pharmacological inhibition of NETs in this context.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON49719

Source
ToetsingOnline

Brief title
NETs induced changes in pediatric HAE

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
respiratoir syncytieel virus bronchiolitis, RSV-bronchiolitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Airway, HAE (human airway epithelial celcultures), NETs (neutrophil extracellular traps), Pediatric

Outcome measures

Primary outcome

We will use the collected cells to obtain pediatric HAE cultures. We will use these cultures as an ex vivo model to study NETs induced changes in the context of RSV infection of the pediatric airways. We will perform measurements on airway mucus (protein expression) and airway epithelial damage (necrosis, apoptosis, loss of differentiation, loss of barrier function, apoptotic gene expression, inflammation markers and inflammatory pathways).

Secondary outcome

n.a.

Study description

Background summary

Viral lower respiratory tract infection (LRTI) caused by respiratory syncytial virus (RSV) is an important cause of childhood morbidity and mortality worldwide. Neutrophil recruitment and neutrophilic inflammation are hallmarks in the pathophysiology of severe RSV-LRTI. There is accumulating evidence that the formation of neutrophil extracellular traps (NETs) in the airways plays a crucial role in the development of severe RSV-LRTI by contributing to mucus plugging and epithelial injury. Therefore, NETs might be a potential target for pharmacological intervention, making it imperative to gain insight into the pathogenetic role of NETs formation in RSV-LRTI. Ex vivo three-dimensional (3D) airway-modelling by the use of Human Airway Epithelial (HAE) cultures allows the study of virus- epithelial airway cell interaction and immunopathology without the use of modified cell lines or animals. However, there is a lack of pediatric specific models. As RSV-LRTI specifically effects infants and the mechanisms underlying respiratory insufficiency due to RSV-LRTI in young children might differ from adults, it is important to develop a pediatric

airway model.

Study objective

1) to determine NETs-induced changes in ex vivo (RSV-infected) pediatric HAE (e.g. mucus hypersecretion and cell death) and 2) to explore pharmacological inhibition of NETs in this context.

Study design

single centre, ex -vivo laboratory study, designed to study NETs induced changes in pediatric airway epithelial cells and airway mucus, with and without RSV co-infection. We will use HAE cultures derived from infants, using a minimally invasive procedure to obtain primary human, pediatric airway epithelial cells. We will perform non - bronchoscopic bronchial cytobrushing to obtain small lower airway epithelial cells for HAE culturing. This is an extension with minor adaptions of a previous PICU study (MEC 06/097). Prior to cytobrushing, patients are already endotracheally intubated for the elective surgery by standard hospital procedures for elective surgery. Additionally, we will test the obtained material for the presence of common respiratory tract virusses (viral respiratory panel).

Study burden and risks

For ethical reasons, bronchoscopic procedures primarily for research purposes are not justified in children. As an alternative, non-bronchoscopic cytobrushing during elective surgery is considered to be an effective and safe procedure in children. No serious risks or adverse events by non-bronchoscopic cytobrushing have been reported. A previous clinical study by Bem1, carried out in the Amsterdam Medical Center - location AMC, reported no adverse events. The subjects of this study are minors and have no direct advantage of their participation in this study. However, respiratory failure in RSV-LRTI is an important cause of childhood hospitalization and research on the mechanisms underlying respiratory failure in RSV-LRTI is therefore of benefit to this age group, which we believe justifies our intended research project.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Age between 2 and 24 months
- No known pulmonary disease
- Endotracheal intubation (for elective surgery)
- No signs of infection (fever, temperature >38.5 C) and no respiratory symptoms (cough, wheeze, snotty) present at moment of intubation.
- No reported respiratory symptoms in the last 7 days prior to surgery (cough, wheeze, snotty)
- Informed consent obtained for both non-endoscopic cytobrushing and serological testing after confirmation of comprehension of the Dutch language.

Exclusion criteria

- Age < 2 months or > 24 months
- Reported pulmonary disorder
- Non-elective endotracheally intubation
- Symptoms of a present or recent infection (T>38.5C in the last 7 days prior to surgery) or reported respiratory symptoms in the last 7 days prior to surgery
- No consent.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO Date:	27-03-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-05-2020
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	NL71577.018.19