The role of innate immunity in the pathogenesis of acute respiratory syncytial virus lower respiratory tract infection:
Repeated measurements of nasopharyngeal type 1 interferon levels in RSV infections

Published: 18-09-2006
Last updated: 20-06-2024

To obtain insight in the role of the innate immune response, especially Type 1 interferons, in the pathogenesis of RSV LRTI. New techniques are used to unravel the local (nasopharyngeal) immunological milieu during viral LRTI. The hypothesis is that...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Observational non invasive

Summary

ID

NL-OMON35329

Source
ToetsingOnline

Brief title
SNOT'R

Condition

- Respiratory tract infections

Synonym
Innate immune response, Viral respiratory tract infection

Research involving
Human

Sponsors and support

Primary sponsor: RSV Research Group van het Wilhelmina Kinderziekenhuis Utrecht, UMCU, onder leiding van Prof. dr. J.L.L. Kimpen, promotor
Source(s) of monetary or material Support: door de onderzoekers zelf en fonds aangevraagd bij de European Society for Pediatric Infectious Diseases

Intervention

Keyword: Innate Immune Response, Repeated measurements, Respiratory Syncyitial Virus, Type 1 interferons

Outcome measures

Primary outcome

1. Disease severity:

Children: Standardised Respiratory Distress Assessment Instrument (RDAI) Score

Elderly: Standardised Adult Physiology And Chronic Health (APACHE) Score,

Respiratory Parameter

2. Virological analysis (nasopharyngeal material):

Quantitative RT-PCR on RSV, hMPV, rhinovirus, adenovirus, PIV 1-4, Flu A en B,

en coronavirus

3. Immunological analysis/cytokine concentrations (nasopharyngeal material):

Interferon-alfa using commercial ELISA

IL-1αβ/α, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12*70, IL-13, IL-15, IL-17,

IL-18, IFN-γ and TNF-α using Luminex

4. Immunological analysis (blood):

Leucocytes and differentiation

Immunophenotyping

Toll-like receptor responses

Secondary outcome

na

Study description

Background summary

Respirator Syncytial Virus (RSV) lower respiratory tract infection (LRTI) is the most common cause of pediatric hospitalisation during the winter season. During the first year of life, 0.5-1% of Dutch children is admitted for RSV infection. Risk factors for RSV bronchiolitis hospitalisation are prematurity (with or without chronic pulmonary disease), neonatal status and congenital heart disease. However, most patients have no identifiable risk factor. Recent literature shows that the elderly population is also at risk for RSV LRTI hospitalisation.

The role of the immune response during RSV infection and during recuperation of serious illness is largely unknown. It is speculated that inadequate viral clearance during the neonatal period is the result of a premature immune system. Indeed, healthy babies show an increase of interferon (IFN) gamma production during the first 12 months of life. Studies also show that a decrease in adaptive immune response during RSV bronchiolitis is associated with an increase in disease severity and that there is a positive correlation between disease severity and viral titers.

Apart from immature T-cel immunity, innate immune responses, such as Toll-like receptor systems and Type 1 interferons, are also suboptimal at birth. TLR4-CD14 complex-mediated tumor necrosis factor (TNF) alpha is largely absent at birth. TLR4 is considered the putative receptor for RSV. Type 1 interferons have a direct anti-viral effect, but also play a role in activation of antigen presenting cells, natural killer (NK) cells and T-cells. Epithelial and plasmoid dendritic cells produce interferon after infection with RSV. However, RSV inhibits TNF-alpha mediated interferon production. Inhibition of interefron production could be an important mechanism by which RSV attempts to evade the immune system. So far, the role of Type 1 interferons during RSV LRTI has not

been studied in humans.

Study objective

To obtain insight in the role of the innate immune response, especially Type 1 interferons, in the pathogenesis of RSV LRTI. New techniques are used to unravel the local (nasopharyngeal) immunological milieu during viral LRTI. The hypothesis is that nasopharyngeal Type 1 interferon concentration is associated with severity of disease during RSV LRTI in children and the elderly.

Study design

Outpatient children (RSV + en RSV -):
Nasopharyngeal aspirate during the outpatient visits.

Hospitalised, non-intubated children (RSV + en RSV -):
Nasopharyngeal aspirate after admittance and 3 times a week, and during outpatient visits, 2 max.

Intubated children (RSV + en RSV -):
Nasopharyngeal aspirate and noseswab after intubation and 3 times a week until extubation. 2 1/2 ml of blood 3 times a week, during regular laboratory work-up, until extubation. For subgroup of children discharged to the pediatric ward of WKZ nasopharyngeal aspirate at ward 3 times a week, and at home once a week for 2 weeks after discharge.

Hospitalised elderly (RSV +):
Nasopharyngeal aspirate after admittance and 3 times a week until discharge.

Hospitalised elderly (RSV -):
Nasopharyngeal aspirate only after admittance.

Study burden and risks

na

Contacts

Public
RSV Research Group van het Wilhelmina Kinderziekenhuis Utrecht, UMCU, onder leiding van Prof. dr. J.L.L. Kimpen, promotor

Lundlaan 6, KE 041.31.1
3584 EA, Utrecht

Nederland
Scientific
RSV Research Group van het Wilhelmina Kinderziekenhuis Utrecht, UMCU, onder leiding van Prof. dr. J.L.L. Kimpen, promotor

Lundlaan 6, KE 041.31.1
3584 EA, Utrecht
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Child = under the age of 13 months (exception: <5 years old for group 3)
Adult = over the age of 18 years
Upper respiratory infection = symptoms of rhinitis with or without mild cough
Lower respiratory infecton = symptoms of hypoxemia, tachypnea, dyspnea, severe cough, and/or repeated apneu's, fever

Exclusion criteria

Child = previous airway morbidity or severe co-morbidity (exception: no exclusion criteria for group 3)
Adult = None

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-10-2006
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	18-09-2006
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	20-12-2007
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	03-11-2008
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	31-08-2010
Application type:	Amendment

Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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	NL12722.099.06