A pilot study of immunorespons in children with Down syndrome after Respiratory Syncytial Virus (RSV) lower respiratory tract infections (LRTI)

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The primary objective is whether a difference in innate and acquired immunorespons on RSV infection exists, in children with DS compared to healthy matched-controls.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Chromosomal abnormalities, gene alterations and gene variants
Study type	Observational invasive

Summary

ID

NL-OMON31485

Source
ToetsingOnline

Brief title
RSV and Down

Condition

- Chromosomal abnormalities, gene alterations and gene variants
- Immune disorders NEC
- Viral infectious disorders

Synonym
Down syndrome, Mongols; Immunodeficiency, physical defense disorder, Trisomy 21

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Down syndrome, Immunorespons, RSV

Outcome measures

Primary outcome

The primary outcome is the difference in immunorespons after RSV LRTI in children with DS and 'healthy' peers. The difference will be stated upon: RSV specific cytokine production; total number of T-cells, B-cells, Antigen Presenting Cells, Natural Killer cells and Dendritic cells; general cytokine expression.

Secondary outcome

Age, sex and ethnic background will be taken into account as variables in the analyses.

Study description

Background summary

Respiratory syncytial virus (RSV) is the single most important cause of lower respiratory tract infections (LRTI) in infants and young children. Seventy percent of infants will be infected with RSV before one year of age, and virtually all children have had a RSV LRTI before the age of 2 years. Most children will develop a minor cold, but in 22% of cases children develop severe RSV bronchiolitis. About 3% of all children are hospitalized, 7-22% of which is in need of mechanical ventilation.
Down syndrome (DS) is the most common chromosomal abnormality among live born infants. DS is associated with a variety of immunological impairments. Lower respiratory tract infection is the most common cause for acute hospital admission in children with DS. In a recent study (article in preparation) we

found an increased incidence of RSV LRTI hospitalization in children with DS. The factors that determine the high risk of RSV LRTI hospitalization in children with DS are currently unclear. Different pathophysiologic mechanisms could play a role. For instance, children with DS appear to have suboptimal immune responses. Thymus development and function is abnormal. The number of B-cells and T-cells are low, especially in the first two years of life. In addition, defective T-cell ex vivo proliferative responses to non-specific and antigenic stimuli, cytokine production and NK-cell responses are thought to play a role in the increased susceptibility to infectious pathogens. Our hypothesis is that an abnormal innate and acquired immunorespons predisposes children with DS for severe RSV LRTI.

Study objective

The primary objective is whether a difference in innate and acquired immunorespons on RSV infection exists, in children with DS compared to healthy matched-controls.

Study design

This is an observational study. In a total of 100 children (50 DS and 50 healthy matched-controls) innate and acquired immunorespons against RSV will be examined. A single venapunction will be done, to acquire 5-10 ml blood (if possible this will be done in combination with a planned diagnostic venapunction).
Part of this blood will be cultured in the presence of live RSV. Cytokine respons will be measured after 5 days. Further, FACS staining will be done to measure the amount of virus specific cells. Stimulation assays will be performed to examine specific T-cell responses. Finally, part of the blood will be used to determine the amount and function of dendritic cells after RSV infection. In case of rest-material and if parental consent has been given, this will be frozen for possible future studies, for which parental consent will be asked again at that time.

Study burden and risks

All participants will undergo one venapunction during a regular visit to the outpatient clinic or during an elective procedure. Patients will not come to the hospital particularly for this study, unless this is not possible otherwise. The amount of time for a venapunction is limited, usually it does not take more than 10 minutes. The risks of a venapunction is negligible. The possibility of a haematoma or prolonged bleeding must be taken into account. The consequences are limited however. In case of unsuspected serious adverse events, this will be reported to both parents and the METC. The most important burden to be taken into account is the venapunction, which can be fearful or stressing for the child. The parent will be asked to accompany the child during

the venapunction to report signals of a high burden for the child, so that in consultation with the parent the procedure will be ceased.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Down syndrome, age 0-12 years; healthy matched-controls

Exclusion criteria

Bronchopulmonary dysplasia, prematurity (gestational age <37 weeks), hemodynamic significant congenital heart disease, immunodeficiencys, current infectious disease, fever in month before inclusion

Study design

Design

Study type:	Observational 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):	03-05-2007
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	02-01-2007
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-08-2008
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL14629.041.06