Multisystem phenotyping of severe ACUte asthma at the Paediatric Intensive Care Unit

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Observational invasive

Summary

ID

NL-OMON54638

Source
ToetsingOnline

Brief title
MACU-PICU

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Asthma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Aanvraag bij Longfonds;Stichting Steun Emma;Stichting Astmabestrijding

Intervention

Keyword: Biomarkers, Multisystem phenotyping, Precision medicine, Severe Acute asthma

Outcome measures

Primary outcome

Severe acute asthma phenotypes at the PICU based on differences in bacterial metabolomics and microbiomics, viromics, breathomics, transcriptomics and cytokine biomarkers.

Secondary outcome

None applicable.

Study description

Background summary

Amongst children, asthma is the most prevalent chronic disease. It is characterized by stable phases and exacerbations, the latter caused by numerous triggers. Although a lot has been gained in the treatment of these exacerbations with inhalation of steroids and bronchodilators, some patients have exacerbations which are refractory to this standard therapy. This is seen as severe acute asthma and for these patients intensification of treatment and admittance to a paediatric intensive care unit (PICU) is necessary. Unfortunately, these refractory exacerbations can progress to respiratory insufficiency and still lead to fatalities. Worldwide, PICU admissions of children with severe acute asthma have increased substantially, surprisingly without an increase in prevalence of asthma, suggesting a change in phenotype. Thus far, therapy for all children admitted to a PICU with severe acute asthma is equal with intensification of bronchodilation (preferably intravenously) and systemic corticosteroids. This one-size-fits-all principle does not seems right for a heterogeneous disease such as asthma and will probably influence time to relief of symptoms as well as length of stay. It can be expected that the immunological basis of the asthma exacerbation differs, depending on age of the child, the trigger of the exacerbation and genetic characteristics, thereby influencing treatment response.
The aim of this study is to identify phenotypes of severe acute asthma in children, using a non-invasive multisystem approach including microbiomics, breathomics, viromics, genomics and immunological biomarkers. Identifying these

asthma profiles may lead to individualized treatment and to new targets for novel therapies.

Study objective

Despite seeing an increase in children admitted to the paediatric intensive care unit for severe acute asthma, we still do not know what the cause of this increase is, and we still only have few drugs we can give these children, regardless of the age of the child and regardless of the trigger, being it a virus, an allergen, or tobacco smoke for instance, causing the severe asthma attack.
Childhood asthma has always been a challenging disease to phenotype, since access to tissue and molecular systems are hampered by the often invasive nature of the techniques necessary to obtain biological samples. Novel techniques now give us the unique opportunity to research various tissues and molecular systems in a non-invasive manner. Although these techniques are now being used in a couple of studies where a multisystem approach is used to phenotype the different forms of childhood asthma, none of these focus on the children with severe acute asthma at the paediatric intensive care unit, a patient group known for having the highest mortality rate.
We hypothesise that severe acute asthma at the paediatric intensive care unit is a clinical diagnosis of a heterogeneous disease which can be characterised by novel biomarkers identified by a non-invasive multisystem approach, leading to personalised treatment.

Study design

The study is designed as an observational cross-sectional diagnostic case-control study for which we use a multisystem -omics approach with easily and non-invasive obtainable tissues and materials to phenotype children with severe acute asthma at the PICU. We will sample 60 children with asthma exacerbations: 30 admitted to the PICU (cases) and 30 age-matched children admitted with asthma to a general ward (controls). Although we hypothesize that children with severe acute asthma at the PICU present heterogeneous phenotypes of asthma, making an observational cohort study possible, we also think these children bear a different phenotype of asthma compared to those with asthma who are not being admitted at the PICU. Therefore we want to add these controls to explore differences between groups presenting with varying severities of illness.

Study burden and risks

Apart from the blood-sampling, which only will be done when a necessary intravenous line is being placed as a standard of care for children with a severe acute asthma attack, all the measurements are non-invasive. There are no risks associated with the participation in this study. Benefit for the

individual patient could be related to the recognition of a phenotype associated with a certain response to treatment, which will enable personalized medicine in the future. As said, since these asthma phenotypes are different in children and adults, and severe acute asthma attacks differ from an asthma exacerbation because the exacerbation seems refractory to treatment, it is important to perform the study in this specific group of patients.

Contacts

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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

- Between 2-18 years of age
- Referred to a PICU with severe acute asthma for which intravenous salbutamol is started (according to the criteria of the Dutch protocol for status

asthmaticus, clinical judgement of the attending physician and asthma scores).
-Written informed consent obtained from the parents/ local guardians/ patient when 12 years of older.
-Patients included in the SysPharmPediA study (NL 55788.041.15) with unstable asthma GINA step 3.

Exclusion criteria

- Cystic Fibrosis
- Previous inclusion in the study

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:	Recruiting
Start date (anticipated):	05-09-2022
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	21-10-2019
Application type:	First submission
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	NL70251.018.19