Cardiovascular Disease in Children with chronic inflammation

Published: 26-10-2016
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Primary objective: study the association of circulating iNKT cell numbers and function with early atherogenesis, as measured by cardiovascular magnetic resonance imaging (MRI). Secondary objectives: a) study the association of circulating iNKT cell...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Observational invasive

Summary

ID

NL-OMON47646

Source
ToetsingOnline

Brief title
CDC study (cardiovascular disease in children)

Condition

- Coronary artery disorders
- Autoimmune disorders
- Appetite and general nutritional disorders

Synonym
Atherosclerosis, coronary disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Nutricia,Wilhelmina Kinderziekenhuis onderzoeksfonds;Nutricia Research Unit Utrecht;Immunopharmacologie (universiteit

utrecht);Topsector Life sciences and Health

Intervention

Keyword: Atherosclerosis, Chronic disease in childhood, Inflammation, Natural Killer T cells

Outcome measures

Primary outcome

iNKT cell numbers and function: numbers will be quantified by flow cytometry,

function will be quantified by in vitro stimulation with iNKT cell ligands

followed by quantitative PCR of iNKT cell cytokines.

Early atherosclerosis: measured by cardiovascular magnetic resonance imaging

(MRI), using aortic wall thickness and volume as the main readout.

Secondary outcome

Secondary study parameters/endpoints

1) Markers of systemic inflammation:

* multiplex immuno assay profiling of circulating inflammatory markers

including cytokines and adipokines will be used to quantify circulating

inflammatory mediators

* phenotyping of circulating immune cell subtypes will be used to quantify

circulating inflammatory cells

2) Cardiac ultrasonography markers for vascular dysfunction:

* screening cardiac ultrasonography including left atrial volume and left

ventricular volume and function

* intima-media thickness measurement

3) Pulse wave velocity measurement for vascular dysfunction

Other study parameters:

1) Anthropomorphic measurements: weight, length, BMI-SD, waist-hip ratio, fat percentage (bio-impedance measurement).

2) Growth: patients and their parents will be asked for permission (signed consent) to retrieve their growth charts from the GGD (gemeentelijke gezondheidsdienst, CB, schoolarts).

3) Nutrition: patients will be asked to complete a nutritional diary for 3 days, which takes 10 minutes a day. Standardized nutritional diaries are used for the cystic fibrosis adolescents already.

4) Medication use: descriptive data, will be derived from the patient information systems (Hix in WKZ/UMC Utrecht).

5) Metabolic profile: fasting glucose/insulin, HbA1c, lipid profile.

6) Physical activity: patients will be asked to fill in a questionnaire. The questionnaire is standardized and internationally published. The questionnaire is used by the child physical activity centre of the hospital already.

Study description

Background summary

Prolonged survival of children with chronic disease often comes at the price of early atherosclerosis. Chronic inflammation plays a primordial role in atherogenesis, and invariant Natural Killer T (iNKT) cells seem one of the important cellular players involved because of their activities in the vascular wall and high circulating numbers in children.

Study objective

Primary objective: study the association of circulating iNKT cell numbers and function with early atherogenesis, as measured by cardiovascular magnetic

resonance imaging (MRI).
Secondary objectives: a) study the association of circulating iNKT cell numbers and function with other markers of systemic inflammation, and b) study the association of established cardiac ultrasonography markers for vascular dysfunction, such as left atrial volume and left ventricular volume and function with early atherogenesis as measured by cardiovascular MRI, and c) study the association between nutrition, growth, surrogate markers for cardiovascular risk (including dyslipidemia, inflammatory parameters, visceral fat mass, pulse wave velocity), and early atherogenesis as measured by cardiovascular MRI.

Study design

Observational, cross-sectional study.

Study burden and risks

The study comprises two invasive procedures: one venous blood withdrawal and one contrast-enhanced MRI procedure. The used contrast agent is gadolinium-based (Gadovist), which is routinely used in pediatric patients. Side effects of Gadovist are very rare, only 1 in 1000 to 1 in 10.000 patients suffers from an acute and transient allergic reaction, usually an itch, nausea, or small bumps on the skin. In extremely rare cases, treatment with antihistamines or adrenalin is required. Futhermore, patients with known contrast allergies or kidney failure will be excluded from the study. In conclusion, the burden and risks of the study are considered minimal.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

General criteria for all groups:
* 12-19 years of age ;Obese adolescents:
Definition according to the international standards of the International Obesity Task Force, see Cole et al, BMJ, 2000. ;JIA adolescents:
* Polyarticular course JIA, including polyarticular JIA and extended oligoarticular JIA, rheumafactor negatieve. These patients often suffer from lifelong rheumatic disease, and are therefore at risk for early atherosclerosis.
* More than 1 year after diagnosis. In first year of disease, patients undergo multiple study procedures, causing a burden on patients. In order to reduce the general burden, this study will focus on patients after their first year of disease.
* BMI-SD < 2 (no obese children). ;Corrected aortic arch anomalies adolescents:
* Corrected aortic arch anomalies, i.e. hypoplastic aortic arch, coarctatio aortae, interrupted aortic arch. These patients are at risk for hypertension and early atherosclerosis.
* BMI-SD (standard deviation from BMI corrected for age and sex) < 2, to prevent including obese children in this group, to prevent obesity being a confounder in later analysis. ;Cystic fibrosis adolescents:
- Established cystic fibrosis, all mutations.
- BMI-SD < 2, to prevent inclusion of obese children so that obesity cannot be a confounder in later analysis. ;Corrected ASD adolescents:
* Corrected ASD.
* No other cardiac anomalies.
* BMI-SD < 2, to prevent inclusion of obese children so that obesity cannot be a confounder in later analysis.
NB. ASD correction < age 1 year has an excellent prognosis and is not associated with enhanced risk of early atherosclerosis.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
* Intoxication (smoking, drug-use)
* Acute illness (fever)
* Mental retardation
* Claustrophobia
* A history of allergic reactions to MR contrast fluids
* Implanted electronic devices (i.e. pacemaker, internal cardioverter-defibrillator, cochlear implants, nerve- and bone stimulators)
* Subjects with ferromagnetic clips in brain, eyes or lungs
* A known reduced kidney function (GFR< 60 ml/min/1.73m2)
* Pregnancy
* Subjects who do not wish to be informed about abnormal findings of the cardiovascular MRI

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):	03-04-2017
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	26-10-2016
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	26-01-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-03-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	17-01-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	07-02-2019
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	NL57924.041.16

Study results

Date completed:	25-06-2019
Actual enrolment:	116