Analysis of immunological and genetic signatures in pediatric inflammatory bowel diseases

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON48142

Source
ToetsingOnline

Brief title
Immunological and genetic profiling in VEO-IBD (Very Early Onset)

Condition

- Gastrointestinal inflammatory conditions
- Immunodeficiency syndromes

Synonym
chronic inflammation of the bowel, Inflammatory Bowel Disease

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Daniel Kotlarz en Christoph Klein;von

Hauner Children's Hospital;I-MU Munich

Intervention

Keyword: Children, Genetics, IBD, Immunology

Outcome measures

Primary outcome

To detect potential disease-causing mutations and subsequently create possible

novel targeted treatment

Secondary outcome

Geen

Study description

Background summary

In inflammatory Bowel Disease (IBD), consisting of Crohn*s disease and ulcerative colitis, it is believed that both genetic predisposition and environmental factors contribute to the etiology. Experimental studies and genetic evidence suggest that chronic intestinal inflammation is complex and triggered by various environmental factors, immunological dysfunctions, defective epithelial barrier function, and imbalances of the microbial flora in genetically susceptible individuals.
Another sub-population within the IBD group is that of much younger children diagnosed with very early onset IBD (VEO-IBD) of which the incidence has dramatically increased over the past decades worldwide. VEO-IBD presents with a phenotype that is significantly different from the forms observed in adults and older children. Children with VEO-IBD often fail to respond to conventional therapies or surgery and its worst forms are life-threatening. Recent studies have shown that in contrast to IBD diagnosed at a later age, the pathogenesis of VEO-IBD is expected to be greatly influenced by inherited factors, due to the young age of onset, increased prevalence of familial disease, and a phenotype that is significantly different. While the number of genes implicated in intestinal disease in model organisms is growing rapidly, only few of these have been systematically tested in human subjects. Many patients with the rare entity of VEO-IBD show severe refractory and life-threatening diseases, therefore innovative and comprehensive studies elucidating the underlying immunological and genetic molecular pathomechanisms are critical. Since VEO-IBD

is a rare condition, centralizing a big international cohort in one laboratory with state-of-the-art equipment and extensive experience is of great importance. Furthermore, it is believed that this centralization will offer substantial understanding of the pathophysiology and subsequently offer novel targeted treatment therapies.

Study objective

In this study it is aimed to investigate the genetic and immunological causes of VEO-IBD in order to improve diagnostics and therapies for patients with this intractable disease. In an explorative approach, state-of-the-art genome-wide screenings on genomic DNA and RNA will be conducted in children with VEO-IBD and their parents (e.g. whole exome sequencing, whole genome sequencing, RNA sequencing) to detect potential disease-causing mutations. The genetic studies will be complemented by analysis of the immune system, microbiome, biomarkers, and environmental factors. It is hypothesized that the genetic and immunological information gained by this study will ultimately lead to the development of diagnostic tools and improvements in health care of children with intestinal diseases.

Study design

An international cohort study in order to explore novel genetic variations associated with VEO-IBD, and to determine the underlying molecular causes of the disease, which in turn might lead to better targeted (tailored) treatment.

Study burden and risks

All included VEO-IBD patients will be asked to donate samples containing blood, saliva, urine, stool, and also additional mucosal biopsies during routine endoscopy. Furthermore, samples containing blood, saliva, urine and stool will be obtained from the parents. All of these biospecimens will be send off to Dr. von Hauner Children's Hospital laboratory in Munich, Germany

A minimal psychological burden and risk is associated with finding out whether or not a particular family carries a mutation. More specifically there is a minimal risk of bruising and infection or bowel perforation, when respectively performing vena puncture or endoscopy. Obtaining other biospecimens show no risk to the patient or parents. On the other hand, since genetic analysis (using blood and urine samples) in VEO-IBD patients is part of standard routine medical diagnostic procedures, participating is also beneficial.

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

1. Patients who are suspected of having or diagnosed with VEO-IBD regardless of race, ethnicity, and gender will be included
2. Diagnosis of IBD (Crohn disease and ulcerative colitis) is based on regular endoscopy, histology, intestinal MRI, video capsule endoscopy or a combination of these (IBD Working Group ESPGHAN, 2014)
3. Both parents of the identified patients will be asked to participate, in order to perform segregation analysis, linkage analysis, or association studies
4. Written informed consent (parents and children (in case of age >12 years)

Exclusion criteria

1. Any patient perceived by the clinical team to be at risk for complications if collection of biospecimens samples for research purposes are taken (e.g., excessive bleeding)
2. No fetal specimens will be taken from pregnant women for prenatal genetic testing
3. No Approved and signed informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2020
Enrollment:	150
Type:	Anticipated

Ethics review

Approved WMO

Date:	21-08-2019
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	NL68606.029.19