The iFAOd study-inflammatory response in long-chain Fatty Acid Oxidation disorders

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In this study we aim to elucidate the effects of inhibited lcFAO on monocyte phenotype and inflammatory activation.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Lipid metabolism disorders
Study type	Observational invasive

Summary

ID

NL-OMON48223

Source
ToetsingOnline

Brief title
iFAOd

Condition

- Lipid metabolism disorders

Synonym
deficiency in beta-oxidation of long-chain fat, long-chain fatty acid oxidation disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Hartstichting beurs 2017T048

Intervention

Keyword: immune system, long-chain fatty acid oxidation, rhabdomyolysis

Outcome measures

Primary outcome

* monocyte phenotype, including monocyte subset percentages and their

expression of key surface proteins, including inflammatory and

anti-inflammatory markers and receptors

* Inflammatory responses, whole blood will be activated with the prototypical

pro-inflammatory TLR4 trigger LPS (lipopolysaccharide) and production of

cytokines will be assessed after 24 h (i.e. IL-6, TNF, IL-12, IL-8)

Secondary outcome

phenotype of other immune cells (e.g. neutrophils, T cells and B cells)

Study description

Background summary

Patients with a genetic defect in lcFAO can suffer from various symptoms induced by catabolism, but rhabdomyolysis (excessive muscle breakdown) is most frequently reported in adults and adolescents. The pathophysiology is still poorly understood. Macrophages, a white blood cell, differentiate from blood monocytes and perform both pro- and anti-inflammatory functions. The mechanisms that control the functions of distinct macrophage subsets remain ill-defined, especially in humans. Recent studies highlight the crucial role of metabolic pathways including fatty acid oxidation in the regulation of macrophages (and monocytes as their more immature precursors).We hypothesize that pro-inflammatory capacities of macrophages could trigger muscle break down in these patients. Using monocytes of lcFAO deficient (lcFAOd) patients, this project aims to understand the role of lcFAO in regulating monocyte and macrophage inflammatory responses. The attained knowledge will significantly strengthen our fundamental understanding on the role of lcFAO in macrophage regulation and will highlight to what extend these defects in monocytes and macrophages can explain the clinical symptoms that the lcFAO deficient patients

experience. Moreover, the results might reveal possible therapeutic targets to arrest the rhabdomyolysis cascade in an early stage, as this is near impossible until date.

Study objective

In this study we aim to elucidate the effects of inhibited lcFAO on monocyte phenotype and inflammatory activation.

Study design

Longitudinal invasive observational study

Study burden and risks

Venous blood will be drawn (maximum of 30 mL) for further investigation of the monocyte phenotype and inflammatory activation. Preferably blood will be drawn at times venous acces is already required for regular care. If this is not feasible blood will be drawn by venapuncture. Venapuncture can be painful and cause hematoma

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Enzymatically confirmed long-chain fatty acid oxidation disorder including VLCAD, LCHAD, MTP, CPT1, CPT2 and CACT deficiency
-18 years old or older

Exclusion criteria

(auto-) immunedisorder

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):	24-09-2020
Enrollment:	15

Type:	Actual

Ethics review

Approved WMO Date:	24-01-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-01-2020
Application type:	Amendment
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	NL67564.018.18