Study the dose and effectiveness of dietary sugar supplementation in congenital muscular dystrophy

Published: 03-01-2017
Last updated: 14-04-2024

The primary objective is to determine the effect of dietary ribose supplementation on muscle function in patients with isolated LGMD as caused by a dystroglycanopathy. The secondary aim is to determine if ribose is well tolerated in this patient...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON43130

Source
ToetsingOnline

Brief title
RiboSup

Condition

- Muscle disorders

Synonym
Dystroglycanopathy; Congenital Muscular Dystrophy

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ZONMW

Intervention

Keyword: Congenital muscular dystrophies, dietary sugars, Dystroglycanopathies

Outcome measures

Primary outcome

Primary study parameters include effectiveness of sugar supplementation on

improved muscle function as investigated by standardized questionnaires and

muscle function tests and a muscle biopsy.

Secondary outcome

Secondary study parameter includes if sugar supplementation is well tolerated

in this patient group.

Study description

Background summary

Dystroglycanopathies are orphan diseases, forming a subgroup of the Congenital Muscular Dystrophies with central nervous system involvement. Less severe forms of the disease result in isolated limb-girdle muscular dystrophy (LGMD) at later age. Currently, no causative treatment exists for any form of the dystroglycanopathies.
The pathogenic mechanism is based on deficient modification of the protein alpha-Dystroglycan (aDG) with glycans. These glycans are composed of monosaccharides that are derived from the food or are synthesized in the body. Deficient aDG glycosylation results in deficient binding of the muscle membrane to the extracellular matrix, thereby resulting in muscular dystrophy. Over 15 different genetic defects have been identified as cause of this group of diseases.
Recently, we discovered the function of one of these genetic defects, ISPD. The ISPD enzyme produces the sugar CDP-ribitol. We found that supplementation of culture patient cells with ribitol and ribose improved the levels of the CDP-ribitol sugar and also restored the glycosylation of aDG. Since ribose has been used as a safe and naturally occurring food supplement in human, these data indicate a potential safe way to intervene in dystroglycanopathy patients due to ISPD mutations.

Study objective

The primary objective is to determine the effect of dietary ribose supplementation on muscle function in patients with isolated LGMD as caused by a dystroglycanopathy. The secondary aim is to determine if ribose is well tolerated in this patient group.

Study design

Patients will be assessed for muscle function and strength, via standardized questionnaires and by clinical chemistry parameters in blood and urine before start of dietary supplementation. After start of therapy, these investigations will be repeated every two months during 8 months. After 6 months, additionally a muscle biopsy will be taken to assess improved muscle function biochemically.

Intervention

Intervention involves daily dietary intake of the monosaccharide ribose.

Study burden and risks

Participants will be asked for a visit to the outpatient clinic at the department of Neurology of the Radboudumc or collaborating institutions abroad. Their medical history will be taken, they will undergo a clinical examination and they will fill out questionnaires. Blood and urine samples will be collected before and during ribose supplementation. Participants will undergo a muscle biopsy of the leg after 6 months of treatment, unless they object against this procedure. This material will be used for biochemical assessment of the response to ribose. Complications of (muscle) biopsies are very uncommon and include hematoma and very localized loss of sensation of the skin (hypesthesia). The dietary monosaccharides are used as safe food supplement. In case of fasting, ribose at much higher concentrations than used in this study were reported to result in lowered blood glucose levels. To avoid such potential risks, patients will take ribose in the fed-state. We classify the risk of this study as negligible.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert grooteplein 10
Nijmegen 6525 GA
NL

Scientific
Radboud Universitair Medisch Centrum

Geert grooteplein 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Confirmed Congenital muscular dystrophy with mutations in ISPD, FKRP, or FKTN
- Dystroglycan dysfunction in muscle
- Normoglycemic before start of supplementation
- Isolated muscle dystrophy, no central nervous system symptoms
- Age >18 years

Exclusion criteria

Persons with contra-indications for a muscle biopsy or who are unwilling to undergo a biopsy, are excluded for that one procedure, but can still be included in the study. Patients with a known condition of severe hypoglycaemia in the fed-state will not be included in this study.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-10-2020
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	03-01-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-08-2020
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL58620.091.16