Cholic acid treatment in Peroxisomal Biogenesis Disorders (Zellweger spectrum): biochemical and clinical effects.

Published: 10-12-2010
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To investigate the effect of cholic acid supplementation on the clinical and biochemical parameters of Zellweger spectrum disorder

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON39837

Source
ToetsingOnline

Brief title
Cholic acid in Zellweger

Condition

- Metabolic and nutritional disorders congenital

Synonym
Peroxisomal biogenesis disorder, Zellweger spectrum disorder

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,nog in aanvraag

Intervention

Keyword: Biochemical and clinical effects, Cholic acid, Peroxisomal biogenesis disorders, Pilot study

Outcome measures

Primary outcome

1- the degree of suppression of endogenous bile acid synthesis

2- change in fat soluble vitamins levels

3- change in weight and length growth

4- side effects of cholic acid suppementation

Secondary outcome

1- change in seizure frequency - change in the obtained developmental mile

stones

2- change liver enzymes - change in fibroscan liver elasticity measurements -

change in liver protein synthesis

3- change in markers of peroxisomal/mitochondrial functioning

Study description

Background summary

Zellweger spectrum disorder is a severe disabling disorder with a short life expectancy. At least some of the clinical abnormalities including severe liver dysfunction, growth retardation and neurological abnormalities in this disorder are caused by the accumulation of bile acid intermediates. Bile acid supplementation by cholic acid has been shown to decrease endogenous bile acid production, stimulate bile secretion and to improve bile flow and micellar solubilization. We hypothesize that cholic acid supplementation improves liver function and alleviates neurological symptoms by suppressing the endogenous bile acid synthesis and stimulating bile flow, thus decreasing the accumulation of toxic and cholestatic bile acid intermediates. In addition, we hypothesize that cholic acid suppletion in mild Zellweger spectrum patients improves

intestinal fat absorption and growth by increasing the amount of intraluminal bile acids, thus promoting micellar solubilization.

Study objective

To investigate the effect of cholic acid supplementation on the clinical and biochemical parameters of Zellweger spectrum disorder

Study design

The original study was an open label pilot study with a 9-month run in period and a 9 months treatment period. We will extend the treatment phase with one additional year.
Cholic acid will be supplemented at a regular dose

Intervention

cholic acid supplementation during 1 year and 9 months

Study burden and risks

Zellweger spectrum disorder is a unique congenital disease and progressive damage starts in utero and continues from birth onwards. Therapeutic treatment from young age is therefore most relevant. This therapeutic study studies clinical outcomes of cholic acid supplementation which are relevant for the participating subjects.
The burden to the subjects is limited as most investigations are performed during 2 standard clinical visits and blood sampling is part of standard care during these visits (650uL blood extra is sampled at each visit). During the standard visits the extra interventions are urine collection using urine collection bags, neurological mile stone determination, fibroscan measurements, handing over the food diary and in those with epilepsy also a diary of convulsions. The neurological evaluation an will be only be a minimal time burden. Fibroscan maeasurement is a one minute, safe, non-invasive and painless procedure. Diet evaluation using a diary and keeping a diary of convulsions is a limited effort for patients or care-takers.
Only one extra visit to the hospital is required (week 26). Length and weight are measured, extra blood sampling is performed (volume 550 uL) and urine is collected using an urine collection bag(minimal volume 5 ml).
Cholic acid is an endogenous substance and excellent safety reports of long term use have been published in one case of Zellweger spectrum and several cases of other bile acid metabolism disorders.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Phenotypically mild Zellweger spectrum disorder.
At least one of the following hallmarks: steatorrhea, elevated transaminases, growth retardation, neurological symptoms

Exclusion criteria

Short life expectancy based on severe multiple organ dysfunction at the time of diagnosis

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2011
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	cholic acid
Generic name:	cholic acid

Ethics review

Approved WMO Date:	10-12-2010
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	23-07-2015
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
EudraCT	EUCTR2010-022046-25-NL
CCMO	NL33339.018.10