Does arginine enhance galactose oxidative capacity in classic galactosemia? A pilot study

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The objective of this study is to evaluate the possible effect of arginine on galactose oxidative capacity in 5 patients with classic galactosemia (homozygous for the p.Q188R mutation).

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

Summary

ID

NL-OMON47197

Source
ToetsingOnline

Brief title
The effect of arginine on classic galactosemia

Condition

- Metabolic and nutritional disorders congenital

Synonym
Galactose-1-Phosphate Uridylyltransferase deficiency, galactosemia

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: - Arginine, - Classic galactosemia, - GALT deficiency, - Therapy

Outcome measures

Primary outcome

The main study parameter is galactose oxidative capacity before and after

arginine supplementation.

Secondary outcome

Secondary outcome measures include erythrocyte GALT enzyme activity, galactose

plasma levels, Gal-1-P plasma levels, and galactitol levels in urine.

Study description

Background summary

Classic galactosemia is a rare inherited metabolic disease that presents in neonatal patients with a life-threatening multi-organ toxic syndrome. Although a galactose-restricted diet quickly relieves the initial severe illness, it fails to prevent long-term complications. Therefore, new therapies are required to improve patient outcome.
Misfolding is a common molecular basis for GALT deficiency in classic galactosemia, leading to protein aggregation. Chemical chaperones as arginine can provide protein stability, thus preventing aggregation and enhancing its residual activity. In a galactosemia bacterial model, arginine has shown to stabilize GALT variant proteins. Accordingly, this might be a promising therapeutic approach for classic galactosemia. As arginine is a well-known amino acid that is therapeutically widely used and has showed no side effects in previous studies, we propose to use it in a pilot study. We aim to evaluate the effects of arginine administration in a classic galactosemia patient in order to determine its possible role in the treatment of this disease.
Human fibroblasts will be cultured to gain further insights on galactose metabolism upon arginine exposure and its mechanism of action.

Study objective

The objective of this study is to evaluate the possible effect of arginine on galactose oxidative capacity in 5 patients with classic galactosemia

(homozygous for the p.Q188R mutation).

Study design

Intervention study with pre-post design, single arm

Intervention

All participants will receive arginine in the form of arginine aspartate (Asparten ®) during 30 ± 5 days, by oral administration (3x/day).

Study burden and risks

The immediate benefit of participation is that general knowledge of classic galactosemia will be extended. If a positive effect of arginine is found, the benefit for the next generation galactosemia patients might be very large, since this could be a first step in the development of a new therapeutic strategy in classic galactosemia. If a new therapy could prevent long-term complication, this would have a large effect on patient's quality of life. However, there is no direct benefit for the participants; no relief of symptoms is expected. Inevitably, side effects might occur, but this chance is estimated to be very small. Participation brings the burden of taking medication 3 times a day during 30 ± 5 days and 2 visits to the clinic where a venapunction and a galactose oxidative capacity will be accomplished. A skin bipsy will be performed once, at the outpatient clinic that patients normally visit. This will limit the burden of participation. Overall we think the potential benefit for the classic galactosemia community outweighs the limited risks and the small burden of the study.

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

- Patient with classic galactosemia, homozygous for the p.Q188R mutation, diagnosed by GALT enzyme activity assay and GALT gene mutation analysis
- Eighteen years of age or older
- Capable of giving informed consent

Exclusion criteria

- Urea cycle disorders (assessed by post prandial amino acid profile in blood)
- Increased level of plasma uric acid

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):	05-12-2017
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Asparten
Generic name:	Arginine Aspartate

Ethics review

Approved WMO Date:	04-08-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	12-10-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	11-01-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2014-002674-36-NL
CCMO	NL49929.068.17