The effect of phenylalanine supplementation on metabolic control in Tyrosinemia Type 1 patients.

Published: 08-12-2016
Last updated: 17-04-2024

The primary objective of this study is to investigate the effect of different levels of oral phenylalanine supplementation on the blood concentration and diurnal variation of phenylalanine and tyrosine in HT1 patients treated with NTBC. This in...

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

Summary

ID

NL-OMON43703

Source
ToetsingOnline

Brief title
Phenylalanine supplementation in Tyrosinemia type 1

Condition

- Metabolic and nutritional disorders congenital
- Protein and amino acid metabolism disorders NEC

Synonym
Hereditary Tyrosinemia Type 1, Metabolic Disease

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Phenylalanine, supplementation, Tyrosinemia Type 1

Outcome measures

Primary outcome

The primary study parameters are phenylalanine and tyrosine concentrations. Their day to day variation (at specific time points) and variation throughout the day will be analysed. Next to this, mean phenylalanine and tyrosine concentrations with and without supplementation of phenylalanine will be analysed.

Secondary outcome

The secondary outcome parameters are NTBC and succinylacetone concentrations. If doses of NTBC are high enough, it is hypothesized that the tyrosine degradation pathway is completely blocked. Thus, the metabolic product succinylacetone will not be formed. However, in regular patientcare increased succinylacetone concentrations are sometimes found. Thus, the question is whether NTBC concentrations are high enough during the complete day. Therefore, the variation of NTBC and the occurence of increased succinylacetone concentrations will be analysed.

Study description

Background summary

Hereditary Tyrosinemia Type 1 (HT1) patients usually present with liver dysfunction and or renal tubular dysfunction with rickets early in life. After the introduction of 2-(2-nitro-4-trifluoro-methylbenzoyl)-1,3-cyclohexanedione (NTBC), problems resolved and life expectancy greatly increased. However, due

to NTBC, which blocks the conversion of tyrosine at an earlier step, tyrosine concentrations increase, making dietary restrictment of tyrosine and its precursor phenylalanine necessary. Recently, some articles report low phenylalanine concentrations in HT1, making phenylalanine supplementation necessary despite possible conversion to tyrosine and resulting increase in tyrosine. Next to that, previous research of us showed a strong diurnal variation of phenylalanine, with extremely low phenylalanine concentrations early in the afternoon. These strong diurnal variation and increase in tyrosine concentrations make more studies on the optimal dose of phenylalanine supplementation necessary.

Study objective

The primary objective of this study is to investigate the effect of different levels of oral phenylalanine supplementation on the blood concentration and diurnal variation of phenylalanine and tyrosine in HT1 patients treated with NTBC. This in order to find a particular dose of phenylalanine in which low phenylalanine as well as high tyrosine concentrations are prevented. In addition to this, NTBC and succinylacetone concentrations are measured in the bloodspots to ensure complete blockade of the tyrosine degradation pathway. Therefore, as secondary objective, blood concentrations and diurnal variation of NTBC and succinylacetone will be investigated.

Study design

This longitudinal study will include two rounds of nutritional supplementation of phenylalanine and has a total length of 24 days. The duration of both rounds of phenylalanine supplementation will be five days and during these days most bloodspot measurements will be done.
The study is open, not placebo controlled and is completely done at home. The study is the follow-up of the study with reference number 2010/061 that measured the day to day and daily fluctuation of the same variables without supplementation of phenylalanine.

Study burden and risks

Patients will be treated with 2 different amounts of phenylalanine supplementation. Phenylalanine supplementation is used in HT1 patients before, without any side effects. Due to possible conversion of phenylalanine into tyrosine, tyrosine concentrations can increase. However, only small amounts of phenylalanine are given. The participating HT1 patients will perform 2 rounds of 13 bloodspots (taken by finger prick). The total duration of the study is 24 days. No extra site visits are necessary. These patients are used to do bloodspots at home. Therefore, no physical and physiological discomfort is expected.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1 Hanzeplein 1
Groningen 9700 RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1 Hanzeplein 1
Groningen 9700 RB
NL

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

Diagnosed with Hereditary Tyrosinemia type 1
Treated with NTBC
Adequate dietary control (tyrosine concentrations: 200-600 µmol/L)

Exclusion criteria

Tyrosinemia type 1 patients with intercurrent infections
Tyrosinemia type 1 patients who received liver transplantation

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-02-2017
Enrollment:	6
Type:	Actual

Ethics review

Approved WMO

Date:	08-12-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL55410.042.16