Effects of short term increase of phenylalanine levels on neuropsychological functions and well-being in adults with phenylketonuria: the *diet for life* study

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To evaluate the effects of short term supplementation of Phe to levels comparable to levels observed in adult patients who fully discontinued their diet on neuropsychological functions and wellbeing of adult patients with PKU.

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

Summary

ID

NL-OMON30968

Source
ToetsingOnline

Brief title
the "Diet for Life" study

Condition

- Metabolic and nutritional disorders congenital
- Inborn errors of metabolism

Synonym
phenylketonuria, PKU

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,SHS international,SHS international (onderdeel van Nutricia/SHS)

Intervention

Keyword: diet, neuropsychological functions, phenylketonuria, wellbeing

Outcome measures

Primary outcome

What is the neuropsychological deficit profile of adults with treated PKU?

Does supplementation of Phe to plasma levels comparable to levels observed in

adult patients who fully discontinued their diet, influence neurocognitive

functioning or wellbeing?

Secondary outcome

Which neurophysiological mechanisms are responsible for neuropsychological

dysfunction in adults with treated PKU? Can network disruption be demonstrated?

Does supplementation of Phe to plasma levels comparable to levels observed in

adult patients who fully discontinued their diet influence network disruption?

This part of the study will be conducted by the department of neurology in the

VUMC. This study will be submitted to the MEC of the VUMC.

Study description

Background summary

Phenylketonuria (PKU; MIM 261600) is an autosomal recessive disorder of phenylalanine (Phe) metabolism caused by a deficiency of the enzyme phenylalanine hydroxylase (PAH; EC 1.14.16.1). Untreated PKU results in severely retarded mental development and neurological abnormalities. Patients with PKU are treated with a Phe-restricted diet and supplementation of all amino acids except Phe. With the introduction of newborn screening and the early institution of the diet, mental retardation due to PKU has been nearly eliminated. At this moment, the most important issue in the treatment of PKU is whether the reduction of the Phe levels, by a strict and socially invalidating diet, is still relevant in adults. Relaxation of the diet in adolescence is common practice and dietary guidelines for adults vary greatly between the different countries.

Study objective

To evaluate the effects of short term supplementation of Phe to levels comparable to levels observed in adult patients who fully discontinued their diet on neuropsychological functions and wellbeing of adult patients with PKU.

Study design

We aim to perform a double blind study with crossover design with repeated measures.

Intervention

During two periods of four weeks each, an additional supplement of aminoacids will be added to the diets of the subjects. During one of the 4 weeks periods the supplement will not contain any Phe or its metabolite tyrosine, but different aminoacids. The other 4 weeks period the supplement will contain the amount of Phe that, added to the Phe intake from the patients* own diet, increases the daily Phe intake to a normal Phe intake for a healthy person of that age and sex. Between the two study periods there will be a washout period of at least 4 weeks in which the patients take their own usual diet.

Study burden and risks

Patients will visit the AMC and/or the VUMC 4 times during the study. They will undergo neuropsychological tests (4x), a MEG scan (2x), dietary evaluation (3x) and send in bloodspots (20x) for Phe measurements. They will complete a questionnaire to evaluate wellbeing 8 times. For 2 periods of 4 weeks each

they will add an extra aminoacid supplement to their own supplement that they take 3 times per day every day.
During a total of 4 weeks patients will have elevated phenylalanine levels. In the literature a reversible decrease of neuropsychological functions has been reported with high phenylalanine levels. In other countries, where the diet is discontinued in adulthood, no problems have been reported. Because in many countries the diet is relaxed in adulthood without evaluation of the possible consequences, it is very important for the safety of the patients to evaluate the effect of high phenylalnine levels on the functioning and the well being of the patients. If no effects are found, a relaxation of the diet in adulthood may be considered. If effects are detected it will be clear to the patients why a strict diet will be necessary.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam
Nederland
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients with PKU aged 18 and older who have been detected by newborn screening and have been continuously treated with a protein restricted diet and supplementation of aminoacids.

Exclusion criteria

Poor dietary adherence with a mean phe value above 1100 umol/l in the year prior to the start of the study
Pregnancy or the wish to conceive within 3 months after the end of the study

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2008
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL19477.018.07