The phenylalanine eat or diet study: direct effects of high or low phenylalanine values on cognitive functioning in adults with PKU.

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Primary objective: To accurately assess the direct functional consequences of high versus low phenylalanine levels in adult patients with PKU, using eye-hand coordination testing in tasks of different cognitive complexity. Secondary objective: To…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Inborn errors of metabolism
Study type	Interventional

Summary

ID

NL-OMON46442

Source
ToetsingOnline

Brief title
The Phe eat or diet study

Condition

- Inborn errors of metabolism

Synonym
Phenylketonuria, PKU

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC

Source(s) of monetary or material Support: Nutricia,Stichting Coolsingel en Nutricia Metabolics Research Fund.

Intervention

Keyword: Adult, Cognitive function, Dieet, Phenylketonuria

Outcome measures

Primary outcome

- Eye Latency.

This is obtained via eye-hand coordination tasks of different cognitive

complexity on a touch screen. Patients will perform eye hand coordination tasks

on 7 occasions: at baseline, at the beginning of each intervention period and

after 2 and 4 weeks during the intervention periods.

Secondary outcome

Obtained with eye-hand coordination tasks

- Task performance

- Saccadic Error

- Correction Latency

- Hand Latency

- Hand Error

Obtained via quality of life questionnaires:

Scores of the different domains of the:

- generic SF-36 questionnaire

- the HADS questionnaire

- the disease specific PKU-Qol questionnaire

Study description

Background summary

Children with phenylketonuria (PKU) adhere to a strict protein-restricted diet from birth. This diet results in acceptable phenylalanine (Phe) levels (<360 µmol/l) and prevents brain damage and overt cognitive impairment. However in adults the necessity of dietary adherence is a topic of debate. Guidelines on dietary adherence in adulthood differ immensely. This is due to a lack of evidence about the effect of dietary adherence on cognitive function in adults with PKU. This lack of evidence is present because there is a lack of objective practical methods to investigate cognitive function.
Recently, the department of neuroscience of the Erasmus MC validated a method for the objective and quantitative assessment of visuomotor functioning using eye-hand coordination tasks. These tests are accurate, take only 30 minutes to perform and, in healthy subjects, show a high test*retest reliability. As visuomotor skills are good predictor of motor development and cognitive functioning the eye-hand coordination tasks are the ideal tests to investigate cognitive function in phenylketonuria. We hypothesise that adult patients with PKU will perform worse on eye-hand coordination tasks if Phe levels are high, and that the effect of high Phe is transient.

Study objective

Primary objective: To accurately assess the direct functional consequences of high versus low phenylalanine levels in adult patients with PKU, using eye-hand coordination testing in tasks of different cognitive complexity.
Secondary objective: To asses quality of life with the disease specific PKU-QoL questionnaire, the generic 36-item Short Form Survey (SF-36) questionnaire and the Hospital Anxiety and Depression Scale (HADS) during high versus low phenylalanine levels in adult patients with PKU.

Study design

A randomized double-blinded placebo controlled cross-over trail.

Intervention

All included patients will be asked to follow a strict protein restricted diet, aiming at Phe levels of < 360 µmol/l (with supplementation of essential amino acids) during the whole study period of 14 weeks, starting 2 weeks before the first intervention period. Patients will be randomly assigned to one of two groups. During the first intervention period of 4 weeks group 1 will start taking Phe-containing capsules (0,8 times their bodyweight in kilograms times 49 mg of Phe. Rounded to multiples of 500 mg.) which they will take daily.

Group 2 will take a placebo capsules. Thereafter there will be a wash-out period of 4 weeks, followed by a second intervention period. During the second periods the patients that took the Phe-capsules will take placebo and visa versa.

Study burden and risks

Patients will visit our outpatient clinic 7 times and we estimate each visit will take approximately 90 minutes. The first visit will take 1 hour extra for dietary advise. During each visit they will perform the eye-hand movement tasks, complete the QoL questionnaires and plasma will be drawn to determine Phe levels and urine will be collected. Furthermore, during the total study period of 14 weeks Phe levels will be measured twice a week in dried blood spots (resulting in a total number of 24 bloodspots). Patients can draw blood for the bloodspots at home, from the finger with a small lancet. The blood is blotted on filter paper can this paper can be given to the investigators during the next visit. The patients know how to do this as they did this regularly throughout childhood.
During 14 weeks the patients will have to follow a stricter protein restricted diet than they usually do, aiming at a Phe level of <360 µmol/L. This is the level that is aimed at during childhood, so patients have experience with the strict diet. A dietician with experience in treating patients with PKU will make a personalised diet plan for each patient and the patients will be able to contact the dietician for advice throughout the study. Patients will be asked to fill in a diet diary.
Previous studies with Phe loading have shown there was a slight effect on mood and concentration in some patients, but that using Phe in large amounts for a short period of time did not have major side effects in adulthood.
The benefits of participating in this study for the patient are that they get a good insight in if and how Phe levels effect their functioning. They can implement this knowledge into their daily life. Furthermore the results of this study will help to create clear guidelines about dietary adherence in adult patients with ET-PKU.

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

- > 18 years of age
- Pre-treatment Phenylalanine level as a neonate of > 600 µmol/l
- The patient was diagnosed with PKU via newborn screening and immediately treated with a protein restricted diet, throughout childhood

Exclusion criteria

- Incapacity to comprehend the Dutch language or test instructions
- Neurological pathologies
- Unwillingness to remove eye make up
- Ocular pathologies/ visual impairment
- Other severe chronic comorbidities including psychiatric conditions that may impair visuo-motor function
- Constraint in motor control of the dominant hand and arm
- In women: pregnancy or the wish to get pregnant in the near future
- In women: The unwillingness to take adequate birth control measures

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-01-2019
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	29-05-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL63107.078.18