An exploratory matched case-control study to measure blood nutrient levels of adult PKU patients on a protein substitute.

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The study*s main objective is to measure blood micro- and macronutrient and amino acid levels in adults with PKU on a protein substitute and compare with age- and sex-matched non-PKU comparison subjects.

Ethical review	Approved WMO
Status	Completed
Health condition type	Inborn errors of metabolism
Study type	Observational invasive

Summary

ID

NL-OMON50188

Source
ToetsingOnline

Brief title
SNAP: Study Nutrients in Adult PKU

Condition

- Inborn errors of metabolism

Synonym
Phenylketonuria / PKU

Research involving
Human

Sponsors and support

Primary sponsor: Nutricia Research

Source(s) of monetary or material Support: Nutricia Research BV

Intervention

Keyword: Phenylketonuria

Outcome measures

Primary outcome

The main outcome parameter in this study is the blood nutritional status.

Secondary outcome

The other outcome parameters in this study are:

• Phe/Tyr Ratio [µmol/L]

• Nutrient intake three-day diet diary will be recorded by the subjects on

three consecutive days (2 weekdays and 1 day in the weekend), including product

or supplement use (see Table 2). Nutrient intake will be calculated at a local

level (e.g. dietician at site) using validated software packages.

• Electronic questionnaire to assess subjective cognitive wellbeing

(FACT-Cognitive Function (Version 3))

Study description

Background summary

Phenylketonuria (PKU) is an inherited metabolic disorder, where subjects are born with a genetic deficiency of the hepatic-based enzyme phenylalanine hydroxylase (PAH) which results in a complete or partial inability to convert phenylalanine (Phe) into Tyrosine (Tyr). The incidence of PKU varies worldwide for instance between 1:4000-1:9000 in Turkey, Ireland and Eastern Europe to 1:100,000-1:200,000 in Finland, Japan and Thailand. Due to the genetic deficit, Phe accumulates in the blood, and there is a shortage of Tyr and its metabolites. Left untreated, PKU leads to severe mental retardation and neurological disabilities.
Dietary management of PKU

The main treatment in PKU consists of dietary restriction of Phe often with Tyr supplementation. Such a diet is strict, and involves limited intake of natural sources of protein, including but not limited to meat, fish, seafood, dairy, eggs, nuts and grains. Unsurprisingly, the restrictive nature of the PKU diet limits dietary intake of several important macronutrients and micronutrients, resulting in it being naturally poor in e.g.: proteins (and associated essential amino acids), essential fatty acids (i.e. EPA and DHA), vitamins and minerals, in particular vitamins D, B6, & B12 as well as selenium, iron, calcium and zinc.
Nutritional status in PKU subjects
Early diet-treated PKU subjects have reported lower status in several essential nutrients and micronutrients, increased body mass index (BMI), altered folate metabolism, plasma lipid peroxidation and other oxidative stresses. Although much research has been done on the nutritional status in PKU, the adult population is still largely understudied. This is partly because most screening procedures were introduced in the 70s and 80s; hence, the *first* groups of early-diagnosed PKU subjects enter now their mid adulthood. Studying adults with PKU comes with various challenges adding to the heterogeneity of this population, e.g. treatment guidelines varied (and still vary) per country and adherence to the PKU diet and supplementation regimen is one of the key challenges in adolescence and adulthood. The latter can be a real threat to the current apparent marginal status of nutrients in PKU as prior studies have indicated that nutrient levels might be dependent on dietary compliance to individualized PKU diet and amino acid supplementation regimens. For instance, most, although not all studies comparing PKU plasma levels of vitamins B6 and/or B12 to reference normal plasma values report endogenous levels in PKU patients trending towards the lower end of this range. These studies generally demonstrate an inverse correlation between plasma Phe levels and plasma B6 and/or B12 levels, suggestive for dietary compliance influences. However, even in cases of adequate dietary compliance to their prescribed diet and amino-acid regimen, lower levels of DHA have been reported.

Study objective

The study*s main objective is to measure blood micro- and macronutrient and amino acid levels in adults with PKU on a protein substitute and compare with age- and sex-matched non-PKU comparison subjects.

Study design

An exploratory matched case-control, multicenter, multi-country study

Intervention

Not applicable

Study burden and risks

Participants are asked to complete an online questionnaire once and to complete a 3-day diet diary. They will need to come to the site once for a study visit where blood will be drawn via venipuncture. The participants will have to be come to site in fasted state and should not exercise intensively for 24 hours before blood sample collection.

The participants do not directly benefit from this study.
There are no risks other than those associated with venipuncture. All other determinations are non-invasive (dietary assessments, questionnaires, anthropometric measurements).

The burden is limited as part of the assessments can be performed at home. One visit is required for the blood sample collection.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Inclusion criteria

1. Age >=18 years
2. Written informed consent
3. Same age- (±3 years) and sex as an included PKU subject

Exclusion criteria

1. For women: Currently pregnant or lactating
2. Current psychiatric disorders
3. Current Substance Use Disorders (as described in DSM V)
4. Current use of psychotropic and/or inotropic medication (exclusion due to inotropic medication use only if main goal or prescription is to alter the contractability of the heart) six weeks prior to V1.
5. Omega-3, antioxidant, (multi)vitamin (other than vitamin D) and/or (multi)mineral supplement use within six weeks prior to entry in the study (for NCRU: prior to V1). Vitamin D supplementation is allowed
6. Severe hepatic, thyroid or renal dysfunction
7. No acute illnesses like flu, diarrhea, or vomiting (subjects should be symptom free for a week prior to V1)
8. Participation in any other clinical intervention studies involving test products concomitantly or within six weeks prior to entry into the study. (for NCRU: prior to V1).
9. Other family members taking part in this study
10. Any condition (e.g. celiac disease, anorexia, bulimia, gastrointestinal tract disorders) or special diet (e.g. vegan or vegetarian diet, professional athletes, people actively aiming to lose weight) that effects the metabolism and/or normal dietary pattern/intake
11. A first or second degree relative with inborn errors of metabolism
12. Living together with someone with inborn errors of metabolism (e.g. partner, spouse or roommate).
13. NCRU specific: Employees of Nutricia Research and/or partners, parents, children and brothers/sisters of employees

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-01-2022
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	07-01-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
ClinicalTrials.gov	NCT03858101

Register	ID
CCMO	NL78867.056.21

Study results

Date completed:	18-01-2023
Results posted:	25-03-2024

First publication
08-03-2024