Effectiveness of methylphenidate in adults with phenylketonuria and attention-deficit/hyperactivity disorder: An N-of-1 series

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We hypothesize that methylphenidate improves ADHD manifestations in adults with (late-diagnosed) PKU.

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24320

Bron
NTR

Verkorte titel
MPH4PKU

Aandoening

Phenylketonuria; ADHD

Ondersteuning

Primaire sponsor: Amsterdam UMC / Amsterdam Public Health (Personalized Medicine)
Overige ondersteuning: Amsterdam Public Health - Personalized Medicine, Amsterdam UMC, 's Heeren Loo

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary outcome measure is Goal Attainment Scaling.

Toelichting onderzoek

Achtergrond van het onderzoek

Phenylketonuria (PKU) is the most common inborn error of amino acid metabolism. In patients who have not been diagnosed by newborn screening, so called ‘late-diagnosed’ patients, symptoms include severe neurodevelopmental disorders including intellectual disabilities and attention-deficit/hyperactivity disorder (ADHD). It is hypothesized that ADHD symptoms in late-diagnosed PKU patients typically present as behavioral problems. These may be caused by low levels of prefrontal dopamine, as a result of impaired monoamine synthesis. Targeting the dopamine imbalance may improve ADHD symptoms and even a broader domain of functioning in late or untreated PKU. Currently, behavioral problems in PKU are mainly treated with antipsychotic drugs that may induce or aggravate parkinsonian features. Methylphenidate (MPH), a dopamine reuptake inhibitor, may be beneficial in treating ADHD symptoms and behavioral problems in PKU by raising brain dopamine availability. The goal of the project is to investigate the effectiveness of methylphenidate for ADHD symptoms in late-diagnosed PKU.

The N-of-1 study is a series of double-blind randomized and placebo-controlled multiple cross-over trials within five participants with a minimum age of 18 years old who are diagnosed with PKU as well as ADHD. Each N-of-1 trial consists of a baseline period, a dose titration phase, three cycles of alternating two 7-day intervention periods each followed by a 7-day washout period, and a follow-up measurement. During the intervention periods, participants will receive twice daily methylphenidate (doses based on age and body weight) or placebo. The primary outcome measure includes the personalized ‘Goal Attainment Scaling’(GAS). Secondary outcome measures are the Strengths and Difficulties Questionnaire (SDQ) (subscale hyperactivity/inattention), the shortened version of the Emotion Dysregulation Inventory (EDI) reactivity index, the personal questionnaire (PQ), and adverse effects.

Doel van het onderzoek

We hypothesize that methylphenidate improves ADHD manifestations in adults with (late-diagnosed) PKU.

Onderzoeksopzet

At the end of each seven-day interventional period, primary caregivers will be contacted to

evaluate GAS scores (primary outcome measure), to go through the personal questionnaire (PQ), to discuss any change in diet, and to discuss possible side effects by using a standardized checklist of side effects of methylphenidate. Also, a dried blood spot will be conducted at the end of each interventional period. The other secondary outcome measures (SDQ and EDI) will be measured at the end of each period (weekly). Both questionnaires will be filled out digitally by primary caregivers using the app m-Path, Castor Electronic Data Capture (EDC) or by using paper forms. Three and six months after terminating the third cycle of the N-of-1 trial, an optional contact moment will take place for follow-up measurements in which the questionnaires will be filled out and the goals and items of GAS and PQ will be discussed again.

Onderzoeksproduct en/of interventie

Participants will receive twice daily methylphenidate or placebo.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Minimum age of 18 years.
- On or off Phe-restricted diet.
- A definite diagnosis of classical PKU according to well-established guidelines.
- Meet DSM-5 criteria for ADHD and diagnosed with ADHD by an expert multidisciplinary team

consisting of an ID physician, a psychologist, and a psychiatrist.
- Suffering from ADHD symptoms for which a dietary intervention would not suffice to improve behavioural problems.
- Presence of a patient’s caregiver for proxy-reports.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Unable to take and/or send in dried blood spots.
- Unable to obtain informed consent from legal representative.
- Presence of ADHD in first- and second-degree relatives.
- Presence of a contra-indication for treatment with methylphenidate (e.g. cardiovascular disease).
- Planned surgery and/or general anaesthesia during the trial.
- Pregnancy.
- Breastfeeding (females).
- During treatment with non-selective, irreversible monoamine oxidase (MAO) inhibitors, or within a minimum of one month of discontinuing those drugs.
- Current treatment with acetazolamide, thiazide-diuretic and sodium bicarbonate, or sympathicomimetics.
- Current substance or alcohol abuse.
- Unable to swallow tablets / capsules.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	N.v.t. / één studie arm
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-09-2021
Aantal proefpersonen:	5

Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Toelichting
N/A

Ethische beoordeling

Positief advies

Datum:	01-07-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9585
Ander register	METC AMC : METC2021_081

Resultaten

Samenvatting resultaten
N/A