BH4 treatment in Phenylketonuria - comparing different practices of dosing

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25048

Source
NTR

Brief title
BH4 dose

Health condition

Phenylketonuria (PKU)

Sponsors and support

Primary sponsor: University Medical Center Groningen
Source(s) of monetary or material Support: Grant application - BioMarin Pharmaceuticals

Intervention

Outcome measures

Primary outcome

The primary outcome of the study is the comparison of Phe levels between the three treatment regimen. The mean, mean standard deviations (SD) and mean coefficient of variation (CV) of the blood phenylalanine concentrations measured 6 times a day of 2 consecutive days, will be compared for 3 different dosage regimen.

Secondary outcome

- The mean SD and CV of the blood tyrosine concentrations measured 6 times a day of 2 consecutive days, compared for 3 different dosage regimen.
- The mean SD and CV of the blood phenylalanine/tyrosine ratio measured 6 times a day of 2 consecutive days, compared for 3 different dosage regimen.
- Time of highest and lowest Phe level during the day
- (When feasible: the kinetics of dried blood spot pterin concentrations).

Study description

Background summary

Rationale: A subset of patients with phenylketonuria (PKU) is treated with tetrahydrobiopterin (BH4). It is unclear if the timing and dose distribution impact metabolic control.
Objective: To compare diurnal Phe and Tyr variation in PKU patients on three different BH4 dosing regimens.
Study design: 3 way cross-over study
Study population: PKU patients treated with BH4
Intervention (if applicable): Each patient receives BH4 either 1) once daily in the morning, 2) once daily in the evening, or 3) twice daily. The total dose BH4 per day is the same in all three regimes. The sequence is randomized.
Main study parameters/endpoints: blood Phe variation, blood Tyr variation, blood Phe:Tyr ratio variation
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: There is no anticipated risk. The burden could be that patients have to measure blood spots more frequently and that patients are used to take the BH4 once daily and they need to remember they have to switch some time from their usual habits.

Study objective

Timing and dosing of BH4 potentially impacts Phe and Tyr variation in PKU patients treated with BH4 and thus potentially impacts outcome.

Study design

Each period will take one week. Consequently, the total study will take 3 weeks.
Participants will start with the allocated BH4 regime at day 1. Day 6 and 7 are the last days of the regime in which patients will collect 6 blood samples per day. As the terminal elimination phase of BH4 is 10 to 33h (4), the time between start of treatment and sampling days are considered to be sufficient for the body to adapt to the new regime. To evaluate this turnover of BH4, participants are asked to take additional morning samples (fasting) at day 3, 4 and 5.

Time schedule of blood sampling:

before breakfast (fasting sample)
in the morning (2 hours after breakfast)
before lunch
in the afternoon (2 hours after lunch)
before the diner
in the evening (2 hours after diner)

Intervention

The study design is a three-way cross-over study in which three different dosing-regimens will be compared. The study exists of the following three periods:
- Taking BH4 once a day in the morning during breakfast
- Taking BH4 once a day in the evening during dinner
- Taking BH4 twice a day, during breakfast (1/2 dose) and during dinner (1/2 dose)
The sequence of these three periods will be randomized using a computer program.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Diagnosed with phenylketonuria by newborn screening.
2. Diagnosed as a BH4-responder after a 48-h BH4 loading test and a treatment trial
3. Currently uses sapropterin as part of treatment (with a minimum of three months)
4. Age ≥ 4 years
5. Good metabolic control for the previous 6 months, meaning 75% of the Phe levels are within therapeutic target levels with a minimum of four values.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
Pregnancy, planning pregnancy or lactation

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2021
Enrollment:	28
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL9613
Other	METC UMCG : not submitted yet

Study results