Pilot study on Ketosis Impact on Signs and Symptoms of Schizophrenia and Bipolar Disorders

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The current pilot study intends to establish the effect of a single dose of dGK on relevant (neuro-)electrophysiological (primary outcome: Pre-Pulse Inhibition (PPI); furthermore on resting EEG, on the ERP P300, cognitive, metabolic, inflammatory,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56800

Source
ToetsingOnline

Brief title
KISSeS

Condition

- Other condition
- Schizophrenia and other psychotic disorders

Synonym
schizophrenia psychotic disorder / bipolar disorder

Health condition

bipolaire stoornissen

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Administration, Bipolar disorder, Ketone Bodies, Olanzapine, oral, Schizophrenia

Outcome measures

Primary outcome

The primary outcome measure is percent change between intervention (dGK ingestion) vs control (isocaloric gold standard drink) in PPI.

Secondary outcome

Secondary outcome measures include percent change between intervention and control drink: in basal EEG, P300 ERP, cognitive test scores;
patient-experienced improvement in energy level, mood, ability to focus (visual analogue scale); metabolic and immune parameters (blood, sweat and saliva biomarkers; indirect calorimetry).

Study description

Background summary

Cumulative evidence points towards a shared disease mechanism underlying schizophrenia spectrum and bipolar disorders (SSD/BD): a dysfunction in energy homeostasis in the brain1,2. The bioenergetic dysfunction-hypothesis provides a comprehensive disease model for both disorders, highlighting the role of multi-level glucose metabolism problems in the brain. Importantly, this is hypothesized as a causative mechanism, instead of an associational one. Therefore, therapeutically restoring energy homeostasis in SSD/BD could be of immense clinical value. While fully glucose-dependent under normal feeding conditions, the brain switches to metabolizing ketones derived from fatty acid oxidation in the liver during fasting/starvation. The ketogenic diet (KD) induces ketosis by greatly restricting carbohydrate intake. Indeed, small

recent studies suggest the KD is effective in treating core SSD/BD symptoms3-6. However, the KD*s restrictive nature hinders its adherence and applicability. We propose that using a well-researched ketone drink can replace the KD, restore brain energy homeostasis, and improve SSD/BD symptoms. This double-blind, controlled crossover pilot study aims to investigate both clinical and mechanistic effects of exogenous ketones in SSD/BD.

Study objective

The current pilot study intends to establish the effect of a single dose of dGK on relevant (neuro-)electrophysiological (primary outcome: Pre-Pulse Inhibition (PPI); furthermore on resting EEG, on the ERP P300, cognitive, metabolic, inflammatory, and patient-experience outcome measures (secondary).

Study design

Aggregated n=1 design: Randomised, double-blind controlled 2-way cross-over study.

Intervention

Oral intake of nutritional drink (50 g dGK versus isocaloric carbohydrate drink). Patients (n=24) will follow a crossover trial, and be randomised in a double-blind fashion to either intervention first (1x50g dGK) or gold standard first (1x50g isocaloric carbohydrate drink). After a 72-hour washout period, patients will crossover to the other condition.

Study burden and risks

At baseline, height, weight, waist circumference will be measured, and clinical measures taken to determine psychiatric symptom severity (Positive and Negative Syndrome Scale; PANSS or Young Mania Rating Scale, YMRS; or Inventory of Depressive Symptomatology - Clinician, IDS-C duration 10 to 45 minutes). On test days, a nutritional drink will be administered (50g dGK or isocaloric carbohydrate drink). The drinks can be considered unpalatable, which will be counteracted by offering sparkling water after nutritional drink ingestion. The safety of dGK is well established, and side effects are infrequent and very mild8-12. An EEG and EMG of the eye muscle (both non-invasive) will be administered using an electrode cap following standard operating procedures (burden to patients consists mainly of not being able to freely move around during EEG measurements, total duration maximum 3 hours on test days). Cognitive tests will be administered on test days (max. 30 minutes). An iv-line will be offered to patients (opt-out possible): single venapuncture on test days, max. 123 ml of blood sampled. Indirect calorimetry will be done on test days: while non-invasive the gas-exchange canopy placed over the head of patients may by some be experienced as claustrophobic. As such, patients can

choose to opt-out of this measurement and still participate in the rest of the study. For the 5-day trial duration, patients will wear a small, watch-sized non-invasive biosensor measuring biomarkers in passive sweat (attached using a skin-safe sticker; minimal to no patient burden), as well as a continuous glucose monitor (CGM: pain-free insertion in the subcutis of upper arm without discomfort). Patients will be asked to collect 3-5 saliva samples every day for 5 days, and to keep a diet and smoking diary, without changing their nutritional and nicotine intake.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients diagnosed with schizophrenia or bipolar disorder who are in at least partial remission receiving standard care
able to give informed consent

age 18 - 65 years old

Exclusion criteria

Acute/florid psychosis, acute mania (unremitted)
inability to give (informed) consent
age < 18 or > 65 years old.
liver function disorder
kidney function disorder
cardiovascular disease
ketone body metabolism disorder
diabetes
pregnancy or lactating

Study design

Design

Study type: Interventional

Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-12-2024
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	30-05-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO Date:	08-10-2024
Application type:	Amendment
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	NL83836.018.23