Effect of 4 weeks of oral 6-bromotryptophan on safety, pharmacokinetics and efficacy in metabolic syndrome individuals (BROMO trial)

Published: 27-02-2023
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To assess safety, pharmacokinetics and efficacy of oral dosage of 6-BT in individuals with metabolic syndrome

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON53935

Source
ToetsingOnline

Brief title
BROMO trial

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes, Diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: 6-bromotryptophan, Glucose homeostasis, Metabolic syndrome

Outcome measures

Primary outcome

The principal outcome will be patient safety and tolerability (biochemical parameters of kidney and liver function and complete blood count, adverse events) in relation to improvements in glucose homeostasis (mixed-meal tests and continuous glucose monitoring).

Secondary outcome

Secondary read-outs will include changes in: immunological profile (ex vivo stimulation of monocytes, and immunophenotyping of peripheral blood mononuclear cells (PBMC)) and gut microbiome composition (16s rRNA sequencing). Also, liver fat content will be determined before and at end of the trial by MRI. As this food derived metabolite is given to humans for the first time, we will also study its pharmacokinetics by measuring serum 6-BT concentrations in serum and urine at different time-points after oral intake.

Study description

Background summary

We identified a novel endogenous plasma microbiome-derived tryptophan metabolite, 6-bromotryptophan (6-BT), which was associated with preserved beta-cell function and diminished circulating T cell count in (T1D) type 1

diabetes patients. Anti-inflammatory and insulin-secratogogue effects were established in in vitro- and murine studies in both the setting of type 1 and type 2 diabetes. Also, 6-BT did not show any toxic effects in cells or in vivo experiments. In order to obtain safety data before we progress to an efficacy study in T1D, we aim to perform a phase I/II trial of 6-BT in metabolic syndrome individuals. If safe, 6-BT may hold a promise as a food supplement in type 1 and 2 diabetes.

Study objective

To assess safety, pharmacokinetics and efficacy of oral dosage of 6-BT in individuals with metabolic syndrome

Study design

A double blinded, phase I/II, dose finding, placebo controlled trial.

Intervention

Participants will be given placebo, 2mg, 4mg or 8mg of 6-BT capsules once daily for 4 weeks (n=9 per arm, total of 36 participants).

Study burden and risks

6-BT is a endogenous (food tryptophan derived) metabolite found in the human circulation. Our previous trail has shown that fecal microbiota transplantations (FMT) can modulate and increase plasma 6-BT levels with a positive association with C-peptide (as marker of pancreatic beta cells function). Additionally, recent investigations have linked higher plasma 6-BT levels with lower risk of kidney disease progression, supporting the health benefits of 6-BT beyond T1D.Also, previous human studies with bromo intake in healthy subjects in much higher dosages was (see protocol chapter k 5.4) and this 6BT food supplement was found to be safe and effective in mouse studies. In tota l subjects will spend 19h on this study, and 403 ml blood will be taken. Venapunction has a small risk of hematoma. MRI scan can be unpleasant but has no health risk just like collecting 24-hours urine and feces.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ

NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Metabolic syndrome AND/OR insulin resistance, defined as:
* Metabolic syndrome: >=3 criteria out of the 5 following criteria:
o fasting plasma glucose >=5.6*mmol/L
o triglycerides >=1.7*mmol/L
o waist circumference >=102*cm
o high-density lipoprotein cholesterol <=1.04*mmol/
o blood pressure >=130/85*mm Hg.
* Insulin resistance: HOMA-IR (>2.5)

• Male
• Caucasian
• 35-70 years old

Exclusion criteria

- Use of systemic medication (except for paracetamol), including proton pump inhibitors, antibiotics and pro-/prebiotics in the past three months or during the study period.
- A history of a cardiovascular event

- A history of cholecystectomy
- Overt untreated gastrointestinal disease or abnormal bowel habits
- Liver enzymes>2.5*fold higher than the upper limit of normal range
- Smoking
- Alcohol abuse
- Exclusion criterion for MRI liver (metal in body, claustrophobic etc.)

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-03-2023
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	27-02-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2023
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	NL83061.018.22