Personalized Glucose Optimisation through Nutritional Intervention

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To obtain insight into the metabolic and lifestyle determinants of postprandial blood glucose responses and to establish the effect of macronutrient manipulation of a 12-week dietary intervention on blood glucose homeostasis in metabolically…

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

Summary

ID

NL-OMON55478

Source
ToetsingOnline

Brief title
The PERSON-study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Lipid metabolism disorders

Synonym
adult-onset diabetes, obesity, overweight, Type 2 diabetes mellitus

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: DSM Food Specialties,FrieslandCampina ,Nutricia,Top Institute Food and Nutrition (TIFN);TKI Agri&Food

Intervention

Keyword: Glucose homeostasis, Insulin sensitivity, Metabolism, Personalized nutrition

Outcome measures

Primary outcome

The primary objective of this study is to establish the effect of a metabolically targeted, macronutrient manipulated 12-week dietary intervention on the change in disposition index (composite marker of first phase insulin secretion and insulin sensitivity) between optimal and suboptimal diet after participants follow an optimal or suboptimal diet for their phenotype (MIR or LIR).

Secondary outcome

As secondary outcomes, we aim to study the effect of 12-weeks of targeted macronutrient manipulation on change in:

1. Tissue-specific insulin sensitivity, glucose tolerance, 24-hour glucose values
2. Body composition and body fat distirbution
3. Circulating metabolites after a high fat mixed meal under fasting and postprandial (high fat mixed meal) conditions
4. Energy metabolism and substrate oxidation during a hyperinsulinemic-euglycemic clamp (2 steps)
5. Baseline blood lipid spectrum
6. Fecal microbiota composition
7. Oral microbiota composition

8. Targeted metabolomics (baseline and during the clamp)

9. Physical and mental performance and well-being.

10. Blood pressure

11. Gene and protein expression in skeletal muscle and adipose tissue.

12. Advanced glycation end-products (AGE) accumulation

13. Carotid artery reactivity

14. Fasting immune metabolism (PBMCs)

15. Outcomes 1-14 listed above in the optimal versus suboptimal diets within

the LIR and MIR groups

16. DNA analysis (buffy coat collection, pre-intervention only)

Study description

Background summary

A healthy lifestyle is an essential element to release the physical and mental potential of every individual and is able to prevent the epidemic development of overweight, and cardio- metabolic diseases. Unfortunately, most people do not manage to incorporate or maintain the recommended changes in their daily lifestyle. This may be due to the fact that people do not perceive the benefits of a healthy lifestyle in the short term, nor the adverse effects of an unhealthy lifestyle. It is increasingly recognized that maintaining well-controlled blood glucose concentrations is essential for remaining healthy and preventing chronic metabolic diseases. Additionally, there is evidence that well-controlled blood glucose concentrations - by boosting physical and mental energy - may be an important determinant of well-being, mental and physical performance. The link between blood glucose and the latter factors has hardly been studied. Moreover, it is not known to what extent these relationships differ in healthy participants and participants with an impaired glucose metabolism. When people feel better, fitter and/or otherwise motivated to follow a dietary advice, for example, by personalized feedback on physiological measures of glucose control or other indicators of health status, the implementation of a healthy lifestyle is expected to be more successful.

Furthermore, despite being compliant to lifestyle advice, the metabolic

flexibility to respond to dietary intervention may vary between individuals. Recent evidence indicates that insulin resistance and metabolic inflexibility may develop separately in different organs, representing different etiologies towards cardio-metabolic diseases. Interestingly, these tissue-specific sub-phenotypes may have a differential response to diet. In a recent ground-breaking study, it was shown that, despite high inter-individual variability in glycemic response, responses to individual meals in daily life could be more accurately predicted by means of an algorithm that included lifestyle factors (diet, physical activity) and microbial composition as compared to a prediction by common practice. The above data suggest that successful lifestyle interventions may require a more personalized approach. Therefore, we hypothesize that phenotype-based dietary intervention optimizes beneficial effects on blood glucose regulation, metabolic health and subsequently mental and physical performance and well-being.

Study objective

To obtain insight into the metabolic and lifestyle determinants of postprandial blood glucose responses and to establish the effect of macronutrient manipulation of a 12-week dietary intervention on blood glucose homeostasis in metabolically different groups and its relationship to physical and mental performance and well-being.

Study design

Two-center dietary intervention study with a double-blind, randomized, controlled parallel design. The metabolic phenotype will be blinded to the participants and researchers.

Intervention

During a period of 12 weeks, each group will receive either a diet optimal for MIR or a diet optimal for LIR with respect to disposition index as determinant of blood glucose homeostasis.

The optimal diet for MIR is a moderate fat content which is high in mono-unsaturated fatty acids (HMUFA) with a macronutrient breakdown of 38 E% from fat (20% MUFA, 10% PUFA, 8% SFA), 48 E% from CHO (35% complex), and 14 E% from protein (35-40% plant protein) (8). The optimal diet for LIR is low in fat, high in protein (LFHP) and increased fiber with a macronutrient breakdown of <28 E% from fat (10% MUFA, 10% PUFA, 8% SFA), 48 E% from CHO (35% complex), and 24 E% from protein (35-40% plant protein), and an additional supplement of 6-12g of soluble fiber per day. The dietary intervention will be supported by products from industrial partners (e.g. extra virgin olive oil, high protein-low fat products, high fiber supplements, etc.).

The dietary intervention will be employed using freely available commercial food products. In addition, some products (which will also be commercially available) will be provided by industrial partners and distributed at the university. To ensure that the main fat source for the HMUFA diet is MUFA, olive oil will be given to the participants. Additionally, a commercially available fiber supplement will be provided and low fat foods (cereals, legumes, pasta, etc.) will be advised to the participants receiving the LFHP diet. The metabolic phenotype will be blinded for the participants and researchers, thus it is unknown whether the provided diet is optimal or suboptimal.

Study burden and risks

The general interest of this study is to obtain insight into the metabolic and lifestyle determinants of postprandial blood glucose responses and to establish the effect of macronutrient manipulation of a 12-week dietary intervention on blood glucose homeostasis in metabolically different subgroups and its relationship to physical and mental performance and well-being. Participants may have personal health benefits if intervention effects are according to expectations. Following the study completion, all participants will have access to all results of the testing performed. These data can provide information about their health status and additional information about their metabolic phenotype, which may positively impact their health.

Participants can experience burdens such as time spent for the study. Participants will have to invest approximately 40 hours in the study, plus an additional 20 hours for the subgroup at UM. The dietary and healthy regimen they will follow can be considered a burden, but also an overall health benefit as both diets are considered healthy diets. Also the collection of fecal and urine samples can be experienced as a burden (collecting the samples storing them at home for up to 24 hours).

The MRI scan does not have any risks associated with it, however some patients can experience claustrophobia. The MRI is only six minutes in Maastricht, which is a significant reduction of a normal MRI scan time, therefore this effect is minimized. Although scanning time at WUR is longer (30 minutes), we will check beforehand whether participants ever experienced claustrophobia.

In addition, participants will undergo a DXA scan. Thereby, they will receive a total radiation dose of <20 µSv (calculated by Heleen Huyten-Erkens, Radiation Expert, Randwyck, Maastricht). The average dose of each person in the Netherlands is 2,5 mSv per year, therefore the dose of the radiation can be neglected (statement by Heleen Huyten-Erkens, Radiation Expert, Randwyck, Maastricht).

The placement of the CGM and ActivPAL, though quite non-obtrusive, can be considered a burden for the participants. The placing of each piece of

equipment will be done by experienced researchers and will be secured by well-practiced measures to minimize issues the participant may encounter. The calibration of the CGM may be considered a burden due to the fingerprick that is required four times a day by a glucose meter.

During the test days, blood will be collected via a venous catheter. Venipunctures can occasionally cause a local hematoma or bruise to occur. Some participants report pain during venipuncture. During visit 3, an adipose tissue biopsy will be taken. The adipose tissue biopsy might cause a local hematoma. The UM subgroup, visit 4, will require a skeletal muscle biopsy. After the muscle biopsy, some participants report pain, which is experienced as muscle pain. More often the muscle feels stiff for a couple of days after the biopsy. To minimize the risk for a hematoma, the area where the biopsy was taken will be compressed for approximately five minutes after placing the steristrips and a waterproof bandage. The place of incision will leave a small scar (~3 mm for adipose tissue biopsy and ~8 mm for skeletal muscle biopsy). During the hyperinsulinaemic-euglycemic clamp there is a small risk of hypo- or hyperglycemia. However, from our own extensive experience, these conditions do not occur very often and can be reversed immediately. A medical doctor is always available during the clamp. Concerning the other study procedures (OGTT and indirect calorimetry), there are no known risks and these measurements are routinely applied in human biology research. Standard operating procedures (SOPs) for each measurement are available on the UM Human Biology Department*s server.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Overweight/obese (BMI >= 25 kg/m2 < 40 kg/m2) Caucasian men and women (age: 40-75 years) who are predominantly muscle (MIR) or liver (LIR) insulin resistant will be included from the general population. Stable body weight for at least 3 months (+/-3 kg).

Exclusion criteria

- Pre-diagnosis of type 1 or type 2 diabetes mellitus
- Renal or hepatic malfunctioning (pre-diagnosis or determined based on ALAT, ASAT and creatinine values)
- Gastrointestinal diseases or abdominal surgery (allowed i.e.: appendectomy, cholecystectomy)
- Food allergies, intolerances and/or dietary restrictions interfering with the study (including special diets, vegetarians and eating disorders)
- Cardiovascular diseases (e.g. heart failure) or cancer (e.g. non-invasive skin cancer allowed)
- High blood pressure (untreated >160/100 mmHg, drug-regulated >140/90 mmHg)
- Diseases affecting glucose and/or lipid metabolism (e.g. pheochromocytoma, Cushing*s syndrome, acromegaly)
- Anemia defined as Hb men <8.5 and women <7.5 mmol/l
- Diseases with a life expectation shorter than 5 years
- Major mental disorders
- Drug treated thyroid diseases (well substituted hypothyroidism is allowed inclusion)
- Other physical/mental conditions that may interfere with study outcomes
- Medication known to interfere with study outcomes (e.g. PPAR-α or PPAR-γ agonists (fibrates), sulfonylureas, biguanides, α-glucosidase inhibitors, thiazolidinediones, repaglinide, nateglinide and insulin, chonic use of NSAIDs)
- Use of certain anticoagulants
- Use of antidepressants (stable use >= 3 months prior to and during study allowed)

- Use of statins (stable use >= 3 months prior to and during study allowed)
- Use of β-blockers (only for the extensive phenotyping participants)
- Chronic corticosteroids treatment (>7 consecutive days of treatment)
- Use of antibiotics within 3 months prior to the study
- Participation in a regular organized sports activities (>4 hours per week)
- Having a restricted dietary pattern interfering with the study diets
(e.g. vegan or Atkins diet)
- Plans to lose weight
- Abuse of alcohol (alcohol consumption >14 units/week) and/or drugs
- Not willing to limit alcohol consumption to 7 drinks per week
- Regular (including use of e-cigarettes)
- Use of strong vitamins or other dietary supplements expected to interfere
with the study outcomes
- Pregnant or lactating women, or women who are planning to become pregnant
- Inability to comply with the study diet
- Blood donation within the last 3 months
- Participation in possibly interfering studies within the last 3 months
- Inability to understand study information and/or communicate with staff
- Unwillingness to be randomized or sign informed consent
- Unwillingness to save data for 15 years.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-06-2018
Enrollment:	1056
Type:	Actual

Ethics review

Approved WMO Date:	18-04-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-08-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	20-12-2018
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL63768.068.17