Is the GLP-1 response to an oral glucose load increased in South Asians as compared to Western-Europeans?

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Studying the GLP-1 response to a 75 grams oraal glucose load in 10 ZA and 10 WE healthy lean males to see whether GLP-1 is involved in the pathogenesis of T2D in ZA. 1. To investigate whether young lean healthy SA males without a family history of...

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

Summary

ID

NL-OMON40806

Source
ToetsingOnline

Brief title
Does GLP-1 play a role in early type 2 diabetes in South-Asians

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
gut peptide GLP-1, sugar disease

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: eigen projectnummer;speaker's fees etc.

Intervention

Keyword: GLP-1, oral glucose tolerance test, South Asians, type 2 diabetes

Outcome measures

Primary outcome

- AUC GLP-1 in SA versus WE

- peak GLP-1 level in SA versus WE

- time to peak GLP-1 in SA versus WE

- iinsulin sensitivity by Matsuda-index in SA versus WE

Secondary outcome

- does peak GLP-1 in plasma precede the peak of plasma insulin?

- insulin sensitivity by Matsuda-index in SA versus WE

- is metabolic flexibility in SA impaired (switch from glucose to lipid

metabolism and vice versa)

Study description

Background summary

People of South-Asian (SA) descent, such as the Surinamese-Hindostani population in the Netherlands (especially the Hague) have a greater risk for type 2 diabetes (T2D) than people of Western-European (white) decent. In addition, T2D develops at younger age and lower BMI than in WE. Furthermore, the disease is accompanied by more and grave cardiovasculair complications in SA. The underlying cause for this increased risk is still not completely elucidated.
In a previous investigation we found that healthy lean young men of SA descent had higher GLP-1 levels following an oral glucose load as compared to matched WE.
GLP-1 is a hormone secreted by the gut that has positive influences on insulin secretion and insulin sensitivity and that delays gastric emptying and decreases appetite. As such it improves glucose metabolisme and induces weight loss. Therapies have been developed that increase plasma GLP-1 levels and by

that improve glucose levels and lead to some (average 3-4 kg) bodyweight loss.
In the above mentioned study (Metabolism 2014 Feb;63(2):226-32) we investigated healthy lean men with a positive family history for T2D. It might very well be possible however that because of that, the SA already had a little insulin resistance and that the increased GLP-1 levels were a compensatory response.
Hence we would now like to study young lean healthy men of SA and WE descent WITHOUT first degree relatives. If then, GLP-1 levels are still higher in SA it is plausible that GLP-1 plays a role in the pathogenesis of T2D in SA.
We will then proceed by investigating whether the increased levels are due to insulin resistance or incretin resistance (OGTT versus isoglycemic [to the OGTT], IVGTT) and the glucose-lowering effect of GLP-1 in SA. In addition, we will study the GLP-1 response in different age and different insulin resistant populations. Furthermore it is worth investigating whether or not GLP-1 suppletion is a worthwhile preventive strategy in SA.
Indeed, in mouse models exogenous GLP-1 also has beneficial effects on the endothelium. In addition, intracerbroventricular injection of GLP-1 in mice activated brown fat activity (BAT). BAT burns triglycerides and glucose and is importantly involved in energy homeostasis. Activating BAT is currently under investigation for the treatment and prevention of obesity and associated metabolic disorders.
Hence if, (shortage of) GLP-1 is involved in the pathogenesis of insulin resistance/T2D in SA we will certainly also investigate the effect of supplying GLP-1 in vascular function and BAT activation.

Study objective

Studying the GLP-1 response to a 75 grams oraal glucose load in 10 ZA and 10 WE healthy lean males to see whether GLP-1 is involved in the pathogenesis of T2D in ZA.

1. To investigate whether young lean healthy SA males without a family history of
T2D also have increased GLP-1 levels following an OGTT
2. To investigate whether the GLP-1 peak indeed precedes the start of the insulin
secretion
3. To investigate whether or not young lean healthy SA males without a family history of T2D already have impaired metabolic flexibility

Study design

non-randomised observational controlled study

Study burden and risks

Procedure:
Medical history and physical examination: bodyweight, length, waist circumference, fat mass by BIA.
Indirect calorimetry before and 30 min after ingestion of oral glucose solution
Intraveneus catheter for blood drawings during 75 grams OGTT of 210 minutes

time frame: 5 hours

Burden: overnight fast, blood drawing from intravenous catheter during study day.
Risks: none

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

- 10 Male healthy volunteers of South Asian descent and 10 male healthy volunteers of western- european descent, born in the Netherlands
- Age > 18 years and * 25 years
- BMI > 20 kg/m2 and < 25 kg/m2

Exclusion criteria

- A first degree (parent or sibling) relative with T2D
- Diabetes mellitus as defined by ADA criteria{2014 12 /id}
- Any significant chronic disease
- Renal, hepatic or endocrine disease
- Clinical cardiovascular disease, including complaints of angina pectoris or intermittend claudicatio
- Smoking
- Use of medication known to influence glucose and/or lipid metabolism
- Recent weight changes or attempts to loose weight (> 3 kg weight gain or loss, within the last 3 months)
- Difficulties to insert an intravenous catheter
- Recent blood donation (within the last 3 months)
- Recent participation in other research projects (within the last 3 months), participation in 2 or more projects in one year

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL
Recruitment status: Recruiting

Start date (anticipated):	12-06-2015
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	25-11-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL49651.058.14
Other	TC 2473