Visualizing beta cells in patients with (postprandial) hyperinsulinemic hypoglycemia after bariatric surgery

Published: 20-07-2015
Last updated: 07-02-2025

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

Summary

ID

NL-OMON44909

Source
ToetsingOnline

Brief title
Visualizing beta cells in post-bariatric hypoglycemia

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Gastrointestinal therapeutic procedures

Synonym
hyperinsulinemic hypoglycaemia; low blood glucose caused by excessive insulin

Research involving
Human

Sponsors and support

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

Intervention

Keyword: bariatric surgery, beta cells, hyperinsulinemische hypoglycaemie

Outcome measures

Primary outcome

The main parameter of the study is the quantitative assessment of pancreatic 68Ga-NODAGA-exendin-4 uptake in patients suffering from persisting HH after RYGB and matched controls.

Secondary outcome

Secondary endpoints are the GLP1 and GIP responses after the MMT, the pancreatic distribution of 68Ga-exendin-4 as assessed by experts from the nuclear medicine department and the correlation between pancreatic 68Ga-exendin-4 uptake and beta cell function.

Study description

Background summary

Hyperinsulinemic hypoglycemia (HH) is a rare complication that occurs 1 to 5 year after gastric bypass surgery. The underlying mechanism of this complication is not yet completely understood. Changes in hormone levels, such as GLP1, after RYGB, nesidioblastosis or an increase in the number of beta cells may be one of the underlying causes. However, several study results are conflicting and it is hypothesized that the patient population with HH after RYGB is heterogeneous and several underlying causes may be present. In order to differentiate between hyperfunction with normal B-cell mass and a general or localized increase in beta cell mass we aim to compare quantitative 68Ga-exendin-4 PET imaging of the pancreas between patients with and without HH after RYGB. Thereby, we aim to increase the insight in the underlying mechanism of HH after RYGB. If different underlying causes can be diagnosed, treatment for HH can be optimized for patients.

Study objective

The main objective is to examine if 68Ga-exendin tracer accumulation (i.e. beta cell mass) differs in patients with persisting HH after RYGB compared to matched patients without HH after RYGB.

The secondary objectives are:
- compare GLP1 and GIP responses after MMT in post-RYGB patients with and without HH
- determine the correlation between measured exendin accumulation and beta cell function and
- evaluate the distribution of 68Ga-exendin over the pancreas and compare between both groups

Study design

For recruiting control individuals, hypoglycemia is excluded using a 14-day continuous glucose monitoring. After recruitment of the participating individuals, all patients will undergo an enrollment check at Rijnstate hospital consisting of a medical interview and a physical examination performed by a qualified physician. Recent blood samples for standard laboratory checks (blood counts, electrolytes, liver enzymes, creatinine, inflammation parameters) will be analyzed. Another visit is needed for an mixed meal test and a glucose-dependent arginine-stimulation test to investigate meal responses and the beta-cell function. At the third visit, a PET/CT scan will be performed at the Radboudumc. 68Ga-NODAGA-exendin-4 will be administered to all patients and the PET/CT scan will be performed 1 hour after injection of the radiopharmaceutical.

Study burden and risks

All individuals will undergo physical examination and blood sampling for standard laboratory parameters. In addition, all patients will undergo amixed meal test and an arginine stimulation test. At the third visit, 68Ga-NODAGA-exendin-4 will be administered intravenously and PET/CT scanning will be performed 1 hour after injection of the tracer. After injection of the radiopharmaceutical, blood samples will be drawn from an intravenous catheter for determination of blood glucose levels and blood pressure will be measured. Injection of the radiopharmaceutical may theoretically result in nausea and headache as has been reported for (much higher doses) Byetta® in therapy studies. In addition, single cases of low blood pressure and low blood glucose levels have been described. Although low blood glucose levels only occurred after accidental heavy overdosing of Byetta®, patients will be closely monitored. Furthermore, in a previous study (CPOP-EX), we did not observe any side or adverse effects after 111In-DTPA-[K40]-exendin-4 injection for all 20 patients included.
The expected radiation exposure will not exceed 5 mSv per PET/CT scan and is therefore considered minimal to little. However, if the technique would indeed

allow sensitive and specific visualization and quantification of beta cell mass in patients with hyperinsulinemic hypoglycemia, this would make further diagnosis and patient specific treatment possible in the future.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

HH group
- Signed informed consent
- >18
- Persisting hyperinsulinemic hypoglycemia after a low-carbohydrate diet and/or insulin suppressive medication for one year.;Controle group
- Signed informed consent
- >18

- RYGB at least 2 years ago
- Normal glucose levels before and after RYGB (fasting glucose between 4 and 6 mmol/l and/or HbA1c between 20 and 42 mmol/mol)
- Score <= 7 on Sigstad's scoring system
- Hypoglycemia excluded by 14-day continuous glucose monitoring
- Individual matched to HH group on age (± 5 years), sex and BMI at time of inclusion (± 2 kg/m2)

Exclusion criteria

HH group
-Anti-diabetic medication in the past 6 months
-Previous treatment with synthetic Exendin (Exenatide, Byetta®) or Dipeptidyl-Peptidase IV inhibitors
-Known liver failure or serum liver values over 2 times the normal values.
-Pregnancy or the wish to become pregnant within 6 months
-Breast feeding
-Kidney failure, i.e. calculated creatinine clearance below 40 ml/min
-Age < 18 years
-No signed informed consent;Additional exclusion for controle group
-Any diabetic history (e.g. including diabetes during pregnancy)
-Previous diagnosed HH
-Sigstad*s dumping score > 7

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	24-11-2016

Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	68Ga-NODAGA-exendin-4
Generic name:	nvt

Ethics review

Approved WMO Date:	20-07-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-08-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	18-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
EudraCT	EUCTR2014-005554-20-NL
CCMO	NL51854.091.15