The physiology of glucagon-like peptide-1 receptor expression in patients with endogenous hyperinsulinism: correlation with histopathology

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Ethical review	Not approved
Status	Will not start
Health condition type	Endocrine disorders congenital
Study type	Interventional

Summary

ID

NL-OMON42359

Source
ToetsingOnline

Brief title
GLP-1-CHI

Condition

- Endocrine disorders congenital
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
CHI, Congenital hyperinsulinism

Research involving
Human

Sponsors and support

Primary sponsor: Nucleaire geneeskunde en radiologie
Source(s) of monetary or material Support: Europese Unie in het kader van een FP7 research project (BetaCure no 602812)

Intervention

Keyword: beta cells, CHI, PET

Outcome measures

Primary outcome

The expression and distribution of the GLP-1R in the pancreas of children (<16 years) with proven endogenous congenital hyperinsulinism by comparison of 68Ga-NODAGA-exendin 4 PET/CT imaging data with autoradiography and histology performed on specimens collected during surgery.

Secondary outcome

• Comparison of the sensitivity of 68Ga-NODAGA-exendin 4 PET/Ct and 18F-DOPA PET/CT for the pre-operative localization of focal CHI and the discrimination between focal and diffuse CHI.

• Analysis of the kinetics of radiotracer uptake in the pancreas of CHI patients.

• Determination of the minimal injected dose of 68Ga-NODAGA-exendin 4 needed for accurate imaging.

• Determination of the effective radiation dose received by children injected with the calculated minimum dose of 68Ga-NODAGA-exendin 4.

• Assessment of the safety (side effects) of 68Ga-NODAGA-exendin 4 as compared to 18F-DOPA.

• Calculation and comparison of the interobserver variability of

68Ga-NODAGA-exendin 4 PET/CT and 18F-DOPA PET/CT

• Evaluation of the clinical outcome parameters (laboratory parameters

(glucose) and dosage of medical treatment) after surgery

Study description

Background summary

We propose to improve the sensitivity and specificity of pre-operative imaging for the localization of focal lesions in CHI and the discrimination between focal and diffuse CHI. This by using a new tracer which binds the glucagon-like-peptide-1 receptor (GLP-1R): 68Ga-NODAGA-exendin-4.

Study objective

The main study aim is the in vivo and ex vivo investigation of the expression and distribution of the GLP-1R in the pancreas of children (< 16 years) with proven endogenous congenital hyperinsulinism who qualify for surgery based on response to medical treatment and genetic analysis (only patients with genetically proven diffuse CHI will be excluded). 68Ga-NODAGA-exendin-4 PET/CT imaging data will be compared with autoradiography and histology performed on specimens collected during surgery.

Study design

Multicenter prospective imaging (pilot) study in which we will compare GLP-1R imaging with the standard imaging technique for pre-operative imaging in patients with CHI.

Intervention

68Ga-exendin PET/CT

Study burden and risks

Injection of the radiolabeled tracer may result in nausea and headache as has been reported for (very high doses (10-100 µg) of) Byetta® in therapy studies. In addition, a decrease of blood glucose levels (0.8 - 2.1 mmol/l has been described after injection of 8 - 14 µg 111In-DTPA-exendin-4 in patients with adult hyperinsulinemic hypoglycaemia (AHH). Importantly, regular monitoring of glucose concentrations led to no serious episodes of hypoglycaemia. Therefore,

no side-effects are anticipated with injection of 0.032 µg/kg of radiolabeled exendin. Patients will however be closely monitored, especially because the compound has not been used before in children. Furthermore, a prophylactic glucose infusion will be started 15 minutes before injection of radiolabeled exendin.
The expected radiation dose will not exceed 13.2 mSv in newborns and declines rapidly with age. In relation to the expected benefit in diagnostic imaging by improving pre-operative non-invasive determination of the type of CHI and localization of the focus of diseased beta cells with higher sensitivity and specificity and the resulting impact on CHI treatment, this additional radiation exposure is acceptable. Especially when taking into consideration that the current challenges in pre-operative localization of focal CHI result in considerable morbidity of the surgical treatment which causes these children to experience severed side-effects and remain dependent on medication for the rest of their lives.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

• Biochemically and clinically proven endogenous congenital hyperinsulinism:
- Unresponsive to medical treatment (diazoxide)
- Indication for 18F-DOPA PET/CT based on mutation analysis
• Standard imaging (18F-DOPA PET/CT) not older than 8 weeks
• <16 years old
• Informed consent signed by parents or legal guardians of the patient.

Exclusion criteria

• Genetically proven diffuse CHI (presenting with a homozygous or compound heterozygous ABCC8/KCNJ11 mutation)
• Calculated creatinine clearance below 40 ml/min
• Evidence of other malignancy than insulin producing tumors in conventional imaging (suspicious liver, bone and lung lesions based on CT)
• Age > 16 years
• No signed informed consent

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-01-2016
Enrollment:	10

Type:	Anticipated

Medical products/devices used

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

Ethics review

Not approved

Date:	29-10-2015
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015□002692□18-NL
CCMO	NL54275.000.15