Effects of INsulin dEtemiR and neutral protaminE hagedorn (nph) insulin on BRain glucOse metabolism: a study in persons with type 1 diabetes

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

Summary

ID

NL-OMON33980

Source
ToetsingOnline

Brief title
Insulin detemir action in cerebro/ INcEREBRO

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Novo Nordisk,Zowel universiteit als industrie

Intervention

Keyword: Brain, Detemir, Glucosemetabolism, Insulin

Outcome measures

Primary outcome

Primary study endpoints:

I. Cerebral metabolic rate of glucose (CMRglu), in brain regions associated

with appetite regulation, as determined by FDG-PET scanning

II. Cerebral blood flow (CBF), in brain regions associated with appetite

regulation, as determined by H2O-PET scanning

Secondary outcome

Secondary study endpoints:

I. Insulin concentrations in the CSF

II. Brain activity in specific regions involved in control of appetite, as

determined by fMRI

III. Weight change

Study description

Background summary

Intensive insulin therapy improves the long-term outcome of diabetes patients, but is also associated with weight gain, a very unwanted side-effect. Insulin detemir is a relatively new basal insulin analogue, which consistently has been shown to result in less weight gain as compared to NPH insulin. This observation has so far not been explained. However, a possible mechanism could be an enhanced effect of insulin detemir in cerebro in communicating satiety signals. Since insulin receptors are abundantly present in the brain, it is of interest to assess whether reduced weight gain is associated with increased

concentrations of insulin detemir in the cerebrospinal fluid (CSF) and whether there are differences in glucose metabolism and blood flow in brain areas potentially involved in appetite regulation.

Study objective

The aim of this study is to determine whether subcutaneous administration of insulin detemir, as compared to NPH insulin, leads to a more pronounced effect on brain glucose metabolism and blood flow in brain regions associated with appetite regulation. Furthermore, we would like to explore whether insulin detemir, as compared with NPH insulin, reaches a higher concentration in the CSF, whether it leads to more activation in appetite related brain areas and whether the changes in appetite control are related to changes in brain glucose metabolism, blood flow and/or insulin concentration in the CSF, as potential explanation for the weight difference of insulin detemir.

Study design

Randomised, open-label cross-over study. Type 1 diabetic patients will be treated on a basal-bolus regimen for two periods of 12 weeks, starting with either insulin detemir or NPH insulin, administered in the evening, the prandial insulin being insulin aspart. PET and fMRI measurements and a lumbar puncture will be performed in the last week of both treatment periods.

Intervention

12 weeks of insulin detemir QD in the evening (+ TID insulin aspart)
12 weeks of NPH insulin QD in the evening (+ TID insulin aspart)

Study burden and risks

We are well aware, that this study can be a really demanding task for our patients. Participants will have to switch to another insulin therapy scheme (although it is possible that they already use or have used the trial insulin before), which can be really hard. After a screening visit they are to visit the research facility five times. These visits will be in the early morning.
The risks associated with participation are the risks of venous/arterial blood drawing, lumbar puncture and radioactivity (<10mSv)during PET scanning, as described in full detail before. We will try to make this study as bearable as possible for our patients. All posible measures will be taken to minimize the discomfort for the participants. All tests will be done by one researcher.
From experience at our own institution, it is known that the participating patients are very enthusiastic during the study, mostly because of their interest in the scientific background of their disease.

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

Type 1 diabetic patients
Age 21-60 years
Male
Diabetes duration minimal 2 years
HbA1c ~ 7,5%

Exclusion criteria

Recent onset of DM
BMI < 18 OR > 35 kg/m2
T2DM

History of major heart/renal disease
Severe untreated proliferative retinopathy
History of recurrent severe hypoglycaemia
(History of) brain disorders
Alcohol abuse
(History of) drug abuse, benzodiazepines, selective beta-blockers, oral steoids, oral anticoagulants
Current psychiatric disease/treatment
(history of) eating disorders
History of severe head trauma accompanied by loss of consciousness
Any endocrine disease not well controlled for at least 3 months
Inability to undergo MRI
Visual acuity < 0.3
Known or suspected allergy to trial product or related products

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-01-2009
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Insulatard
Generic name:	neutral protamine hagedorn (NPH)
Registration:	Yes - NL intended use

Product type:	Medicine
Brand name:	Levemir
Generic name:	Detemir
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Novorapid
Generic name:	aspart
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	26-02-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-03-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2010
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
EudraCT	EUCTR2007-007255-13-NL
ClinicalTrials.gov	NCT00626080
CCMO	NL20992.029.08