The effect of exenatide compared to insulin glargine on cardiac function and metabolism in type 2 diabetic patients with congestive heart failure: a randomized-controlled trial

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In this study we will assess the effects of exenatide on cardiac metabolism and function in patients with T2DM and CHF. We will address the following hypothesis: exenatide improves global cardiac function in CHF patients with T2DM, by favorable...

Ethical review	Approved WMO
Status	Completed
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON35173

Source
ToetsingOnline

Brief title
CARDEXINE

Condition

- Heart failures
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetic cardiomyopathy, diabetic heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Eli Lilly,zowel universiteit als industrie

Intervention

Keyword: cardiac metabolism, exenatide, heart failure, type 2 diabetes

Outcome measures

Primary outcome

I. what are the effects of 26-week exenatide compared to insulin glargine

treatment in 42 patient with T2DM and CHF (NYHA II-IV) on global cardiac

function, measured as ejection fraction (EF) using cardiac magnetic resonance

(CMR).

Secondary outcome

I. changes in regional intramural systolic and diastolic myocardial function

assessed by CMR and strain analysis.

II. cardiac oxygen consumption, cardiac efficiency and (stress) perfusion, as

assessed by PET.

III. patients* performance, measured by a 6-min. walk test and exercise

capacity with VO2max test.

Study description

Background summary

Patients with type 2 diabetes mellitus (T2DM) are at high risk of developing congestive heart failure (CHF) due to the high presence of diabetic cardiomyopathy (DCM) and ischemic heart disease. The concomitant occurrence of T2DM and CHF is associated with excessive mortality rates. Recently, several classes of blood-glucose lowering drugs have been related to an elevated risk

of CHF. Consequently, not only caution should be exercised when exposing high-risk, but otherwise asymptomatic T2DM patients to these potentially harmful agents, but more importantly, safely lowering of blood-glucose in T2DM patients with concomitant CHF may be extremely challenging. Glucagon-like peptide (GLP)-1 receptor agonists, a novel class of blood-glucose lowering agents, have been reported to improve cardiac function in CHF patients with T2DM. Whether GLP-1 receptor agonists act directly on the myocardium is presently unknown, since the beneficial effects may be secondary to the concomitant improvements in metabolic control. Exenatide is one of the currently available GLP-1 receptor agonist that has durable effects on metabolic control and simultaneously decreases body weight in patients with T2DM.

Study objective

In this study we will assess the effects of exenatide on cardiac metabolism and function in patients with T2DM and CHF. We will address the following hypothesis: exenatide improves global cardiac function in CHF patients with T2DM, by favorable effects on cardiac metabolism leading to improvement of cardiac efficiency.

Study design

Using a comparator-controlled, parallel-group study design, T2DM CHF patients (NYHA class II-IV) who have not achieved a target HbA1c of <=6.5% with metformin, will be treated with either exenatide (5 µg BID for 4 weeks, subsequently increased to 10 µg BID for the remainder of the study) or insulin glargine (initiated at 10 IU/day; titrated according to fasting blood glucose concentrations based on general protocol-defined guidance) during a 26-week period, to allow the evaluation of a direct GLP-1 receptor agonist mediated effect. We expect that with the use of non-invasive imaging techniques, including PET, MRI and echocardiography, myocardial function and oxidative metabolism can be detailed and the effect of both treatment regimes be evaluated. We will also compare the myocardial function and metabolism of these patients with those of healthy BMI- and age-matched controls.

Intervention

interventiongroup: exenatide 5 mcg BID first 4 weeks, subsequently increased to 10 µg BID for the remainder of the study

comparatorgroup: insulin glargine, initiated at 10 IU/day; titrated according to fasting blood glucose concentrations based on general protocol-defined guidance during a 26-week period

The healthy controls will not receive the studymedication

Study burden and risks

We are aware of the inconvenience that is imposed on the participants in this study. After a screening visit, they have to visit the research facility 8 times. The visit duration ranges between approximately one hour to f4 and a half hours. The risk associated with participation are the risks of venous blood drawing, intravenous infusion and radioactivity (<10 mSv) during the PET scanning, as described in full detail earlier. We will try to make this study as bearable as possible for our patients. Appropriate measures will be taken to minimize discomfort for the participants. All tests will be done by one researcher.

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

- Patients:
Type 2 diabetic patients
Male and postmenopausal female
Age 18 years and above
Metformin therapy (stable, maximum tolerable dose for 2 months)
HbA1c 6.5-10%
Confirmed congestive heart failure (NYHA, functional class II-IV)
Ejection Fraction (EF)<50%
Stable standard therapy for their cardiac condition for 3 months prior to entering the study;- Healthy controls:
Male and postmenopausal female
Age 18 years and above
No known acute or chronic disease

Exclusion criteria

- Patients:
Type 1 diabetes
Serious renal (creatinine clearance< 50 ml/min) or liver impairment
(Receiving treatment for) malignant disease
Cardiovascular event< 3 months prior to inclusion
Acute congestive heart failure
Any reason for not being able to sustain the imaging studies (impairment to understand the aim of the study/procedures, implanted devices, claustrophobia, atrial fibrillation, orthopnoe)
Contraindications for the use of exenatide/insulin
Use of insulin, thiazolidiones, (other than study) incretin-based therapies within 4 months of screening
Chronic use of glucocorticoids, NSAIDs or centrally acting drugs (>2 weeks) within 2 weeks immediately prior to screening;- Healthy controls:
Chronic use of any drug
Impaired glucose tolerance (as assessed by a 75-g oral glucose tolerance test)

Study design

Design

Study phase:	4
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	30-11-2009
Enrollment:	62
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Byetta
Generic name:	Exenatide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lantus
Generic name:	Insuline Glargine
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	13-02-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	08-04-2009
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	23-11-2009

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-04-2010
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-07-2010
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	EUCTR2008-005325-10-NL
ClinicalTrials.gov	NCT00766857
CCMO	NL24661.029.08