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Effect of exenatide in type 2 diabetic patients with congestive heart failure

Submission date
12/07/2011

Recruitment status
No longer recruiting

Registration date
04/08/2011

Overall study status
Completed

Last Edited
19/04/2017

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The hormone glucagon-like peptide-1 (GLP-1) may have a beneficial effect on heart function beside its well-known action of lowering blood sugar. It was recently shown that GLP-1 improves left ventricular hemodynamics (heart blood flow) in dogs with advanced dilated cardiomyopathy (enlarged heart). This was accompanied by an increase in myocardium (heart muscle) uptake of glucose, without any change in levels of insulin, suggesting that GLP-1 has an insulin-like effect on the myocardium. Some human studies also demonstrate beneficial effects of GLP-1 on the heart. Short-term treatment with GLP-1 of patients with acute myocardial infarction (heart attack) improves heart function, as does long-term treatment of patients with congestive heart failure (CHF). The aim of this study is to find out whether the drug exenatide, which mimics GLP-1, improves hemodynamic functions in type 2 diabetic patients with CHF.

Who can participate?
Type 2 diabetic patients aged 18-80 with heart failure

What does the study involve?
Participants are randomly allocated to be treated with either exenatide or placebo (dummy drug) over 6 hours. After a break of 18 hours, they are treated with the other drug for another 6 hours. Heart function and blood pressure are monitored during the study. Blood samples are taken at the start of the study, at 30 minutes and every hour until 6 hours to measure blood levels of exenatide.

What are the possible benefits and risks of participating?
Not provided at time of registration

Where is the study run from?
Stockholm South General Hospital (Södersjukhuset AB) (Sweden)

When is the study starting and how long is it expected to run for?
January 2008 to June 2010

Who is funding the study?
Eli Lilly Amylin Alliance (USA)

Who is the main contact?
Dr David Nathanson
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2006-005220-16

Study information

Scientific Title
A double-blinded cross-over clinical trial investigating hemodynamic effects of exenatide on diabetic patients hospitalized for congestive heart failure

Study objectives
Investigate whether exenatide improves hemodynamic functions in type 2 diabetic patients with chronical left ventricular heart failure and the safety of this drug in an acute setting.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Swedish Central Ethical Review Board, 01/09/2009, ref: MPA 151:2007/25520

Study design
Single-center randomized two-period crossover double-blind study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Left venticular heart failure and Type 2 diabetes mellitus

Interventions
Patients are investigated in a supine position throughout the study. Patients are randomized to receive either 0.12 pmol/kg/min intravenous exenatide or placebo during a 6 hour infusion. After a wash-out period of 18 hours, another 6 hour infusion of either exenatide and placebo is given, i.e. patients are there own controls. During the study, heart function and invasive arterial blood pressure are monitored with a pulmonary artery catheter (Schwann-Ganz) and a catheter with an arterial line, respectively.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Exenatide

Primary outcome(s)
1. Serum biomarkers like BNP, NEFA, plasma glucose, S-insulin, S-C-peptide are monitored at multiple time points during the infusions
2. Serum levels of exenatide as follows:
2.1. During infusion (exenatide vs placebo), CI and PCWP are measured at baseline, 1 hour, 3 hours and 6 hours.
2.2. During the 18 hour washout period, another two measurements are made and infusion is repeated (exenatide vs placebo) with new measurements (baseline, 1 hour, 3 hours and 6 hours)
2.3. Blood samples are drawn at baseline (0) and at 30 min and every hour, until 6 hours (totally 7 blood samples are drawn)

Key secondary outcome(s)
1. Mean arterial blood pressure
2. Mean pulmonary arterial pressure
3. Tolerability of exenatide in this acute setting

Completion date
16/06/2010

Eligibility

Key inclusion criteria
1. Type 2 diabetes patients with LVHF and NYHA class III or IV symptoms of heart failure who are admitted to the hospital for management of decompensated chronic heart failure

2. A stable period of 24 hours using established therapy, i.e. ACE/ARB-inhibitors, beta-blockers, aldosterone-inhibitors and diuretics
3. Patients who are monitored with a pulmonary artery catheter for clinical purposes
4. In subjects without known diabetes, diabetes will be confirmed by at least two fasting plasma glucose levels exceeding 7 mmol/l or a random plasmaglucose exceeding 11,0 mmol/l according to the American Diabetes Association definition of diabetes
5. Male and female subjects
6. 18-80 years of age

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Type 1 diabetes (autoantibody positive)
2. Need of inotropic agents, nitroglycerin-infusion or aortic balloon device
3. Unstable LVHF despite maximal oral treatments and i.v. diuretics
4. Significant ischemic heart disease (defined as angina-limited exercise or unstable angina); documented acute myocardial infarction (MI) within the previous 8 weeks
5. Active myocarditis; malfunctioning artificial heart valve
6. Symptomatic primary pulmonary disease; serious arrhythmias, defined as a history of ventricular flutter or fibrillation other than that occurring within 24 hours after acute MI
7. History of sudden cardiac death or symptomatic ventricular tachycardia within 3 months before study entry; second or third degree atrioventricular block, unless the patient has a functioning implanted pacemaker
8. Supine systolic blood pressure <85 mm Hg or >200 mm Hg
9. Primary renal impairment (creatinine clearance < 30 ml/min)
10. Uncorrected hypokalemia or hyperkalemia (potassium <3.5 mmol/l or >5.5 mmol/l)
11. Significant anemia (Hb < 90 g/l), or treatment with another investigational agent within 30 days before study entry
12. Severe gastrointestinal disease, including gastroparesis
13. Pregnancy or lactation
14. History of drug abuse
15. Presence or history of allergic reaction or intolerance to multiple drugs
16. Subjects considered by the Investigator as unsuitable candidates to receive an investigational drug
17. Known history of, or concomitant medical condition that might interfere with the evaluation

of study medication
18. No minor subjects (<18 years of age) or pregnant women will be participating in the study

Date of first enrolment
31/01/2008

Date of final enrolment
16/06/2010

Locations

Countries of recruitment
Sweden

Study participating centre
Karolinska Institutet
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Sweden
11883

Sponsor information

Organisation
Stockholm South General Hospital (Södersjukhuset AB) (Sweden)

ROR
https://ror.org/00ncfk576

Funder(s)

Funder type
Industry

Funder Name
Eli Lilly Amylin Alliance (USA)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/04/2012		Yes	No
Results article	results	12/01/2016		Yes	No