Postprandial Lipemia, Inflammation, and Vascular Function in Diabetes modulated by dapagliflozin

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To explore the inflammatory changes of dapagliflozin compared with placebo on postprandial lipemia and postprandial leukocyte activation, oxidative stress and endothelial function in men with type 2 diabetes mellitus using insulin.

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

Summary

ID

NL-OMON46285

Source
ToetsingOnline

Brief title
PLEIADES-dapa

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Lipid metabolism disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerose, postmeal fat influence

Research involving
Human

Sponsors and support

Primary sponsor: Sint Franciscus Gasthuis

Source(s) of monetary or material Support: Stichting Onderzoek Interne Specialismes Franciscus Gasthuis

Intervention

Keyword: Diabetes Mellitus, Postprandial inflammation, Postprandial lipemia, SGLT2

Outcome measures

Primary outcome

Main study endpoint will be postprandial leukocyte activation, measured by

CD35, CD11b and CD66b.

Secondary outcome

Secondary endpoints will be postprandial lipemia (plasma apoB, HDL-c, LDL-c,

total cholesterol and triglycerides), oxidative stress (lipoperoxidase) and

vascular function (arterial pulse wave velocity and arterial pulse wave

analysis). Furthermore, we will measure fasting and postprandial levels of free

fatty acids and b-hydroxybutyrate, to explore the molecular mechanisms involved

in SGLT2 inhibition related to lipid metabolism.

Study description

Background summary

Few studies have proven to be efficient in reducing cardiovascular risk in diabetes. Recently, a SGLT2-inhibitor showed a significant reduction in cardiovascular mortality without a clear mechanism for this reduction. Treatment with dapagliflozin will reduce postprandial hyperlipidemia and thus reduce postprandial leukocyte activation, diminish the generation of postprandial oxidative stress and improve postprandial vascular dysfunction in men with type 2 diabetes mellitus.

Study objective

To explore the inflammatory changes of dapagliflozin compared with placebo on

postprandial lipemia and postprandial leukocyte activation, oxidative stress and endothelial function in men with type 2 diabetes mellitus using insulin.

Study design

Randomized, double blind pilot study.

Intervention

Two oral fat load tests (OFLTs) will be performed. After the first OFLT, volunteers will be randomly assigned to receive 12 weeks of either dapagliflozin daily or a placebo. Twelve weeks later the OFLT will be repeated.

Study burden and risks

The use of a SGLT-2 inhibitor daily has been established to be a safe and effective treatment for type 2 diabetes mellitus. Volunteers will be hospitalized on 2 different days (day 1, day 85) for approximately nine hours each day and receive an oral fat load. Glucose will be monitored and controlled according to an individual algorithm. The volunteers* general practitioner will be informed on their participation. A total of 222ml (111ml for each postprandial test) of blood will be drawn. Volunteers will be allowed to drink only water during the tests. There is a theoretical risk of hypoglycemia but no excessive risk is involved. Volunteers receive 250 euros for full participation. Furthermore, volunteers will be informed and given advice if they turn out to have an increased cardiovascular risk or any other condition.

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

- Age of 18 years of older
- Male sex
- Diabetes mellitus type II on intensive insulin treatment (three times short acting and once daily long acting)(unchanged for >10 weeks prior to inclusion
- Stable glucose regulation last 6 months (HbA1c >6.5% - <9%)
- Provision of informed consent prior to any study procedure

Exclusion criteria

- Current smoking
- Impaired renal function (MDRD <60 ml/min/1.73m2)
- Recent use of SGLT2 inhibitior (past 6 months)
- Recent cardiovascular event (past 6 months) (myocardial infarction, coronary artery bypass grafting, stroke)
- Severe hyperglycemic events in the past 6 months (hyperglycemie > 20mmol/l requiring hospital admission)
- Provision of informed consent prior to any study procedure
- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site)
- Previous enrollment in the present study
- Participation in another clinical study with an investigational product during the last 6 months

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2017
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Forxiga
Generic name:	Dapagliflozin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-11-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-02-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 21590
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2016-001417-24-NL
CCMO	NL57393.101.16
OMON	NL-OMON21590

Study results

Date completed:	28-12-2018
Actual enrolment:	14