

Dapagliflozin on cholesterol metabolism in DM2: dissecting its effect on dyslipidemia by using stable isotope based cholesterol and glucose fluxes

Published: 07-04-2016

Last updated: 20-04-2024

to investigate the effect of 5 weeks dapagliflozin 1dd 10mg treatment on glucose and cholesterol fluxes in patients with type 2 diabetes on stable rosuvastatin treatment.

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

Summary

ID

NL-OMON43515

Source

ToetsingOnline

Brief title

DICE study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym

cholesterol, diabetes mellitus

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: unrestricted grant Astra Zeneca

Intervention

Keyword: cholesterol flux, dyslipidemia, glucose flux, type 2 diabetes

Outcome measures

Primary outcome

effect of 5 weeks dapagliflozin 10mg on top of rosuvastatin treatment on LDL de novo lipogenesis compared to rosuvastatin 10mg therapy only or no medication

Secondary outcome

Effect of 5 weeks dapagliflozin 10mg on:

- Change in VLDL secretion and clearance (as determined by 2H3 Leucine enrichment) and relation to plasma CETP, PLTP and HDL subfractions
- (dietary) Triglyceride fluxes (as determined by 1,2,3,4-13C16 * palmitate to measure FFA remnant uptake).
- hepatic and peripheral insulin sensitivity (2 step Hyperinsulinemic normoglycemic clamp with 2H2enriched glucose:) and energy expenditure including carbohydrate oxidation and fatty acid oxidation rates in breathing air
- liver fat content (MRI liver)
- change in fecal microbiome composition
- cholesterol and bile salt excretion

Study description

Background summary

Type 2 diabetes is associated with increased cardiovascular risk which is driven by hyperglycemia en dyslipidemia. A few years ago, a new glucose lowering medication of the SGLT2 inhibitors class (Dapagliflozin).was registered in the Netherlands. Dapagliflozin has been tested in relatively

large studies and was effective in reducing HbA1c levels; however, a sideeffect of all SGLT2 inhibitors is the increase in plasma cholesterol (LDL, HDL and triglyceriden) with 5-8%. We would like to investigate what is mechanism is driving the increased plasma cholesterol (hepatic cholesterol synthesis, increased (dietary) intestinal cholesterol uptake in de darm or decreased excretion of cholesterol) and moreover whether this dyslipidemia might reduce the beneficial cardiovascular effects of glucose lowering by dapagliflozin.

Study objective

to investigate the effect of 5 weeks dapagliflozin 1dd 10mg treatment on glucose and cholesterol fluxes in patients with type 2 diabetes on stable rosuvastatin treatment.

Study design

open label single arm intervention study

Intervention

dapagliflozin 10mg once daily for 5 weeks and rosuvastatin 10mg 1dd during 9 weeks

Study burden and risks

Patients will bring 5 visits to the AMC (total 46 hours) during 13 weken; in total 470 ml blood is drawn. Infusion of stable isotopes, liver MRI and hyperinsulinemic clamp procedures are a safe and standard procedure at our department (METC 2013_071) and are not associated with increased risk. Rosuvastatin and dapagliflozin have been registered in the Netherlands and are frequently used in patients with type 2 diabetes and their use is not associated with increased risks. In conclusion, this is a low-moderate risk study and we feel that the burden of the study and its potential risks do not outweigh the benefits of increased pathophysiological insight into the drivers of dyslipidemia upon SGLT2 use in patients with type 2 diabetes mellitus.

Contacts

Public

Academisch Medisch Centrum

Meibergdreef 9 kamer F4-159.2
Amsterdam 1105 AZ
NL

Scientific

Academisch Medisch Centrum

Meibergdreef 9 kamer F4-159.2

Amsterdam 1105 AZ

NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

- Male or postmenopausal female patients with type 2 diabetes mellitus(HbA1C *6.5% - <8.5%)
- At least 12 weeks of stable dose metformin treatment, FPG<13.2 mmol/l
- LDL cholesterol >2.5 mmol/l
- Willing to switch used statin to rosuvastatin 10mg once daily for 9 weeks
- 18-75 years of age
- Ability to provide informed consent

Exclusion criteria

- History of cardiovascular event
- Smoking
- exogenous insulin use
- Creatinin clearance < 60ml/min
- Alcohol abuse (>4 units/day)
- AST or ALT elevation (>2.5x upper limit)
- Contraindication to MR scanning (i.e. pacemaker, metallic foreign body, claustrophobia)

Study design

Design

Study type: Interventional

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Basic science

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 06-09-2016

Enrollment: 12

Type: Actual

Ethics review

Approved WMO

Date: 07-04-2016

Application type: First submission

Review commission: METC Amsterdam UMC

Approved WMO

Date: 24-08-2016

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
CCMO	NL56045.018.15