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The effect of variation of fatty substances found in the blood on patients with type 2 diabetes

Submission date
19/10/2020

Recruitment status
No longer recruiting

Registration date
09/11/2020

Overall study status
Completed

Last Edited
09/11/2020

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
High blood sugar and fat content are well-recognised risk factors for causing the formation of obstructive plaques in arteries which lead to cardiovascular disease, for example heart attacks. From earlier studies, we know that after eating, high sugar and fat content in the blood seems to have an association with cardiovascular risk in both healthy persons and individuals with type 2 diabetes. This study aims to examine the effect on the body of variation of fat levels in the blood compared to constant fat levels, during a constant high sugar state.

Who can participate?
This study is open to individuals with type 2 diabetes and non-diabetic individuals between the ages of 30 - 65 years with a body mass index between 27 - 40 kg/m² (overweight or obese).

What does the study involve?
This study includes one screening visit and two procedural visits during which participants will have sugar infused into their blood. Blood will be drawn at various time points during the procedure for analysis. Participants will be closely monitored by trained medical and nursing staff throughout the procedure. There will be one week break between visit 2 and visit 3 to prevent the carried over effects of infusions. We expect individual participants would be in the study for 3-4 weeks in total.

What are the possible benefits and risks of participating?
Benefits: No immediate benefits, however, the knowledge gained in the study will help the management of diabetes in the future.
Risks: Potential for a reaction to the fatty substance given by the drip and discomfort from the cannula (plastic needle). A fully advanced life support trained research doctor will be present at all times to manage any emergency situation that arises however this is a rare occurrence. All the potential risks will be fully disclosed and discussed with potential participants at screening before he/she consents to take part in the study.

Where is the study run from?
University of Hull (UK)

When is the study starting and how long is it expected to run for?
June 2014 to October 2021

Who is funding the study?
University of Hull (UK)

Who is the main contact?
Prof. Thozhukat Sathyapalan, thozhukat.sathyapalan@hey.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Prof Thozhukat Sathyapalan

ORCID ID
http://orcid.org/0000-0003-3544-2231

Contact details
Academic Diabetes, Endocrinology and Metabolism
Hull Royal infirmary
Brocklehurst Building
Anlaby Road
Hull
United Kingdom
HU3 2RW
+44 (0)1482675312
thozhukat.sathyapalan@hey.nhs.uk

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
154259

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 154259

Study information

Scientific Title
Effect of acute fluctuations of hyperlipidaemia on insulin resistance and cardiovascular risk in patients with type 2 diabetes

Study objectives
Fluctuation in triglyceride levels confers risk of oxidative stress, beta-cell function and platelet function that is in addition to that predicted by the plasma mean triglyceride value alone.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/12/2014, NRES Committee Yorkshire & The Humber - South Yorkshire (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, UK; +44 (0)207 104 8079; southyorks.rec@hra.nhs.uk), ref: 14/YH/1169

Study design
Pilot cross-sectional non-randomised non-CTIMP

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
Assessing risk of fluctuating lipid levels compared to constant hyperlipidaemia during constant hyperglycaemic state on endothelial function and oxidative stress parameters in type 2 diabetes

Interventions
This study includes one screening visit and two procedural visits. There will be a one week break between visit 2 and visit 3. We expect he or she would be in the study for 3-4 weeks in total. All the participants have a screening assessment to ensure their eligibility for the study and will be required to complete a consent form. The screening includes medical history (including pre-existing conditions and concomitant medications), physical examinations (measurement of height, weight, hip and waist circumference, and resting blood pressure) and blood tests. In women, a pregnancy test will be done before entering the study. Female participants will be asked to use a barrier method for contraception if required during the test.

For visit 2, participants will be required to fast for 12 h, not take their antiplatelet medication (e. g. aspirin) for 72 h before the test, not take their metformin and blood pressure medication on

the evening before and the morning of the visit. Participants will also be requested to stop their lipid lowering medication i.e statins 4 weeks before entering the study. A cannula (plastic needle) will be inserted in both forearms. A hyperglycaemic state will be maintained using 20% Dextrose Infusion followed by continuous 20% IV Lipid infusion 90 ml/h and unfractionated heparin. Another cannula will be inserted in the back of the hand and subjected to controlled heat to allow for blood sample collection. A blood sample will be collected at various time points throughout the test.

A similar procedure will be repeated on visit 3 (1 week after visit 2). A hyperglycaemic state will be maintained using 20% Dextrose Infusion followed by intermittent 20% IV Lipid infusion 90 ml /h and unfractionated heparin for 2 hours followed by Normal Saline 45 ml/h for 2 h before re-starting 20% IV Lipid infusion 90 ml/h and unfractionated heparin.

Blood glucose will be checked before sending participants home. Participants should expect to stay in the centre for approximately 8 h. The expenses for travel and parking fees will be reimbursed. Because of the inconvenience of having to spend 8 h in the diabetes centre for the procedure, we will reimburse participants £50 per procedure. However, participants would not be eligible for the reimbursement if they are on state benefit because it might invalidate their benefits.

Intervention Type
Other

Primary outcome measure
1. Beta cell function assessed by insulin measurements taken at fasting and every 10 min from T-30 to T0 and T340 to T360, and hourly during the whole procedure
2. Oxidative stress markers measured using blood samples drawn during visit 2 and 3 before, at the end of 2 h, 4 h and 6 h of the fatty substance infusion and will be centrifuged followed by analysis using the flow cytometer

Secondary outcome measures
Platelet activation/inhibition measured using blood samples drawn during visit 2 and 3 before, at the end of 2 h, 4 h and 6 h of the lipid infusion and will be centrifuged followed by analysis using the flow cytometer

Overall study start date
01/06/2014

Completion date
15/10/2021

Eligibility

Key inclusion criteria
Diabetes arm:
1. Aged 30 - 65 years
2. BMI 27 - 40 kg/m²
3. History of T2DM on diet with or without metformin

Control arm
1. Aged 30 - 65 years
2. BMI 27 - 40 kg/m²

Participant type(s)
All

Age group
Adult

Sex
Both

Target number of participants
32

Key exclusion criteria
Diabetes arm:
1. Current smoking
2. Pregnancy/breastfeeding/trying to conceive
3. Participants on anti-diabetes medications except metformin
4. Participants on beta blocker/ thiazide diuretics
5. History of chronic kidney disease stage 3, ALT >3x upper limit of normal and active thyroid disease
6. History of recent cardiovascular event in last 12 weeks
7. History of coagulation disorders
8. History of bronchial asthma
9. History of allergy to insulin, soy oil, purified egg (intralipid)
10. History of taking lipid lowering agents within last 2 weeks
11. Unwilling to be informed to their GP about their participation

Control arm:
1. Current smoking
2. Pregnancy/breastfeeding/trying to conceive
3. History of chronic kidney disease stage 3, ALT >3x upper limit of normal and active thyroid disease
4. History of recent cardiovascular event in last 12 weeks
5. History of coagulation disorders
6. History of bronchial asthma
7. History of diabetes mellitus
8. Participants on beta-blockers or thiazide diuretics
9. History of allergy to insulin, soy oil, purified egg (intralipid)
10. History of taking lipid lowering agents within last 4 weeks
11. Unwilling to be informed to their GP about their participation

Date of first enrolment
20/12/2020

Date of final enrolment
20/06/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Hull Royal infirmary
Centre for Diabetes, Endocrinology and Metabolism Research
Brocklehurst Building
220-236 Anlaby Road
Hull
United Kingdom
HU3 2RW

Sponsor information

Organisation
Hull and East Yorkshire Hospitals NHS Trust

Sponsor details
Office 13, 2nd Floor Daisy Building
Castle Hill Hospital
Cottingham
England
United Kingdom
HU16 5JQ
+44 (0)1482461903
james.illingworth@hey.nhs.uk

Sponsor type
Hospital/treatment centre

Website
http://www.hey.nhs.uk/

ROR
https://ror.org/01b11x021

Funder(s)

Funder type

University/education

Funder Name
University of Hull

Alternative Name(s)
HU

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
20/09/2021

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request. Hull and East Yorkshire R & D department will monitor all data collected including safety data throughout the course of the study. The data stored will only have the participant's study number and initials on it. Data will be collected in participant's case notes and a case report form (CRF) designed specifically for the study in line with the sponsor's guidelines and Good Clinical Practice. Data will be collected by the study team. This will include research nurses and medical practitioners. Data will be anonymized and will only be identified by the participant identification number. Data will be collected and retained in accordance with the Data Protection Act 1998. Data will include anthropometric measurements, laboratory investigations which include full blood count , urea, creatinine & electrolytes, liver function test, thyroid function test, HbA1C, creatinine kinase, total cholesterol, triglycerides, LDL and HDL, Insulin and oxidative stress markers (endothelial microparticles) will be examined by local laboratory protocol. Data will can be made available from July 2021 and will be available for 5 years.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version v2	24/06/2014	09/11/2020	No	No

HRA research summary	28/06/2023	No	No