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Targeting subjects with high numbers of particles that carry "bad cholesterol" in the blood to best prevent type 2 diabetes

Submission date
26/07/2017

Recruitment status
No longer recruiting

Registration date
28/07/2017

Overall study status
Completed

Last Edited
23/08/2023

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
Type 2 diabetes is a worldwide health burden leading to other diseases and death. It develops when our body is not responding well to the important actions of insulin. Insulin is a hormone that helps our body to function well and to make use of the food that we eat. If the body is not responding well to insulin, the sugar will accumulate in the blood leading to the diagnosis of diabetes. Having excess weight increases the chance of becoming diabetic. Type 2 diabetes can be prevented by weight-loss. However, there is a need to identify the overweight or obese patients who will most likely become diabetic in order to best prevent this disease. Having high numbers of particles that carry cholesterol in the blood (or apoB) could increase the chance for developing diabetes. This is because high blood apoB decreases the function of our tissues, like fat and muscle, which decreases their response to insulin. Accordingly, we believe that targeting subjects with high blood apoB with weight-loss programs would lead to maximal prevention of type 2 diabetes among a population of overweight and obese subjects. The aim of this study is to identify those who are high risks of developing type 2 diabetes based on certain markers in their blood samples.

Who can participate?
Adults aged 45 to 74 years old who are overweight

What does the study involve?
Participants are asked to follow a healthy weight-loss program for six month using a low-calorie diet, which is based on the Canadian Food Guide. To encourage this, participants meet with dieticians for one hour each month. Participants are encouraged to maintain their normal activity level during the six months. Participants are asked to keep a three day food intake record at the beginning and end of the study. Participants are followed up with blood tests to analyse their cholesterol levels in their blood.

What are the possible benefits and risks of participating?
Participants may benefit from being enrolled in a weight-loss program under close nutritional and medical supervision. They also may benefit from having access to in-depth medical

examination using combinations of tests that are only accessible through medical research. There are no direct risks with participating.

Where is the study run from?
Montreal Clinical Research Institute (Institut de Recherches cliniques de Montréal (IRCM))

When is the study starting and how long is it expected to run for?
October 2007 to August 2014

Who is funding the study?
Canadian Institutes of Health Research (Canada)

Who is the main contact?
Dr May Faraj

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
IRCM research protocol # 2009-33

Study information

Scientific Title
Targeting hyperapoB to reduce the risk of type 2 diabetes in obese subjects; mechanism of action

Study objectives
The plasma concentration of apoB-lipoproteins (i.e. plasma apoB) associates positively with:
1. Baseline risk factors for type 2 diabetes (systemic insulin resistance, glucose-induced hyperinsulinemia, delayed postprandial fat metabolism, inflammation and ex vivo white adipose tissue dysfunction and inflammation) in overweight and obese subjects.
2. Amelioration of these risk factors for type 2 diabetes following a 6-month hypocaloric diet

Ethics approval required
Old ethics approval format

Ethics approval(s)
Montreal Clinical Research Institute (Institut de Recherches cliniques de Montréal (IRCM)) Human ethics board, 01/03/2010, ref: 2009-33

Study design
Single-centre interventional for 6-months

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
No participant information sheet available'

Health condition(s) or problem(s) studied
ApoB-lipoproteins and risk for type 2 diabetes

Interventions
Participants are asked to follow a hypocaloric diet for six months. The diet is administered during individual sessions by two registered dietitians. Daily energy needs are calculated as basal metabolic rate, measured by an indirect calorimetry, multiplied by a sedentary physical activity factor of 1.4, from which 500 kcal were subtracted.

Participants are counseled to follow a balanced diet based on the Canadian Food Guide and Health Canada (45-65% carbohydrate, 20-35% fat and 15-35% protein). To encourage compliance, subjects met monthly with the dietitians for one hour, during which body weight is also recorded.

Participants are encouraged to maintain their habitual (i.e. sedentary) activity level during the six month intervention. Prior to the baseline and post-intervention metabolic testing, subjects undergo a weight stability period of four weeks (± 2 kg), with their weight being verified weekly at the the study centre.

Intervention Type
Behavioural

Primary outcome measure
1. Plasma apoB-lipoprotein profile is measured using an automated analyzer at baseline and seven months
2. Body composition is measured using dual-energy X-ray absorptiometry (DXA) at baseline and seven months
3. Systemic glucose-induced insulin secretion and sensitivity is measured using a Botnia clamp at baseline and seven months
4. Plasma inflammatory markers are measured using commercial hsELISA kits on blood samples at baseline and seven months
5. Postprandial plasma clearance and oxidation rates of a 13C-labeled high fat meal is measured using isotope ratio mass spectrometry at baseline and seven months
6. Gynoid white adipose tissue function is measured ex vivo using in situ lipoprotein-lipase activity technique at baseline and seven months
7. Gynoid white adipose tissue genetic and protein expression of inflammatory markers is measured using RT-PCR and immunoblot, respectively at baseline and seven months

Secondary outcome measures
1. Blood pressure is measured using an automated machine at baseline and seven months
2. Waist and hip circumferences is measured using a measure tape at baseline and seven months
3. Metabolic rate and macronutrient oxidation rates are measured using indirect calimetry at baseline and seven months
4. Dietary intake is measured using 3-day food intake records at baseline and six months (directly at the end of the hypocaolic diet)
5. Plasma C-peptide is measured using a commercial RIA kit at baseline and seven months
6. Fatty acids are measured using a commercial kit at baseline and seven months
7. ApoB48 is measured using a commercial hsELISA kit at baseline and seven months
8. apoA-1 is measured using an automated analyzer at baseline and seven months
9. PCSK9 is measured using a commercial hsELISA kit at baseline and seven months

Overall study start date
01/10/2007

Completion date
01/08/2014

Eligibility

Key inclusion criteria
1. Having a body mass index (BMI) > 27 kg/m2
2. Aged between 45 and 74 years
3. Having confirmed menopausal status (FSH ≥ 30 U/l) for women
4. Non-smoker
5. Sedentary (less than 2 hours of structured physical exercise (ex: sports club) per week)
6. Low alcohol consumption: less than 2 alcoholic drinks/day

Participant type(s)
Healthy volunteer

Age group
Mixed

Sex
Both

Target number of participants
82

Total final enrolment
59

Key exclusion criteria
1. Abnormal physiological values necessitating rapid medical intervention:
1.1. Elevated risk of cardiovascular disease (>20% of calculated Framingham Risk Score)
1.2. Fasting glycaemia > 7.0 mmol/L
1.3. Blood pressure >160/100 mmHg
1.4. Hb < 100 g/L
1.5. Creatinin > 135 µmol/L
2. AST or ALT > 3 times upper normal level
3. Suffering from:
3.1. Claustrophobia
3.2. Type 1 or 2 diabetes
3.3. Un-treated thyroid disease
3.4. Cardiovascular or vascular disease with an event occurring less than 6 months ago
3.5. Event of cancer in the last 3 years
3.6. Chronic inflammatory disease such as rheumatoid arthritis or lupus
4. Abnormal blood coagulation
5. Presently following or have followed in the past 3 months :
5.1. Oestrogen treatment
5.2. Hormone replacement therapy (except thyroid hormone at a stable dose)
5.3. Corticosteroids, nerve sedatives
5.4. Hypertension treatment
5.5. Hyperlipidemia treatment
5.6. Anticoagulant treatment
5.7. Weight-loss, psycho-active or adrenergic agonist medications
6. Substance abuse
7. Have exceeded the annual total allowed radiation dose (like X-ray scans and/or tomography in the previous year or in the year to come) according to the physician’s judgement.
8. Lack of time to participate in the full length of the study (33 weeks)
9. All other medical or psychological conditions deemed inappropriate according to the physician

Date of first enrolment
01/03/2010

Date of final enrolment
01/11/2013

Locations

Countries of recruitment
Canada

Study participating centre
Montreal Clinical Research Institute (Institut de Recherches cliniques de Montréal (IRCM))
110, Avenue des Pins Ouest
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Sponsor information

Organisation
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+1 514 987 5500
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Sponsor type
Research organisation

Website
https://www.ircm.qc.ca

Organisation
Université de Montréal

Sponsor details
Faculty of Medicine, Department of Nutrition
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Sponsor type
University/education

Website
https://nutrition.umontreal.ca/

ROR
https://ror.org/0161xgx34

Funder(s)

Funder type
Government

Funder Name
Canadian Institutes of Health Research

Alternative Name(s)
Instituts de Recherche en Santé du Canada, Canadian Institutes of Health Research (CIHR), CIHR_IRSC, Canadian Institutes of Health Research | Ottawa ON, CIHR, IRSC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Canada

Results and Publications

Publication and dissemination plan
Baseline data are already published in peer reviewed journals and presented at national and international conferences.

Intention to publish date
15/12/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study is not expected to be made available as we did not seek consent from participants to share their data publically. Additional sample and data analysis can be conducted in collaboration with Dr May Faraj

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other publications	baseline data	01/05/2013		Yes	No

Other publications	baseline data	01/09/2015		Yes	No
Other publications	baseline data	28/09/2015		Yes	No
Other publications	baseline data	01/01/2017		Yes	No
Results article	results	01/07/2018	05/08/2019	Yes	No
Other publications	Post hoc analysis	01/02/2021	23/08/2023	Yes	No
Other publications	Post hoc analysis	24/03/2023	23/08/2023	Yes	No
Results article		01/05/2019	23/08/2023	Yes	No