Changes in intracellular metabolism and inflammatory function of circulating and adipose tissue depot-specific CD14+ cells in obesity and diabetes mellitus

Published: 15-02-2016
Last updated: 19-04-2024

In this study we will investigate the intracellular metabolism and inflammatory state of CD14+ cells from blood and different adipose tissue depots in subjects with type 2diabetes mellitus compared to lean and obese healthy controls.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational invasive

Summary

ID

NL-OMON42823

Source
ToetsingOnline

Brief title
Characteristics of CD14+ cells in obesity and diabetes mellitus

Condition

- Diabetic complications

Synonym
adipose tissue chronic low-grade inflammation, inflammation of the adipose tissue

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Vidi grant voor Rinke Stienstra

Intervention

Keyword: adipose tissue (AT), metabolism, monocytes, Type 2 diabetes mellitus (T2DM)

Outcome measures

Primary outcome

To determine metabolic pathways important for inflammatory function of CD14+ cells from blood, visceral and subcutaneous adipose tissue by gene expression analysis (human microarray platform by affymetrix) using a bioinformatics approach.

To determine the intracellular metabolism of CD14+ cells from blood and adipose tissue by measurements of metabolites in cell lysates or supernatants of the (cultured) immune cells and by analysis of intracellular metabolic signalling pathways on protein and gene expression level.

Secondary outcome

To determine the differences in inflammatory potential of CD14+ cells isolated from lean, obese and diabetic subjects by histological assessment of adipocyte size, macrophage infiltration and formation of crown-like structures in the different adipose tissue depots and by measurements of plasma cytokines and cytokines released upon stimulation of cultured cells isolated from the blood.

Study description

Background summary

The adipose tissue is a metabolically highly active tissue affecting many other tissues such as the liver, skeletal muscle and vasculature. The adipose tissue produces and secretes a wide variety of proteins. Adipose tissues can differ in their metabolic characteristics dependent on their anatomical location, namely the visceral and subcutaneous depots. Obesity is accompanied by an accumulation of the adipose tissue mass as well as a hypertrophy and abnormal secretory function of adipocytes. Furthermore, obesity is associated with an increased infiltration of monocytes and macrophages into the adipose tissue, leading to impaired lipid and glucose metabolism that is driven by an enhanced state of inflammation. Therefore, the adipose tissue associated with a more pro-inflammatory state is known to play a central role in the link between obesity and insulin resistance. However, underlying mechanisms leading to adipose tissue inflammation still remain elusive.
Recent research has revealed that the inflammatory function of macrophages is determined by their metabolic status and is thereby influenced by the metabolic environment that the cell is exposed to. Thus, different adipose tissue depots might differentially influence the metabolism and thus inflammatory function of monocytes and macrophages. Moreover, we hypothesize that the adverse metabolic milieu in obese, insulin-resistant adipose tissue, i.e. high glucose levels (hyperglycemia), hypoxia and elevated free fatty acid levels, is leading to a shift in macrophage metabolism towards glycolysis and thereby dictates the development of adipose tissue inflammation during obesity.

Study objective

In this study we will investigate the intracellular metabolism and inflammatory state of CD14+ cells from blood and different adipose tissue depots in subjects with type 2diabetes mellitus compared to lean and obese healthy controls.

Study design

In this case-control study, the intracellular metabolism and inflammatory function of CD14+ cells isolates from the blood and the adipose tissue will be characterized in lean and obese healthy human volunteers as well as in T2DM patients. To this purpose, paired samples of visceral adipose tissue, subcutaneous adipose tissue (each approximately 5g) and blood will be obtained from 45 subjects undergoing elective abdominal surgery, such as cholecystectomy. Prior to the surgical procedure, subjects will undergo anthropometric measurements (BMI). Blood will be drawn to determine hsCRP, plasma glucose, HbA1c, plasma insulin and plasma lipids and to isolate CD14+ cells for a detailed phenotypic characterization. During the surgery, adipose tissue biopsies of approximately five grams will be obtained from both the abdominal subcutaneous and omental visceral depots. Fractions of these biopsies will immediately be stored in transport medium for further processing and analysis at the laboratory of Internal Medicine.

Study burden and risks

The additional burden for the subjects associated with this study is minimal. There is a small risk of bleeding at the place where the adipose tissue biopsies will be obtained. This could directly be treated by the surgeon. Moreover, a blood sample of 20 ml will be taken prior to the surgery when the patient is already anaesthetized. Thus, there will be no extra physical or psychological discomfort associated with the participation in the study and the risks which are already associated with the surgery will not be increased. This study is not directly beneficial for the individual subjects, but the results obtained from this study might increase our understanding of innate immune cells and their intracellular metabolism in relation to the development of diabetes. This in turn, could be of great importance in developing future therapeutics for obese patients with diabetes.

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

group 1 (males and females): age: 35-75 years, body mass index (BMI) of 19-25 kg/m2;group 2 (males and females): age: 35-75 years, body mass index (BMI) of >25 kg/m2 ;group 3 (males and females): age: 35-75 years, body mass index (BMI) of >25 kg/m2, diagnosis of T2DM

Exclusion criteria

any presence of a chronic or acute inflammation and/or autoimmune disorder, any anti-inflammatory medication, metabolic diseases, endocrine diseases and chronic and/or acute inflammatory diseases (high sensitivity C-reactive protein > 1 mg/liter)

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-07-2016
Enrollment:	45
Type:	Actual

Ethics review

Approved WMO

Date:	15-02-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL55814.091.15

Study results

Results posted: 26-05-2019

First publication
26-05-2019