The effect of a high-fat meal on the immune system

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Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24430

Bron
Nationaal Trial Register

Verkorte titel
SHAKE study

Aandoening

atherosclerosis
innate immune memory
high-fat challenge

slagaderverkalking
geheugen van het aangeboren afweersysteem
vetrijke maaltijd

Ondersteuning

Primaire sponsor: Radboud University Medical Center
Overige ondersteuning: Radboud University Medical Center

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The primary endpoint is the TNFa production upon ex vivo stimulation with LPS of monocytes isolated 72h after the consumption of high-fat shake.

Toelichting onderzoek

Achtergrond van het onderzoek

Background of the study:

Atherosclerosis is characterized by a persistent inflammation of the arterial wall. Monocyte-derived macrophages are the most abundant immune cells in atherosclerotic plaques. It has recently been shown that not only immune cells of the adaptive immune system, but innate immune cells as well are able to adopt a long-term pro-inflammatory phenotype upon stimulation. This nonspecific memory of innate immune cells is mediated by epigenetic and metabolic reprogramming and is termed "trained innate immunity." Previous findings from our lab have shown that not only bacterial components such as LPS, but also pro-atherogenic particles such as oxidized LDL can induce trained immunity in monocytes. Interestingly, this memory-effect of trained immunity indicates that even temporary triggers could induce the persistent inflammation in atherosclerosis.

Triglyceride-rich lipoproteins (TRL) have been identified as an important independent risk factor for atherosclerosis. Moreover, elevated plasma levels of these lipoproteins are associated with increased pro-inflammatory markers. TRLs, however, are characterized by alternating plasma levels, with brief elevations following (fat containing) meals. Notably, a high-fat meal not only contributes to the transient increase of TRL plasma levels, but also induces a brief elevation in LPS levels by briefly increasing the permeability of the gut.

We now aim to investigate whether a single high-fat meal can induce trained innate immunity, since this concept might explain how brief postprandial effects can translate into a long-term pro-inflammatory and pro-atherogenic monocyte phenotype.

Objective of the study:

The primary objective is to determine whether a high-fat meal can induce a persistent pro-inflammatory monocyte phenotype, characterized by an increased cytokine production capacity upon ex vivo stimulation. Secondary objectives are metabolic and epigenetic reprogramming of monocytes at these time points as well as the capacity of serum, isolated before and 1-6h after an oral fat load, to induce an increased cytokine production in healthy human monocytes.

Study design:

Cross-over high-fat challenge intervention study.

Study population:

Healthy human volunteers, aged between 18 and 40 years.

Intervention:

A single high-fat challenge (milkshake containing 95g of fat) and ‘control’ shake (comparable to an average breakfast).

Primary study parameters/outcome of the study:

Blood will be drawn at t=0h (before) and at t=1h, t=2h, t=4h, t=6h, t=24 and t=72h after an oral fat load and at the same time points after a ‘control’ shake. The primary endpoint is the monocyte TNFa production upon ex vivo stimulation with LPS (TLR4 ligand) at t=72h.

Secundary study parameters/outcome of the study:

Additional secondary endpoints are the monocytes’ inflammatory phenotype as assessed by flowcytometry analysis , epigenetic and metabolic reprogramming and serum induced inflammation.

Doel van het onderzoek

Atherosclerosis is characterized by a persistent inflammation of the arterial wall. Monocyte-derived macrophages are the most abundant immune cells in atherosclerotic plaques. It has recently been shown that not only immune cells of the adaptive immune system, but innate immune cells as well are able to adopt a long-term pro-inflammatory phenotype upon stimulation. This nonspecific memory of innate immune cells is mediated by epigenetic and metabolic reprogramming and is termed "trained innate immunity." Previous findings from our lab have shown that not only bacterial components such as LPS, but also pro-atherogenic particles such as oxidized LDL can induce trained immunity in monocytes. Interestingly, this memory-effect of trained immunity indicates that even temporary triggers could induce the persistent inflammation in atherosclerosis.

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Onderzoeksopzet

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Onderzoeksproduct en/of interventie

A single high-fat challenge (milkshake containing 95g of fat) and ‘control’ shake (comparable to an average breakfast).

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Age between 18 and 40 years

- LDL cholesterol < 3.5 mmol/l, fasting triglycerides < 2 mmol/l

- No previous cardiovascular events

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Smoking within the year before study entry

- Diagnosed with any long-term medical condition that can interfere with the study (i.e. renal failure, cardiovascular disease, diabetes, rheumatoid arthritis etc.)

- Medication (with the exception of oral contraceptives) or supplement use (i.e. omega3)

- BMI < 18 or > 27 kg/m2

- Previous vaccination within 3 months prior to study entry

- Current infection or clinically significant infections within 1 month before study entry (defined as fever > 38.5°C)

- Allergic to cow milk/dairy products

- Pregnancy/lactation

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Enkelblind
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	04-03-2019
Aantal proefpersonen:	15
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Positief advies

Datum:	08-11-2018
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL7347
NTR-old	NTR7612
Ander register	Radboudumc : 107808

Resultaten