Influence of saltintake on Microcirculation and immune System

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In this study we aim to elucidate effects of dietary sodium intake on:1. Body weight and blood pressure2. Microcirculation by studying the capillary network during high and low sodium conditions.3. Adaptive and innate immune system by studying...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON50531

Source
ToetsingOnline

Brief title
DYNAMICS-2

Condition

- Immune disorders NEC
- Vascular hypertensive disorders

Synonym
high blood pressure, hypertension

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: immune system, microcirculation, salt, sodium

Outcome measures

Primary outcome

The primary endpoint will be body weight and blood pressure, as represented by the mean arterial pressure. Several secondary endpoints are proposed.

Secondary outcome

Concerning effects of sodium intake on microcirculation, the endpoint will be capillary density and perfusion as assessed by Sidestream Darkfield (SDF) imaging and retinal vascular imaging, in response to a high and a low sodium diet. We will investigate whether changes in these parameters correlate with changes in the macrocirculation. The influence of administration of nitroglycerin, an endothelial-independent vasodilator, on microcirculatory changes in the setting of either low or high salt intake will also be examined. Concerning the effects of sodium intake on the immune system, we will assess T-lymphocyte populations (i.e. IL-17, Th17), neutrophil subpopulations, and monocyte subpopulations, by flow cytometry in different sodium conditions.

Study description

Background summary

Cardiovascular disease (CVD) is the leading cause of (premature) death in the world. Arterial hypertension is one of the most important risk factors for developing CVD. Currently in developed Western countries daily salt intake is 8 to 12 grams, well above the recommended daily intake. There is accumulating evidence from human studies that high sodium intake is an important contributor to development of hypertension and subsequent cardiovascular events. For a

substantial time, it was thought that sodium increases blood pressure via an increase in extracellular volume. However, this assumption was challenged by several sodium balance studies. Instead, recent animal studies point to a role for the microcirculation and the immune system. These findings have not been confirmed in human subjects. We want to investigate two patient groups that are known to have alterations in their microcirculation as well as with alterations in their immune system, possibly making them more susceptible to salt-sensitive hypertension. In these patients, we want to assess whether they demonstrate a sodium-induced body weight or blood pressure increase and if so, whether this is related to microcirculatory or immunological changes. These two groups comprise patients with type 1 diabetes mellitus (DM1) and psoriatic arthritis.

Study objective

In this study we aim to elucidate effects of dietary sodium intake on:
1. Body weight and blood pressure
2. Microcirculation by studying the capillary network during high and low sodium conditions.
3. Adaptive and innate immune system by studying circulating T-lymphocyte subpopulations,
neutrophil subpopulations, and monocyte subpopulations.

Study design

This study has a randomized experimental interventional cross-over study design.

Intervention

dietary intervention: low sodium diet (<50 mmol Na+/d) vs high sodium diet (>200 mmol Na+/d)

Study burden and risks

Although this study is investigating two different systems of the human body, it uses the same dietary intervention. When our hypotheses will be confirmed by this study, further knowledge about the relation between microcirculation, immune system, salt intake and hypertension in humans will be provided. Better understanding of pathophysiological mechanisms in patients known to be prone for (salt-sensitive) hypertension is necessary in order to provide support for new therapeutical strategies. Also, current recommendations to reduce salt intake <5 grams daily will be supported. Furthermore, it will strongly emphasize the use of this lifestyle modification in primary prevention of hypertension. Morover, new therapeutic targets can be revealed, and possibly point out a role for immunomodulating therapy in treatment of hypertension.

Participating in this research project will not lead to personal benefit. However, little to no burden is expected when participating in this study. Participants are asked to adhere to a low (<50 mmol Na+) and high sodium diet (>200 mmol Na+) for two weeks each in random order. This intervention causes no harm to the subject, as average sodium intake in males in the Netherlands corresponds to 150-200 mmol daily. The patients will be asked to visit our research department five times which will take approximately nine hours in total. The study visits comprise venous blood drawings, collection of 24-hour urine samples and 24-hour ambulant non-invasive measurements of central and peripheral haemodynamics as well non-invasive assessment of microcirculation. Four (two times two) skin biopsies will be performed, which will be very small in size and will cause only very minor to no scarring. All measurements will cause minimal to no burden to the patient. During two study visits patients will receive one spray of sublingual nitroglycerin. This might cause transient headache and dizziness, but because of the short half-life of nitroglycerin, this effect will last a maximum of 30 minutes.

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

All patients
- Male between 18 and 40 years of age
- Non-treated office blood pressure * 140/90 mmHg
- A body mass index * 30 kg/m2
- Capable of giving written informed consent and able to comply with the requirements and restrictions listed in the informed consent form, DM1 patients
- Known with Diabetes Mellitus type 1
- With or without microalbuminuria defined as:
o either albuminuria 20-200 mg/L in a morning urine sample
o or albuminuria 30-300 mg/24 hrs collected in a 24-hours urine collection
o or albumin-to-creatinin ratio 2,5-25 mg/mmol in a morning urine sample.
- Stable renal function (creatine clearance > 60 ml/min and < 6 ml/min per year decline)
with or without on stable therapy with RAAS inhibiting agents
- HbA1c levels below 10.0% (86 mmol/mol) during the 6 months preceding the study
- Multiple injections of insulin a day, Psoriatic arthritis patients without IL-17 inhibitors
- Known with psoriatic arthritis, stable disease activity (mild or in remission) as clinically
assessed by the treating rheumatologist
- Stable renal function (creatinin clearance > 60 ml/min and < 6 ml/min per year decline, no
overt proteinuria)
- Without use of IL-17 inhibitors, IL-10 inhibitors, IL-23 inhibitors, and leflunomide, Psoriatic arthritis patients with IL-17 inhibitors
- Known with psoriatic arthritis, stable disease activity (mild or in remission) as clinically
assessed by the treating rheumatologist
- Stable renal function (creatinin clearance > 60 ml/min and < 6 ml/min per year decline, no
overt proteinuria)
- Use of IL-17 inhibitors at least 3 months before screening

Exclusion criteria

Patients meeting any of the following exclusion criteria are not to be enrolled in the study:
- An office blood pressure >140/90 mmHg
- A body mass index > 30 kg/m2
- Use of systemic corticosteroids
- Use of NSAIDS >2 times a week
- A major illness in the past 3 months or any significant chronic medical illness that the Investigator would deem unfavourable for enrolment, including chronic inflammatory diseases, excluding the diseases of interest (DM1 and psoriatic arthritis)
- A history of any type of malignancy within the past 5 years with the exception of successfully treated basal cell cancer of the skin
- A history of any renal disease
- A history of any auto-immune disease other than DM1 and psoriatic arthritis
- A history of cardiovascular disease (in the past 6 months) defined as documented coronary artery disease including myocardial infarction, (un-)stable angina pectoris or acute coronary syndrome, precutenaous transluminal coronary angioplasty, coronary artery bypass grafting, cerebrovascular disease including ischemic and hemorrhagic stroke or a subarachnodial bleeding, or peripheral artery disease including aortic aneurysmata
- A history of eye-surgery, glaucoma or retinal eye disorder
- A history, within 3 years, of drug abuse (including benzodiazepines, opioids, amphetamine, cocaine, THC, methamphetamine)
- A history of alcoholism and/or drinking more than 3 units of alcohol per day. Alcoholism is defined as an average weekly intake of >21 units for males. One unit is equivalent to 8 g of alcohol: a half-pint (~240 mL) of beer, 1 glass (125 mL) of wine or 1 (25 mL) measure of spirits
- Smoking or use of tobacco products less then 30 days ago
- Any other issue that in opinion of the Investigator could be harmful to the subject or compromise interpretation of data

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	54
Type:	Anticipated

Ethics review

Approved WMO Date:	14-01-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-03-2020
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

ID: 25435
Source: NTR
Title:

In other registers

Register	ID
Other	....
CCMO	NL63332.018.18
OMON	NL-OMON25435