The Dynamics Study: Influence of NaCl intake on Microcirculation and Immune sytem

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In this study we aim to elucidate effects of dietary sodium intake on:1. Microcirculation by studying the capillary network during high and low sodium conditions.2. Adaptive and innate immune system by studying circulating T-lymphocyte…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON40222

Source
ToetsingOnline

Brief title
Dynamics study

Condition

- Immune disorders NEC
- Vascular hypertensive disorders

Synonym
blood pressure, capillary density, microcirculation, sodium, Th17 cells

Research involving
Human

Sponsors and support

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

Intervention

Keyword: hypertension, immune system, microcirculation, sodium

Outcome measures

Primary outcome

Several primary endpoints are proposed.

1. Microcirculation

A. To assess the effect of dietary sodium intake on capillary recruitment and capillary perfusion determined by capillary density, proportion of perfused density, microculatory flow index and tortuosity, assessed by SDF-imaging, nailfold capillaroscopy and retinal vascular imaging.

B. To assess whether high sodium-induced changes in microcirculation can be restored by nitroglycerin, being a NO donor to the capillary vessel bed.

2. Immune system

A. To assess whether different sodium intakes (high or low salt diet) will lead to changes in circulating T-lymphocyte subpopulations (e.g., Th17 cells).

Secondary outcome

1. Microcirculation

C. To assess if microcirculatory changes in response to dietary sodium are related to macrocirculatory changes, displayed by measurement of central and peripheral blood pressure by use of continuous finger arterial pressure (FinAp) waveform registration with the semi-automatic device Nexfin® and by using radial pulse waveforms with the semi-automatic device Sphygmocor®.

3. Other

A. To assess whether different sodium intakes will lead to changes in eNOS and RNA expression and sulfation of glycosaminoglycans (GAGs) of the skin. This study is in line with other studies of our group studying the influence of dietary salt intake (SALT and SALT-2 study). Due to used storage conditions with formalin, techniques such as mass spectrometry, PCR or western blot are not possible to perform on skin biopsies collected in the SALT studies. Therefore we would like to use skin biopsies of this study in order to perform these techniques. The skin biopsies derived from the SALT-studies will be used to relate the effects of sodium intake on T-cell subpopulations, as part of the current protocol, to influx of inflammatory cells into the skin (macrophages and T-cells).

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. Structural and functional changes of the microcirculation, consisting of all arterial vessels that respond to increasing pressure by a myogenic reduction in lumen diameter, as well as the capillaries and venules, are thought to play an important role in the pathophysiology of hypertension. These microvessels have an important role in the transportation of oxygen and nutrients to tissue cells, and thus their adequate perfusion is essential for tissue and organ function. A high salt diet can lead to changes in microvascular structure and function independent of changes in blood pressure. Human studies on influence of salt intake on microcirculation are mainly performed in hypertensive subjects, so differentiation between the effect of salt intake or hypertension

by itself, or their combination remains difficult. Another, recently revealed, contributor in the onset of hypertension is the immune system. Over the last year there has been emerging evidence that both innate and adaptive immune responses contribute to vascular dysfunction and hypertension. Recent groundbreaking studies have linked the immune system to sodium homeostasis, and consequently salt-sensitive hypertension. However these studies were only carried out in animals or in vitro with human cells.

Study objective

In this study we aim to elucidate effects of dietary sodium intake on:

1. Microcirculation by studying the capillary network during high and low sodium conditions.
2. Adaptive and innate immune system by studying circulating T-lymphocyte subpopulations during high and low sodium conditions.

Study design

This study is a randomized experimental interventional cross-over study design

Intervention

All subjects will be asked to adhere to a low sodium diet (50 mmol Na/day)) and a high sodium diet (200 mmol Na/day) for two weeks each in random order. Furthermore, all subjects will receive one spray of nitroglycerin 0.4 mg sublingual during the study visit 1 and 2.

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 vivo are 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 and high sodium diet for two weeks each in random order. The subjects 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. Two skin biopsies will be performed. All measurements will cause minimal to no burden to the patient. During two study visits subjects 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

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Male between 18 and 40 years of age

- Healthy, as determined by a responsible and experienced physician, based on a medical evaluation including medical history, physical examination (PE) and laboratory tests carried out in the screening visit.
- Non-treated office blood pressure <= 130/85 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

Exclusion criteria

- An office blood pressure >130/85 mmHg
- A body mass index > 30 kg/m2
- 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
- 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
- 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:	Recruitment stopped
Start date (anticipated):	15-07-2016
Enrollment:	18
Type:	Actual

Ethics review

Approved WMO

Date:	22-04-2014
Application type:	First submission
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: 28966
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL44788.018.13
OMON	NL-OMON28966