Influence of NaCl intake on Microcirculation and Immune system

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28966

Source
Nationaal Trial Register

Brief title
Dynamics

Health condition

Salt, Sodium, Microcirculation, Immune system, Zout, Natrium, Microcirculatie, Immuunsysteem

Sponsors and support

Primary sponsor: Academic Medical Center
Source(s) of monetary or material Support: Academic Medical Center

Intervention

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.

Study description

Background summary

Background of the study:

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.

Objective of the study:

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.

Hypotheses

1. Low salt intake will lead to improved microcirculatory structure and function, thereby lowering peripheral vessel resistance and leading to decreased blood pressure, and possibly prevent blood pressure associated end-organ damage.

2. High salt intake will lead to impaired microcirculatory structure and function, thereby increasing peripheral vessel resistance, leading to increased blood pressure.

3. Nitroglycerin, a endothelial-independent source of nitric oxide, will restore high sodiuminduced
changes in microcirculation.

4. High sodium intake will lead to upregulation of inflammatory cells, such as Il-17 producing Th-17 cells.

5. Sodium excess will lead to macrophage influx in the interstitium of the skin, restructuring of the lymphcapillary network, and enhanced eNOS expression.

Study design

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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.

Contacts

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Eligibility criteria

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 enrollment, 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, percutaneous 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
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2014
Enrollment:	18
Type:	Anticipated

Ethics review

Positive opinion

Date:	11-09-2014
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 40222
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL4633
NTR-old	NTR4785
CCMO	NL44788.018.13
OMON	NL-OMON40222

Study results

Summary results

None