The role of glycosaminoglycans and macrophages in salt-sensitivity of blood pressure

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55197

Source
ToetsingOnline

Brief title
SALT-3

Condition

- Other condition

Synonym
Blood pressure, salt-sensitivity

Health condition

Fysiologie van natrium- en volumebalans

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Nierstichting

Intervention

Keyword: Blood pressure, Extracellular volume, Skin, Sodium

Outcome measures

Primary outcome

The primary objective of this study is to explore in DKK and CKD patients the

effects of dietary sodium on body fluid volume, as measured by BP, weight and

bio-impedance measurements.

Secondary outcome

Secundary study parameters are expressed as the effect of salt intake on:

- Skin sodium concentration

- Microcirculatory changes

- Glycosaminoglycan metabolism

- Macrophage activation and lymphangiogenesis

- Microbiome content

Study description

Background summary

The role of sodium consumption in blood pressure (BP) regulation and extracellular fluid (ECF) maintenance is a heavily debated topic. For a substantial time, it was thought that sodium increases BP solely via an increase in ECF. However, this assumption was challenged by several sodium balance studies. Sodium intervention studies revealed two different mechanisms which are relevant for sodium homeostasis. Highly sulphated glycosaminoglycans (GAGs) in the interstitial space and the endothelium facilitate a third

compartment for non-osmotic sodium buffering. In various patients groups, increased sodium buffering as measured with 23Na-MRI is associated with sodium-sensitive hypertension. This finding suggests a causal relation between non-osmotic sodium buffering and sodium-mediated BP development. Furthermore, it has been demonstrated that interstitial sodium buffering is associated with the activation of macrophages and alterations in the lymphangiogenesis and microcirculation, which in turn relate to BP. There is also increasing literature on the influence of the gut microbiome in the absorption of macronutrients, including salt, while salt intake also has a major influence on the composition of the gut microbiome. It is still unclear how this correlates with blood pressure changes.

Study objective

The aim of this study is to investigate in salt-sensitive kidney patients the effect of two different dietary sodium regimens on BP and body fluid volume. Furthermore, we aim to evaluate the way in which new sodium handling mechanisms (interstitial sodium storage, glycosaminoglycan metabolism, immune system activation, microcirculatory changes and microbioma) are involved in this effect.

Study design

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

Intervention

High salt diet (>200 mmol Na+ daily) for 1 week and low salt diet (<50 mmol Na+ daily) for 1 week, each in random order.

Study burden and risks

The burden of this study consists of a total of 3 study visits in which they spend about 10 hours in the hospital. Furthermore we ask patients to visit the hospital 6 times for hand-in their collected 24-hour urine or pick up the automatic device for 24-hour BP measurements, this will take ad maximum 50 minutes extra in the AMC. All participants will be asked to adhere to a low and high Na+ diet and collect 24-hour urine samples during these diets. The study comprises extra venous blood drawing and various extra diagnostic test. Invasive measurements with sodium biopsies are also part of the study visits. At present sodium homeostasis and the pathophysiology behind salt-sensitivity in kidney patients is not well understood. In clinical pratice kidney patients are advised to restrict their sodium consumption, however this is very difficult for most patients.

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)

Inclusion criteria

All subjects:
- Men and women Between 18 and 75 years of age
- 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

Microalbuminuric type 2 diabetes patients:
- Known with Diabetes Mellitus type 2
- Either albuminuria (20-200 mg/L in a morning urine sample / 30-300 mg/24 hrs)
- Stable renal function (eGFR 45-90 ml/min/1.73m2) with or without on stable therapy with RAAS inhibiting agents
- HbA1c levels below 10.0% (86mmol/mol) during the 6 months preceding the study

Nondiabetic CKD patients
- Known with CKD stage 2 - 3a
- Stable renal function during the 6 months preceding the study (eGFR 45-90 ml/min/1.73m2) with or without on stable therapy with RAAS inhibiting agents
- Albuminuria (> >200 mg/L in a morning urine sample / 500 - 3000mg/24 hrs)

Exclusion criteria

- 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 of any significant chronic medical illness that the Investigator would deem unfavourable enrolment, including chronic inflammatory diseases, excluding the diseases of interest (DM2 and CKD) ;
- A history of any type of malignancy within the past 5 years with the expectation of successfully treated basal cell cancer of the skin;
- 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 haemorrhagic stroke or a subarachnodial bleeding, or peripheral artery disease including aortic aneurysmata;
- A history of eye surgery, glaucoma of retinal 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 9 g of alcohol: a half-pint (~ 240mL) of beer, 1 glass (125 mL) of wine or 1 (25ml) measure of spirits;
- Smoking or use of tobacco products less than 30 days ago;
- Any other issue that in opinion of the Investigator could be harmful to the subject or compromise interpretation of the 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:	Recruiting
Start date (anticipated):	01-07-2020
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	13-02-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-09-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	15-09-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

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	NL70705.018.19