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

No registrations found.

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

Summary

ID

NL-OMON20689

Source
NTR

Brief title
SALT-3

Health condition

Salt-sensitive hypertension - chronic kidney disease - diabetic kidney disease

Sponsors and support

Primary sponsor: Amsterdam UMC, location AMC
Source(s) of monetary or material Support: Dutch Kidney Foundation (projectcode 18OKG12)

Intervention

Outcome measures

Primary outcome

The primary outcome is to explore in DKD and CKD patients the effects of dietary sodium on body fluid volume, as measured by BP, weight and bio-impedance measurements.

Secondary outcome

The evaluation of the attribution of new sodium handling mechanisms (skin sodium storage, glycosaminoglycan metabolism, microcirculatory changes, immune system activation) to the response of body fluid volume to different salt intakes.

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. We want to investigate these new mechanisms in the sodium-mediated BP development in kidney patients. These patients are characterized by sodium sensitivity, but yet it is unknown whether in these patients GAG associated non-osmotic sodium buffering and macrophage activation is relevant for sodium induced BP. With the SALT-3 study we aim to investigate the effect of two different dietary sodium regimens on BP and body fluid volume in salt-sensitive kidney patients. Furthermore, we aim to evaluate the way in which new sodium handling mechanisms (interstitial sodium storage, glycosaminoglycan metabolism, immune system activation, microcirculatory changes) are involved in this effect.

Study objective

1. DKD patients are salt-sensitive due to a decreased sodium buffering capacity (damaged ESL). As a consequence a high sodium diet will lead to water retention, resulting in increased ECF, body weight and blood pressure.

2. CKD patients are salt-sensitive due to a decreased level of functional nephrons. These patients show a BP response to high sodium because of non-osmotic sodium buffering saturation in constant high sodium concentrations.

Study design

Screening visit and one study visit after each diet.

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 one week each in random order.

Contacts

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Eligibility criteria

Inclusion criteria

All subjects:
- Age between 18 and 40 years;
- Office BP ≤ 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;
- With microalbuminuria defined as: Either albuminuria 20-200 mg/L in a morning urine sample; or albuminuria 30-300 mg/24 hrs collected in a 24-hours urine collection; or albumin-to-creatinin ratio 2.5-25 mg/mmol in a morning urine sample
- 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% (86 mmol/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;
- With albuminuria defined as: Either albuminuria >200 mg/L in a morning urine sample; or albuminuria 500 – 3000 mg/24 hrs collected in a 24-hours urine collection; or albumin-to-creatinin ratio >25 mg/mmol in a morning urine sample

Healthy volunteers:
- 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.

Exclusion criteria

- An office BP >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 and >14 units for women. One unit is equivalent to 9 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 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
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-03-2020
Enrollment:	75
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	02-03-2020
Application type:	First submission

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
NTR-new	NL8420
Other	METC AMC : METC 2019_271

Study results