The effects of capsaicin and tea on sodium and water homeostasis as measured by osmoregulation and blood pressure.

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1. To assess whether acute TRPV1 activation by capsaicin or ENaC down regulation by flavonoids modulate osmoregulation in healthy subjects2. To assess whether capsaicin and flavonoids affect blood pressure

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON40691

Source
ToetsingOnline

Brief title
PEPPER study

Condition

- Cardiac disorders, signs and symptoms NEC
- Electrolyte and fluid balance conditions

Synonym
hyponatremia, syndrome of inappropriate antidiuresis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Capsaicin, flavonoids, osmoregulation, TRPV1

Outcome measures

Primary outcome

The primary endpoint is the control period-subtracted change in serum sodium induced after an oral administration of capsaicin or tea, with and without WL.

Secondary outcome

Secondary endpoints hold plasma osmolality, co-peptin, vasopressin (AVP), RAAS hormones as well as urinary volume, urinary sodium excretion, and urinary osmolality. Also, blood pressure, body weight and body temperature will be measured.

Study description

Background summary

Hyponatremia, defined as a plasma sodium concentration <135 mmol/L, is the most common electrolyte disorder found worldwide. Hyponatremia is independently associated with increased morbidity and mortality in various groups of patients and in the general population. Attention deficits, gait disturbances, falls, fractures and osteoporosis are all important consequences of chronic hyponatremia. Thus, disturbed osmoregulation leading to hyponatremia has important impact on general health. The pathophysiology of hyponatremia however is incomplete. Generally, excess of water is regarded as the main cause of a low serum sodium concentration. Central and local compensation mechanisms become more active when a change of sodium concentration or plasma osmolality is detected. The reason why some subjects, despite these compensation mechanisms, still develop hyponatremia is largely unknown. Our group just discovered a significant association between plasma sodium concentration and

synonymous single nucleotide polymorphism (SNP) in the TRPV1 gene. TRPV1 is a protein that can be activated by its ligand capsaicin (i.e., the active purgent of red hot chili). Modulation of TRPV1 expression and activation by capsaicin administration is hypothesized to induce hyponatremia. Flavonoids include a huge group of naturally occurring organic compounds and seem to exhibit effects on sodium and water homeostasis as well. Animal studies have demonstrated that flavonoids down regulating the epithelium sodium channel (ENaC) in the kidney, preventing sodium reabsorption and stimulating natriuresis as a consequence. Consumption of flavonoids may put subjects at risk of development of hyponatremia. To our knowledge, the effects of both capsaicin and tea on hydration status have not been studied in human subjects so far.

Study objective

1. To assess whether acute TRPV1 activation by capsaicin or ENaC down regulation by flavonoids modulate osmoregulation in healthy subjects
2. To assess whether capsaicin and flavonoids affect blood pressure

Study design

A single-blinded randomized cross-over interventional study

Intervention

Capsaicin and tea (flavonoids) will be administered to examine the effects on osmoregulation, kidney function and blood pressure with and without a concurrent water load (WL). For the WL, 20mL/kg water has to be ingested in 20 minutes. For the WL warmish water will be used.

Study burden and risks

Nature and extent of the burden and risk associated with participation, benefit and group relatedness: When our hypotheses will be confirmed by this study, further knowledge about the relation between capsaicin, activated TRPV1, flavonoids, ENaC downregulation, disturbed osmoregulation and sodium concentration in humans will be provided. Better understanding of pathophysiological mechanisms in vivo are necessary in order to provide support for new therapeutic strategies and epidemiological approaches. Participating in this research project will not lead to personal benefit or to group level benefit. Little to no burden is expected when participating in this study. Subjects will visit our research department 4 times, totaling 19 hours. During these visits venous blood will be drawn totaling approximately 158 mL. Subjects will be asked to collect 24-h urine thrice. This study aims to unravel one of the pathophysiological mechanisms leading to hyponatremia. At the very long run various groups of patients might benefit from the results, particularly patients at risk for hyponatremia, such as elderly subjects, subjects using

diuretics, subjects with heart failure or renal failure.

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 *135/85 mmHg
- Body Mass Index (BMI) * 30kg/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 * 135/85 mmHg
* A body mass index * 30 kg/m2
* unwillingness to quit temporally being exposed to spicy food
* 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 succesfully treated basal cell
carcinoma of the skin.
* A history of any renal disease
* A history of any blood clotting disorders
* 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 (MI), (un-)stable angina pectoris or acute coronary syndrome (ACS), precutenaous
transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), cerebrovascular disease,
including ischaemic and hemorrhagic stroke or a subarachnoidal bleeding (SAB), or peripheral artery disease,
including aortic aneurysmata (AA).
* A history, within three years, of drugs abuse, including benzodiazepines, opioids, amphetamines, cocain and
Cannabis (THC).
* A history of alcoholism and/or drinking more than 3 units of alcohol per day. Alcoholism is defined as an average
weekly intake > 21 units for males. One unit is equivalent to 8 g Of alcohol: a half-pint (240mL of beer), 1 glass
(125mL) of wine or one measure (25mL) of hard liquor.
* Smoking or usage of tabacco products less than 30 days ago.
* Any other issue that in opinion of the investigator could be harmful to the subject or comprise interpretation of data.

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-01-2015
Enrollment:	24
Type:	Actual

Ethics review

Approved WMO

Date:	24-12-2014
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

No registrations found.

In other registers

Register	ID
CCMO	NL48629.018.14