The effect of dietary salt intake on proximal tubular endocytic function

Published: 09-05-2017
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To investigate whether dietary salt intake influences proximal tubular endocytic function.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON45413

Source
ToetsingOnline

Brief title
SALT

Condition

- Nephropathies

Synonym
proteinuria, urinary protein loss

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: kidney, proteinuria, sodium, tubule

Outcome measures

Primary outcome

Proximal tubular endocytic function.

Secondary outcome

Blood pressure, RAS components, kidney function, serum and urine electrolytes,

body fluid composition

Study description

Background summary

Albuminuria is strongly and independently associated with the risk of end-stage renal disease. Higher sodium intake is associated with increases in urine albumin excretion both in healthy subjects and in chronic kidney disease, and dietary sodium restriction reduces albuminuria, partially independently of blood pressure. A healthy person's urine is virtually devoid of the relatively large serum protein albumin, which was classically attributed to optimal glomerular filtration barrier function. In contrast, recent reports indicate significant filtration of this protein and a greater quantitative role for proximal tubule cells in reabsorbing filtered albumin to minimise albuminuria. The endocytic receptors megalin and cubilin mediate proximal tubular reabsorption of numerous filtered proteins. These include albumin and smaller proteins that are more readily filtered by virtue of their low molecular weight, such as retinol-binding protein (RBP), vitamin d-binding protein (DBP) and *2-microglobulin (*2M). The very few factors that are known to regulate megalin and cubilin expression include tumour growth factor-* (TGF-*) and angiotensin II. Preliminary results from animal experiments by our group and others indicate that the renal expression of megalin and cubilin is inversely correlated with dietary sodium intake.This remarkable finding could offer an additional explanation for the antiproteinuric effect of dietary sodium restriction beyond differences in protein filtration. To our knowledge, the effects of interventions in dietary sodium intake on proximal tubular endocytic function have not been studied in humans.
Urinary extracellular vesicles (uEVs) are constantly excreted by tubular epithelial cells, and they can be readily isolated from spot urine samples. It is assumed that their composition mimics the membrane expression of proteins in the cells they derive from. Hence, isolation and analysis of uEVs could allow for a *liquid kidney biopsy* under various experimental conditions at no risk or significant burden to the study participant. Cubilin and megalin can be

detected in uEVs.

Study objective

To investigate whether dietary salt intake influences proximal tubular endocytic function.

Study design

Intervention study

Intervention

All participants will be sequentially placed on a low salt and a high salt diet.

Study burden and risks

All participants are placed on a dietician-prescribed liquid low salt diet during 8 days. In this period, participants are asked not to consume other drinks than water, tea or a specific lemonade provided by the investigators. In the last 4 days, dietary salt is supplemented via 1000-mg NaCl capsules, 14 per day, to reach a high salt intake. On the day before commencement of the diet (day 0), days 4 and 8, participants collect 24-hour urine, and blood pressure is measured during 24 hours using a wearable device (ABPM). To avoid potential interference, participants are asked to refrain from strenuous physical exercise (sports) and sexual intercourse on these specific days. After finishing 24-hour urine collection and ABPM, participants drink 300 mL of water. Upon arrival in the Erasmus MC, a fasted blood sample is drawn, spot urine is collected, participants are weighed and a body composition measurement is performed. For the latter, we use the Body Composition Monitor device, which quickly measures fluid distribution via electrodes placed on hands and feet in a non-painful, noninvasive manner. After this, participants can commence their next dietary phase (day 5) or leave the study (day 9).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Age 18-30 years
- Male sex

Exclusion criteria

- Use of any medication
- Smoking
- History of hypertension, cardiovascular / metabolic / renal / urogenital / hepatic disease, substance abuse
- eGFR < 90 mL/min/1.73 m2 (calculated using the CKD-EPI equation)
- Albuminuria > 20 mg/10 mmol creatinine in spot urine
- Hypertension at screening visit (>140/90 mmHg by office blood pressure measurement)
- Urinary tract infection at screening visit
- Participation in evening or night shift work during the study period and the week before enrolment
- BMI > 27 kg/m2
- Inability to adhere to the study protocol (due to language or cognitive disability)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-05-2017
Enrollment:	8
Type:	Actual

Ethics review

Approved WMO

Date:	09-05-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL61199.078.17