Effect of a standard oral salt loading test on the renin-angiotensin-aldosterone system in healthy subjects - assessment of reference values

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- assessment of age dependent reference values (ages 20 - 70 yrs) for plasma renin (activity and concentration), serum aldosterone and 24h urinary aldosterone (free and metabolites) during a regular diet and after a 3 day oral salt loading test-...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Adrenal gland disorders
Study type	Interventional

Summary

ID

NL-OMON39385

Source
ToetsingOnline

Brief title
RAAS changes after salt loading

Condition

- Adrenal gland disorders

Synonym
adrenal hypertension, primary aldosteronism

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W,CIS bio international, 91192 Gif/Yvette Cedex, France,fabrikant renine assay

Intervention

Keyword: reference values, renin-angiotensin system, sodium chloride

Outcome measures

Primary outcome

Changes in renin-angiotensin-aldosterone system (RAAS) after an oral salt

loading test. The following RAAS parameters will be measured: plasma renin

concentration, plasma renin activity, serum aldosterone, urinary aldosterone

(free + metabolites)

Secondary outcome

Influence of OC's on previously described RAAS parameters before and after salt

loading.

Study description

Background summary

Recent data have shown primary aldosteronism (PA) to be the most frequent cause of secondary hypertension, with reported prevalence rates of 5-12% among hypertensive subjects in hypertension units as well as in primary care centers. Diagnosing PA is clinically relevant, as causal treatment is feasible in case of a aldosteron producing adrenal tumour - hypertension can be cured through an adrenalectomy. in case of bilateral adrenal hyperplasia, targeted drug therapy can be offered.
The diagnostic approach of PA contains 3 subsequent phases: screening hypertensive subjects (plasma potassium, renin and aldosteron measurements), confirmation tests (demonstrating increased plasma and/or aldosteron levels in serum and/or urine after oral/intravenous salt loading, several test protocols) and localisation studies (MRI/CT, adrenal venous sampling).
Screening for PA in hypertensive patients is usually done by measuring serum aldosterone (increased in PA) and plasma renin (decreased in PA). The ratio of these measurements - called the aldosterone- renin ratio - is currently the

most frequently used screening test to detect PA. Plasma renin can be assessed by measurement of enzyme activity (plasma renin activity, PRA), in which the generation of angiotensin-I is measured with a RIA. PRA measurements have some disadvantages: chilled specimen collection, time consuming and relative large intra- and interassay variation coefficients. Alternatively, plasma renin concentration (PRC) can also be assessed. Advantages of the PRC compared to PRA are: specimen collection at room temperature, possibility of automated analysis and less intra- and interassay variation.
Until now, reference values for plasma renin in healthy and hypertensive subjects have been based on PRA measurements. Although the influence of age on plasma renin and aldosterone levels has been recognized long time ago, age dependent reference values are presently not available.
Oral contraceptives (OC's) affect the renin-angiotensin-aldosterone system, through stimulation of the hepatic angiotensinogen synthesis by the ethinylestradiol component. OC's result in a slight increase of PRA (from more endogenous substrate) and a decrease of plasma renin secretion (slight increase of angiotensin-II inhibits renin secretion through negative feedback mechanism).
An alternative screening method for PA is to assess the urinary aldosterone secretion. Aldosterone is secreted into urine as free-aldosterone and as several metabolites (mainly aldosterone18-glucuronide en 3alpha,5beta-tetrahydroaldosterone). It has been suggested that a normal 24-hour urinary aldosterone excretion excludes the presence of PA, but data are limited.

Study objective

- assessment of age dependent reference values (ages 20 - 70 yrs) for plasma
renin (activity and concentration), serum aldosterone and 24h urinary aldosterone (free and metabolites) during a regular diet and after a 3 day oral
salt loading test

- validation of plasma renin concentration assay against PRA

- to evaluate the effect of OC's on plasma renin concentration and PRA measurements

Study design

Diet intervention study.

Intervention

All participants will be exposed to a standard oral salt loading test.

Study burden and risks

- 2 venapunctions (blood volume 1st venapunction: 21.5 ml, 2nd venapunction
19.5 ml)
- 24 hour urine collection (2x)
- answering a few sreening questions:
a. medication
b. past medical history
- limited physical examination: blood pressure (2x), body weight, height

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

healthy male and female subjects with a normal blood pressure (RR < 140/90 mmHg)

Exclusion criteria

- hypertension (RR>140/90mmHg)
- past medical history of heart failure
- elevated liver enzymes (ALAT, ASAT, gGT, AF > 1.5 URL)
- renal insufficiency (serum creatinine > 110 micrmol/l)
- diabetes mellitus (any type)
- pregnancy
- use of specific drugs: antihypertensives, nonsteroidal anti-inflammatory drugs, diuretics, potassium supplements

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-11-2006
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	05-10-2006
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	11-06-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL13692.042.06