Licorice Influences on cortisol/cortisone, electrolytes and blood pressure

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To assess the effect of a fixed dose of licorice with a specified amount of glycyrrhizic acid on blood pressure, potassium and sodium levels and cortisol/cortisone balance in normotensive subjects. In order to explore individual genetic influences,...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON46407

Source
ToetsingOnline

Brief title
LICORICE study

Condition

- Other condition

Synonym
High bloodpressure, hypertension

Health condition

bloeddruk, elektrolyten, cortison/cortisol balans

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Blood pressure, Cortisol/cortisone, Electrolytes, Licorice

Outcome measures

Primary outcome

The primary outcome will be the difference in 24-hour ambulatory systolic and diastolic blood pressure after exposure to a fixed dose of licorice

Secondary outcome

Secondary outcome parameters will be the difference in cortisol/cortisone ratio, potassium, sodium and aldosterone excretion in 24h urine collection. Furthermore, the difference in concentrations of plasma potassium, sodium, eGFR, creatinine, aldosterone and plasma renin activity will be measured. In addition, we will determine the individual weight at the end of the run-in period (screening) and at the end of the intervention period. Finally, an exploratory analysis for single nucleotide polymorphisms in the gene encoding for 11-beta-hydroxysteroiddehydrogenase will be performed in those five participants with the greatest increase in blood pressure

Study description

Background summary

Glycyrrhizic acid is known to induce pseudohyperaldosteronism, which results in a reduction of the selective conversion of cortisol to cortisone. Cortisol has a much higher affinity for the mineralocorticoid receptor compared to cortisone

and causes activation of the mineralocorticoid receptors, resulting in hypertension, increased sodium retention, excessive renal potassium loss, low renin and reduced aldosterone levels. There is no worldwide consensus of the legal upper use limit specified for the maximum amount of glycyrrhizic acid that may be present in foods and supplements. The European Food Safety Authority (EFSA) determine a maximum level of glycyrrhizic acid in confectionery of 1500 mg/kg. However, this amount is often exceeded by manufacturers. A maximal level of 100 mg/person/day glycyrrhizic acid ingestion in adults is considered to be safe for the majority of the population, but many individuals exceed the recommended amount. Licorice induced hypertension has been focus of a few studies, but the individual susceptibility to licorice exposure and variations in blood pressure and urinary excretion of cortisol/cortisone ratio has not been systematically assessed.

Study objective

To assess the effect of a fixed dose of licorice with a specified amount of glycyrrhizic acid on blood pressure, potassium and sodium levels and cortisol/cortisone balance in normotensive subjects. In order to explore individual genetic influences, blood samples of participants with significant changes will be considered by investigating the existence of genetic single nucleotide polymorphisms.

Study design

Controlled clinical experiment

Study burden and risks

In total, this study will take approximately 3 weeks to complete. During this period study participants will be asked to visit the Academic Medical Centre on 5 occasions. These visits will take approximately 15 minutes to 30 minutes. The first visit concerns a screening, which will be conducted two weeks before the start of the study. Participants will be screened by measuring blood pressure clinically and completing a standard case record form. Information concerning the study period will be provided. During the second and fourth visit, participants will be weighted, blood sampling will be performed and the participants will be requested to perform 24h urinary collection prior to the visits. Furthermore, a 24h ambulatory monitoring of the blood pressure will be performed, starting directly after the visit.
The risks associated with this study consists of the possible side-effects of liquorice ingestion regarding the mineralocorticoid effect of glycyrrhizic acid. These risks are considered low. Licorice consumption for 8 weeks at a dose of 2 mg/kg has been shown to have no significant hazardous effect on serum potassium and cortisol/cortisone levels. In addition, the exposure period of our study is very brief further minimizing the risk associated with licorice

exposure. There are no direct health benefits that relate to study participation. The indirect benefit of participating in this study is the awareness of the possible individual susceptibility and subsequent safety of the described effects of glycyrrhizic acid after a short period of daily licorice ingestion.

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

- Willing and able to participate in the study protocol
- Written informed consent
- Age 18-60 years
- Office diastolic blood pressure maximal 90 mmHg and office systolic blood pressure maximal 140 mmHg

- BMI > 18 or < 35 g/m2
- No use of medication which affects the primary or secondary outcome measurements such as diuretics, antihypertensive drugs and NSAIDs < six weeks before start of the study
- Willing to adhere to the study protocol
- Accessible veins on arm(s) as determined by examination at information meetings

Exclusion criteria

- Allergy to one of the ingredients of licorice
- Office blood pressure >140/90 mm
- Reported alcohol consumption > 28 units/week or recreational drug use
- Existing cardiovascular diseases
- Use of medication which affects the primary or secondary outcome measurements such as diuretics, antihypertensive drugs and NSAIDs < six weeks before start of the study
- Currently on a medically prescribed diet, or slimming diet
- Potassium <3.5 mmol/l
- eGFR <60
- Excessive ingestion of licorice (>200 gr/week) or >3 litre of licorice tea per week
- Pregnancy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-02-2018
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	29-01-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-04-2018
Application type:	Amendment
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

ID: 26713
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
CCMO	NL64405.018.17
OMON	NL-OMON26713