A double blind, randomized placebo-controlled cross-over study on the cardiovascular effects of Salvia miltiorrhiza extract (Danshen) in patients with hypertension and hyperlipidemia

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Ethical review	Approved WMO
Status	Pending
Health condition type	Lipid metabolism disorders
Study type	Interventional

Summary

ID

NL-OMON35218

Source
ToetsingOnline

Brief title
Cardiovascular effects of Salvia miltiorrhiza extract (Danshen)

Condition

- Lipid metabolism disorders
- Vascular hypertensive disorders

Synonym
elevated levels of lipids in the blood, hyperlipidemia

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: MKB-bedrijf Cinmar Pharma

Intervention

Keyword: Cardiovascular diseases, Hyperlipidemia, Salvia miltiorrhiza, Traditional Chinese Medicine

Outcome measures

Primary outcome

Outcome parameters will be assessed in the 4th week of each treatment period.

To study the effect of Danshen on hyperlipidemia, in particular

LDL-cholesterol, but also HDL-cholesterol, total cholesterol, total

triglycerides, apolipoprotein B plasma levels and LDL oxidation will be

measured.

Secondary outcome

Blood pressure will be quantified by 24-h Ambulatory Blood Pressure Monitoring

and office blood pressure monitoring (during 20 min. period). Endothelial

function will be assessed by both the forearm vasodilator response to infusion

of acetylcholine and nitroprusside into the brachial artery, quantified by

venous occlusion strain gauge plethysmography, and by measuring flow-mediated

dilatation of the brachial artery by ultrasound. Ischemia-reperfusion injury

will be determined by measuring flow-mediated dilatation of the brachial artery

after applying increasing periods of forearm ischemia. Furthermore, plasma

biomarkers of oxidative stress (e.g. TBARS) and vascular inflammation (e.g.

hsCRP) will be sampled. In addition, markers of hemostasis (e.g. von Willebrand

factor), and hemorheological parameters, such as blood viscosity, will be

determined. Insulin sensitivity will be assessed by use of the QUICKI index.

Study description

Background summary

Cardiovascular Disease (CVD) is the leading cause of death worldwide. Mortality due to CVD has declined as a result of both primary (general population without a history of CVD) and secondary prevention (patients with a history of CVD) initiatives. The best approach to the problem is the treatment and prevention of risk factors for CVD. Hypertension and hyperlipidemia belong to the main risk factors of the development of atherosclerotic cardiovascular disease.

Extracts of the plant Salvia miltiorrhiza (Chinese name *Danshen*) have been used as traditional Chinese medicine in the treatment of cardiovascular diseases, such as angina pectoris and myocardial infarction. In China, Danshen has been extensively studied in clinical trials over the last decades. However, the methodological quality of these studies was poor, and reliable conclusions from these studies could not be drawn. Several preclinical studies point towards promising effects of Danshen on risk factors of atherosclerotic cardiovascular diseases, such as hyperlipidemia and hypertension. Danshen has potent antioxidant properties and is shown to have promising effects on endothelial dysfunction and ischemia-reperfusion injury. Therefore, we want to investigate the cardiovascular effects of Salvia miltiorrhiza extract (Danshen) in a well-controlled clinical study.

Study objective

Our primary objective is to determine the effect of Salvia miltiorrhiza extract (Danshen) on hyperlipidemia, in particular LDL-cholesterol. Secondary objective is to investigate the effect of Danshen on hypertension. Further objectives are to determine its effect on endothelial dysfunction and ischemia-reperfusion injury, and to explore its effect on markers for oxidative stress and vascular inflammation, and on hemorheological parameters and hemostasis, and on insulin sensitivity.

Study design

This is a single-centre, placebo-controlled, randomized, double-blind, cross-over study.

Intervention

The study will consist of two treatment periods of four weeks with a washout

period of four weeks. Total duration 12 weeks. In one treatment period, Danshen (3 capsules, orally administered twice daily) will be given, in the other treatment period, a similar dosing schedule with placebo capsules will be used.

Study burden and risks

Salvia miltiorrhiza extract (Danshen) has been used for hundreds of years by large populations. No serious side effects have been described. The cannulation of the brachial artery (under local anaesthesia), and the venous blood samples will give some local discomfort. Both flow-mediated dilatation and plethysmography will cause temporary and completely reversible numbness and discomfort in both hands due to inflation of the wrist-cuffs. The subjects may benefit from participating in this study when Danshen appears to improve vascular function and risk factors. A subject fee is to be provided.

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: 40-70 (50% men / 50% women)
* Women:
- postmenopausal, or
- use of contraceptive pill
* Hyperlipidemia
- elevated level of triglycerides: > 1.7 mmol/L
- elevated level of LDL-cholesterol: > 3.5 mmol/L
- reduced level of HDL-cholesterol: < 1.03 mmol/L
* Hypertension:
- systolic pressure > 90 mm Hg
- diastolic pressure > 140 mm Hg
* Signed informed consent

Exclusion criteria

* Smoking
* Alcohol or drug abuse
* History of cardiovascular disease (myocard infarct, angina pectoris, CVA, CI)
* Diabetes mellitus
* Pregnancy
* Concomitant (chronic) use of:
- ACE-inhibitors
- Statins
- Anticoagulant drugs
- > 1 antihypertensive drug
- High-dose antihypertensive medication (above defined daily dose)
- (Antioxidant) vitamin supplements
* Clinically significant liver disease (3 times the upper normal limit of ALAT,ASAT,AF, *GT or LDH)
* Clinically significant anemia (male Hb < 6,9 mmol/L, female < 6,25 mmol/L)
* Abnormal creatinine clearance (adjusted for age of subject)
* Participation to any drug-investigation during the previous 90 days

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2011
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO Date:	15-11-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-06-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL37508.091.11