The Evening vs Morning Polypill Utilization Study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON37659

Source
ToetsingOnline

Brief title
TEMPUS

Condition

- Coronary artery disorders
- Central nervous system vascular disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
cardovascular disease, dyslipidemia, hypertension

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cardiovascular, chronotherapy, combination pill, polypill

Outcome measures

Primary outcome

• Difference in LDL cholesterol between treatment regimen

(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in mean 24 hour ambulatory systolic BP between treatment regimen

(evening administration RHP vs morning administration RHP vs administration of individual agents)

Secondary outcome

• Difference in lipid fractions between treatment regimen

(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in platelet function between treatment regimen

(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in 24 hour ambulatory BP parameters between treatment regimen

(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in central blood pressure between treatment regimen
(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in cardiovascular risk score (Framingham) between treatment regimen
(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in adherence (electronic event monitoring) between treatment regimen
(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in adverse events between treatment regimen
(evening administration RHP vs morning administration RHP vs administration of individual agents)

• Difference in participant acceptability between treatment regimen
(evening administration RHP vs morning administration RHP vs administration of individual agents)

Study description

Background summary

It is expected that a single pill administered on fixed time will simplify medication intake for patient compared to several separate agents on various times, thereby controlling the cardiovascular risk better. However, the components of the polypill need to be administered on various time points. In clinical practice, anti-hypertensives are generally prescribed for use in the morning, whereas some statins are recommended for use in the evening. There is evidence that the reduction in LDL achieved with some statins is superior when taken in the night, but it is unclear whether the additional reduction in LDL (and the reported improvement in BP control when aspirin is taken in the evening) is offset by a reduction in adherence when taking medication in the evening. The current goal is to assess what the optimal treatment regimen is for cardiovascular medication in terms of the change in mean LDL cholesterol levels and ambulatory systolic BP, and adherence to therapy.

Study objective

The primary aim of the trial is to assess what the optimal treatment regimen for acetylsalicylic acid, a statin and two BP-lowering agents is (administered as in regular care in individual agents, a fixed-dose combination pill administered in the evening or administered in the morning), in terms of the change in mean ambulatory systolic BP and/or LDL cholesterol levels in individuals at intermediate or high risk of cardiovascular disease.

Study design

Randomized cross-over study with 75 participants.

Intervention

Eligible individuals willing to participate in the trial will receive the polypill and the components of the polypill for a total of 18-24 weeks; a random sequence of 6 weeks morning, 6 weeks evening administration and 6 weeks administration of the individual agents. After every treatment sequence laboratory blood examination and ambulatory blood measurements will be performed.

Study burden and risks

Measurements:
None of the study measurements are dangerous. Routine blood samples taken may be associated with somen bruising, discomfort and local irritation. There is also a smal risk of infection whenever the skinbarrier is broken by a needle.
The ABPM may be incomfortable due to 24 hours measurement every 30 minutes, including at night. This last measurement may be inconvenient.

Medication:
The polypill combination cardiovascular medication will be an unapproved medication. However all the ingredients in both of the polypill combinations used in this trial are well knowm midicines with well established efficacy and safety profiles. Although all the drugs in the polypill haven been used for many years there are possible risks that both polypill may cause side effects. These are generally mild and infrequent and are usally resolved immediatly by stopping the medication. Side effects of the components of the polypills can include low bloodpressure, dizziness, headache, nausea, mild stomach pain, heartburn, ulceration, abdominal pain, constipation, flatulance, bleeding, gout, cough, fatique, liver problems, ans muscle pain, tenderness or weakness. As with any medication an allergic reaction is possible such as skin rash, itching, difficulty breathing or swelling of the face, but this is quite rare.

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

Adults (>= 18 years) with:
- (A) established atherothrombotic cardiovascular disease (CVD)- history of ischaemic heart disease, ischaemic stroke or transient ischaemic attack, or peripheral vascular disease.
OR
- (B) a 5 year cardiocvascular risk of at least 10% (Framingham risk equation, New Zealand Guidelines Group approach).;- The trial investigator and the specialist from the department of Vascular Medicine considers that the polypill components are indicated according to current guidelines at the doses in the Red Heart Pill 2c.

Exclusion criteria

Individuals will NOT be eligible if one or more of the following criteria are satisfied:
• Contraindication to any of the components of the polypill (e.g. known intolerance to aspirin, statins, or ACE inhibitors; pregnancy or likely to become pregnant or breastfeeding women during the treatment period). Such contrindications are fully listed in the Investigator Brochure.
• The treating doctor or trial doctor considers that changing a participant*s cardiovascular medications would put the participant at risk (e.g. symptomatic heart failure, high dose β-blocker required to manage angina or for rate control in atrial fibrillation, accelerated hypertension, severe renal insufficiency, a history of severe resistant hypertension).;Other potential reasons for exclusion include:
• Known situation where medication regimen might be altered for a significant length of time, e.g. current acute cardiovascular event(s), planned coronary bypass graft operation.
• Unlikely to complete the trial (e.g. life-threatening condition other than cardiovascular disease) or adhere to the trial procedures or attend study visits (e.g. major psychiatric condition, dementia).
• Women of child bearing potential should be on a medically accepted form of contraception (oral or implanted contraception, IUD or tubal sterilisation). If there is any possibility of pregnancy, prior to randomisation a blood or urine pregnancy test will be performed. Final decisions about eligibility will be made at the discretion of the trial Investigator and potential trial participant, in light of any additional requirements or guidance from local ethics committees and other regulatory bodies.
• Night shift worker

Study design

Design

Study type:	Interventional

Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-08-2012
Enrollment:	75
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	acetylsalicylic acid 75mg
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	-
Generic name:	hydrochlorothiazide 12,5mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	lisinopril 10mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	simvastatin 40mg
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Red Heart Pill 2C
Generic name:	acetylsalicylic acid 75mg, simvastatin 40mg, lisinopril 10mg, hydrochlorothiazide 12,5mg

Ethics review

Approved WMO Date:	09-05-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	15-06-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	24-07-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
EudraCT	EUCTR2011-001120-38-NL
ClinicalTrials.gov	NCT01506505
CCMO	NL39698.041.12