TEMPUS - The Evening vs Morning Polypill Utilization Study;A randomised controlled cross-over trial to evaluate evening versus morning administration of a cardiovascular polypill

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Ethical review	Not approved
Status	Will not start
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON35965

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: Financiering door de afdeling vasculaire geneeskunde UMC Utrecht. Geen externe geldstromen.

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)

* Difference in mean 24 hour ambulatory systolic BP

(evening administration RHP vs. morning administration RHP)

Secondary outcome

* Difference in cholesterol spectrum

(evening administration RHP vs. morning administration RHP)

* Difference 24 hour ambulatory BP parameters

(evening administration RHP vs. morning administration RHP)

* Difference in cholesterol spectrum

(administration RHP vs. administration individual agents)

* Difference 24 hour ambulatory BP parameters

(administration RHP vs. administration individual agents)

* Diffence in cardiovascular risk score

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

* Difference in adherence

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

* Difference in adverse events

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

* Difference in participant acceptability

(evening administration RHP vs. morning administration RHP vs. administration

individual agents)

Study description

Background summary

In clinical practice, antihypertensives 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. Current product labelling recommends night use for simvastatin and does not state a timing preference for aspirin or blood pressure lowering medicines. There is therefore uncertainty concerning the best timing of administration of the polypill. This uncertainty will be addressed by this trial.

Study objective

The aim of the study is to measure whether there is a difference in LDL cholesterol levels or the 24 hour ambulatory blood pressure in individuals at high risk of cardiovascular disease when the polypill is taken in the morning compared with the evening.

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 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 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 5% (SCORE)

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 considers that changing a participant*s cardiovascular medications would put the participant at risk (e.g. symptomatic heart failure, high dose *-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, 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 workers.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	75
Type:	Anticipated

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

Not approved

Date:	20-01-2012
Application type:	First submission
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
CCMO	NL36047.041.11