Chronotherapy with aspirin for reduction of cardiovascular disease

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

Summary

ID

NL-OMON55498

Source
ToetsingOnline

Brief title
TImE ASPIRIN

Condition

- Other condition
- Coronary artery disorders

Synonym
cardiovascular diseases

Health condition

cardiovasculaire aandoeningen

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: aspirin, cardiovascular disease, circadian rhytm

Outcome measures

Primary outcome

Effect of aspirin intake at bedtime compared with intake at morning on cardiovascular disease

Secondary outcome

* Time of the day of primary outcome: it is expected that bedtime aspirin reduces the primary outcome more during morning hours (6-12h) compared with the rest of the day.

* Safety: severe or moderate bleeding events according to established definitions.

* Side-effects

* Cost-effectiveness: patients* quality of life (EQ-5D-5L) will be registered at randomization and after that with a frequency of twice per year during follow-up to calculate QALYs. Health care utilization data are extracted from electronic patient records and data from the primary care. Health care use will be translated into cost using Dutch reference prices.

* Subgroup analyses will be performed for gender and age (18-50, 50-65, 65-85 and 85+).

Study description

Background summary

Aspirin is a cornerstone in the secondary prevention of cardiovascular disease because of its inhibitory effects on platelet aggregation. Although not supported by evidence, aspirin is usually taken at morning. There is evidencethat is may be more benificial to take aspirin at bedtime instead of on awakening. Because it has been shown that platelet reactivity follows a clear circadian rhythm, with a peak of platelet reactivity during the morning (6-12 AM). Importantly, studies have shown in meta-analyses that high platelet activity is predictive of adverse cardiovascular outcomes in patients with stable CVD. Given this knowledge, it is highly likely that the morning peak of platelet reactivity contributes to the morning peak of CVD and that reduction of morning platelet activity prevents cardiovascular events during morning hours. This may be achieved by intake of aspirin at bedtime instead of on awakening assuming that intake at morning would be too late.

Study objective

The aim of this comparative effectiveness research is to determine the effect of intake of aspirin before bedtime in comparison with aspirin on awakening in patients already using aspirin for secondary prevention of CVD.

Our primary objective will be to assess the major adverse cardiovascular events, defined as the composite of death from cardiovascular causes, nonfatal myocardial infarction or nonfatal stroke, transient ischemic attack, need for repeat revascularization by redo-CABG or repeat percutaneous intervention (the *cardiovascular endpoints*).

Our secondary objectives are:
* Time of the day of primary outcome: it is expected that bedtime aspirin reduces the primary outcome more during morning hours (6-12h) compared with the rest of the day.
* Safety: severe or moderate bleeding events according to established definitions.
* Side-effects.
* Cost-effectiveness: patients* quality of life (EQ-5D-5L) will be registered at randomization and after that with a frequency of twice per year during follow-up to calculate QALYs. Health care utilization data are extracted from electronic patient records and data from the primary care. Health care use will be translated into cost using Dutch reference prices.
* Subgroup analyses will be performed for gender and age.

Study design

This study follows a parallel double blinded placebo controlled randomized clinical trial design.

Intervention

After patient's written informed consent, subjects will be randomised between aspirin at awakening or at bedtime in treatment periods of 4 years.

Study burden and risks

Totally, the study will have a duration of max. 4 years. The participants, all using aspirin, will be randomized to a study arm: (1) aspirin after awakening + placebo before bedtime, (2) placebo after awakening + aspirin before bedtime. Participants will continue to use their own aspirin preparation as delivered by their pharmacy. An identical placebo will be packaged in their multidose drug dispensing (MDD) by the MDD company.
In addition, the participant will receive 10 questionnaires during the duration of the study.

Subjects will not be exposed to any experimental drug. Therefore, participation in the study will not involve any safety risks for subjects. Nevertheless, subjects will be instructed about the (very small) risk of bleeding associated with aspirin use.

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

patients who already use low-dose aspirin for secondary prevention of cardiovascular events and use a multidose drug dispensing

Exclusion criteria

Insufficient knowledge of the Dutch language
Patients currently participating in another (clinical) trial or study

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-10-2019

Enrollment:	5805
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	acetylsalicylic acid cardio teva 80 mg
Generic name:	acetylsalicylic acid
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	30-11-2018
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	08-01-2019
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-09-2019
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	03-04-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	30-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

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	EUCTR2018-001328-21-NL
CCMO	NL65448.058.18

Study results

Date completed: 28-02-2022

Actual enrolment: 328