Effects of low-dose aspirin taken at bedtime on blood pressure of subjects with who use aspirin for prevention of recurrent cardiovascular events: the Aspirin In Reduction of Tension II (ASPIRETENSION II) Study

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

Summary

ID

NL-OMON34181

Source
ToetsingOnline

Brief title
ASPIRETENSION II

Condition

- Other condition

Synonym
hypertension

Health condition

hypertensie

Research involving
Human

Sponsors and support

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

Intervention

Keyword: aspirin, blood pressure, circadian rhythm, platelets

Outcome measures

Primary outcome

Effect of aspirin intake at bedtime compared with intake at morning on blood

pressure (24-h ambulatory blood pressure measurement)

Secondary outcome

- the effect of aspirin at bedtime compared with aspirin at morning on platelet

function

- effects of different time of intake on potential side effects and compliance

- potential effect modification of the effect on blood pressure by genes

involved in blood pressure regulation

Study description

Background summary

Aspirin is a cornerstone in the secondary prevention of cardiovascular disease because of its inhibitory effects on platelet aggregation. It reduces the risk of recurrent cardiovascular events with about a quarter. Although not supported by evidence, aspirin is usually taken at morning. There are several reasons why it may be more beneficial to take aspirin at bedtime instead of on awakening.

First, one of the most important modifiable risk factors for cardiovascular disease is arterial hypertension. Aspirin is usually assumed to have no effects on blood pressure. However, in two randomized clinical trials of Hermida et al. among (otherwise healthy) grade I hypertensive subjects (140/90-159/99 mmHg), aspirin intake at bedtime decreased 24h blood pressure with 6.8/4.6 and 7.2/4.9 mmHg, whereas use of aspirin at morning slightly increased blood pressure (2.6/1.6 and 1.3/0.8 mmHg). We have demonstrated that aspirin at bedtime decreases both plasma renin activity over 24h and excretion of catecholamines and cortisol in 24h urine compared to morning intake. Decreased activity of these pressor systems forms a biologically plausible explanation for the finding that aspirin at bedtime may reduce blood pressure whereas aspirin at morning does not.
The effect of aspirin at bedtime versus on awakening on blood pressure has never been studied in a clinically relevant group of patients, i.e. patients already using aspirin for the secondary prevention of recurrent atherothrombotic events who mostly use also a wide variety of concomitant (antihypertensive) drugs. If time of intake has an effect, this could lead to a very simple improvement of therapy at no extra cost.

Second, it has been convincingly shown that there is a morning peak in platelet reactivity, which might partly explain the increase in cardiovascular events in the early morning (highest incidence between 6 and 12 AM). Coming in an upright posture can lead to increased platelet activity and platelets can also be stimulated by the early morning increase of sympathetic activity (which starts few hours before awakening).
Since platelet reactivity has a circadian rhythm, time of intake of aspirin may influence its inhibitory effect on platelets. It has been argued that intake of aspirin at bedtime could better prevent the early morning increase in platelet reactivity than intake at morning assuming that intake at morning would be too late.

Study objective

The aim of our project is to study whether treatment with aspirin at bedtime compared with intake at morning has additional benefits in patients using aspirin to prevent recurrent cardiovascular events.
1. Our primary objective is to study the effect of 100 mg aspirin intake at bedtime compared with 100 mg aspirin intake at morning on blood pressure (24h ambulatory blood pressure measurements (ABPM)) in patients who use aspirin for secondary prevention of recurrent atherothrombotic events.
2. As a secondary objective, we will study the effect of aspirin intake at bedtime compared with at morning on platelet function. Furthermore, we will address differential effects on potential side effects and compliance, as well as potential effect modification of the effect on blood pressure by genes involved in blood pressure regulation.

Study design

The design of our study is a prospective, randomized, open-label, blinded endpoint, (PROBE) crossover trial.

Intervention

After patient's written informed consent and screening, subjects will be randomised between aspirin at awakening and at bedtime in two treatment periods of 3 months. Before the start of the study period there will be a screening visit during which a blood sample and questionnaire is taken. After both treatment periods there will be a short visit of half an hour to complete questionnaires and take a blood sample. After both periods blood pressure will be measured for 24 hours and urine will be collected for 24 hours.

Study burden and risks

Totally, the study will have a duration of 6 months. Patients will take pills during the whole study period: 3 months aspirine in the morning and 3 months aspirine in the evening, the order depending on the randomisation of the subject. Subjects will not be exposed to any experimental drug. The study drug is aspirin, but only subjects that were already using aspirin before the study will be included. 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. They will be informed about signs and symptoms and will receive emergency contact numbers in order to guarantee a low threshold for clinical presentation if necessary.

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 have a stable blood pressure (with or without therapy) of 149/94 or lower.

Exclusion criteria

- blood pressure of 150/95 or higher
- change in blood pressure lowering medication within the last three months
- regular use of non-steroidal anti-inflammatory drugs (NSAID's)
- shift workers

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-06-2011
Enrollment:	250
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ascal
Generic name:	Carbasalate Calcium
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-01-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-02-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2010-024448-13-NL
CCMO	NL34954.058.10