QTc-prolongation due to combinations of drugs - a prospective study with a focus on pharmacokinetic and pharmacogenetic risk factors

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In this study we will study the incidence of QTc-interval prolongation when combinations of 2 or more QTc-prolonging drugs are prescribed. Also we will investigate if QTc-prolongation is more frequent in patients with higher drug plasma...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac arrhythmias
Study type	Observational invasive

Summary

ID

NL-OMON30361

Source
ToetsingOnline

Brief title
QTc-prolongation due to combinations of drugs

Condition

- Cardiac arrhythmias

Synonym
heart rhythm disturbances, QTc-prolongation

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: drug safety, pharmacogenetics, pharmacokinetics, QTc-prolongation

Outcome measures

Primary outcome

The primary outcome is the incidence of prolonged QTc-interval during use of all combinations of QTc-interval prolonging drugs

Secondary outcome

1. Are drug concentrations in patients with clinically significant prolongation of the QTc-interval higher compared to patients without prolongation of the QTc-interval?

2. For the pharmacogenetic analysis we will compare the presence of variant alleles, as dichotomic variabele, in both groups with the *2-test.

Study description

Background summary

The QTc-interval on the ECG represents the duration of the action potential in the ventricle plus the repolarisation-time. Subjects with a prolonged QTc-interval have an increased risk for heart rhythm disturbances and acute cardiac death. There are more than 50 drugs that prolong the QTc-interval, some of which have been withdrawn from the market.
The exact risk of QTc-prolongation with simultaneous use of 2 or more QTc-prolonging drugs is unknown. Possibly there are synergistic effects, resulting in an increased risk with drug combinations. Genetic risk factors may further contribute to the risk of QTc-prolongation.
With the introduction of an electronic prescription system in the ErasmusMC we can now easily identify all patients using combinations of 2 or more QTc-prolonging drugs. The physician receives an automatic alert when prescribing such combinations, that are mostly ignored, as scientific evidence for handling these alerts is not available.

Study objective

In this study we will study the incidence of QTc-interval prolongation when combinations of 2 or more QTc-prolonging drugs are prescribed. Also we will investigate if QTc-prolongation is more frequent in patients with higher drug plasma concentraties, or in patients that are identified as *poor metabolisers*.
The goal is to develop guidelines to handle interaction-alerts, by quantifying the risk of presecribing combinations of QTc-prolonging drugs. This may lead to improved drug safety for patients in the Erasmus MC.

Study design

Prospectieve cohort study, including all patients in whom a combination of 2 or more QTc-interval prolonging drugs is prescribed.
In the hospital pharmacy all drug interactions that could lead to QTc-interval prolongation are screened. The responsible pharmacist or clinical pharmacologist farmacoloog, after consultation of the treating physician, will approach the patient for participation in this study.
After obtaining informed consent an ECG will be made and blood will be sampled for pharmacokinetic and for pharmacogenetic analyses.

Study burden and risks

ECG monitoring and a single vena puncture form a minimal risk for the patient

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

All patients for whom a combination of 2 or more QTc-interval prolonging drugs have been prescribed.

Exclusion criteria

No written informed consent obtained.
Patients in whom life expectancy or clinical situation is such that a risk of heart rhythm disturbances is irrelevant to clinical care.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-01-2007

Enrollment:	3000
Type:	Actual

Ethics review

Approved WMO Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL14327.078.06