Effects of vernakalant and flecainide on atrial contractility in patients with atrial fibrillation

Published: 01-05-2012
Last updated: 26-04-2024

Primary Objective: to compare the atrial contractility by means of echocardiography between patients receiving flecainide and vernakalant i.v. after conversion to sinus rhythmSecondary Objective(s): 2a. To compare the conversion rate of AF between...

Ethical review	Approved WMO
Status	Pending
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON37797

Source
ToetsingOnline

Brief title
Vernakalant versus flecainide: atrial contractility

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Atrial fibrillation, Flecainide, Pharmacological cardioversion, Vernakalant

Outcome measures

Primary outcome

Echocardiography to evaluate atrial contractility after conversion to sinus

rhythm

Secondary outcome

2a. conversion rate to sinus rhythm

2b. recurrence of AF at one month follow-up

Study description

Background summary

Pharmacological cardioversion has the advantage of not requiring sedation or anaesthesia.[1] Unfortunately, many of current available anti-arrhythmic drugs have potential proarrhythmic and negative inotropic effects and may be contraindicated in certain patient groups such as postoperative patients. [2] Vernakalant is a relatively new anti-arrhythmic drug (AAD) for rapid conversion of recent-onset atrial fibrillation to sinus rhythm. Vernakalant is a multi-channel blocker which acts preferentially in the atrial ion channels. In this way it has minimal ventricular effects and consequently has a lower risk of potentially dangerous arrhythmia*s compared to other anti-arrhythmic drugs.[3, 4] Vernakalant exerts its anti-arrhythmic activity by means of frequency-dependent blockade of cardiac sodium channels as well as blockade of early-activating potassium channels important in atrial repolarization. The blockade of these channels results in a prolongation of the atrial refractory period and increase of the atrial action potential duration.[4-6] During atrial fibrillation there is a higher frequency. Thus, the frequency-dependent blockade results in an increased block of sodium channels during the fibrillation resulting in a higher effectiveness of the treatment.[5] Vernakalant has a half-life of about 3 hours.[7] The conversion rate in patients presenting with AF with short duration (< 48 hours) varies between 52-59% with a time to conversion varying between 11-14 minutes. [3, 8-10] The incidence of serious adverse events is low in patients using vernakalant. The described adverse events (AE*s) were of minor clinical significance.

Compared to other anti-arrhythmic drugs it has no clinically significant proarrhythmic risk. No cases of torsades de pointes, sustained ventricular tachycardia or ventricular fibrillation were described. [3, 10]
Studies have shown that recovery of atrial contraction is delayed in patients undergoing direct current cardioversion compared to patients undergoing pharmacological cardioversion.[11, 12] We could recently demonstrate that blockade of the ultra-rapid delayed rectifier current IKur can acutely restore atrial contractility after spontaneous cardioversion of AF in goats.[13] This effect was caused by elevation of the atrial plateau potential which enhances Ca2+ influx in atrial myocytes by reverse mode Na/Ca exchange.[14] We hypothesize that vernakalant, the only clinical available IKur blocker so far, enhances atrial contractility after cardioversion of AF. Enhanced atrial contractility after cardioversion of AF might reduce thromboembolic risks and improve hemodynamics after cardioversion of AF.
Assessment of the effect of vernakalant on atrial contractility after cardioversion requires the presence of sinus rhythm. As atrial contractility after vernakalant administratrion cannot be compared to predrug values (before exposure to vernakalant the patients are in AF), the effect of vernakalant needs to be compared to a control compound with comparable effects with the exception of the IKur block. Flecainide is widely used for cardioversion of AF, blocks (as vernakalant) sodium channels, and lacks IKur blocking properties. Thus, the goal of our study is to compare the atrial contractility of patients who are treated with vernakalant i.v. to patients who are treated with flecainide i.v.

Study objective

Primary Objective: to compare the atrial contractility by means of echocardiography between patients receiving flecainide and vernakalant i.v. after conversion to sinus rhythm
Secondary Objective(s):
2a. To compare the conversion rate of AF between patients receiving flecainide and
vernakalant i.v.
2b. To compare the recurrence rate of AF four weeks after successful cardioversion between
patients receiving flecainide and vernakalant i.v.

Study design

This is an observational pilot study to compare the atrial contractility after pharmacological conversion in patients receiving vernakalant or flecainide. The patients are included at our first heart aid department where AF is diagnosed. When the treating cardiologist decides to apply pharmacological cardioversion, the patient will be asked to participate. After obtaining informed consent, the patient will be randomized to receive flecainide or vernakalant intravenously.

Patients randomized to vernakalant will receive a 10-minute infusion of 3 mg/kg vernakalant, followed by a 15 minute observation period. If the patient is still in atrial fibrillation, an additional 10-minute infusion of 2 mg/kg vernakalant will be given. Patients randomized to flecainide received a 10-minute infusion of 2 mg/kg (maximal 150 mg) flecainide. If the patient is still in AF 1 hour after the infusion, electrical cardioversion will be performed according to protocol. If conversion to sinus rhythm occurs within 60 minutes after start of the infusion, one of the secondary endpoints (2a) will be reached. The time point of conversion to sustained (> 1 minute) sinus rhythm will be noted. An echocardiography evaluating the atrial contractility (primary endpoint, 1) will be performed during sinus rhythm, this can be after pharmacological, electrical or spontaneous cardioversion. This is not part of the regular therapy. All baseline characteristics and echocardiographic measurements will be noted in a case record form. These include demographic characteristics, medical history, use of anti-arrhythmic drugs, previous rhythm control, data on electrocardiogram and echocardiogram. Patients will be continuously monitored for at least 1-4 hours after ending the intravenous treatment. Four weeks after the cardioversion patients will visit the outpatient clinic by their own cardiologist for follow-up. This is part of the regular treatment. During this visit we will evaluate the heart rhythm by electrocardiography (2b). We will also perform a second echocardiography, determining the same parameters as the first echocardiography. This is not part of the regular treatment. See figure with study flow chart and numbered objectives.

Intervention

Administration of vernakalant or flecainide

Study burden and risks

During this study two extra echocardiographies will be performed. Both during regular visits, meaning that there is no extra visit necessary. There are no risks related to an echocardiography.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL
Scientific

Medisch Universitair Ziekenhuis Maastricht

P. Debyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- patients presenting with paroxysmal or persistent AF;- eligible for treatment with flecainide or vernakalant infusion to restore sinus rhythm;- receiving adequate anticoagulant therapy (or having an episode of AF lasting < 24 hours)

Exclusion criteria

- atrial flutter;- contra-indications for receiving flecainide or vernakalant infusion according to MUMC+ protocol (unstable hemodynamic condition, LVEF < 40%, inadequate potassium levels, acute ischaemia, sinus node dysfunction);- age < 18 years

Study design

Design

Study phase:	4
Study type:	Interventional

Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2012
Enrollment:	50
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Tambocor
Generic name:	Flecainide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Vernakalant
Generic name:	Brinavess
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	01-05-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	25-06-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2012-001898-90-NL
CCMO	NL39854.068.12