The influence of sunitinib on contractility of human atrial trabeculae

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON34277

Source
ToetsingOnline

Brief title
Sunitinib and cardiotoxicity/ SunCar

Condition

- Heart failures

Synonym
cardiotoxicity, Heart failure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: KWF

Intervention

Keyword: Cardiotoxicity, Ischemia-reperfusion, Sunitinib, Tyrosine kinase inhibitor

Outcome measures

Primary outcome

The developed force in ex vivo atrial trabeculae during standardized

stimulation.

Secondary outcome

The difference in averaged maximal speed of tension development during

contraction between two trabeculae.

The difference in averaged maximal speed of tension reduction during relaxation

between two trabeculae

Study description

Background summary

Recently, sunitinib (a tyrosine kinase inhibitor that is used for treatment of metastasic renal carcinoma and gastrointestinal stroma tumors) has been associated with development of heart failure, possibly by off-target inhibition of AMP-protein kinase. We hypothesize that sunitinib reduces the contractile ability of myocardium and the tolerance against ischemia-reperfusion and that activators of AMP-protein kinase such as atorvastatin and AICAR reverse this unwanted effect of sunitinib.

Study objective

The primary objective of the study is to investigate the effect of sunitinib on ex-vivo atrial contractile force in absence and presence of ischemia-reperfusion.
A secondary objective is to explore if atorvastatin or AICAR prevent sunitinib-induced deterioration of contractile function of human atrial trabecels

Study design

In vitro study on human tissue

Study burden and risks

The use of human atrial tissue derived from patients undergoing heart surgery is an unique way of studying human tissue with minimal effort or risks for the patient.
At our department of cardiothoracic surgery all relevant clinical data at baseline and follow up (including the involved surgeon, postoperative plasma troponin levels and occurrence of supraventricular tachycardias) are stored in a prospective observational database. Since one of the surgeons routinely amputates the atrial auricle when he introduces the extracorporal circulation, we have the opportunity to compare plasma troponins and incidence of supraventricular tachycardia between patients in whom their auricles were excised (n=209) with those patients in whom this procedure was not performed (n=1401). Average 8-hour plasma troponin concentrations were 6.1 +/- 13.9 and 5.8 +/- 12.6 microgram/l respectively (not significant). In 24% of the 209 patients in whom the auricle was amputated, and in 23.7 % of the 1401 patients in whom the auricles remained in situ, a supraventricular tachycardia developed (Dr. L. Noyez, personal communication). Based on these data, we conclude that sampling of atrial (auricular) tissue at the time of introduction of extracorporal circulation does not pose the patient at significant additional risk.

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

• Age > 18 years
• Willing to sign informed consent
• Planned elective CABG surgery with extracorporal circulation

Exclusion criteria

• Use of theophylline
• Use of sulfonylureas
• Use of oral antiarrhythmics
• Atrial arrhythmias
• Right ventricular failure

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-01-2011
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	22-10-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL33248.091.10