Bosentan improves clinical Outcome of adults with congenital heart disease or mitral valve lesions who undergo CArdiac surgery

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To investigate whether an endothelin-1 receptor antagonist improves exercise capacity (peak V*O2) in adults with CHD or with mitral valve lesions who undergo cardiac surgery.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON36241

Source
ToetsingOnline

Brief title
BOCA

Condition

- Cardiac valve disorders
- Cardiac and vascular disorders congenital

Synonym
aangeboren hartafwijking, open hart operatie risico

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ICIN,Actelion Pharmaceuticals

Intervention

Keyword: bosentan, cardiac surgery, CHD, mitral valve surgery

Outcome measures

Primary outcome

Primary endpoint of the study is the exercise capacity (peak V*O2) six weeks post-operatively.

Secondary outcome

Secondary endpoints of the study are 1) on the intensive care unit a) hemodynamics b) Sequential Organ Failure Assessment (SOFA) score and c) hours of hospitalization 2) at discharge the right ventricular function (assessed by transthoracic echocardiography) 3a) six weeks post-operatively the right ventricular function (assessed by transthoracic echocardiography) b) the quality of life 4) twelve weeks post-operatively a) right ventricular function (assessed by transthoracic echocardiography) b) differences in clinical status and symptoms

Study description

Background summary

Cardiac surgery relieves symptoms and increases life expectancy in cardiac patients, with and without congenital heart disease (CHD). However, surgery involves many risks of complications, including right ventricular failure. Right ventricular failure is often difficult to treat and is characterized by edema, oliguria, hypotension, and in severe cases shock, multi organ failure and death. Clinical factors contributing to right ventricular failure are mechanical pulmonary ventilation, pre-existing pulmonary hypertension, having CHD or mitral valve lesions and undergoing cardiac surgery.

Cardiac surgery exposes patients to high partial pressures of oxygen, air embolism, and the release of cytokines. The endothelin-1 cytokine release, initiated by the cardiopulmonary bypass, induces vasoconstriction of the pulmonary arterioles resulting in elevation of the pulmonary vascular resistance (PVR). Heart failure patients with higher PVR have been shown to have significantly lower exercise capacity measured by peak V*O2. Interventions affecting the PVR influence the right ventricular function, as shown in patients with chronic thrombo-embolic pulmonary hypertension before and after surgery. Moreover, studies on cardiac surgery have shown a decline in systolic right ventricular function post-operatively compared to pre-operative values, when cardiopulmonary bypass was used. This decline can persist for many years, emphasizing the importance of RV protection peri-operatively.
Reducing the right ventricular afterload, the PVR, is shown to be effective in patients with pulmonary arterial hypertension treated with bosentan, an endothelin-1 receptor antagonist. We hypothesize treatment of patients peri-operatively with bosentan will reduce the PVR, which consequently improves the clinical outcome measured by exercise capacity.

Study objective

To investigate whether an endothelin-1 receptor antagonist improves exercise capacity (peak V*O2) in adults with CHD or with mitral valve lesions who undergo cardiac surgery.

Study design

A prospective randomized open label assessment with blinded end-points (PROBE-design). Total duration of the study is 17 weeks with 5 weeks pre-operative and 12 weeks post-operative treatment with bosentan.

Intervention

The treatment group receives a starting dose of 62.5 mg tablet bosentan twice daily for four weeks followed by 125 mg tablet of bosentan twice daily one week prior to and 12 weeks after surgery. The other group receives no study medication.

Study burden and risks

The trial medication has a low but potential risk of reversible liver damage, which will be monitored regularly (by laboratory testing of liver transaminases). Other side effects of bosentan are rare, the most common being headache, dizziness and peripheral edema, The additional burden for the patients mainly consists of the time needed for the investigations: history taking + physical examination (15 min) and cardiopulmonary exercise testing (60

min).

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

Adults with CHD or with mitral valve lesions who undergo cardiac surgery.

Exclusion criteria

* Current treatment with bosentan
* Systemic arterial pressure < 85 mmHg
* Incapable of giving informed consent

* Ejection fraction below 30 %
* Hypersensitivity to bosentan or any of its help substances
* Moderate to severe liver disease: Child-Pugh class B or C
* Raised plasma transaminases level > three times limiting value.
* Simultaneous use of cyclosporine A
* Percutaneous Transluminal Angioplasty procedures

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	07-10-2011
Enrollment:	110
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tracleer
Generic name:	bosentan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2010-021450-18-NL
ClinicalTrials.gov	NCT01184404
CCMO	NL32984.018.10