BICYCLE trial.

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20429

Source
NTR

Brief title
BICYCLE

Health condition

Pulmonary arterial hypertension
Exercise induced
Congenital heart disease
Advanced treatment
Cardiopulmonary exercise test
Pulmonale arteriële hypertensie
Inspanningsgebonden
Congenitale hartziekten
Cardiopulmonale inspanningstest

Sponsors and support

Primary sponsor: Academic Medical Center - University of Amsterdam
Source(s) of monetary or material Support: Academic Medical Center - University of Amsterdam

Intervention

Outcome measures

Primary outcome

The primary objective of this study is to determine change in mean pulmonary arterial pressure at peak exercise in adult congenital heart disease patients with exercise-induced pulmonary arterial hypertension before and after treatment with bosentan, compared to patients treated with placebo.

Secondary outcome

To determine:

1. Cardiopulmonary exercise capacity: i.e. peak oxygen consumption, VE/VCO2 ratio, O2 pulse;

2. Pulmonary hemodynamics: i.e. systolic pulmonary arterial pressure, pulmonary vascular resistance, pressure-flow relationships during and at peak exercise;

3. Right ventricular function: i.e. TAPSE, TEI index, TDI-S, right ventricular dimensions;

4. Laboratory parameters:
i.e. NT-pro BNP, troponin T;

5. NYHA functional class;

6. Quality of life: assessed by TAAQOL-CHD, SF-36 and Minnesota CHD-HF questionnaire.

Study description

Background summary

Rationale:

Pulmonary arterial hypertension (PAH) can be a rapidly progressive disorder and is associated with a high mortality rate, despite medical intervention. With the availability of effective therapy, early disease detection is an important strategic objective to improve treatment outcomes. Resting echocardiography is currently the recommended screening modality for high-risk population groups. However, it is clear that abnormalities in resting hemodynamics (and symptoms) are late sequelae of the pathobiological processes that begin in the distal pulmonary arteries. Exercise stress may unmask early pulmonary vascular dysfunction, however the definition, clinical significance, and natural history of ‘exercise PAH’ remain undefined. However, based on clinical experience and literature the prevalence is estimated at ~ 20%.Treatment with endothelin receptor blockers has shown a beneficial influence on

the clinical performance in patients with exercise induced PAH due to systemic sclerosis and primary pulmonary hypertension. Whether endothelin receptor blockers decrease pulmonary pressures and improve clinical outcome in patients with exercise induced pulmonary arterial hypertension due to congenital heart disease is unknown.

Objective:

Identify congenital heart disease patients with exercise-induced pulmonary arterial hypertension. Analyze changes in pulmonary arterial pressures at peak exercise in patients with exercise induced pulmonary arterial hypertension before and after treatment with bosentan, compared to placebo.

Study design:

Randomized placebo controlled trial with a study period of 26 weeks.

Study population:

Adult congenital heart disease patients with exercise induced pulmonary arterial hypertension (n=40) from the Academic Medical Centre, Amsterdam.

Intervention:

After randomization one group (n=20) receives a 125 mg tablet of Bosentan twice daily for 6 months. The other group (n=20) receives placebo for 6 months.

Main study parameters/endpoints:

To determine wether bosentan (endothelin receptor inhibitor) decreases mean pulmonary arterial pressure at peak exercise in adult congenital heart disease patients with exercise induced pulmonary arterial hypertension. Furthermore the change in cardiopulmonary exercise capacity and right ventricular function will be investigated.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

All investigations, blood analysis excepted, are non-invasive and free of risk. The burden for the patients mainly consists of the time that is consumed by the investigations, namely: history taking + physical examination (15 min); Quality-of-Life- score (15 min); laboratory tests (electrolytes, creatinine, urea, albumin and neurohormones, troponin T); 12 lead electrocardiogram (10 min); exercise echocardiography (30 min); cardiovascular exercise testing (30 min).

The trial medication has a potential risk of liver damage, which will be monitored regularly by laboratory testing of liver transaminases.

Study objective

In adult congenital heart disease patients with exercise-induced pulmonary arterial hypertension, treatment with bosentan lowers the mean pulmonary arterial pressure, which may result in improvement of the cardiopulmonary circulation, cardiopulmonary exercise capacity and quality of life.

Study design

Patients are requested to visit the outpatient clinic at baseline, at 3 and 6 months follow-up.

Intervention

When all baseline procedures have been performed and the investigator has observed that all inclusion and none of the exclusion criteria apply, patients are randomised by the investigator using a computerized randomisation tool. Randomisation is performed by the investigator after informed consent has been contained. Eligible patients are randomly assigned to one of the following treatment arms:

1. 6 months of treatment with bosentan 125 mg twice a day;

2. 6 months of treatment with placebo twice a day.

The starting dosage of bosentan is 62,5 mg twice a day. Trial medication is doubled after 4 weeks to reach study dose, after checking liver parameters.

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Adult (>18 years) and mentally competent;

2. Open or closed septal defect (ASD I/II, VSD, AVSD);

3. Open or closed systemic-to-pulmonary shunt (PDA);

4. Presence of X-PAH:

A. One of the following criteria, at peak exercise:

i. mPAP > 34 mmHg with CO ≤ 10 l/min;

ii. mPAP > 40 mmHg with CO ≤ 15 l/min;

iii. mPAP > 45 mmHg with CO ≤ 20 l/min;

iiii. mPAP > 50 mmHg with CO ≤ 30 l/min.

B. And a PVR (slope pressure/flow plot) of > 2.5 mmHg/l/min.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Incapable of giving informed consent;

2. Pregnancy or lactation (a pregnancy test is offered to every female patient within fertile age);

3. Women of child-bearing age who are sexually active without practising reliable methods of contraception;

4. Substance abuse (alcohol, medicines, drugs);

5. Subjects who are not able to perform cardiopulmonary exercise testing;

6. Any cardiac operation < 6 months before inclusion;

7. PAH of any aetiology other than the one specified in the inclusion criteria;

8. Impairment of organic function (renal, hepatic);

9. Arterial hypotension (systolic blood pressure < 85mmHg);

10. Anaemia (Hb < 10g/L, or <6.21 mmol/L);

11. Significant valvular disease, other than tricuspid or pulmonary regurgitation;

12. Chronic lung disease or total lung capacity < 80% predicted value;

13. History of significant pulmonary embolism;

14. Other relevant diseases (HIV infection, Hep B/C infection);

15. Subjects with known intolerance to bosentan or their constituents;

16. Prohibited medication: Any medication listed below which has not been discontinued at least 30 days prior to inclusion:

A. Unspecified or other significant medication (glyburide or immunosuppression);

B. PAH therapy (endothelin receptor antagonists, PDE-5 inhibitors, prostanoids);

C. Medication which is not compatible with bosentan or interferes with its metabolism (inhibitors of CYP2C9, CYP3A4) or medication which may interfere with bosentan treatment according to the investigator.

Study design

Design

Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2013
Enrollment:	40
Type:	Anticipated

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL3595
NTR-old	NTR3746
Other	METC AMC : 2012-004067-41
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A