Hyperoxic Exercise in Type 2 Diabetes.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20199

Source
NTR

Brief title
Hyperoxic Exercise in Type 2 Diabetes

Health condition

Diabetes type 2

Sponsors and support

Primary sponsor: Erasmus MC, University Medical Center Rotterdam
Source(s) of monetary or material Support: Diabetes Fonds

Intervention

Outcome measures

Primary outcome

The relative improvement in whole-body insulin sensitivity. An insulin sensitivity index (SI) will be calculated by using
the minimal model (Bergman et al 1985); a higher SI indicates enhanced insulin sensitivity. Acute-phase insulin
secretion (AIRG) and glucose effectiveness (SG) were also determined from the IVGTT (Bergman et al 1985).

Secondary outcome

1. Relative improvements in vascular function parameters using forearm plethysmography (change in forearmbloodflow in ml/100g forearm/min after nitriprusside/acetylcholine);

2. Cardiovascular fitness (VO2max);

3. Systemic blood pressure;

4. Body composition;

5. Lipid metabolism;

6. Glycemic control.

In 12 subjects from the control group and 12 subjects from the intervention group: GLUT-4 expression in the muscle, mitochondrial enzymatic activity and muscle fiber morphologic characteristics from muscle biopsy analysis.

Study description

Background summary

Rationale:

Type 2 diabetes patients frequently suffer from physical deconditioning and vascular disease. Although the exact mechanisms are unclear, microvascular changes and endothelial dysfunction appear to inhibit the oxygen transport and uptake in peripheral skeletal muscle of type 2 diabetes patients. Hyperoxic-training has been shown a safe intervention to increase exercise capacity and energy expenditure and is now routinely used for athletes (‘live-high, train-low’) and COPD patients. Furthermore, in COPD patients normalisation of oxygen saturation improves insulin sensivity.

Objective:

This research project aims to investigate (1) whether hyperoxic interval training improves insulin resistance, endothelial dysfunction, cardiovascular fitness, lipid metabolism and glycemic control in the treatment of deconditioned non-insulin dependent type 2 diabetes patients (2) the pathophysiological role of endothelial dysfunction and insulin resistance on the adaptive response to exercise.

Study design:

Substudy 1 (dosefinding study): intervention study;
Substudy 2 (training intervention study): double-blind placebo controlled intervention study.

Study population:

48 deconditioned (non-)insulin dependent type 2 diabetes patients.

Intervention:

After inclusion, 12 patients will participate in the dosefinding study (substudy 1). The remaining 36 subjects will be randomised and blinded to 16 weeks of progressive 30-45 min cycle ergometer interval training, applied 3 times a week while breathing either hyperoxic (100%O2, 4-8 L/min) or normoxic (21%O2-79%N2, 4-8L/min) humidified air (=placebo) through a nasal tube.

Main study parameters/endpoints:

The main study parameter and end-point is the relative improvement in whole-body insulin sensitivity.
Secondary end-points are relative improvements in vascular function parameters using forearm plethysmography, cardiovascular fitness, systemic blood pressure, body composition, lipid metabolism, glycemic control, GLUT-4 expression in the muscle, mitochondrial enzymatic activity and muscle fiber morphologic characteristics.

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

Before inclusion subjects will undergo a physical examination and X-ECG to exclude cardiovascular disease and assess cardiorespiratory status. A group of 12 subjects will undergo a submaximal exercise test while obtaining arteriovenous blood samples to optimize oxygen flow during exercise (substudy 1). The other 36 participating subjects will be asked to attend a total of 48 supervised exercise sessions of 45 min (substudy 2). To minimize the risk for a hypoglycemic event during the first 2 weeks of the exercise intervention, capillary blood glucose will be measured following exercise. If necessary medication will be adjusted. Independent of oxygen concentration in the air mixture, patients are expected to improve their physical fitness and metabolic control. Beside the direct therapeutic effects, both interventions are expected to improve general health and well-being.

Although unlikely, in theory hyperoxic exercise training might worsen diabetes related retinopathy. Therefore, an experienced ophthalmologist will monitor and stage diabetic retinopathy before and after the 16 weeks training program. Dual energy x-ray absorptiometry will be used to assess changes in body composition. Frequently sampled intravenous and forearm venous occlusion plethysmography following intrabrachial infusions of methacholine and sodium nitroprusside will be applied. A muscle biopsy will be obtained from the non-dominant vastus lateralis muscle after local anesthesia in 24 subjects (12 from the control and 12 from the intervention group). To prevent bleeding complications patients using low molecular weight heparin derivates and oral anti-coagulants will be excluded. Furthermore a compressive bandage will be applied for 12 hours. The procedure will be performed under aseptic conditions to prevent infectious complications. Participating subjects will visit the clinical research unit 9 times over a 5 months time period, equivalent to a 22 hours time load. Over a period of 20 weeks multiple arterialised and venous blood samples (equivalent to 258 cc) will be drawn through an intravenous/arterial catheter.

Study objective

Type 2 diabetes patients frequently suffer from physical deconditioning and vascular disease. Although the
exact mechanisms are unclear, microvascular changes and endothelial dysfunction appear to inhibit the
oxygen transport and uptake in peripheral skeletal muscle of type 2 diabetes patients. Hyperoxic-training has
been shown a safe intervention to increase exercise capacity and energy expenditure and is now routinely
used for athletes (‘live-high, train-low’) and COPD patients. Furthermore, in COPD patients normalisation of
oxygen saturation improves insulin sensivity.

Study design

All participants will receive:

1. Interview;

2. Clinical research and blood pressure measurements;

3. Food diary for three days;

4. Carry an activity monitor for seven days (Actigraph accelerationdevice);

5. Exercise ECG during cycle ergometer interval training;

6. Whole body DEXA measurement;

7. Fundus photography;

8. Frequently sampled intravenous glucose tolerance during three hours;

Intervention

After inclusion, 12 patients will participate in the dosefinding study (substudy 1). The remaining 36 subjects will be randomised and blinded to 16 weeks of progressive 30-45 min cycle ergometer interval training, applied 3 times a week while breathing either hyperoxic (100%O2, 10-15 L/min) or normoxic (21%O2-79%N2, 10-15 L/min) humidified air (=placebo) through mask.

Contacts

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Eligibility criteria

Inclusion criteria

1. Type 2 diabetes according to WHO criteria for over 2 years;

2. VO2peak 60-90% of age-predicted value as measured on a cycle-ergometer;

3. Motivated and willing/able to travel 3 times a week to ErasmusMC and participate in a supervised exercise
intervention program.

Exclusion criteria

1. Use of Beta-blocker therapy, low molecular heparin, exogenous insulin therapy (for

exercise intervention only),
use of oral anti-coagulans therapy;

2. Decompensatio cordis, angina pectoris, myocardial infarction or positive signs of cardiac ischaemia on the ECG during the incremental exercise test;

3. Orthopaedic impairments that would limit participation in the training program;

4. Co-morbidity such as renal failure or > grade III retinopathy or previous diabetic foot ulcer;

5. Cerebro-vascular disease (CVA), neurological diseases or deficits;

6. A history of glaucoma or high intraocular pressure will be contraindication for dilated fundus reflex photography.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-05-2010
Enrollment:	48
Type:	Anticipated

Ethics review

Positive opinion

Date:	27-04-2010
Application type:	First submission

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	NL2175
NTR-old	NTR2299
Other	MEC / EudraCT : 2009-125 / 2009-011448-20 ;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A