The cardiovascular effects of hyperoxia during and after CABG surgery

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1. To study the effect of different target PaO2's on myocardial damage, hemodynamics, microcirculation and organ perfusion in CABG patients.2. To study underlying mechanisms of hyperoxia by determining differences in oxidative stress response...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON38987

Source
ToetsingOnline

Brief title
Cardiovascular effects of hyperoxia

Condition

- Coronary artery disorders

Synonym
coronary bypass surgery (for coronary artery stenosis)

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: CABG, circulation, hyperoxia, intensive care

Outcome measures

Primary outcome

Hemodynamic parameters: myocardial injury (CK-MB and hs-troponine-T)

The primary endpoint was chosen because of its ability to provide proof-of-concept for the cardiovascular effects of hyperoxia. If indeed myocardial injury is found, a variety of secondary endpoints may support the relevance this has for hemodynamics, organ perfusion, etc. Effects on clinical endpoints, such as length-of-stay, mortality, etc, can only be anticipated to show-up in much larger clinical trials.If indeed hyperoxia shows unfavourable effects on most hemodynamic, perfusion-related and metabolic endpoints, such large trials are unlikely to ever be performed.

Secondary outcome

-hemodynamics

-microcirculation

-oxidative stress

-tissue/organ perfusion

-clinical endpoints (duration of mechanical ventilation, length of stay, mortality).

Study description

Background summary

Although the deleterious effects of hypoxia are well known, most physicians are less aware of the potential harmfull effect of hyperoxia. To avoid hypoxia, the tendency to supply extra oxygen to patients is widespread. Increasing evidence shows that hyperoxia has important circulatory effects, with decreased cardiac output (CO) and increased systemic vascular resistance (SVR), resulting in increased infarct size and increased mortality after myocardial infarction and cardiac arrest. The underlying mechanisms are unknown, but could relate to increased formation of reactive oxygen species (ROS), which not only causes vasoconstriction, but also other untoward effects, such as reperfusion damage. Hyperoxia is frequently, >20% of the mechanical ventilation time, encountered in the Intensive Care. Patients who underwent a coronary bypass graft operation (CABG) may be especially vulnerable to the detrimental cardiovascular effects of hyperoxia because of fluctuations in cardiac function due to other causes (such as blood loss and fluid shifts) post-surgery. However, many physicians still feel that increased arterial oxygen pressure (PaO2) represents a salutary oxygen reserve not only post-surgery but also during cardiopulmonary bypass (CPB). PaO2 measurements of >200 to 300 mmHg during CPB are no exception, as confirmed by our own pilot data. Therefore, we chose to investigate the cardiovascular effects of hyperoxia in patients during and after CABG surgery together with the proposed mechanisms by which hyperoxia exerts its effects. We will compare standard patient care, using supra-normal PaO2 levels, with oxygen levels titrated to normal physiological range.
We hypothesize that hyperoxia during and post CABG surgery has unfavourable effects on myocardial injury, hemodynamics, microcirculation, and organ perfusion, due to increased oxidative stress (ROS) affecting endothelium-derived vaso-active factors.

Study objective

1. To study the effect of different target PaO2's on myocardial damage, hemodynamics, microcirculation and organ perfusion in CABG patients.
2. To study underlying mechanisms of hyperoxia by determining differences in oxidative stress response between the hyperoxic patients and the normoxemic groups.

Study design

Randomized, prospective clinical trial

Intervention

We will investigate current practice (1, 2; group I) with titrated oxygen levels (group II).
group I: target PaO2 on CBP during aortic clamp time 200 * 220 mmHg, PaO2 at

ICU of 130-150 mm Hg
group II: : After intubation FiO2 will be decreased to 40% (provided that O2 saturation remains > 96%). Target PaO2 on CBP during aortic clamp tima 130 * 150 mmHg, PaO2 at ICU 80 * 100 mmHg

Study burden and risks

The risk and burden for study subjects are small. Blood sampling is combined with sampling for normal care of patients. SDF measurements and urine sampling are not a burden for patients. Since the titrated oxygen levels administered to the patients are based on the pO2 measured in blood and pulse oximetry and the oxygen levels are within the range of normal physiological levels, we do not expose the patients to 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
-Non-emergent CABG surgery
-Hb * 7.5 mmol/l
-BSA * 1.9 m2

Exclusion criteria

-Non-elective surgery
-Combined cardiac surgery (heart valve combined with CABG surgery)
-Off-pump-CABG
-Presence of pre/perioperative intra-aortic balloon pump
-Medical history positive for COPD

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-11-2013
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Conoxia
Generic name:	oxygen
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	17-05-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-10-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2013
Application type:	Amendment
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

ID: 27282
Source: NTR
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-001743-31-NL
CCMO	NL43882.029.13
OMON	NL-OMON27282