Changes in VC, DLCO, DLNO and exhaled breath after an one-hour oxygen dive with a PO2 of 190 kPa as an indication for pulmonary oxygen toxicity.

Published: 01-02-2012
Last updated: 15-05-2024

Primary Objective: 1. Will an exposure to oxygen with a PO2 = 190 kPa lead to changes primarily in DLno compared to DLco?Secondary Objectives: 1. After an exposure to oxygen with a PO2 = 190 kPa for one hour, are the changes primarily located in the...

Ethical review	Approved WMO
Status	Pending
Health condition type	Respiratory disorders NEC
Study type	Interventional

Summary

ID

NL-OMON35888

Source
ToetsingOnline

Brief title
pulmonary functional changes after an oxygen dive

Condition

- Respiratory disorders NEC

Synonym
pulmonary oxygen toxicity; oxygen induced lung damage

Research involving
Human

Sponsors and support

Primary sponsor: Koninklijke Marine

Source(s) of monetary or material Support: Ministerie van Defensie - Koninklijke Marine

Intervention

Keyword: diffusing capacity, exhaled breath, pulmonary oxygen toxicity, spirometry

Outcome measures

Primary outcome

Changes in DLno, DLco VC and EB compared to baseline after air and oxygen

dives.

Secondary outcome

Changes in oxidative stress status compared to baseline after air and oxygen

dives.

Study description

Background summary

Breathing of oxygen during a longer time with a partial pressure (PO2) of more than 50 kPa can lead to pulmonary oxygen intoxication (POT). The most mentioned changes which can be found are atelectasis, interstitial oedema, inflammation and finally fibrosis. Although this kind of lung damage in principle is reversible, the continuation of breathing oxygen will eventually lead to irreversible lung damage as can be seen in Acute Respiratory Distress Syndrome (ARDS). Nowadays, changes in lung function are used as an indicator for the development of POT. Most mentioned indicators arethe decrease in vital capacity (VC) and diffusing capacity for carbon monoxide (DLco).

Based on the changes in VC Clark & Lambertsen (1970) introduced the Unit of Pulmonary Toxicity Dose (UPTD) in the early seventies. By using the UPTD one could predict the median decrease of the VC after being exposed to oxygen with a given PO2 during a specific time. For example a 450 UPTD exposure could lead to a median VC decrease of 2%. A derived application of this UPTD format is being used in the anaesthesia and intensive care setting where it is a rule of the thumb that breathing 100% oxygen (PO2 of about 100 kPA) may not last longer than 24 hours. Although this median decrease of VC is most often used, it is suggested that not VC but DLco detects POT earlier and better than VC (Clark 1970, Lowry 2002, Thorsen 1993, van Ooij 2011). The preference for this

VC indicator was mainly motivated by its easy handling by laymen which stood in contrast with the difficult measurement of DLco.

In contrast to the seventies Dlco can nowadays easier and faster be measured. With the development of new techniques it is possible to determine also the diffusing capacity for nitric oxide (DLno). An advantage of this new method is that it is capable to measure the specific alterations in the alveolo-capillary membrane. By using DLno one could detect where POT generates; in the alveolar membrane (Dm) or in the capillary of the lung vascular bed (VC). A disadvantage of both techniques are that they can only be used in cooperative persons. Using it in an IC setting is not possible.
With the introduction of the electric nose (also called e-nose) this could be used for IC-patients, in contrast to DLco and DLno. The e-nose is able to measure volatile organic components (VOC) in the exhaled air. In the apparatus there are nano sensors which can bind specific VOC's. By analyzing these VOC's one can determine different VOC-patterns (EB) which can be used in recognizing a specific disease like f.e. asthma and emphysema. In the earlier phase of POT inflammation is one of the key features. Due to this inflammation changes in EB could develop which can be detected by e-nose. This would offer us an ideal method for IC-patients to see whether POT is developing or not. Unfortunately, no studies have been published regarding this theory.

Our hypothesis is that breathing oxygen with a PO2 of 190 kPa during 60 minutes will lead to changes in DLno earlier than in DLno. In contrast VC will show no significant changes after this exposition. Furthermore this kind of oxygen will specific changes in EB as measured with the e-nose.

Study objective

Primary Objective:
1. Will an exposure to oxygen with a PO2 = 190 kPa lead to changes primarily in DLno compared to DLco?

Secondary Objectives:
1. After an exposure to oxygen with a PO2 = 190 kPa for one hour, are the changes primarily located in the Dm or in the Vc?
2. Is there a specific EB measurable after an exposure to oxygen with a PO2 = 190 kPa for one hour?

Study design

This study is a randomized cross-over trial in which the subjects are measured during three days.

Study day 1: baseline measurement will be done in which we measure VC, DLco, DLno and EB for 6 times within a period of 24 hours. The subject will not be

exposed to either oxygen or pressure. With these measurements we will study any diurnal rhythm effect which could confound our measurements. We call this study day "Baseline day".

Study day 2: during this day the subject will make a wet dive to 9 meters during 60 minutes. He will either breath 100% oxygen (active exposure) or air (control, PO2 max 40 kPa) in random order. Before the dive and 5 times after the dive VC, DLco, DLno and EB will be measured at the same time points as during the baseline measurements. Besides, in 15 subjects venous blood sample (two times) will be taken to determine the oxidative stress (OS) status before and after the oxygen exposure. In this way we can see what the personal oxidative burden is due to this kind of oxygen exposure.

Study day 3: this one is congruous as day 2 but now the subjects will breath the other type of breathing gas. In other words: if on day 2 oxygen was breathed he will now breath air during the dive. The time points for measuring VC, DLco, DLno and EB will be the same as on day 1 and day 2. This also concerns the venous blood samples.

Intervention

Every subject will perform one dive with air and one with 100% oxygen. These dives will be done in random order.

Study burden and risks

Benefits:
For military oxygen diving as well as intensive care medicine it is of importance to know at which level and duration of breathing oxygen will lead to POT. By using the proper indicators it will help oxygen divers to plan their oxygen dives better or an intensivist to administer oxygen for each patient to the right duration.

Risks assessment, group relatedness and burden:
Within the scope of this study the subjects will be imposed to some life-style restrictions concerning eating, drinking and sporting. To our opinion this regime will not disproportionate infringe their private life.

The measurements of VC, DLco, DLno and EB are not invasive, simple and complications are not known. As DLco has to be corrected for Hb a fingertip blood sample will be necessary to measure Hb. The burden of the fingertip blood sampling is in our opinion minimal and complication is not to be expected. To measure the oxidative stress status venous blood must be taken (vena mediana cubiti). This venous puncture is concerned simple and the possible complication is hematoma due to leakage of venous blood out of the puncture vessel.

Any well performed in-water dive has some risk of DCS. The risk of DCS associated with this dive simulation can be considered as very small (0.1%). Besides, this diving profile lays well within the maximal diving time of the used diving tables (300 minutes).
During an oxygen dive to 9 meter, there is a risk of the occurrence of an epileptic insult due to cerebral oxygen toxicity. Using the articles of Arieli (2002) and Butler (2004) this riks can be determined at below 5%. This estimations are based on oxygen divers who are subjected to exertion. As our subjects will not perform any exercise we expect the risk of an insult due to cerebral oxygen toxicity to be substantially less than 5%. If nevertheless an insult does occurs the proper action will be taken according to "Noodplan Neurologische Zuurstof Vergiftiging" (NZV) (see section K6).

All in all, we think the burden of these simulations can be considered low, and less than with a real, wet oxygen dive.

Contacts

Public
Koninklijke Marine

Postbus 10.000
1780 CA Den Helder
NL
Scientific
Koninklijke Marine

Postbus 10.000
1780 CA Den Helder
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Fit to dive, certified military oxygen diver, normal spirometry and diffusing capacity

Exclusion criteria

reduced Tiffeneau-index (FVE1/SVC), reduced diffusing capacity (DLCO, DLNO), recent lower pulmonary tract infections

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2011
Enrollment:	25
Type:	Anticipated

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

ID: 23480
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL35768.018.11
OMON	NL-OMON23480