Difference in time until onset of symptoms and recovery between hypobaric and normobaric hypoxia

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This study aims to answer the following questions: 1. Is there a difference in the time to onset of the first symptom between HH and NH?2. Is there a difference in the severity of symptoms between HH and NH?3. Is there a difference in the time to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56865

Source
ToetsingOnline

Brief title
Hypobaric vs normobaric hypoxia

Condition

- Other condition

Synonym
oxygen deficiency, Reduction in blood oxygen saturation

Health condition

hypoxie symptomen en resipiratoire veranderingen bij hypoxieblootstelling bij gezonde deelnemers

Research involving
Human

Sponsors and support

Primary sponsor: Koninklijke luchtmacht
Source(s) of monetary or material Support: Ministerie van Defensie

Intervention

Keyword: hypobaric hypoxia, normobaric hypoxia, physiological response, symptoms

Outcome measures

Primary outcome

Difference in time until onset of the first hypoxia symptom and the severity of hypoxia symptoms between Hypobaric Hypoxia (HH) in the hypobaric chamber and Normobaric Hypoxia (NH) in the ROBD at a simulated altitude of 18000 ft. The endpoint is an composite endpoint. At an altitude of 18,000 ft, we expect all test subjects to experience hypoxia symptoms. In the unlikely event that they do not feel their own symptoms. The crossing of their TUC will be considered their first sign of hypoxia. In the unlikely event that test subjects will not experience symptoms and the TUC will not be crossed, censoring will be applied.

Secondary outcome

Secondary parameters:

I. Difference in time to initiation of recovery (after recognition of the third symptom) between HH and NH.

II. Difference in severity of symptoms in HH and NH.

III. Difference in respiratory and oxygenation parameters during the different exposures to hypoxia, by measuring the following parameters:

a. Oxygen saturation (SpO2)

b. Rate of decline of SpO2

c. Respiratory Rate (RR)

d. Tidal volume (TV)

e. Minute ventilation (Ve)

f. Partial pressure of end tidal CO2 (PETCO2)

g. Partial pressure of end tidal O2 (PETO2)

Study description

Background summary

When flying at altitude, aircrew of the Royal Netherlands Air Force (RNLAF), are dependent on either a pressurized cabin and/or an oxygen delivery system for protection against the effects of hypoxia. In the event of oxygen delivery equipment failure or cabin depressurization, it is essential for aircrew to recognize their hypoxia symptoms and initiate emergency procedures. Inability of aircrew to initiate emergency procedures can lead to impairment of cognitive functioning (McMorris 2017, Aebi 2020) and at extreme altitudes (>18,000 ft) may eventually lead to loss of consciousness with fatal results (Cable 2002). The Time of Useful Consciousness (TUC) is the duration a person can function effectively in a hypoxic environment. During a hypoxic event a decrease in the partial pressure of oxygen in the ambient air (PO2) causes a decrease in the inspired partial pressure of oxygen (PiO2) and alveolar oxygen pressure (PAO2), this results in a lower partial pressure of oxygen in arterial blood (PaO2) (Dehart 2002). The TUC depends on the altitude, the rate of decompression and the individual*s reaction to hypoxia, and can range from seconds to minutes (Dehart 2002). After this point, a person may still be conscious, but would be unable to initiate and follow the proper emergency procedures due to cognitive impairment (Dehart 2002, Leinonen 2021, Hohenauer 2022). These procedures are to descend the aircraft to a safe flying altitude <10000 ft (;3048 m) and if available, switch the onboard oxygen system to high pressure breathing.

Aircrew of the RNLAF receive hypoxia training every five years in accordance with NATO standards. The purpose of this training is to teach aircrew to recognize their hypoxia symptoms such as tingling, warm sensations, fatigue (Dehart 2002) and initiate *recovery* within their TUC using standardized emergency procedures (Cable 2010). Normally, aircrew is encouraged to initiate recovery after recognizing their third hypoxia symptom. Currently, in this training, altitude is simulated in a hypobaric chamber (HC) by reducing the atmospheric pressure within the chamber. This induces hypobaric hypoxia (HH). This training is costly, time-consuming, and has a risk of decompression

sickness (Rice 2003, Smart 2004). To limit the risk of decompression sickness, subjects denitrogenate by breathing 100% oxygen, for the duration of 30 minutes before exposure (Rice 2003, Dehart 2002). In addition, during this training, aircrew do not perform flight-related tasks, making it difficult for them to translate their experiences during training to the effects hypoxia may have on their performance during flight.

The Reduced Oxygen Breathing Device (ROBD) was introduced in RNLAF for hypoxia training purposes to solve these issues. The ROBD was designed to induce normobaric hypoxia (NH), by lowering the fraction of inspired oxygen (FiO2), without changing the ambient pressure. One of the advantages of the ROBD over HC, is that it can be integrated with a flight simulator. This allows aircrew to train hypoxia recognition and recovery in a realistic environment. Another advantage of the ROBD is that there is no risk for decompression sickness and doesn*t require any pre-breathing/denitrogenation. Furthermore, it is transportable, which makes it possible to train air crew at their own air force base.

For the ROBD training to be able to replace the HC training effectively, the time until onset of hypoxia symptoms should be the same. It should also offer the same symptom severity to allow the aircrew to initiate recovery within their TUC. The severity of hypoxia symptoms is dependent on the magnitude of changes in O2 and CO2 content in the blood (Leinonen 2021, Drechsler 2023). Several studies show that respiratory parameters differ between HH and NH during acute exposure (Self 2011, Savourey 2003 and 2007). They reported lower O2 content (PaO2 (Savourey 2003) or SpO2 (Savourey 2003 and 2007) in HH compared to NH. In addition, Self (2011) showed that the decrease in O2 content was faster in HH compared to NH. Savourey (2003 and 2007) found a higher respiratory rate (RR) in HH compared to NH. Self (2011) also showed a steeper rate of decline in cerebral O2 saturation in HH vs NH measured with a forehead sensor. Furthermore, lower partial pressure of CO2 in arterial blood pressure (PaCO2) (Self 2011) and partial pressure of end tidal CO2 (PETCO2) (Savourey 2007) values were reported in HH compared to NH. The results of these studies may indicate an earlier onset of symptoms and more severe symptoms in HH compared to NH, leading to an earlier initiation of recovery.

Self (2011) investigated the difference in the number of hypoxia symptoms reported between HH and NH at a simulated altitude of 25000 ft. He found that subjects reported more symptoms in the first minute of exposure to HH, compared to NH but not after three and four minutes. To the best of our knowledge, there are no studies comparing the until onset of hypoxia symptoms or the time until initiation of recovery between HH and NH. In addition, the effect of differences in ventilatory parameters between HH and NH and their relation to time to the until onset of hypoxia symptoms, has also not been studied

The results of this study will offer a better understanding of the physiological and subjective differences between HH and NH. It may be used to

assess effectiveness of ROBD training compared to HC training. In addition, it may be used to improve ROBD hypoxia training.
More realistic training offers air crew a better chance of successful recovery in a real-world scenario.

Study objective

This study aims to answer the following questions:
1. Is there a difference in the time to onset of the first symptom between HH and NH?
2. Is there a difference in the severity of symptoms between HH and NH?
3. Is there a difference in the time to recovery between HH and NH?
4. Are there differences in ventilatory parameters between HH and NH?
5. What is the correlation between ventilatory parameters and the time to the onset of symptoms?
6. What is the correlation between ventilatory parameters and the time to recovery?

Study design

This will be a randomised crossover research. We will use a repeated within subject measure design where every test subject will follow a hypobaric and a normobaric hypoxia session. During the sessions, altitude up to 18000ft will be simulated with either hypobaric hypoxia or normobaric hypoxia. There will be a minimum of three days between the two sessions. Symptoms will be registered continuously as well as ventilatory and oxygenation parameters.

Intervention

Each test subject will undergo a hypobaric hypoxia- and a normobaric hypoxia session

Study burden and risks

Subjects will participate in both hypoxia sessions taking approximately two hours each (including pre-flight and post-flight briefing). There will be a minimum of three days between the sessions. Subjects will be exposed to hypobaric and normobaric hypoxia which may cause hypoxia symptoms such as paraesthesia, shortness of breath, dizziness, nausea and headache. This will last for the duration of the exposure to hypoxia. The subject might feel tired after exposure. Subjects will be continuously monitored, and an instructor will be available to administer additional 100% oxygen to those who want it or neglect to do so in accordance with the guidelines. There is always a flight surgeon readily available on site during all hypoxia training sessions for medical questions and emergencies. Subjects have access to the flight surgeon

on call 24/7.

Contacts

Public
Koninklijke luchtmacht

Kampweg 53
Soesterberg 3769DE
NL
Scientific
Koninklijke luchtmacht

Kampweg 53
Soesterberg 3769DE
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Aircrew between 18 and 62 years old
Previous hypoxia training
In possession of an active aeromedical certificate (fit to fly)
Willing and able to provide informed consent

Exclusion criteria

Significant adverse event after a previous hypoxia training

Ear drum perforation in medical history
Claustrophobia
Pregnancy
Exposure to altitude for longer than one week higher than 8000ft 3 months prior to research
Smokers
Does not comprehend study requirements and/or is unable to comply with study procedures or pre-session restrictions

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-08-2024
Enrollment:	34
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	08-07-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

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
CCMO	NL85548.058.24