Hyperbaric OXygen therapy for ACute Acoustic Trauma

Published: 04-08-2021
Last updated: 09-11-2024

This study has been transitioned to CTIS with ID 2024-517739-35-00 check the CTIS register for the current data. The objective of this study is to investigate whether hyperbaric oxygen therapy twice-daily for five days (HBOT5) is superior to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hearing disorders
Study type	Interventional

Summary

ID

NL-OMON55905

Source
ToetsingOnline

Brief title
HOXACAT

Condition

- Hearing disorders

Synonym
Acute Acoustic Trauma, Acute Hearing Loss

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Stichting Ziektekostenverzekering Krijgsmacht

Intervention

Keyword: Acute Acoustic Trauma, Corticosteroids, Hyperbaic Oxygen Therapy, Sensorineural Hearing Loss

Outcome measures

Primary outcome

The main study endpoint is the absolute hearing gain on all affected

frequencies (>= 20 dB) after between patients in HBOT5 and HBOT10 groups.

Secondary outcome

Additional audiometric outcomes include relative hearing gains and speech

discrimination at 100%, these will be compared between the both treatment arms.

Study description

Background summary

Acute acoustic trauma (AAT) is a form of acute sensorineural hearing loss caused by blast injury or high impact noise. AAT is relatively common in the military, AAT has continued to a mass veteran disability at a 13-18% annual rate in the USA. Of the 2.35 million unique cases of auditory system disability at the end of 2013, approximately 870,000 are attributed to the Gulf War era and approximately 551,000 from exposure during operations in Iraq and Afghanistan.5 In the United States military, the estimated costs for compensation and care of hearing loss and auditory system approaches $1.2 billion for over 1.8 million Veterans.6 These numbers are not published for the Dutch military.

In the Netherlands, the treatment protocol in the military is the combination therapy of hyperbaric oxygen therapy (HBOT) and oral corticosteroids. The rationale for this therapy is that corticosteroids may reduce the inflammatory response while HBOT reduces the amount of hypoxia caused by the acoustic trauma. Several preclinical studies have shown beneficial effects of HBOT in AAT models. Lamm et al. assessed the effects of HBOT in an experimental AAT model in guinea pigs. They showed an alleged preventive effects of HBOT in 14 out of 26 guinea pigs. Hu et al. reported that HBOT can reduce the noise induced threshold shift and decrease cochlear damage during chronic noise exposure in guinea pigs.

Intense noise produces mechanical damage to the cochlea, which directly leads to disruption of the hair cell stereocilia. Pilgramm et al. demonstrated in an animal model that 60 h after acoustic trauma, the number of inner ear sensory cells that had suffered morphological damage was lower in the group receiving HBOT than in the group without HBOT. Kuokkanen (1997)12 and (2000)13 showed a lesser amount of threshold shift and fewer missing hair cells among rats that were treated with HBOT following 60 shots (162 dB) with an assault rifle. Colombari et al. found in an animal experiment with acute acoustic damage that the number of injured cochlear outer hair cells decreased and that their functionality improved after HBOT.

Clinically, it was shown that the combination therapy of HBOT and corticosteroids has additional benefit to corticosteroids alone, and that early treatment is key. However, in current practice patients have to undergo ten days of HBOT and seven days of corticosteroid treatment (60 mg/day). In the military, these ten days of treatment affect the employability of the soldier and may have strategic consequences for decision making for military officers. Therefore, the military is interested in reducing the amount of treatment days for patients with AAT. It has already been shown that addition of two HBOT sessions a day is as effective as one HBOT session a day in sudden sensorineural deafness. However, no such studies exists for AAT. The aim of this study is to investigate whether hyperbaric oxygen therapy twice-daily for five days (HBOT5) is as effective in hearing loss recovery as hyperbaric oxygen therapy once daily for ten days (HBOT10) for AAT.

Study objective

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The objective of this study is to investigate whether hyperbaric oxygen therapy twice-daily for five days (HBOT5) is superior to hyperbaric oxygen therapy once daily for ten days (HBOT10) in obtaining hearing loss recovery after AAT. This will be determined by comparing audiometric outcomes at final follow-up.

As secondary objective, the amount military personnel recovering to the Dutch Military Hearing Standards will be assessed using the Clinical Recovery Score, which is based on the guidelines from the Committee on Hearing and Equilibrium (see figure 3). Furthermore, the frequency and severity of adverse events (AEs) will be assessed.

Study design

This study is a randomized superiority trial (1:1 allocation) comparing two different treatment protocols of hyperbaric oxygen therapy (twice daily for 5 days [HBOT5] versus once daily for 10 days [HBOT10]). This design is chosen

because the standard of care in the Dutch military for acute acoustic trauma is hyperbaric oxygen therapy once daily for 10 days with corticosteroids (60 mg/day for 7 days). However, practically the use of 10 days of HBOT hinders employability of military personnel. Therefore, a randomized superiority trial is performed. Included patients will be randomized to treatment with HBOT5 (intervention group) or HBOT10 (comparator). Patients will be treated at the Department of Hyperbaric Medicine at the Amsterdam University Medical Centre, Academic Medical Centre, Amsterdam, the Netherlands. Concomitant therapy with corticosteroids 60 mg per day for 7 days is given in both groups (standard practice). Patients will be seen by the hyperbaric physician before the start of hyperbaric treatment. During hyperbaric sessions patients will be under supervision of the hyperbaric physician and a separate appointment will be scheduled at the end of treatment, at which side-effects of treatment will be evaluated. Audiometry will be measured at presentation at the otolaryngology clinic. Follow-up audiometry will be measured one month after the last HBOT session.

Intervention

The investigation treatment is hyperbaric oxygen therapy twice daily for five days while the comparator treatment is hyperbaric oxygen therapy once daily for ten days. Hyperbaric oxygen therapy will be performed in a multi-person recompression chamber, where subjects breathed 100% oxygen via a built-in breathing mask at a pressure of 240 kPa for 90 min, including three 5 min *air breaks*.

Study burden and risks

HBOT is a very safe treatment method with very few serious adverse effects. Adverse effects are often mild and reversible but could, potentially, be severe and life threatening. As a consequence, strict precautions must be taken while administering HBOT to avoid those complications. In addition, proper installation and maintenance of a HBOT facility and adequate staffing with specifically trained personnel is pivotal.

Barotrauma
Barotrauma is a general term to indicate injury to a tissue through the action of differential pressures and it can occur in body areas where tissue and gas interface, such as the middle ear, the sinuses and the lungs. Middle ear barotrauma is the most commonly reported acute side effect of HBOT, and it was reported to occur in 2% of patients. A prospective study reported that almost one-fifth of all patients experienced some ear pain or discomfort related to problems in middle ear pressure equalization, that can be resolved with tympanostomy tubes, while visual otological examination confirmed barotraumatic lesions in 3.8% of patients. Barotrauma can be avoided by careful patient selection, excluding patient with contraindications for HBOT such as emphysema,

by patient education and by the termination of HBOT when early symptoms occur. Pulmonary barotrauma is a potential problem mainly during the decompression phase of HBOT since the volume of gas in the lungs increases due to the reduced pressure and this extra volume needs to be breathed out. However, the occurrence of this complication has only been reported in sporadic cases.

Any time that the environmental pressure is changed, all of the air spaces within the body must remain in balance with these changes. If they do not, discomfort will result. Study participants may experience this discomfort in their ears, and very rarely, sinus space or tooth discomfort. If discomfort occurs, study participants will be asked to advise a hyperbaric team member immediately so that corrective action can be implemented. If a study participant*s lungs do not ventilate adequately during pressure changes, he/she may suffer a leak of pulmonary air into the chest, or into the bloodstream. Such a leak could cause problems with the lungs such as a dry cough, chest pain or burning, or central nervous system function such as confusion, altered sensation, loss of consciousness, paralysis or even death. These complications are rare, and every effort will be made to exclude all study participants who may be at high risk of these side effects.

Effects on the brain
Hyperbaric oxygen may affect the brain and produce one or more signs or symptoms, including muscle twitching, anxiety, confusion and dizziness. If the situation is not corrected a generalized seizure may result (this occurs in roughly 1 in 4000 treatments at 2.4 ATA). This is quickly corrected by removing the oxygen. Again, this does not happen often, and every effort has been made to exclude all study participants who may be at an increased risk of this side effect.

Fire
Although increases in oxygen concentration can cause an increased risk of fire, the hyperbaric chamber has been specially designed to minimize this risk. Only cotton clothing and bedding, provided by chamber staff, will be used when study participants are in the chamber to minimize this risk.

a. Level of knowledge about mechanism of action
Oxygen is considered as a drug and it can be administered easily under normobaric conditions, but administering oxygen at pressures higher than 1 ATA requires compression. This is usually done by having the patient breathe pure oxygen or mixtures with other gases while being inside an airtight chamber in which the pressure is greater than 1 ATA. Three primary mechanisms are believed to be involved in the potential beneficial effects: bubble size reduction and elimination in case of decompression sickness and gas embolism (commonly called decompression illnesses or DCI), the achievement of hyperoxia in target organs, and the potential enhancement of immune and healing mechanisms through the correction of pre-existing hypoxia in target organs.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amstedam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amstedam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Diagnosed with AAT based on audiometry after high impact noise-exposure at the Department of Otorhinolaryngology, Central Military Hospital.
- First visit to the Department of Otorhinolaryngology between 24 and 72 hours after the acoustic trauma.
- Age >= 18 years old.
- Minimum hearing loss: >= 30 dB on one tested frequency, or >= 25 dB on two tested frequencies, OR >= 20 dB on three tested frequencies.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded:
- Subject does not speak fluent Dutch
- History of idiopathic sudden sensorineural loss.
- History of radiation therapy in the head and neck region.
- Previous acute acoustic trauma (before current trauma) with objectified hearing loss.
- Current or previous use of ototoxic drugs with objectified complaints before the current visit.
- Known presence or history of vestibular schwannoma or cholesteatoma.
- Current otitis media.
- Epilepsy.
- Known presence of untreated pneumothorax.
- Known Chronic Obstructive Pulmonary Disease Gold IV grade or other pulmonary disease with severe air trapping.
- Known severely reduced cardiac ejection fraction.
- Implanted device that is not proven to be compatible with HBOT.
- Claustrophobia that interferes with taking place in hyperbaric chamber.
- Inability to equalize middle ears using Valsalva manoeuvre. (If so, patients are offered tympanostomy tubes if they wish to participate before being excluded.)
- Current pregnancy.
- Use of adriamycin, bleomycin, cisplatin, or doxorubicin in previous six months.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-01-2022
Enrollment:	84
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Oxygen
Generic name:	Oxygen
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	04-08-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-08-2021
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

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-517739-35-00
EudraCT	EUCTR2020-005741-17-NL
CCMO	NL76096.018.21
Other	NL9123