the effect of hyperbaric oxygen therapy on immune response and oxidative stress

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To explore the effects of HBOT on immunologic parameters and oxidative stress.

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

Summary

ID

NL-OMON48412

Source
ToetsingOnline

Brief title
HOIROS study

Condition

- Autoimmune disorders
- Bacterial infectious disorders
- Gastrointestinal therapeutic procedures

Synonym
Immuun response and reactive oxygen species, inflammation & oxidative stress

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van defensie.

Intervention

Keyword: Anesthesiology, Hyperbaric Oxygenation, Immune system, Oxidative stress

Outcome measures

Primary outcome

Immunologic effects defined by neutrophil intracellular ROS generation,

phagocytosis assays, plasma cytokine concentrations, HLA-DRA mRNA expression,

malondialdehyde concentration and ex vivo whole blood stimulation.

Secondary outcome

NA

Study description

Background summary

Hyperbaric oxygen therapy

HBO consists of breathing 100% oxygen under higher than normal atmospheric pressure:
usually 1.5-2.8 atmosphere absolute (ATA). This increases plasma and tissue oxygen levels,
and decreases hypoxia. HBOT is commonly used in the treatment of decompression sickness, carbon monoxide intoxication, arterial gas embolism, necrotizing soft tissue infections, chronic skin ulcers, severe multiple trauma with ischemia and ischemic diabetic foot ulcers.

HBOT and immunologic response

Several reports have been published in regards to the immunologic effects of HBO on specific patient populations (for instance patients with Crohns Disease) and animals. For example it has been shown to alter signaling pathways such as Hypoxia Induced Factor (HIF) and heme-oxygenase (HO), both involved in tissue response to hypoxia and wound repair. Furthermore, the production of pro-inflammatory cytokines and chemokines (IL-1, IL-6, TNF-alfa) is suppressed by HBO. [1] Also, in general, oxidative stress is recognized to play a role in stem cell mobilization and promoted wound healing. [2].
However, to our knowledge, there are no reports in regards to the immunologic

effects of HBO in healthy individuals. We have performed a search of literature but found no such articles. In our study we will investigate the effect of HBO on the immunologic parameters and oxidative stress factors:

HBOT and surgery

Previous data by Yang and colleagues on animals demonstrated that HBO inhibits TNF- * production during intestinal ischemia-reperfusion [3] with a beneficial effect, mediated by decreased production of both TNF-* and IL-1*, on indomethacin-induced enteropathy [4]. Preconditioning with HBO might be useful as an adjunct for various types of surgery. For instance, a better outcome in left ventricular function was demonstrated after on-pump coronary artery bypass surgery after pretreatment with three HBO sessions [5]. The positive role of HBO in human surgery has further been demonstrated in other cardiovascular [6, 7], orthopedic surgery [8], and after liver transplantation, as reported by Franchello et al. which documented a reduction of ischemic areas and an increase of intrahepatic arterial vascularisation by collateral vessels after 20 HBO sessions in a patient affected by Hepatic Artery Thrombosis (HAT) after liver transplantation [9] Bosco et al performed a prospective randomized, double blind study in which they evaluated the post-operative biological and clinical effects of single hyperbaric-treatment the day before surgery for pancreatic ductal adenocarcinoma [10]. This study showed that HBOT significantly decreased the serum IL-6 level which was associated with biliary fistula. It also showed significantly less pulmonary infections in patients in the HBO group. However, IL-8 and IL-12 were not affected by HBO exposure. A recent meta-analysis of our group showed that post-operative HBO had a positive effect on colorectal anastomoses in rats [11]. This study effect was most prominent on colorectal anastomoses in rats without a malignancy and in ischemic anastomoses. To investigate the full potential of HBO to prevent anastomotic leakage in human patients undergoing colorectal surgery, a pilot study should be performed in due time. However, all earlier studies have been conducted on animals or specific patient populations. To understand the underlying mechanisms of HBOT, we first need to determine the immunologic effects of HBO in healthy volunteers.

Study
We initiated the present pilot study to evaluate effects of HBOT on the immune response and oxidative stress in healthy young, male volunteers. These findings will help guide further re-search and sample size assumptions.

Study objective

To explore the effects of HBOT on immunologic parameters and oxidative stress.

Study design

Pilot of a prospective cohort study.

A total of 15 healthy volunteers will undergo the HBOT sessions. The volunteers will receive a total of three HBOT sessions with 24-hour intervals. Hyperbaric treatment will consist of three treatments breathing 100% air at a pressure of 2.4 atmosphere absolute. The total duration of one treatment is 110 minutes (total of 80 minutes of breathing 100% oxygen with 5-minute breaks on normal air, total session time: 110 minutes)

Laboratory findings will be obtained before and after the 3 HBOT sessions according to schedule below. In total, six 10.5 ml blood samples will be drawn from the volunteers, adding up to 63 ml in total. 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. Inclusion, treatment and assessment of outcomes will be done in an outpatient clinic-setting.

Blood sample schedule.
- Directly before session one * T0
- Directly after session one * T1
- Directly before session two * T2
- Directly after session two * T3
- Directly after session three * T4
- 24 hours after session three * T5

Intervention

The volunteers will receive a total of three HBOT sessions. Hyperbaric treatment in the intervention group will consist of three treatments breathing 100% air at a pressure of 2.4 atmosphere absolute. The total duration of one treatment is 110 minutes (total of 80 minutes of breathing 100% oxygen with 5-minute breaks on normal air, total session time: 110 minutes)

Study burden and risks

The risk of this study is considered negligible. 63ml blood sampling is a relatively small amount and harmless in healthy volunteers. Hyperbaric oxygen therapy is routinely used in the treatment of for instance different wound healing problems. Risks associated with HBO include ear and/or sinus complaints (squeeze/perforations), myopia, acute oxygen toxicity (seizures) and decompression illness.
* Ear and/or sinus complaints include middle ear and sinus squeeze, due to an inability to or late equalizing. This presents as acute pain and if not dealt with, may result nose or ear bleeding and in case of middle ear squeeze result in perforation of the ear drum. The overall risk to develop ear and sinus

complaints is reported to be 2-3%.1,2
* Visual changes due to myopia have been reported in up to 60 to 70% of patients, but these changes are reversible and mostly mild. No lasting effects are seen in patients receiving less than 50 treatment sessions (as is the case in this protocol).2,3
* Acute oxygen toxicity results in seizures when the central nervous system is exposed to a toxic level of oxygen. These symptoms resolve quickly en without residue once the exposure to high level of oxygen is diminished. The clinical HBO protocol takes this into account by limiting oxygen breathing to sections 20 minutes before a 5-minute break breathing room air. The risk to develop acute oxygen poisoning is reported to be 0.02 to 0.3% in a clinical setting.4,5
* Given that patients breathe 100% oxygen, there is no risk of decompression illness.

[1] D. T. Fitzpatrick, B. A. Franck, K. T. Mason, et al. Risk factors for symptomatic otic and sinus barotrauma in a multiplace hyperbaric chamber. Undersea Hyperb Med, vol. 26, nr. 4, pp. 243-7, 1999.
[2] E. M. Camporesi. Side effects of hyperbaric oxygen therapy. Undersea Hyperb Med, vol. 41, nr. 3, pp. 253-7, 2014.
[3] Churchill S, Deru K, Wilson G, Cable R, Bell JE, Weaver LK. Rates of visual acuity change in patients receiving hyperbaric oxygen in monoplace and multiplace chambers. Undersea Hyperb Med 2016;43:217-23.
[4] S. Yildiz, S. Aktas, M. Cimsit, et al. Seizure incidence in 80,000 patient treatments with hyperbaric oxygen. Aviat Space Environ Med, vol. 75, nr. 11, pp. 992-4, 2004.
[5] S. Hadanny, O. Meir, Y. Bechor, et al. Seizures during hyperbaric oxygen therapy: retrospective analysis of 62,614 treatment sessions. Undersea Hyperb Med, vol. 43, nr. 1, pp. 21-8, 2016.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male
- Healthy
- Age 18-40
- Be able to read and understand Dutch

Exclusion criteria

- Language barrier
- Unable to give informed consent
- Unfit for hyperbaric oxygen therapy as assessed by the hyperbaric physician

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-10-2019
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	23-09-2019
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
CCMO	NL69684.018.19