Hyperbaric High Pressure Oxygen Therapy in Post-COVID Syndrome and ME/CFS

ClinicalTrials.gov ID NCT06118138

Sponsor Charite University, Berlin, Germany

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Study Details Tab

Study Overview

Brief Summary

The objective of this observational study is to document symptom progression in 60 patients with myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) who undergo Hyperbaric Oxygen Therapy (HBOT) following COVID or other infections. Participants will receive HBOT treatment as an additional option after completing the Chronic Fatigue Syndrome CARE (CFS_CARE) study and will be invited to take part in this observational study. Patients will complete health evaluations in the form of questionnaires, including the 36-Item Short Form Health Survey (SF-36), to assess changes in ME/CFS-related symptoms after HBOT. Rather than evaluating the efficacy of HBOT itself, the study will focus on observing and documenting these changes. Its goal is to offer valuable insights into symptom progression in ME/CFS patients receiving HBOT, which can serve as a foundation for future interventional randomized controlled trials.

Detailed Description

Following mild to moderate COVID infection, around 10% of individuals develop post-COVID syndrome (PCS) characterized by symptoms like fatigue, exercise intolerance, cognitive impairment, headaches, and muscle pain (Kedor et al., 2022). Some PCS patients may later be diagnosed with ME/CFS, a severe and chronic disease triggered by infections (Renz-Polster & Scheibenbogen, 2022). ME/CFS presents symptoms such as debilitating fatigue, exercise intolerance, post-exertional malaise (PEM), headaches, muscle pain, cognitive impairment ("brain fog"), orthostatic intolerance, autonomic dysfunction, sleep disturbances, and a general feeling of illness. Currently, no curative therapy for ME/CFS exists. Therapeutic procedures for ME/CFS mainly focus on symptom management, but evidence-based and standardized treatments are urgently needed due to the high number of patients and the impact on healthcare (Renz-Polster & Scheibenbogen, 2022). Off-label drug and non-drug approaches are used, but their effectiveness lacks sufficient evidence from controlled trials.

ME/CFS and PCS may have different underlying pathomechanisms, with some patients showing endothelial dysfunction and reduced blood flow (Haffke et al., 2022). Enhancing blood flow and promoting the formation of new capillaries is a potential therapeutic approach due to the presumed role of reduced blood flow. In this regard, Hyperbaric Oxygen Therapy (HBOT) is under investigation as a treatment for ME/CFS and PCS, showing promising results in trials (e.g., Zilberman-Itskovich et al., 2022; Robbins et al., 2021; Kjiellberg et al., 2022; Akarsu et al., 2013). This non-interventional observational study aims to document symptom progression in 60 patients with ME/CFS who underwent HBOT following COVID or other infections. The study does not focus on evaluating the efficacy of HBOT itself.

ME/CFS patients currently participating in the Chronic Fatigue Syndrome CARE (CFS_CARE) study at Klinik Bavaria in Kreischa will have the opportunity to receive HBOT treatment as a supplementary offer from the clinic upon completion of the CFS_CARE study. Additionally, these patients will be invited to participate in this observational study during the final CFS_CARE presentation at the 12-month mark. HBOT is performed as part of the Conformité Européenne (CE) certificate, as an outpatient procedure within standard clinical practice, and independent of the study focus. Throughout the HBOT treatment, patients will undergo health assessments and symptom evaluations four weeks after treatment initiation and four weeks after completing the HBOT sessions. To facilitate this, patients will receive a link to a RedCap file containing questionnaires, including those previously utilized in the CFS_CARE study (36-Item Short Form Health Survey (SF-36), Munich Berlin Symptom Questionnaire (MBSQ), Chalder Fatigue

Questionnaire, Bell Score). Completing the questionnaires typically requires approximately 45 minutes. The questionnaires will be collected every two months over 12 months, resulting in a total follow-up period of 10 months. A follow-up visit at the outpatient clinic is scheduled for four weeks after HBOT is completed.

The study's primary endpoint is to identify improvements in physical function following HBOT. This will be achieved by utilizing the SF-36 Physical Function (PF) questionnaire, which commonly serves as the primary endpoint in clinical trials focused on ME/CFS. It has been shown that an increase of at least 10 points in the SF-36 PF (range 0 - 100 = healthy) defines clinically relevant improvement ("a little better"), and an increase of 20 points defines greater clinical improvement ("much better") (Brigden 2018). Therefore, an increase of at least 10 points 4 weeks after HBOT is defined as a response and assessed as the primary endpoint.

The study-related measures do not pose significant risks or additional burdens to participants aside from the time required to complete the questionnaires. However, it has the potential to generate valuable knowledge regarding HBOT as a potential treatment for ME/CFS. To date, there has been no documentation of the efficacy of HBOT in ME/CFS through a clinical trial employing objective methods. The results of this observational study are expected to serve as the foundation for a potential interventional randomized controlled trial (RCT).

Official Title

Observational Study of Hyperbaric High Pressure Oxygen Therapy (HBOT) in Patients with Post-COVID Syndrome (PCS) and Myalgic Encephalomyelitis/chronic Fatigue Syndrome (ME/CFS)

Conditions

Post-COVID ME/CFS

Intervention / Treatment

- Combination Product: Hyperbaric oxygen therapy (HBOT)

Other Study ID Numbers

- HBOT
- 01EP2201 (Other Grant/Funding Number) (OTHER_GRANT: BMBF)

Study Start (Actual)

2023-07-15

Primary Completion (Estimated)

2025-12-31

Study Completion (Estimated)

2025-12-31

Enrollment (Estimated)

60

Study Type

Observational

Resource links provided by the National Library of Medicine

MedlinePlus (https://medlineplus.gov/) related topics: Fatigue (https://medlineplus.gov/fatigue.html) Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (https://medlineplus.gov/myalgicencephalomyelitischronicfatiguesyndrome.html) Oxygen Therapy (https://medlineplus.gov/oxygentherapy.html)

Genetic and Rare Diseases Information Center (https://rarediseases.info.nih.gov/gard) resources: Chronic Graft Versus Host Disease (https://rarediseases.info.nih.gov/diseases/10964/chronic-graft-versus-host-disease)

FDA Drugand Device Resources (https://clinicaltrials.gov/fda-links)

Contacts and Locations

This section provides contactdetails forpeople who can answerquestions aboutjoining this study,and information on where this studyis takingplace.

To learn more,please see the Contacts and Locations section in How to Read a Study Record (https://clinicaltrials.gov/study-basics/how-to-read-study-record#contacts-and-locations).

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Participation Criteria

Researchers look forpeoplewho fita certain description,called eligibility criteria.Some examples ofthese criteriaare a person's generalhealth conditionorpriortreatments.

Forgeneral informationaboutclinicalresearch,read Learn AboutStudies (https://clinicaltrials.gov/study-basics/learn-about-studies).

Eligibility Criteria

Description

Inclusion Criteria:

- Participants between the ages of 18 and 65 years who have previously participated in the CFS_CARE study and have been diagnosed with ME/CFS
- ME/CFS diagnosis based on the Canadian Consensus Criteria (CCC), characterized by exercise intolerance and symptom worsening lasting for a minimum of 14 hours
- Disease severity determined by a Bell Score ranging from 30 to 70
- Plan to undergo 20 or 40 days of Hyperbaric Oxygen Therapy (HBOT)
- Consent provided by the patient

Exclusion Criteria:

- Unwillingness to consent to the storage of pseudonymized clinical data as a part of the study
- Pregnancy
- Presence of medical conditions that could potentialy pose a risk during Hyperbaric Oxygen Therapy (HBOT) (e.g., heart failure, pulmonary disease, major depression, panic attacks)
- Acute infection (e.g., COVID, HIV, or hepatitis)

Study Population

Sixty male or female patients, aged between 18 and 65 years, will be included in the study. ME/CFS patients currently participating in the CFS_CARE study through the Bavaria Clinic in Kreischa will have the opportunity to receive HBOT treatment as an additional option provided by the clinic upon completion of the CFS_CARE study. Additionally, these patients will be invited to participate in this observational study during the final CFS_CARE presentation at the 12-month mark.

Ages Eligible for Study

18 Years to 65 Years (Adult, Older Adult)

Sexes Eligible for Study

All

Accepts Healthy Volunteers

No

Sampling Method

Non-Probability Sample

Study Plan

This section provides details of the study plan, including how the study is designed and what the study is measuring.

How is the study designed?

Design Details

Observational Model : Cohort
Time Perspective: Prospective

Groups and Interventions

Intervention/Treatment
Combination Product: Hyperbaric oxygen therapy (HBOT) • HBOT is a medical treatment employed for various conditions. It entails breathing 100% oxygen within a pressurized chamber known as a hyperbaric chamber. This oxygen-rich environment promotes healing and aids in combating specific infections. In this study, the investigators will administer HBOT using a hyperbaric chamber set to 2 times the normal atmospheric pressure, indicated as 2 atmosphere absolute (ATA). This pressure surge enhances oxygen dissolution into the bloodstream, surpassing levels achievable at sea level. The pressure will be raised incrementally, followed by HBOT sessions lasting for a total of 90 minutes. The 90-minute sessions include brief 5-minute intervals for ambient air every 20 minutes to ensure safety and comfort. Treatment will be conducted five days a week over eight weeks. Supervised by competent healthcare professionals, HBOT is considered safe, with potential side effects primarily stemming from heightened pressure and, in rare cases, oxygen toxicity.

What is the study measuring?

Primary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Improvement in Physical Function (PF) as measured by the Short Form 36 Health Survey Questionnaire (SF-36).	The Short Form 36 Health Survey (SF-36) is an established and widely used health-related quality of life measure. The Physical Function (PF) domain asks patients to report limitations on ten mobility activities, such as walking specified distances, carrying groceries, and bathing or dressing. Scores are weighted and transformed into a scale ranging from 0 (greatest possible health restrictions, i.e., severe disability) to 100 (no health restrictions). An intra-patient change of 10 points in SF-36-PF from baseline to week four is considered clinically meaningful.	4 weeks after completion of HBOT therapy

Secondary Outcome Measures

Outcome Measure	Measure Description	Time Frame
Duration of improvement in Physical Function (PF) as measured by the Short Form 36 Health Survey	Duration of the effect of HBOT therapy as assessed by SF-36 PF. Intra-patient change in physical and mental fatigue from baseline to follow-up points will be documented as indexed by the SF-36 PF.	Collected every 2 months over a total of 12 months after

Questionnaire (SF-36)		completion of HBOT therapy
Improvement in physical and mental fatigue as measured by the Chalder Fatigue Scale	The Chalder Fatigue Scale measures the extent and severity of tiredness and has been used in multiple randomized trials of behavioral interventions in patients with ME/CFS. Each of the 11 items is answered on a 4-point scale with an overall score ranging from 0 (asymptomatic) to 33 (maximum symptomology). Intra-patient change in physical and mental fatigue from baseline to follow-up points will be documented as indexed by the Chalder Fatigue Scale.	Collected every 2 months over a total of 12 months after completion of HBOT therapy
Improvement in functional disability as measured by the Bell disability scale	The Bell disability scale is a standard assessment in ME/CFS that evaluates functional ability in adult ME/CFS patients. Eleven statements describe patient status such as level of symptoms at rest, level of symptoms with exercise, activity level, and ability to perform work, travel and self care. Its score ranges from 0 (bedridden) to 100 (no symptoms). Intra-patient change from baseline to follow-up points will be documented as indexed by the Bell score.	Collected every 2 months over a total of 12 months after completion of HBOT therapy
Improvement in disease severity based on self-reported symptoms as measured by the Munich Berlin Symptom Questionnaire (MBSQ)	The Munich Berlin Symptom Questionnaire (MBSQ) is a questionnaire for ME/CFS that captures the Institute of Medicine (IOM) and Canadian Consensus Criteria (CCC) as well as a total of 44 symptoms from 8 domains on a scale of 0 – 4 for frequency and severity. From this, a score for total symptom severity ranging from 0 (not present) to 352 (very severe) is calculated. Intra-patient change from baseline to follow-up points will be documented as indexed by the MBSQ.	Collected every 2 months over a total of 12 months after completion of HBOT therapy
Improvement in muscle strength as measured by the hand grip strength (HGS) test	The Hand Grip Strength (HGS) test is a simple yet effective measurement of muscular strength. It involves gripping a dynamometer (or other grip strength measurement device) with maximal force using the dominant hand. The device measures exerted force in kilograms or pounds. Hand grip strength reflects overall muscle strength providing insights into a person's physical health, functional capacity, and potential muscular deficiencies. Intra-patient change in hand grip strength (HGS) from baseline to week four.	4 weeks after completion of HBOT therapy
Assessment and documentation of tolerability	Assessment and documentation of tolerability with a questionnaire that is collected at the end of the HBOT therapy	On the day of completion

		of HBOT therapy
Improvement in orthostatic tolerance as measured by the National Aeronautics and Space Administration (NASA) 10 Minute Lean Test	The NASA 10-Minute Lean Test evaluates a person's susceptibility to gravitational effects. In post-COVID ME/CFS research, it probes cardiovascular and autonomic nervous system issues stemming from a SARS-CoV-2 infection. During the test, an person lies flat on their back with a slightly elevated head, while blood pressure and heart rate are monitored during a controlled tilt to a head-down position. In about 10 minutes, this provides valuable insights into cardiovascular adaptability and potential dysregulation, aiding understanding of symptoms like dizziness, fatigue, and palpitations in long-COVID patients. Intra-patient change in the NASA 10 Minute Lean Test from baseline to week four.	4 weeks after completion of HBOT therapy
Improvement in exercise capacity measured by the 1–Minute Sit-to-Stand Test	The 1-Minute Sit-to-Stand Test is a validated and reliable test for quantifying exercise capacity. In this test, the person starts in a seated position and is instructed to stand up and sit down as many times as possible within a one-minute period. The test provides valuable insights into a person's muscle strength, endurance, and overall physical fitness. Intra-patient change in the 1-minute Sit-to-Stand Test from baseline to week four.	4 weeks after completion of HBOT therapy

Collaborators and Investigators

This is where you will find people and organizations involved with this study.

Sponsor

Charite University, Berlin, Germany

Collaborators

- KLINIK BAVARIA Kreischa
- Vivantes Klinikum im Friedrichshain

Investigators

- Principal Investigator: Carmen Scheibenbogen, Prof. Dr., Charite University, Berlin, Germany

Publications

General

These publications are provided voluntarily by the person who enters information about the study and may be about anything related to the study.

- Kedor C, Freitag H, Meyer-Arndt L, Wittke K, Hanitsch LG, Zoller T, Steinbeis F, Haffke M, Rudolf G, Heidecker B, Bobbert T, Spranger J, Volk HD, Skurk C, Konietschke F, Paul F, Behrends U, Bellmann-Strobl J, Scheibenbogen C. A (https://pubmed.

prospective observationalstudy ofpost-COVID-19 chronic fatigue syndrome following thefirstpandemic wave in Germanyand biomarkers associated with symptom severity.NatCommun.2022 Aug 30;13(1):5104.doi: 10.1038/s41467-022-32507-6.Erratum In:NatCommun.2022 Oct12;13(1):6009.doi:10.1038/s41467-022-33784-x. (https://pubmed.ncbi.nlm.nih.gov/36042189)

- Renz-PolsterH,ScheibenbogenC.[Post-COVIDsyndrome with fatigue and exercise intolerance:myalgic encephalomyelitis/chronic fatigue syndrome]. Inn Med (Heidelb).2022 Aug;63(8):830-839.doi: 10.1007/s00108-022-01369-x.Epub 2022Jul13.German. (https://pubmed.ncbi.nlm.nih.gov/35925074)
- Haffke M,FreitagH,RudolfG,SeifertM,DoehnerW,Scherbakov N,Hanitsch L,Wittke K,BauerS,Konietschke F,PaulF,Bellmann-StroblJ,KedorC,ScheibenbogenC,Sotzny F.Endothelialdysfunction and altered endothelialbiomarkers in patients with post-COVID-19 syndrome and chronic fatigue syndrome (ME/CFS). J TranslMed.2022 Mar22;20(1):138.doi:10.1186/s12967-022-03346-2. (https://pubmed.ncbi.nlm.nih.gov/35317812)
- ZilbermanItskovichS,CatalognaM,Sasson E,Elman-Shina K,Hadanny A,Lang E,FinciS,Polak N,Fishlev G, KorinC,ShorerR,Parag Y,Sova M,EfratiS.Hyperbaric oxygen therapy improves neurocognitive functions and symptoms ofpost-COVIDcondition:randomized controlled trial.SciRep.2022 Jul12;12(1):11252.doi: 10.1038/s41598-022-15565-0. (https://pubmed.ncbi.nlm.nih.gov/35821512)
- Robbins T,GonevskiM,Clark C,BaituleS,Sharma K,MagarA,PatelK,Sankar S,KyrouI,AliA,Randeva HS. Hyperbaric oxygen therapy forthe treatmentoflong COVID:early evaluation ofa highlypromising intervention.Clin Med (Lond).2021 Nov;21(6):e629-e632.doi:10.7861/clinmed.2021-0462. (https://pubmed.ncbi.nlm.nih.gov/34862223)
- Kjellberg A,Abdel-Halim L,HasslerA,ElGharbiS,Al-EzerjawiS,Bostrom E,Sundberg CJ,Pernow J,Medson K, KowalskiJ H,Rodriguez-Wallberg KA,Zheng X,Catrina S,Runold M,Stahlberg M,Bruchfeld J,Nygren-BonnierM, Lindholm P.Hyperbaric oxygenfortreatmentoflong COVID-19 syndrome (HOT-LoCO):protocolfora randomised,placebo-controlled,double-blind,phase IIclinicaltrial.BMJ Open.2022Nov2;12(11):e061870.doi: 10.1136/bmjopen-2022-061870. (https://pubmed.ncbi.nlm.nih.gov/36323462)
- Akarsu S,Tekin L,Ay H,CarliAB,Tok F,Simsek K,Kiralp MZ.Theefficacy ofhyperbaric oxygen therapy in the managementofchronic fatigue syndrome.Undersea HyperbMed.2013 Mar-Apr;40(2):197-200. Erratum In:Undersea HyperbMed.2013 May-Jun;40(3):312. (https://pubmed.ncbi.nlm.nih.gov/23682549)

Study Record Dates

These dates track the progress ofstudy record and summary results submissions to ClinicalTrials.gov.Study records and reported results are reviewed by the NationalLibrary ofMedicine (NLM)to make sure they meetspecific quality controlstandards before being posted on the public website.

Study Registration Dates

FirstSubmitted
2023-11-01

FirstSubmitted thatMetQC Criteria
2023-11-01

FirstPosted
2023-11-07

Study Record Updates

LastUpdate SubmittedthatmetQC Criteria
2025-02-11

LastUpdate Posted (Estimated)
2025-02-12

LastVerified
2024-09

More Information

Terms related to this study

Keywords Provided by Carmen Scheibenbogen, Charite University, Berlin, Germany

Post-COVIDSyndrome
Long COVID
Chronic Fatigue Syndrome

AdditionalRelevantMeSH Terms

Disease
Pathologic Processes
MuscularDiseases
MusculoskeletalDiseases
Encephalomyelitis
Neuroinflammatory Diseases
Nervous System Diseases
NeuromuscularDiseases
Chronic Disease
Disease Attributes
Fatigue Syndrome,Chronic
Syndrome

Plan forIndividualParticipantData (IPD)

Plan toShare IndividualParticipantData (IPD)?

No

Drug and device information,study documents,and helpfullinks

Studies a U.S.FDA–Regulated DrugProduct

No

Studies a U.S.FDA–Regulated Device Product

No

ProductManufactured in and Exportedfrom the U.S.

No