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Effects of dronabinol on breathlessness and exercise capacity in chronic lung disease

Submission date	Recruitment status	[_] Prospectively registered
28/12/2021	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
14/01/2022	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
19/10/2022	Respiratory	[_] Record updated in last year

Plain English summary of protocol
Background and study aims
Breathlessness (dyspnea) is the most common and frequently debilitating symptom in patients with chronic obstructive pulmonary disease (COPD). The aim of this study is to determine if dronabinol improves dyspnea intensity and exercise tolerance in patients with COPD.

Who can participate?
Patients over 18 years old with COPD

What does the study involve?
Participants are randomly allocated to receive 6 weeks of oral dronabinol and 6 weeks of placebo (or vice versa) over two periods with an intervening 8- to 12-week washout period.

What are the possible benefits and risks of participating?
The results of this study will help to determine if dronabinol has a novel use in COPD patients with breathlessness. The side effects of the medication include nausea, vomiting, anxiety, confusion and sleepiness.

Where is the study run from?
VA Loma Linda Healthcare System (USA)

When is the study starting and how long is it expected to run for?
January 2011 to October 2020

Who is funding the study?
VA Loma Linda Healthcare System (USA)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
Effects of dronabinol on dyspnea and quality of life in patients with chronic obstructive pulmonary disease: a randomized cross-over trial

Study objectives

To determine if dronabinol improves dyspnea intensity and thereby exercise tolerance in chronic obstructive pulmonary disease (COPD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/12/2011, Institutional review board, VA Loma Linda Healthcare System (11201 Benton St, Loma Linda, CA 92357, USA; +1 (0)9 825 7084, ext. 2264; Sunbeam.Obomsawin@va.gov), ref: 00929, Prom# U28

Study design
Prospective randomized double-blind placebo-controlled single-centre crossover study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet: Aimee D. Rodriguez; research coordinator at the VA Loma Linda Healthcare System; Aimee.Rodriguez@va.gov

Health condition(s) or problem(s) studied
Chronic obstructive pulmonary disease (COPD)

Interventions
Participants are randomized to either the study drug or the placebo arm for Phase I and crossed over to the other arm during Phase II. Each study phase consists of a 2-week run-in period followed by a 4-week treatment period. Depending on the arm of the study they are in, subjects start on either placebo or dronabinol 5 mg capsules orally. During the run-in period, the number of capsules of the study drug is gradually increased from one per day up to four per day. In case of adverse effects such as lightheadedness, subjects are asked to decrease the number of capsules per day to the last tolerated level. On completion of the first phase, each patient undergoes an 8- to 12-week washout. This is followed by crossover to a similarly structured Phase II.

Run-in period I (2 weeks)
Day 0: fill out questionnaire packet and answer adverse drug reaction
Screen and perform Incremental Shuttle Walk Test (ISWT)
- start dronabinol 5 mg by mouth or placebo daily x 3 days.
Day 3: answer adverse drug reaction screen
- if no adverse effects are reported, increase the dose to 5 mg by mouth twice a day

Day 6: answer adverse drug reaction screen
- if no adverse effects are reported, increase the dose to 5 mg by mouth three times a day
Day 9: answer adverse drug reaction screen
- if no adverse effects are reported, increase the dose to 5 mg by mouth four times a day
Day 12: answer adverse drug reaction screen
- if no adverse effects are reported, continue 20 mg daily in divided doses
**Note: Sham titration conducted of the placebo arm following the exact same schedule as laid out above

Treatment period I (4 weeks)
1. Group A receives doses of oral dronabinol (Δ9-THC)
2. Group B receives a placebo that is identical in appearance

Followed by a wash-out period (8-12 weeks)

The groups will then be crossed over so that during Phase II, group A will receive a placebo and group B will receive dronabinol.

Phase II
Run-in II and treatment period II will be conducted with an identical protocol to run-in I and treatment period I, respectively.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Dronabinol

Primary outcome measure
1. Sensation of dyspnea measured using the Borg dyspnea scale at rest and post exercise
2. Exercise capacity measured using shuttle walk distances before and after Phase I and II of the study
3. Sensation of dyspnea measured using PSFDQ scores before and after Phase I and II of the study

Secondary outcome measures
1. Fatigue measured using the Borg fatigue score at rest and post exercise
2. Respiratory symptoms and quality of life measured using SGRQ scores before and after Phase I and II
3. Quality of life measured using GDS scores before and after Phase I and II
4. The number of adverse events during the study measured using telephone follow up on a biweekly basis

Overall study start date
06/01/2011

Completion date
03/10/2020

Eligibility

Key inclusion criteria
1. Diagnosis of COPD as defined by the American Thoracic Society (ATS) and European Respiratory Society (ERS)
2. Remained dyspneic despite maximal medical therapy indicated for their level of disease
3. Completed a pulmonary rehabilitation program (including reconditioning exercise, education, and support group meetings) prior to study enrollment
4. Aged over 18 years old

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
50

Total final enrolment
24

Key exclusion criteria
1. Pre-enrollment urine drug screen positive for THC
2. Chronic hypercapnia ($paCO_2$ >45 mmHg)
3. Anemic (hemoglobin <7 g/dl)
4. Pregnant
5. Known allergy to sesame seeds, sesame oil or dronabinol
6. Uncompensated acute heart failure
7. History of neuromuscular disease

Date of first enrolment
29/07/2013

Date of final enrolment
22/10/2019

Locations

Countries of recruitment
United States of America

Study participating centre
VA Loma Linda Healthcare System
11201 Benton St
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Sponsor information

Organisation
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Hospital/treatment centre

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https://ror.org/03z6z3n38

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
VA Loma Linda Healthcare System

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal. The study protocol is available on request. The statistical analysis plan is within the manuscript and supplemental material is available on request.

Intention to publish date
01/01/2022

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the subsequent results publication.

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		05/04/2019	19/10/2022	No	No