Beta-alanine supplementation in patients with chronic obstructive pulmonary disease (COPD) following a neuromuscular electrical stimulation (NMES) training program.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON25510

Source
NTR

Brief title
BASE-ELECTRIC

Health condition

Chronic obstructive pulmonary disease (COPD); Exercise intolerance; Muscle dysfunction.

Sponsors and support

Primary sponsor: Board of Directors CIRO
Source(s) of monetary or material Support: Lung Foundation, the Netherlands

Intervention

Outcome measures

Primary outcome

Exercise tolerance, defined as cycle endurance time. Cycle endurance time will be determined with the constant work-rate test (CWRT), performed on an ergometer at 75% of the maximal work rate (pre-determined by a cardiopulmonary exercise test; CPET) to volitional exhaustion.

Secondary outcome

Exercise capacity - by means of CPET and six minute walking test (6MWT).
Quadriceps muscle function - by means of isometric and isokinetic quadriceps strength and endurance (computerized dynamometer) and maximal dynamic isotonic strength (one-repetition maximum; 1-RM).
Body composition - by means of Dual-energy X-ray Absorptiometry.
Muscle characteristics (after m. vastus lateralis muscle biopsy) - Structural and metabolic parameters as well as markers of oxidative stress and inflammation will be measured with dedicated methodology.
(Fasted) systemic factors (after obtaining fasting venous blood) - Systemic beta-alanine, taurine and histidine levels as well as systematic markers of oxidative stress and inflammation at rest will be measured with dedicated methodology.
Cognitive function - executive functioning will be assessed using the Modified Wisconsin Card Sorting Test (M-WCST), and divided attention will be examined via the Stroop Colour-Word Test (SCWT).
Lung inflammatory and oxidative stress biomarkers - by measuring volatile organic compounds (VOCs) and fractional nitric oxide (NO) concentration in exhaled breath (FENO).
Physical activity - by means of activity monitors (Actigraph GT9X).
Functional mobility - by means of the Short Physical Performance Battery (SPPB) mobility test.
Dyspnoea - by means of the Modified Medical Research Council (mMRC) dyspnoea scale.
Health-related quality of life - by means of the COPD Assessment Test (CAT).
Anxiety and Depression - by means of the Hospital Anxiety and Depression Scale (HADS).
Fatigue - by means of the subjective fatigue subscale of the Checklist Individual Strength (CIS-Fatigue).
Problematic activities of daily life - by means of the Canadian Occupational Performance Measure (COPM).
Compliance - by means of a patient diary and documenting remaining tablets at end of study.
Patient safety/side effects - by means of a patient diary en personal check-ups.

Additional outcomes are used to characterize patients at baseline. Pulmonary function will be assessed using post-bronchodilator spirometry, whole body plethysmography and diffusion capacity. Furthermore, respiratory muscle strength, using maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) measurements, will be determined. An arterial blood sample is collected to determine arterial blood gases at rest. Additionally, patient characteristics as age, gender, level of education, marital status, smoking status, exacerbation/hospitalisation frequency and medical history (Charlson Comorbidity Index; CCI), medication and/or oxygen use will be assessed at baseline during an intake interview.

Study description

Background summary

Exercise intolerance is common in patients with chronic obstructive pulmonary disease (COPD) and, although multifactorial, it is largely caused by lower-limb muscle dysfunction. Research has shown that patients with severe to very severe COPD have significantly lower levels of muscle carnosine, which acts as a pH buffer and antioxidant. Beta-alanine is the rate-limiting precursor to carnosine synthesis and BA supplementation has been shown to consistently elevate muscle carnosine in a variety of populations. Hence, it is very plausible to hypothesize that beta-alanine supplementation in COPD patients following a neuromuscular electrical stimulation (NMES) training program (as part of pulmonary rehabilitation; PR) will increase muscle carnosine levels, which in turn will result in a positive effect on exercise tolerance and lower-limb muscle function.

Study objective

It is hypothesized that beta-alanine supplementation in patients with COPD following a neuromuscular electrical stimulation (NMES) training program (as part of pulmonary rehabilitation; PR) will increase muscle carnosine levels, which in turn will result in a positive effect on exercise tolerance and lower-limb muscle function. These adaptations may translate into improved functional capacity during activities of daily living and improved quality of life.

The primary targets of both exercise training and BA supplementation are the muscles of ambulation. Nevertheless, it seems reasonable to hypothesize that an enhanced bio-availability of carnosine in the body, by means of beta-alanine supplementation, may have an anti-oxidative effect in both the lungs and the brain.

Study design

The regular PR program at CIRO consists of a baseline assessment, followed by an inpatient PR program and is ended with a post-rehabilitation assessment. After completion of the baseline assessment and obtaining informed consent, an additional study-related appointment is scheduled with included patients approximately 1 week prior to the start of the PR program. This additional testing day will be repeated after the rehabilitation period. Study duration per subject will be approximately 10 to 12 weeks.

During the regular (baseline and post) assessments, the following outcomes will be measured: exercise capacity and endurance, quadriceps muscle function, body composition, physical activity, functional mobility, dyspnoea, health-related quality of life, anxiety and depression, fatigue, problematic activities of daily life, pulmonary function and patient characteristics.

The study-related appointments include: fasting venous blood sampling, a vastus lateralis muscle biopsy (optional, not required), two cognitive function tests (M-WCST and SCWT) and two tests for lung inflammatory biomarkers (VOC and FeNO measurements).

During the PR program 80 sessions of high-frequency NMES (75Hz), being the primary exercise modality, will be applied. Patient safety and compliance will be constantly monitored during the PR program.

Intervention

Oral beta-alanine (sustained-release Carnosyn®; 3.2 g/day) or identical looking placebo supplementation for a duration of 8-10 weeks.

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Eligibility criteria

Inclusion criteria

- COPD, GOLD group B or D
- Modified Medical Research Council (mMRC) dyspnoea score ≥3
- Clinically stable according to the pulmonary physician, i.e. no exacerbation and/or hospitalization within the previous 4 weeks.
- Age between 40-80 years
- Cycle endurance time is 100-300 seconds.
- Quadriceps muscle strength <80% predicted
- Attending the regular inpatient pulmonary rehabilitation program in CIRO and receiving NMES as the primary muscle training modality.

Exclusion criteria

Patients will be excluded if they meet at least one of the following criteria: instable cardiac disease, use of anabolic steroids during PR program, history of drugs/alcohol abuse,

vegetarianism, inability to understand the Dutch language, self-reported beta-alanine supplementation in the past 3 months, participation in a PR program within the past 12 months, inability to perform a cardiopulmonary exercise test.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-04-2020
Enrollment:	68
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Positive opinion

Date:	02-03-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 56353
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8419
CCMO	NL68757.091.19
OMON	NL-OMON56353

Study results

Summary results
N/A