Protein Supplementation to Enhance Exercise Capacity in COPD during Pulmonary Rehabilitation

SUPPLEMENTARY APPENDIX

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Appendix 1: supplement acceptability survey

Nutritional Supplementation to Enhance Exercise Capacity in COPD Patients

Thank you for taking part in this survey.

1. Since starting the supplement, which of the following applies to your appetite? Please circle below.

1. Increased 2. Decreased 3. Stayed the same.

2. How satisfied are you with the taste of your supplement? Please Circle below.

1 = Not satisfied at all 2 = slightly satisfied 3 = satisfied 4 = very satisfied

3. What did you like or dislike about the supplement?

4. If it was available, would you continue to take your supplement? Please circle below.

   1. Yes 2. No

5. What can be changed about the supplement to make you more likely to take it?

6. What do you think about having to take it twice a day?

Appendix 2: Pulmonary rehabilitation and methodology of outcome measures

Pulmonary Rehabilitation (PR)

PR is a comprehensive out-patient programme consisting of one hour of exercise training and one hour of education which participants attend twice a week for a total of 12 sessions. The PR programme is supervised by respiratory physiotherapists and follows the British Thoracic Society (BTS) guidelines (1). The exercise training portion starts with a warm-up and is followed by low intensity aerobic exercises such as cycling, treadmill walking and level walking, and resistance exercise, such as progressive resistance of upper and lower body with free weights, step up, thigh muscle training with or without weight cuffs and sit to stand. Intensity of exercises depended upon the tolerance of each individual. The education offer includes but is not limited to: stress management, signs of chest infection, early recognition of exacerbation, dyspnoea and symptom management, nutrition, techniques using inhalers and nebulisers, energy conservation, smoking cessation and chest clearance techniques. Education topics were delivered by a multidisciplinary team.

Outcome measurements

Spirometry (FEV_1, FVC and FEV_1/FVC ratio):

To confirm the diagnosis of COPD, post-bronchodilator hand-held spirometry was performed using a Micro 1 Handheld Spirometer (CareFusion, *Basingstoke*, UK), which follow the ATS/ERS standards of lung function (2). Participant were seated in upright position with the head slightly elevated during the test. Tests were repeated three times to conform with published quality-assurance criteria (3).

Primary outcome: exercise capacity

The primary outcome was the difference in change in ISWT distance (in meters) from baselines between groups. The ISWT was conducted based on European Respiratory Society and American Thoracic Society recommendations (4). Two cones were placed a distance of 9m apart. The course was 9m in length and the cones are placed with an inset of 0.5 m from either end. An audio recording has the test instructions played to avoid any variation in the test. Heart rate, blood pressure, level of dyspnoea using Borg scale, and oxygen saturation were measured prior and immediately after the test. Participants were required to perform the ISWT before enrolling in PR twice to overcome a learning effect and the higher distance was used in analysis.

Secondary outcomes

Questionnaires

CAT and SGRQ were used to assess health-related quality of life (5, 6), levels of anxiety and depression was assessed by HADS (7), breathlessness was assessed by mMRC and BORG (8), and the risk of malnutrition was assessed MUST (9).

Physical activity monitoring

Participants were asked to wear a step counter pedometer (Yamax Digi-walker SW-200) on the left side of waist (10), and recorded all daily steps for 14 days, except when showering and sleeping, before starting the PR program and for 14 days after PR completion. A diary card was provided for each period.

Sit to Stand – Five Test

Participants were instructed to sit on a straight-backed chair without arms, with feet flat on the floor and hands folded across the chest, and asked to stand up and sit down without using arm

support as fast as possible five times. A stop watch was used to count the time (11). For those who cannot do the manoeuvre, the test was terminated.

Handgrip strength

A Jamar smart handheld dynamometer (Patterson Medical Ltd, *Warrenville*, Illinois, USA) was used to measure the highest isometric strength of forearm muscles and the hand. The test was conducted by holding the device following specific guidelines (12). The average of the best two measurements were used for the analysis.

Body weight, height and composition

Body weight was measured in light clothing using a digital scale (EB4074C, *Anaheim*, US) while height was measured using a wall-mounted stadiometer without shoes.

To measure body composition, a Bodystat Touch 1500 (Bodystat Ltd, Douglas UK) was used. Participants were instructed to be in supine position and rest for three to four minutes. Two electrodes were placed on the anterior surface of the right hand and right ankle.

Waist, hip, and mid-thigh circumference

Participants were asked to stand up with feet closed together, both hands close to the body, and relaxed. A stretch- resistant tape was placed at the top of the iliac crest and the lower margin of the lowest palpable rib with the measurement taken at the end of normal exhalation to measure the waist. For the hip, the tape was used horizontally to measure the widest portion of the buttocks with the measurement taken at the end of normal exhalation. For the thigh, measurement was made directly under gluteal fold with tape horizontal to the floor. All measurements were repeated twice, and the mean was calculated with both measurements within 1 cm difference.

Participants experience using oral nutritional supplements (ONS)

At the end of the trial, participants were provided with a survey regarding their experience using nutritional supplementation during PR (Appendix 1).

Appendix 3: Demographic data and baseline characteristics of subjects with COPD divided into two groups; completers and non-completers.

The mean age of the participants was 72 ±8 years: 62% were male, and 62% were ex-smokers. The non-completers had a trend towards higher numbers of exacerbations and hospital admissions but these were not significant when compared with completers (p >0.05). Our participants were mainly GOLD 2 and 3, with median FEV_1 1.3L (57% predicted). There were no significant differences between the groups in the ISWT, weight, FFM, FM, physical activity measured by steps, CAT, anxiety and depression scores, risk of malnutrition, and STS5 (p > 0.05). A difference in the SGRQ scores between the two groups was not statistically significant (p >0.05). Overall, there were no statistical differences in baselines characteristics between completers and non-completers.

Table 1: Demographic data and baseline characteristics of subjects with Chronic Obstructive Pulmonary Disease (COPD) divided into two groups; completers and non-completers.

Subjects Demographics	**Total population (68)**	**Completers (44)**	**Non-completers (24)**	**p-value** completers vs. non-completers
Age (years)	72 ±8	73 ±8	70 ±9	0.16
Male n (%)	42 (62%)	28 (64%)	14 (58%)	0.67
Female n (%)	26 (38%)	16 (36%)	10 (42%)	
Active smoker n (%)	26 (38%)	15 (34%)	11 (46%)	0.34
Ex-smokers n (%)	42 (62%)	29 (66%)	13 (54%)	

Smoking history (pack-years)	41 (28-58)	45 (28-61)	39 (30-58)	0.75
Exacerbation within last year	1 (0 – 2)	1 (0 – 2)	2 (0 – 3)	0.09
Hospitalisation due to exacerbations within last year n (%)	15 (22%)	7 (16%)	8 (33%)	0.09
Medications				
SABA n (%)	44 (65%)	31 (70%	13 (54%)	0.18
LABA n (%)	40 (59%)	25 (57%)	15 (63%)	0.65
SAMA n (%)	0	0	0	^
LAMA n (%)	36 (53%)	24 (55%)	12 (50%)	0.70
ICS n (%)	33 (49%)	19 (43%)	14 (58%)	0.20
Other non-Respiratory medications n (%)	60 (88%)	38 (86%)	22 (92%)	0.52
Diabetes n (%)	0	0	0	^
Pulmonary function				
FEV_1 (L)	1.3 (1 – 1.9)	1.6 (1.1 – 2.4)	1.2 (1.1 – 1.2)	0.77
FEV_1 (% predicted)	58 (39 – 70)	64 (43 – 74)	49 (37 – 60)	0.89
FEV_1/FVC %	52 ±12	54 ±12	51 ±13	0.36
Anthropometric measurements				
Weight (kg)	69 ±14	71 ±14.6	66 ±12	0.13
Waist circumference (cm)	93 ±13	94 ±14	90 ±11	0.30
Hip circumference (cm)	100 ±10	101 ±10	98 ±8	0.33
Mid-thigh circumference (cm)	57 ±8	58 ±7	56 ±9	0.46
Body composition				

Fat mass (kg)	25 ±6	25 ±6	24 ±6	0.49
BMI kg/cm^2	24 (21 – 27)	24 (21 – 27)	24 (21 – 27)	0.98
FFM (kg)	45±11	47.9 ±12	41.9 ±3.7	0.11
FFMI (kg/m^2)	15.3 ±3	15.8 ±3	14 ±1	0.60
Functional outcomes				
ISWT (m)	266 ±134	267 ±130	264 ±144	0.94
mMRC grade	3 (2 – 3)	3 (2 – 3)	3 (2 – 3)	0.82
(R) Handgrip (kg)	27 ±9	28 ±10	24 ±7	0.09
(L) Handgrip (kg)	25 ±8	27 ±9	23 ±5	0.05
STS5 (sec)	10.3 (8.6 – 12.8)	11 (7 – 15)	9.8 (10 – 10)	0.70
Questionnaires				
CAT	20 ±7	19 ±7	21 ±7	0.34
Anxiety scores (HADS)	7 ±4	6 ±4	8 ±4	0.25
Depression scores (HADS)	6 (3 – 9)	6 (3 – 8)	7 (2 – 12)	0.45
SGRQ total	49 ±17	46 ±16	55 ±18	0.07
SGRQ symptoms	61 ±21	57 ±22	68 ±17	0.07
SGRQ activity	67 ±20	66 ±18	71 ±23	0.30
SGRQ impact	35 ±18	32 ±17	42 ±20	0.06
MUST	0	0	0	0.99
Physical activity (steps/ day)	3014 (1765 – 5914)	4102 (2148 – 6385)	3687 (1532 – 5841)	0.93

Data are presented as n (%), mean ±SD or median IQR. p value represent a comparison between completers and non-completers. ^ No data to compare with.

Abbreviations: SABA, Short-acting beta-agonists; LABA; Long-acting beta-agonists; SAMA, Short-acting muscarinic antagonist; LAMA, Long-acting muscarinic antagonist; ICS, Inhaled corticosteroids; BMI, FEV_1, Forced Expiratory Volume in 1 second; FEV_1%, Predicted Forced Expiratory Volume in 1 second; FEV_1/FVC, calculated ratio between both measurements; BMI, Body Mass Index; FFM, fat-free-mass; FM, fat-mass; FFMI, fat-free-mass index; ISWT, incremental shuttle walk test; mMRC; modified medical research council dyspnoea scale; (R) handgrip, right handgrip; (L) handgrip, left handgrip; STS5, five repetition sit to stand; CAT; COPD assessment test; HADS, hospital anxiety and depression scale; SGRQ, St. George's respiratory questionnaire; MUST, malnutrition universal screening tool.

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