DANISH MEDICAL JOURNAL

Brief Research Report

Dan Med J 2022;69(11):A03220185

High-protein diet during pulmonary rehabilitation in patients with chronic obstructive pulmonary disease

Nana Møgelberg[1], Randi Tobberup[1], Grith Møller[1], Nina Skavlan Godtfredsen[2], Annette Nørgaard[3] & Jens Rikardt Andersen[1]

1) Department of Nutrition, Exercise and Sports, University of Copenhagen, 2) Department of Pulmonary Medicine, Copenhagen University Hospital – Hvidovre Hospital, 3) The Pulmonary and Allergy Clinic, Hellerup, Denmark

Dan Med J 2022;69(11):A03220185

ABSTRACT

INTRODUCTION. The prevalence of cachexia in patients with chronic obstructive pulmonary disease (COPD) is high and associated with reduced quality of life, increased mortality and morbidity. We aimed to test the effect of a high protein diet combined with exercise on fat-free mass (FFM), functional capacity, symptom burden and dyspnoea.

METHODS. Outpatients with COPD and severe or very severe (GOLD grade III-IV) disease and malnutrition commencing pulmonary rehabilitation were randomised to a high-protein diet or standard care. FFM was measured by bio-impedance analysis (BIA), mid-upper arm circumference (MUAC) and mid-thigh circumference (MTC), peripheral muscle function by six-minute walking distance (6MWD) and handgrip strength (HGS), symptoms by the COPD Assessment Trial (CAT) and dyspnoea by the Medical Research Council dyspnoea scale and Borg scores; all at baseline and after 12 weeks.

RESULTS. Ten out of 13 randomised patients completed the trial. The intervention group was superior to the control group with respect to 6MWD (97 ± 93 m, p = 0.04) at 12 weeks. No differences were observed between the groups in HGS, anthropometrics, symptom burden or dyspnoea.

CONCLUSION. In patients with COPD attending rehabilitation, a high protein diet combined with physical exercise had a clinically relevant effect on walking distance.

FUNDING. none.

TRIAL REGISTRATION. NCT04888182.

Chronic obstructive pulmonary disease (COPD) is a heterogeneous, progressive respiratory disease [1]. Malnutrition, including cachexia, is common [2] and is associated with reduced quality of life and exercise performance, increased gas trapping, lower diffusing capacity, peripheral muscle weakness, increased complications and mortality [3]. Pulmonary cachexia is a complex syndrome that includes reduced food intake and varying degrees of inflammation leading to anorexia, and metabolic changes including reductions in appetite sensations and elevated resting energy expenditure [4].

Supplementation of calories has shown positive effects on functional exercise capacity and quality of life [5, 6], but the effect of protein supplementation in malnourished patients remains unknown. Thus, the hypothesis of the study was that a high protein diet and exercise may improve fat-free mass (FFM), functional capacity, symptom burden and dyspnoea in malnourished COPD patients.

METHODS

Consecutive patients with severe COPD (stage III or IV [7]) who were at nutritional risk (NRS 2002, [8]) and had been referred for pulmonary rehabilitation (PR) by their general practitioner or outpatient clinic were randomised to receive dietary counselling (DC) aiming to reach a high protein diet as a supplementary component to PR or standard PR. Terminal or lung-transplanted patients and patients with severe comorbidities preventing the intervention were excluded. All participants gave informed consent. The regional ethical scientific committee and the Danish Data Protection Agency approved the protocol.

Both groups participated in the PR, which consisted of a group-based, supervised physical training with endurance and resistance training twice weekly for 12 weeks (120 min./week). The patient education sessions lasted 60-90 min. after the exercise sessions.

The intervention group (IG) received DC by experienced dieticians, aiming at a protein intake of ≥ 25 E%. An oral nutritional supplement (Atpro 200; 1,570 kJ and 92 g protein per 100 g) was used to supplement the patients' diet to reach ≥ 25 E%/protein/day. The control group (CG) received no DC or nutritional supplementation.

The Harries and Benedict equation [9] with an individual activity and stress component was used. Dietary assessment was performed by 3 × 24-hour diet recall interviews (two weekdays and one weekend day) at baseline and at 12 weeks calculated using the Master Diætist System, Denmark® containing the Danish food composition tables.

Muscle function was assessed by the six-minute walking distance (6MWD) and handgrip strength (HGS) (Saehan DHD-1 Digital Hand Dynamometer, SH1001). FFM was measured by bio-impedance analysis (BIA) (BIA-101, RJL). Mid-upper arm circumference (MUAC) and mid-thigh circumference (MTC) were measured on the dominant side. The COPD Assessment Trial (CAT) Test [10] was used to measure global symptoms. Dyspnoea was measured by the Medical Research Council dyspnoea scale, and Borg score for perceived exertion during physical activity was measured before and after the 6MWD test [11, 12].

Compliance with the nutritional intervention was assessed by three-day 24-hour diet recall interview and return of the ATPRO 200 packages. Adherence to the PR programme was recorded.

Statistical analyses used one-way analysis of covariance (ANCOVA). In the analysis of 6MWD, gender and forced expiratory volume in the first second (FEV1) were included as covariates.

RESULTS

Among the 70 patients screened, 13 patients were randomised to intervention (n = 7) or control (n = 6). Three men from the CG withdrew their consent during the study period. Two patients were admitted to the hospital and one was lost to follow-up. Thus, ten patients were included in the analysis (**Table 1**).

TABLE 1 Baseline characteristics of patients.

	Intervention group (N = 7)	Control group (N = 3)
GOLD: severe/very severe, n	3/4	0/3
FEV1, mean ± SD, % predicted	29.4 ± 6	29.4 ± 6
FEV1/FCV, mean ± SD, %	40.6 ± 8	36.3 ± 8
Comorbidities, n		
Cardiovascular diseases, n	2	1
Osteoporosis	2	2
Pulmonary cachexia	4	2
Medication, n		
Glucocorticoids	5	2
Anti-inflammatory treatment	1	0
Smoking	1	0
Sex, n		
Male/female	3/4	0/3
Age, mean ± SD, yrs	68.3 ± 12	71.7 ± 2
Body weight, mean ± SD, kg	65.4 ± 17	51.4 ± 11
BMI, mean ± SD, kg/m^2	22.2 ± 5	21.0 ± 3
Weight loss[a], n	4	2
FFM, mean ± SD, kg	45.7 ± 11	36.6 ± 4
FFMI[b], mean ± SD, kg/m^2	15.5 ± 3	15.0 ± 1

FEV1 = forced expiratory volume in the 1st sec.; FCV = forced vital capacity; FFM = fat-free mass; FFMI = Fat-free Mass Index; GOLD = Global Initiative for Chronic Obstructive Lung Disease; SD = standard deviation.
a) Unintentional weight loss of ≥ 5% over the 3 mos.
b) FFMI = FFM/height^2.

The IG reduced 6MWD by 9.8 m and the CG by 42.5 m after 12 weeks of rehabilitation. After adjustments for gender and FEV1, the 6MWD mean group difference was 97.1 m (p = 0.04). No differences were observed between the two groups on any other endpoints (**Table 2**).

TABLE 2 Changes in functional capacity, anthropometrics, symptom burden and dyspnoea from baseline to after 12 weeks of intervention.

	Intervention group (N = 7)		Control group (N = 3)		
	baseline	after 12 wks	baseline	after 12 wks	ANCOVA (p-value)
Functional capacity, mean ± SD					
6MWD, m	325.4 ± 84.4	315.6 ± 113.8	309.0 ± 32.5	266.5 ± 122.3	97.1 (0.04)
HGS	34.6 ± 10.7	33.7 ± 11.0	27.7 ± 3.5	27.7 ± 6.0	–2.7 (0.39)
Anthropometrics, mean ± SD					
FFM, kg	45.7 ± 11.1	45.9 ± 10.9	36.6 ± 3.8	36.3 ± 4.6	1.6 (0.23)
MUAC, cm	25.8 ± 3.5	26.3 ± 4.6	25.8 ± 5.4	24.8 ± 5.4	1.0 (0.43)
MTG, cm	46.1 ± 7.0	44.2 ± 7.2	45.8 ± 6.3	44.7 ± 11.0	–0.8 (0.69)
Symptom burden, mean ± SD					
CAT	20.4 ± 6.0	21.6 ± 5.9	22.3 ± 6.7	24.7 ± 3.1	–1.7 (0.45)
Dyspnoea, mean ± SD					
Borg scale:					
Before 6MWD	1.4 ± 1.6	1.6 ± 1.8	1.0 ± 1.4	2.0 ± 0	–0.7 (0.6)
After 6MWD	5.5 ± 1.2	5.6 ± 1.9	7.0 ± 0	7.0 ± 2.8	0.3 (0.9)
MRC	3.7 ± 1.3	3.4 ± 1.0	4.3 ± 0.6	4.0 ± 1.0	–0.2 (0.8)

6MWD = 6-minute walking distance; ANCOVA = one-way analysis of covariance; CAT = COPD Assessment Trial; FFM = fat-free mass; HGS = handgrip strength; MRC = Medical Research Council Dyspnoea Scale; MTG = mid-thigh grip; MUAC = mid-upper arm circumference; SD = standard deviation.

Compliance with the PR was 75 ± 27% (IG) and 81 ± 7% (CG). The IG increased the protein intake from 17.1 E% (1.2 g/kg/d) to 18.6 E% (1.3 g/kg/d), reaching 66 ± 23% compliance with the protein goal. The CG altered the protein intake from 13.1 E% (1.0 g/kg/day) to 12.1 E% (1.0 g/kg/day). The caloric intake of the IG was 1,752 kcal/day (94% of the requirement) at baseline and 1,755 kcal/day (87% of the requirement) at 12 weeks, whereas the CG increased their intake from 1,539 kcal/day (96% of the requirement) to 1,644 kcal/day (100% of the requirement).

DISCUSSION

Maintenance of peripheral muscle function (6MWD) was detected in the IG compared with a deterioration in the CG despite low statistical power. No group difference was detected as far as the remaining outcomes were concerned.

6MWD is a valid and reliable measure of exercise capacity in COPD patients, and a reduction is expected in these patients [13]. This correlates well with mortality risk [13] and post-operative complications [14]. Previous studies have reported conflicting results. Improved muscle endurance [15-18], muscle strength [16, 17], symptoms [16] and FFM [16, 17] have been identified. Conversely, a lack of any group effect has been reported on muscle endurance [19, 20], muscle strength [18, 20], dyspnoea [18, 19], symptoms [18-20] and FFM [19, 20]. The discrepancy in studies reporting the effect of nutritional support on physical capacity, FFM and symptoms in malnourished patients with COPD may be explained by methodological variations with respect to patients, duration, nutritional interventions, exercise elements and choice of outcome measurements [13].

The strength of the present study is the supplementation of an inexpensive protein powder to the patients' habitual diet with a high degree of acceptance. Although the goal of at least 25 E% of protein was not reached, the IG had 40% higher protein intake than the CG after 12 weeks. The main weakness of the study was the small sample size. Conducting multiple analysis on the small sample size might have introduced type-1 error.

CONCLUSION

In patients with COPD attending rehabilitation, a high protein diet combined with physical activity had a clinically relevant effect on peripheral muscle function.

Correspondence *Grith Møller.* E-mail: gmp@nexs.ku.dk

Accepted 15 September 2022

Conflicts of interest none. Disclosure form provided by the author is available with the article at ugeskriftet.dk/dmj

References can be found with the article at ugeskriftet.dk/dmj

Cite this as Dan Med J 2022;69(11):A03220185

REFERENCES

1. Schols AM, Ferreira IM, Franssen FM et al. Nutritional assessment and therapy in COPD: A European respiratory society statement. Eur Respir J. 2014;44(6):1504-20.
2. Akner G, Larsson K. Undernutrition state in patients with chronic obstructive pulmonary disease. A critical appraisal on diagnostics and treatment. Respir Med. 2016;117:81-91.
3. Calder PC, Laviano A, Lonnqvist F et al. Targeted medical nutrition for cachexia in chronic obstructive pulmonary disease: a randomized, controlled trial. J Cachexia Sarcopenia Muscle. 2018;9(1):28-40.
4. Schols AMWJ. Pulmonary cachexia. Int J Cardiol. 2022;85(1):101-10.
5. Nguyen HT, Collins PF, Pavey TG et al. Nutritional status, dietary intake, and health-related quality of life in outpatients with COPD. Int J Chron Obstruct Pulmon Dis. 2019;14:215-26.
6. Ferreira IM, Brooks D, White J et al. Nutritional supplementation for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012;12:CD000998.
7. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2018 Report. Global Initiative for Chronic Obstructive Lung Disease, 2018. https://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf (23 May 2021).
8. Kondrup J, Rasmussen HH, Hamberg O et al. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr. 2003;22(3):321-36.
9. Roza AM, Shizgal HM. The Harris Benedict equation reevaluated: resting energy requirements and the body cell mass. Am J Clin Nutr. 1984;40(1):168-82.
10. Jones PW, Harding G, Berry P et al. Development and first validation of the COPD Assessment Test. Eur Respir J. 2009;34(3):648-54.
11. Borg G. Perceived exertion as an indicator of somatic stress. Scand J Rehab Med. 1970;2(2):92-8.
12. Bestall JC, Paul EA, Garrod R et al. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. Thorax. 1999;54(7):581-6.
13. Singh SJ, Puhan MA, Andrianopoulos V et al. An official systematic review of the European Respiratory Society/American Thoracic Society: measurement properties of field walking tests in chronic respiratory disease. Eur Respir J. 2014;44(6):1447-78.
14. Datta D, Lahiri B. Preoperative evaluation of patients undergoing lung resection surgery. Chest. 2003;123(6):2096-103.
15. Efthimiou J, Fleming J, Gomes C et al. The effects of supplementary oral nutrition in poorly nourished patients with chronic obstructive pulmonary disease. Am Rev Respir Dis. 1988;137(5):1075-82.
16. Sugawara K, Takahashi H, Kashiwagura T et al. Effect of anti-inflammatory supplementation with whey peptide and exercise therapy in patients with COPD. Respir Med. 2012;106(11):1526-34.
17. van Wetering CR, Hoogendoorn M, Broekhuizen R et al. Efficacy and costs of nutritional rehabilitation in muscle-wasted patients with chronic obstructive pulmonary disease in a community-based setting: a prespecified subgroup analysis of the INTERCOM trial. J Am Med Dir. 2010;11(3):179-87.
18. Laviolette L, Lands LC, Dauletbaev N et al. Combined effect of dietary supplementation with pressurized whey and exercise

training in chronic obstructive pulmonary disease: a randomized, controlled, double-blind pilot study. J Med Food. 2010;13(3):589-98.

19. Gurgun A, Deniz S, Arg&;n M, Karapolat H. Effects of nutritional supplementation combined with conventional pulmonary rehabilitation in muscle-wasted chronic obstructive pulmonary disease: a prospective, randomized and controlled study. Respirology. 2013;18(3):495-500.

20. Ahnfeldt-Mollerup P, Hey H, Johansen C et al. The effect of protein supplementation on quality of life, physical function, and muscle strength in patients with chronic obstructive pulmonary disease. Eur J Phys Rehabil Med. 2015;51(4):447-56.