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Original article

The effect of enteral nutrition support on muscle function capacity and pulmonary functions in malnourished patients with Chronic Obstructive Pulmonary Disease

Duygu Degirmenci[1], Habibe Şahin[2], Meltem Soylu[3]
[1]Ordu University, Health Science Faculty, Department of Nutrition and Dietetics, Cumhuriyet Campus, Ordu, Turkey; [2]Erciyes University, Health Science Faculty, Department of Nutrition and Dietetics, Melikgazi, Kayseri, Turkey; [3]Nuh Naci Yazgan University, Health Science Faculty, Department of Nutrition and Dietetics, Erkilet, Kayseri, Turkey - E-mail: msoylu@nny.edu.tr

Summary. Patients with Chronic Obstructive Pulmonary Disease (COPD) usually have a decreased muscle function capacity and pulmonary functions. The purpose of this study was to determine the effect of enteral nutrition support given in addition to diet on muscle function capacity, forced expiratory volume in second (FEV1) and tiffeneau index (FEV1/FVC) in malnourished patient with COPD. Forty patients with body mass indexes (BMI) below 18.5 kg/m^2 were included in the study. Nutrition education was given to all patients then the patients were divided into two groups as treatment and control. Treatment group consumed two bottles of enteral nutrition product in addition to oral nutrition for three months. The muscle powers of the patients were measured with handgrip dynamometer and their FEV1 and FVC values were determined with pulmonary function tests, and tiffeneau indexes were calculated in the beginning and at the end of the study. In conclusion, enteral nutrition support increased hand grip strength and FEV1 without any significant effect on FEV1/FVC values in malnourished patients with COPD.

Key words: COPD, enteral nutrition support, FEV1, FEV1/FVC, hand grip strength

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory disorder of the lung and whole body caused mainly by tobacco smoking, and is characterized by progressive and persistent airflow obstruction (1). COPD is the fourth leading cause of death worldwide (2) whereas according to the results of the "Study of Disease Burden" conducted in Turkey in 2004, COPD is the third leading cause of death, and 26 thousand people die every year due to COPD in our country (3). It is estimated that the global burden of COPD will increase in the near future due to continuing exposure to risk factors related to COPD and the aging of the population (2).

The treatment of COPD requires a multidisciplinary approach including pharmacological, surgical and oxygen therapies along with physiotherapy, psychotherapy and nutritional therapy (4). Malnutrition is frequently observed in patients with COPD. Overall, 10-45% of patients with COPD are malnourished, and it is evident that malnutrition and under-nutrition are important prognostic factors for COPD patients (5). Chronic inflammatory processes, tissue hypoxia, muscle atrophy, anabolic hormone deficiency, and an increased resting metabolic rate all contribute physiologically to weight loss in patients with COPD (6). Malnutrition in COPD causes reduction in body fat and muscle mass through decreasing protein synthesis irrespective of lung function. Malnutrition can limit the exercise capacity by causing dysfunctions in diaphragm and other respiratory muscles and lead to emphysematous changes in parenchyma. In addition, it has been considered that malnutrition affects the respiratory control center and reduces respiratory minute/volume and the ventilatory response to hypoxia and hypercapnia thus increases the incidence of acute respiratory failure in COPD patients (1,4,7).

Nutritional support is a critical part of the treatment plan for the patient with COPD. Proper care to prevent malnutrition will have a significant impact on quality of life and overall patient outcomes. The primary objective of nutrition support is to meet the calculated nutritional requirements thus prevent weight loss. Nutrition support shows positive effects on weight gain and provides functional recovery in the lungs by increasing energy intake (1,8,9,10). These patients may have increasing fatigue, dyspnea, and early satiety, which affect their ability to eat and consume enough calories. Therefore, under these circumstances, it is important to provide nutrition that has high calorie density. This will also help to minimize abdominal distention that may cause discomfort while eating (8). Nutritional intervention consists of oral supplementation and enteral nutrition to prevent weight loss and muscle mass depletion. Frequent small amounts of oral nutrition supplement ONS are preferred in order to avoid postprandial dyspnea and satiety as well as to improve compliance (6,11-13). Therefore, this study was performed to investigate the effects of enteral nutrition support in addition to diet on the muscle function capacity and some parameters of pulmonary function in COPD patients with malnutrition.

Materials and Methods

Participants and Study Design

This study was designed as a prospective, controlled, randomized trial to investigate the influence of enteral nutrition support along with the diet on muscle function capacity and pulmonary function in patients with COPD.

At the beginning, 63 patients were included in the study. However, 16 patients from the treatment group were excluded from the study because they did not consume the products regularly. Four patients from the control group and three patients from the treatment group expired without completing the study. The study was completed with 40 patients with 80% power (β = 0.20) and 95% confidence level (α = 0.05) by power analysis. Out of 40 patients with COPD, 29 patients hospitalized at Clinic of Chest Diseases and 11 outpatients admitted to the clinics of Pulmonary Disease in Trabzon Ahi Evren Thoracic and Cardiovascular Surgery Training and Research Hospital between January and November 2014 were enrolled in the study. The inclusion criteria were receiving a diagnosis of COPD by specialist doctors, having BMI below 18.5 kg/m^2, being over 18 years old, cognitively intact, not pregnant and lactating.

Patients were given verbal and written information about the study, and written informed consent was obtained from all individual participants. This study was initiated with the permission of the administration Trabzon Ahi Evren Thoracic and Cardiovascular Surgery Training Hospital dated 20/12/2013 and the decision of Erciyes University Medical Faculty Ethics Committee, Approval No: 2013/759.

Patients who were not confined to bed and not depending on respiratory devices and agreed to participate in the study were randomly distributed into control and treatment groups consisting of 20 patients in each after being informed about the investigation. Patients in treatment group received two packs/day of enteral nutrition support (Nutrivigor, Abbott) in addition to their diets for 12 weeks whereas control group had no nutritional support. Enteral nutrition product used in this study had a formula that provides an energy intensive complete and balanced nutrition for people who are malnourished or under risk of malnutrition and/or loss muscle mass. The product consists of 18 g protein, 11 g fat, 39 g carbohydrates, 1.2 g HMB, 1.7 g fructooligosaccharides, 352 mg calcium and 12 μg vitamin D in 220 ml volume.

Data Collection and Measurements

Demographic data (age, gender, education level, etc.) and information concerning the smoking, alcohol consumption, disease and treatment statuses of the patients participated in the study were collected through face to face interviews by researchers. Income levels were determined based on the patients' personal statements.

The body weight of the patients was determined with 0.1 kg precision digital scale (King, EB817). The height of individuals was measured by a stadiometer with 10-200 kg±100 g and 60–200 cm±1 mm sensitivity (MK-150, Turkey) while the person in light clothing was standing without shoes, feet were together, and head was maintained in the Frankfort Horizontal Plane position (triangle of eyes in alignment with the upper side of auricle). The body mass index (BMI, kg/m^2) values were calculated through dividing the weight (kg) by height (m) square.

Nutritional statuses of patients were evaluated with NRS-2002 form proposed by The European Society for Clinical Nutrition and Metabolism (ESPEN) for the hospitalized patients. NRS-2002 form was composed of two parts. In the first part, the severity of the disease, food intake (presence of reduction) and weight loss within three months were questioned. If the answers to all of the questions were "no", no question from second part was asked, and weekly scans were continued. If the response to any of the questions was "yes", it was passed to the second part evaluating the malnutrition and disease severity. The severity of the disease was scored as absent (0 points), mild (1 point), moderate (2 points) and severe (3 points). Patients having a total score of three or above was considered as under risk of malnutrition (14).

A 24-hour food consumption of individuals was determined by the researchers using the backward reminder method. Daily energy, macro and micro nutrients intakes of individuals were determined by evaluating the food consumption data with BeBis (Pasifik Company, Türkiye).

The handgrip strength was measured with hydraulic hand dynamometer (Jamar, Lafayette Instrument Company, USA) while the patient was standing with a 45° angle between the arm and the body. The average of two measurements of the both hands was recorded as the result.

Pulmonary function tests were carried out with spirometer (ZAN 100, ZAN Messgerate Gmbh, Germany) by three measurements, and the best curve was used for the determination of forced expiratory volume in 1st second (FEV1), forced vital capacity (FVC) values. The measurements were performed in the beginning and at the end of the study to compare energy and nutrient intake, hand grip strength, FEV1, FVC and FEV1 / FVC values obtained prior to and after the treatment.

Statistical Analysis

The analysis of the data was performed with Statistical Package for the Social Sciences (SPSS version 23). The frequency analysis for demographic characteristics and responses to questionnaires of individuals participated in the study were performed, and introductory statistics values were calculated. Kolmogorov-Smirnov test was used for normality testing of the data, and homogeneity of group variance was determined with Levene test. Student's t-test for independent groups (for the differences between control and treatment groups) and paired t-test for dependent groups (for the differences between the values obtained before and after the treatment) were used. Spearman rank correlation coefficient was calculated in order to determine the relationships between variables. Chi-square test was performed in order to examine the dependence between questions, and Pearson chi-square values were calculated, when the expected frequency was less than 5, Fisher's Exact or G-test (likelihood ratio) was performed. Statistical significance levels were considered as α = 5% for all calculations and interpretations.

Limitations of the Study

Because the nutritional habits, smoking and alcohol consumption, disease and treatment histories of the patients were recorded by the investigators with face to face interviews, the exaggerated or missing information may be given by the participants. Sixty three patients were included in the study during data collection process, but some elderly people in treatment group did not regularly consume enteral nutritional product or stopped consuming enteral nutritional product before the completion of the study. For this reason, 16 patients from the treatment group were excluded from the study. Younger patients were more aware and eager of using enteral nutrition support that resulted in a significantly lower mean age in the treatment group than the control group.

Results

The average age of the patients included in the study was 74.70 ± 10.31, the average duration of disease was found as 11.98 ± 1.08 years. The mean BMI of the patients was 17.18 ± 1.24 kg/m^2 which are below 18.5

kg/m² in accordance with the methodology of the study.

The 72.5% of the patients were hospitalized in clinic and the remainings (27.5%) were outpatient. Most of the patients (62.5 %) was retired because of their age thus 90% of patients had social security (social security institution, pension fund and bagkur) (p>0.05). The distribution of the demographic characteristics of the patients was shown in Table 1. According to the NRS-2002 score, the scores of all patients were above 3 which indicates malnutrition, and 50% of the patients stated that they lost weight in the last 3 months.

The history of smoking in 100%, alcohol consumption in 25% and other chronic diseases in 45% of the patients were recorded. According to the results questionnaires, 47.5% of the individuals skipped meals due to anorexia and slept late, and the skipped meal was lunch in 42.5% of the participants. It was determined that 32.5% of the subjects had no snack.

No significant differences were determined between control and treatment groups in regard to handgrip strength and pulmonary function test. There was no difference between individuals in the control group concerning the hand grip strength (p>0.05) whereas handgrip strength increased significantly (p<0.001) after the enteral nutrition support in COPD patients

Table 1. Distribution of some demographic characteristics of COPD patients

Variables	Treatment		Control		Total	
	n	%	n	%	n	%
Gender						
Male	20	100.0	19	95.0	39	97.5
Female	-	-	1	5.0	1	2.5
			-			
Age (year)						
55-64	5	25.0	4	20.0	9	22.5
65-74	6	30.0	4	20.0	10	25.0
>75	9	45.0	12	60.0	21	52.5
		χ=6.000; *p*=0.199				
Educational Background						
Illiterate	2	10.0	1	5.0	3	7.5
Primary school	12	60.0	17	85.0	29	72.5
Secondary school	2	10.0	1	5.0	3	7.5
High school/University	4	20.0	1	5.0	5	12.5
		χ=0.00092; *p*=0.222				
Monthly Income Level						
Lower than the minimum wage	13	65.0	16	80.0	29	72.5
Higher than the minimum wage	7	35.0	4	20.0	11	27.5
		χ=1.129; *p*=0.288				
Smoking						
Yes	0	0.0	1	5.0	1	2.5
Stopped	20	100.0	19	95.0	39	97.5
			-			

*Pearson Chi-square; p<0.05; ** Fisher's exact Chi-square; p<0.05

with low physical activity levels in treatment group (Table 2).

At the end of study, increases in FEV1 values were observed in control and treatment groups but the increase in FEV1 was significant ($p<0.05$) solely in patients supported with enteral nutrition support. There were slight but not significant ($p>0.05$) decreases in FEV1/FVC values in both groups at the end of the study compare to the initial values (Table 3).

Discussion

Malnutrition is frequently observed in patients with COPD. Overall, 10-45% of patients with COPD are malnourished, and it is evident that malnutrition and under-nutrition are important prognostic factors for COPD patients (4). The main reason for malnutrition is inability to meet increased energy requirements, depending on the hypermetabolism and increased breathing, with deteriorating food intake resulting from breathing difficulties (1,4,6,7).

Table 2. Effects of enteral nutrition support on hand grip strength of COPD patients

	Treatment	**Control**	p^a
	$\bar{X} \pm Sx$ (Lower-upper limit)	**$\bar{X} \pm Sx$ (Lower-upper limit)**	
Hand grip strength (kg) before treatment	26.09±7.67 (16.00-48.75)	25.70±6.36 (9.00-35.00)	0.863
Hand grip strength (kg) after treatment	26.80±7.51 (17.50-49.00)	25.56±5.73 (11.00-34.50)	0.561
p^b	**0.000****	0.474	

** p<0.05; **Paired t-test; p<0.05; p^a: Comparison of experimental and control groups; p^b: The comparison of measurements performed before and after treatment*

Table 3. Effects of Enteral Nutrition Support on Pulmonary Function of COPD Patients

Variables	**Treatment**	**Control**	p^a
	$\bar{X} \pm Sx$ (Lower-upper limit)	**$\bar{X} \pm Sx$ (Lower-upper limit)**	
FEV1 (L/sn)			
Before treatment	39.60±22.53 (16.00-94.00)	44.30±17.92 (18.00-89.00)	0.470
After treatment	43.35±18.94 (19.00-95.00)	46.60±11.59 (22.00-63.00)	0.517
p^b	**0.034****	0.472	
FEV1/FVC			
Before treatment	80.05±29.45 (43.00-136.00)	82.45±27.54 (53.00-136.00)	0.792
After treatment	73.65±21.41 (40.00-112.00)	75.85±19.58 (48.00-128.00)	0.736
p^b	0.066	0.120	

** p<0.05; **Paired t-test; p<0.05; p^a: Comparison of experimental and control groups; p^b: The comparison of measurements performed before and after treatment*

COPD is generally seen in smokers, males, and elderly with low socioeconomic status (1, 9). In our study, 97.5% of the patients were male and the majority of the patients (77.5%) were over 75 years old. In the presented study, the mean age of the patients participating in the study were found as 74.70 ± 10.31 which is similar to results of the studies conducted in Turkey and indicating the COPD, a disease of advanced age, is seen more frequently in patients aged over 60 years (15,16).

The prevalence of COPD is higher in men than women due to higher smoking rate and more professional exposure. Thus the majority of COPD patients admitted to hospital were male which can be considered as the reason for higher proportion (97.5%) of men participated in the presented study (Table 1). Smoking is known as the most important cause of COPD, the risk of development of COPD in smokers is around 40-70% which significantly increases with age (17). The lungs of smokers are exposed to more oxidative damage and blood antioxidant levels have been found lower than non-smokers. The oxidant-antioxidant imbalance contributes to lung damage thus the risk of the development of COPD in smokers also increases. In studies related to the smoking history in patients with COPD, it was found that cigarette consumption increases the risk of COPD (18,19). In a study conducted on 276 patients with COPD in Japan, 75.3% of the patients had stopped smoking and 22.4% of them were still smoking (20). Similarly, all of the patients participated in the presented study used to smoke and only one patient was still smoking tobacco in control group.

Low level of education is one of the risk factors affecting the prevalence of COPD. In a study comparing the control group (without COPD) to patients with COPD, low education level was observed in patients with COPD (21). Similar results were found in our study indicating the vast majority of the COPD patients were illiterate, literate or primary school graduates (Table 1).

Low socioeconomic status is another risk factor affecting the prevalence of COPD. Intrauterine growth failure, poor living conditions, malnutrition, childhood respiratory infections and exposure to cigarette smoke have been reported to be associated with the development of COPD (22,23). In the present study, the majority of patients was on low-income and retired (Table 1) which is consistent with the study of Yılmaz (24) who reported that 100% of the COPD patients had lower income compare to their expenses.

Other diseases are commonly seen in patients with COPD and these diseases also have significant impacts on the prognosis of COPD. Some of the diseases evolve independently from COPD whereas some others have causal relationship with COPD (25). Comorbidity defines one or more concomitant diseases that are directly related to or not related to COPD. In all over the world, it is well known that at least two of the most common chronic diseases including COPD are present in 25% of the individuals aged over 65 years, and 10% of the elderly suffer from three or more concomitant diseases. Similarly, in this study, other diseases apart from COPD were determined in 45.0% of patients. Comorbid diseases commonly encountered in patients participating in the presented study were cardiovascular diseases, hypertension and benign prostatic hyperplasia (BPH).

In this study, BMI of the patients was lower than 18.5 kg/m^2 in accordance with the study design. Decreased body weight has been identified as a poor-prognostic factor in patients with COPD and the survival time is reported to be only 2 to 4 years in patients with severe disease who are lean and have a forced expiratory volume percentage in one second (FEV1%) of less than 50% (19). It has also been reported that COPD patients with a body mass index (BMI) of <20 kg/m^2 have a higher risk of acute exacerbations as compared to COPD patients with a BMI of 20 kg/m^2 or greater, and that patients exhibiting weight loss during a 1-year observation period are more prone to acute exacerbations than those who do not exhibit weight loss over the same period (26). Furthermore, body weight has been demonstrated to be positively correlated with the forced expiratory volume in one second (FEV1), exercise tolerance and diffusing capacity of the lung, even in patients with stable-phase COPD (5). Providing the daily energy requirements in COPD is of importance because insufficient energy intake causes destruction in muscle protein, weight loss and cachexia.

In our study, no significant difference was determined between COPD patients in control and receiving enteral nutrition support considering the FEV1 measurements in both sampling times (p>0.05). However, a significant increase (p<0.05) was observed in FEV1 values after the enteral nutrition support whereas no statistically significant difference was detected in FEV1 / FVC (Table 3). It is still unclear that whether body weight loss is one of the causes of the severe deterioration in lung function or in severe lung disease. However underweight COPD patients more likely have tendency towards low diffusion capacity, air trapping and severe airway obstruction than overweight COPD patients (1,5). In a study performed on 79 patients with COPD, positive correlations have been reported between FEV1 and BMI and between lean body mass index (FFMI) and FEV1 (27). Lazarus et al. (28), suggested a positive relationship between lean body mass and lung function. In a study conducted on 32 patients with COPD who were obese and overweight, exercise capacity were significantly higher compared to patients with normal lean tissue mass and lower BMI (29).

Hand grip strength is considered as an objective measurement for evaluating the performance of the upper extremity. Hand grip strength is not only associated with upper limb muscle strength but also it is associated with overall body and pulmonary muscle strength. The reason for the decrease in lean body mass in patients with COPD is the enhanced muscle proteolysis. Glucocorticoids play a role in muscle proteolysis. Glucocorticoids, in one hand, enhance proteolysis and on the other hand, activate amino acid mobilization for gluconeogenesis by inhibiting transport of amino acids to the muscle and protein synthesis (30). In a study investigating the hand grip strength in patients with COPD, it has been claimed that hand grip strength of patients were significantly lower compared to a control group composed of healthy individuals and also associated with the deterioration of cardiac function in patients with COPD (31). In contrast, Heijdra et al. (30) who compared the muscle strength of COPD patients with healthy subjects, have determined that the patients participated in their study had normal lean body mass. These authors reported no significant difference between patients and healthy individuals concerning the grip strength and suggested that COPD patients with normal lean body mass index had not too severe peripheral muscle dysfunction. In the presented study, similar to the findings of Heijdra et al. (30) no significant difference was determined between control and treatment groups concerning the hand grip strength (p>0.05). The lack of difference in hand grip strength in this study may be due to presence of randomly selected COPD patients in control and treatment groups. However, enteral nutrition support significantly increased (p<0.05) hand grip strength of the patients whereas no significant difference (p>0.05) was observed between the hand grip strength measurements in the beginning and at the end of the study in patients who did not receive nutrition support (Table 2).

The results of this study have shown that enteral nutrition support in malnourished COPD patients increases FEV1 without any effect on FEV1/FVC ratio. Enteral nutrition support contributes to the treatment of disease by meeting the increasing energy demand as well as providing protein support. In some studies (6,7,12,13) functional recovery has been achieved with the increases in energy intake in the patients having enteral nutrition support. However, double-blind, controlled, long-term studies are needed in cachectic COPD patients receiving enteral nutrition support.

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Correspondence:
Asst. Prof. Dr. Meltem Soylu
Nuh Naci Yazgan University, Health Science Faculty,
Department of Nutrition and Dietetics, Erkilet, Kayseri, Turkey.
Phone: :+9035232400 00/443,
E-mail: msoylu@nny.edu.tr