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The effect of supplemental oxygen on 6-minute walk test in chronic obstructive pulmonary disease patients

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Abstract

Introduction: Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease that associated with abnormal airflow during respiration. It has been demonstrated that supplemental oxygen used in the time of exercise testing has a considerable positive effect in cases with COPD.
Objectives: Present study was aimed to investigate the possible effects of supplemental oxygen on the outcomes of 6-minute walk test (6MWT).
Patients and Methods: COPD cases were randomly divided into two groups (n= 50/each). Group1; patients who received nasal oxygen during the 6MWT, and group two were patients who did not receive supplemental oxygen during the test.
Results: The Shapiro-Wilk test showed that the distribution of all parameters in two groups followed the normal distribution. The total distance walked was 431.54±40.76 m in the intervention group and 399.08±49.94 m in the control group, with a significant difference between the two groups (P= 0.001). After 6MWT, the mean of SpO_2 in the intervention group was significantly higher than the control group (P= 0.002) and the degree of dyspnea was significantly lower than the control group (P= 0.031).
Conclusion: Overall, supplemental oxygen has significant positive effects in COPD patients, but definitive commentary is needed for further studies.
Trial registration: The trial protocol was approved by the Thai Clinical Trials Registry (identifier: TCTR20220122001; https://www.thaiclinicaltrials.org, ethical code; IR.MUI.MED.REC.1396.308.3).

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Introduction

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease that associated with abnormal airflow during respiration (1,2). It has been reported that the rate of lung malignancies, cardiovascular disease, and other respiratory complications is higher in these patients (3). Aforementioned condition is usually induced by long-term exposure to annoying gases or particulate matter, especially in cigarette smoke, and accompanied by cough, breathing trouble, sputum overproduction, and wheezing (4,5). Furthermore, chronic bronchitis, irritation of the bronchial tubes and emphysema, destruction of bronchioles due to exposure to cigarette smoke, are the two most reported disorders related to COPD (6). In cases with COPD, pulmonary complications and weakness of skeletal muscles lead to sedentary life style and alterations in functional status (7). Precise evaluation of the functional status in these patients plays a crucial role in recommending suitable therapy and respiratory rehabilitation programs(7).

As we all know, submaximal exercise tests like the 6-minute walk test (6MWT), as an easy and cost-effective test, can be used for evaluation of aerobic capacity and ability to execute a defined exercise. In the beginning, 6MWT was introduced for the assessment of subjects with cardiovascular problems but continuously, it was recommended in several other conditions such as COPD, interstitial lung diseases and hypertension of pulmonary artery (8,9). The functional capacity of the cases is evaluated by measuring the distance covered over a time of six minutes. Furthermore, the outcome of this test presents helpful information about physiological function of neuromuscular

Key point

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease that associated with abnormal airflow during respiration. The present study was aimed to investigate the possible effects of supplemental oxygen on the outcomes of 6-minute walk test (6MWT). Based on our results, supplemental oxygen has significant positive effects in COPD patients, further studies are still needed for this aspect of COVID-19 patients.

and cardiovascular systems, body metabolism and blood circulation (10).

It has been demonstrated that supplemental oxygen used in the time of exercise testing has a considerable positive effect in cases with COPD (11,12). Some underlying mechanisms such as reduced dynamic hyperinflation, delayed lactic acidosis and lessened pressure of pulmonary artery are involved in aforementioned positive effects (12,13); however the issue is open to discussion. Additionally, enhanced oxygen consumption in respiratory and skeletal striated muscles was observed in COPD subjects by using supplemental oxygen (12).

Objectives

Due to the high concern of COPD and the importance of various diagnostic methods as well as supportive therapies, the present study was aimed to investigate the possible effects of supplemental oxygen on the outcomes of 6MWT in the group of patients with COPD.

Patients and Methods

Study design and patients

Our study was conducted from May 2017 to September 2019 in the internal medicine department of Al-Zahra hospital of Isfahan university of medical sciences, Isfahan, Iran. Written consent was obtained from each patient and participation in the present survey was voluntary. Demographic information of patients including age, gender, weight and height were written in special forms. All patients were clinically assessed by a physician. Accordingly, the clinical presentations and risk factors of the subjects were determined based on their medical records and self-reports of them.

Before entering, the measure of hemoglobin in the blood, serum levels of thyroid hormones and echocardiographic parameters were conducted. Patients with anemia, hyperthyroidism, the body mass index (BMI)> 30 kg/m^2, and the ejection fraction (EF) <60% were excluded. The acceptable inclusion criteria were; (I) definitive diagnosis of moderate to severe COPD, (II) weeks without exacerbations), (III) lack of acute coronary syndrome, (IV) FEV1/FVC ratio of less than 0.7, and 50 %< FEV<80% (stage 2) and 30 %< FEV<50% (stage 3), (V) a cigarette smoking history of more than 10 pack-year and (VI) ability to walk. Patients with complications during the test were excluded from the study. A total of 100 cases with definitive diagnosis of COPD that were able to finish the 6MWT, without using additional oxygen or having to stop before completing the test, were included in our study. Participants were randomly divided into two groups (n= 50/each). Group one: patients who received nasal oxygen during the test (2 L/nin), as an intervention group; and group two: patients who did not receive supplemental oxygen during the test, as a control group. It was important to note that patients were unaware that the oxygen capsule was full or empty.

The 6-minute walk test protocol

The present test was performed based on the American Thoracic Society guidelines (14). Prior to the beginning of study, all patients received a comprehensive explanation about the 6MWT. Additionally, subjects were asked to stop the test if they experienced any pain in their chest, respiratory problems, vestibular problems, dizziness and leg cramps. The patients were asked to walk 30 meters for six minutes (walk back and forth) as soon as the test began. The total distance walked was measured and compared between the two groups. In addition, oxygen saturation (SpO_2), self-experienced dyspnea (using the Borg CR10 Scale) (15), heart rate (HR), and fatigue (based on the Borg scale) (16) were measured before and after the 6MWT. The SpO_2 was measured using a portable pulse oximeter (NONIN Medical Inc., Plymouth, MN).

Statistical analysis

In the current study, the extracted data were analyzed by statistical package for social science (SPSS) software, version 25.0 (SPSS Inc., Chicago, IL, USA). Data were analyzed by Shapiro-Wilk normality tests. The statistical analysis was conducted by independent *t* test and pair *t* test. The significant level was set at *P* value less than 0.05.

Results

Male patients (n = 100) were distributed to the two groups (n = 50/each) (Figure 1). The intervention group, received 2 L/m nasal oxygen during the test, while the control group did not receive supplemental oxygen during the test. The Shapiro-Wilk test showed that the distribution of all parameters in two groups followed the normal distribution. Mean ages in the two groups were 62.46 ± 10.94 years, and 60.48 ± 9.25 years, respectively. There is no meaningful statistical difference between ages in the two groups of COPD subjects ($P = 0.33$). The baseline demographic and characteristics of the COPD patients were summarized in Table 1. Based on the measured forced expiratory volume in one second (FEV1) in percent, significant airflow limitation was present in all patients. Additionally, all patients of this study were smokers (Table 1).

The results of some assessed parameters during the 6MWT are summarized in Table 2. The total distance walked was 431.54 ± 40.76 meter in the intervention group and 399.08 ± 49.94 meter in the control group, with a significant difference between two groups ($P = 0.001$). After 6MWT, the mean of SpO_2 in the intervention group was significantly higher than the control group ($P = 0.002$) and the degree of dyspnea was significantly lower than the control group ($P = 0.031$). There is no significant statistical difference between other evaluated variables at the baseline and end of 6MWT ($P > 0.05$)

The mean of total distance walked in the patients with gold stage 2 (n=77) was 428.77 ± 77 (m) and in the patients with gold stage 3 (n=23) was 370.26 ± 54.45 (m) ($P < 0.001$). There are a significant difference between BMI of patients

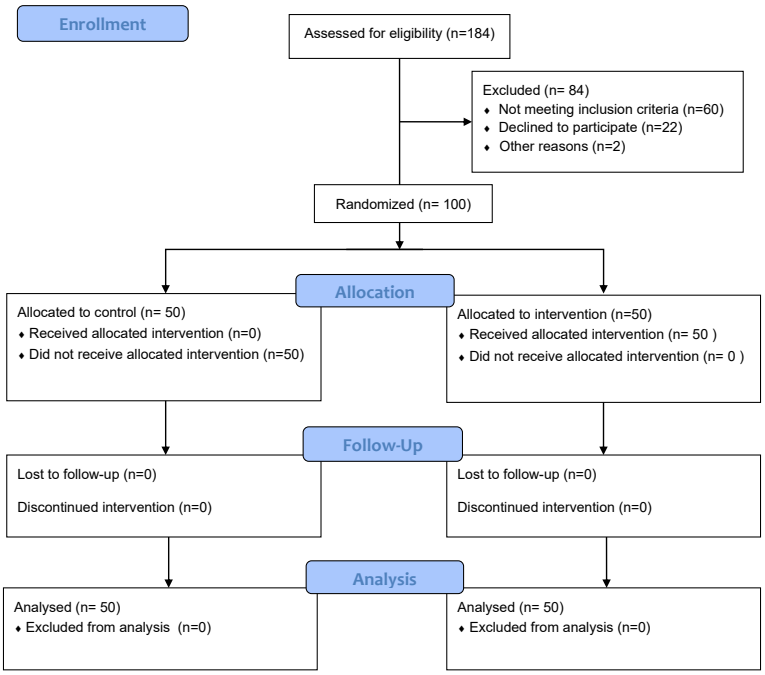

Figure 1. Flow diagram of the study.

with gold stage 2 and 3 of COPD (24.86 ± 3.87 kg/m^2 and 22.95 ± 3.46 kg/m^2, respectively). Table 3 shows the evaluated parameters in the 6MWT, which are compared in gold stage 2 and 3 patients.

Discussion

As we all know, COPD, as a common respiratory disease, is a leading cause of mortality all over the world (17). It has been reported that mortality rate of COPD is associated with some factors such as BMI, FEV1, exercise capacity and degree of dyspnea (18). As previously mentioned, we investigated the possible effects of supplemental oxygen on the outcomes of 6MWT in the group of patients with COPD. The 6MWT is an accessible test that gives us valuable information about the integrated function of the respiratory, muscular and cardiovascular systems and also reflects the practical exercise level for daily activities (19). So far, some studies have indicated that the 6MWD is a better mortality predictor than the FEV1 in cases with severe COPD. It has been proposed that the distance

Table 1. Demographic and characteristics of the COPD patients in two groups of intervention and control

Parameter	Intervention (N=50)	Control (N=50)	P value
Age (year)	62.46±10.94	60.48± 9.25	0.33
Height (cm)	172.34±9.07	170.74±8.24	0.35
Weight (kg)	72.10±12.47	71.7±13.20	0.87
BMI (kg/m^2)	24.28±3.75	24.563.97±	0.72
SBP (mm Hg)	127.13±20.25	130.24±7.72	0.35
DBP (mm Hg)	83.08±10.17	79.19±11.80	0.11
Smoking (pack-year)	38.92±30.64	32.19±18.23	0.19
FVC (%)	61.96±19.31	72.83±14.72	0.003
FEV1 (%)	50.82±20.56	60.45±17.37	0.015
FEV1/FVC	63.92±14.39	64.44±15.01	0.86

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV1, forced expiratory volume in one second; FVC, forced vital capacity.

Table 2. The results of some assessed parameters during the 6MWT

Parameter	Intervention	Control	*P* value[a]
Distance (M)	431.54±40.76	399.08±49.94	0.001*
Dyspnea, Borg Index			
Baseline	1.53±0.78	1.32±0.74	0.17
End	4.42±1.35	5±1.29	0.031*
P value[b]	<0.001	<0.001	
Heart rate (beats/min)			
Baseline	95.38±9.33	94.78±7.14	0.71
End	116.38±9.70	119.7±8.61	0.07
P value[b]	<0.001	<0.001	
Spo_2			
Baseline	89.52±2.03	90.30±2.19	0.06
End	91.14±2.15	89.70±2.37	0.002*
P value[b]	<0.001	0.001	
Fatigue, Borg index			
Baseline	2.06±0.71	2.02±0.74	0.78
End	5.46±1.18	5.66±1.25	0.41
P value[b]	<0.001	<0.001	

[a] Independent *t* test; [b] Paired *t* test.

Table 3. The evaluated parameters in the 6MWT, which are compared in gold stage 2 and 3 patients

Parameter	Gold stage 2 (n=77)	Gold stage 3 (n=23)	*P* value[a]
Distance (M)	428.77± 77	370.26± 54.45	<0.001*
Dyspnea, Borg index			
Baseline	1.24±0.66	2.02±0.8	<0.001*
End	4.22±1.03	6.35±0.93	<0.001*
Heart rate (beats/min)			
Baseline	94.99±8.67	95.39±6.94	0.83
End	117 ±9.82	121.52±6.13	0.04*
Spo_2			
Baseline	90.21±2.25	88.91±1.31	0.01*
End	90.21±2.25	88.91±1.31	0.01*
Fatigue, Borg index			
Baseline	1.92±0.73	2.43±0.5	0.002*
End	5.29±1.13	6.48±1.03	<0.001*

[a] Independent *t* test.

walked in the 6MWT predicts mortality in COPD cases (20, 21). In the present study, the total distance walked was 431.54 ± 40.76 (m) in the intervention group and 399.08 ± 49.94 (m) n the control group, with a significant difference between the two groups ($P = 0.001$). Jolly and co-workers investigated the effects of oxygen therapy during activity in subjects with advanced COPD without severe resting hypoxemia (11). Based on the result of their study, the total distance walked in patients who received supplemental oxygen was higher than those who did not receive but unlike our study, the difference between the two groups was not significant.

COPD mainly affects the lungs but also produces other systemic complications. Nutritional abnormality is one of the considerable consequences of COPD that generally characterized by low BMI (22). A relationship between COPD and low BMI has been well presented in previous studies. We found a significant difference between BMI of patients with gold stage 2 and 3 of COPD (24.86 ± 3.87 and 22.95 ± 3.46, respectively) was seen. Moreover, as previously mentioned, all patients under study were smokers. Perhaps one of the causes of low BMI in patients with gold stage 3 of COPD is smoking. Previous papers were indicated that cigarette smoking is associated with the lower caloric intake (22).

Some studies have suggested smoking as one of the reasons for the effective decrease in BMI. In our study, it is not possible to make a definite statement about the cause of decreased BMI in stage 3 COPD patients compared to stage 2, since respiratory abnormalities themselves reduce energy intake and most importantly, the relation between low-BMI and respiratory mortality was also reported in non-smoker cases (23,24). Furthermore, most patients did not report accurate information on the number of cigarette smoking (pack-year) and therefore it was not possible to accurately examine the relationship between smoking and other variables. Therefore, it seems that lower BMI in patients with gold stage 3 of COPD is associated with simple malnutrition.

Among the various complications of COPD, dyspnea, sensation of respiratory displeasure, is of great importance (15). It has been reported that the degree of dyspnea predicts health associated quality of life (15). The precise underlying mechanism of dyspnea is unclear but it has been suggested that mechanical dissociation, dynamic hyperinflation, weakness of inspiratory muscles and gas exchange anomalies involved in pathogenesis of this condition in COPD (15). None of the tools and software that are presently available to assess the degrees of dyspnea is accurate enough. In the present study, the administration of supplemental oxygen reduced dyspnea in COPD patients. In our investigation, the Modified Borg Dyspnea Scale (MBS) was applied for evaluation of dyspnea pre/after 6MWT. The MBS is a reliable evaluation tool for determining the degrees of dyspnea (0 to 10 rated scale). Kendrick et al, in their study demonstrated usefulness of the modified 0-10 Borg scale in assessing the degree of dyspnea in patients with COPD and asthma (25).

Conclusion

Increasing the walked distance in the 6MWT in a group of patients who received supplemental oxygen may indicate sufficient coordination between cardiovascular system, skeletal system and respiratory muscles. Besides, decreased dyspnea in these subjects can be associated with increased coordination of respiratory muscles and respiratory movements. Overall, supplemental oxygen has significant positive effects in COPD patients; however, definitive commentary is needed for further studies.

Limitations of the study

The small sample of the patients and also single-center study were the main limitations of the present trial study.

Authors' contribution

In the present study, FG, FS and SS were the principal investigators. FG and SS were included in designing the study. FS was participated in writing the initial format of the manuscript. All authors confirmed the accuracy of all parts of the present manuscript and approved it for publication.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The study was approved by the ethics committee of this university (ethical code #IR.MUI.MED.REC.1396.308.3). Accordingly, informed consent was obtained from all the patients. The trial protocol was approved by the Thai Clinical Trials Registry (identifier: TCTR20220122001; https://www.thaiclinicaltrials.org). Besides,

ethical issues (including plagiarism, data fabrication and double publication) have been completely observed by the authors. This paper was extracted from the residency thesis of Fatemeh Sajjadfar, at the department of internal medicine, Isfahan university of medical sciences.

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