

Consequences of aerobic resistance exercise combined with Liprimar in the treatment of Chronic obstructive pulmonary disease

Yanping Liu, Huiyao Wang, Bingjie Nie, Yahua Liu

The third Clinical Medical College of Xinjiang Medical University (Cancer Hospital).

Abstract *Background:* Aerobic resistance exercise is fundamentally required for the patients with COPD at a stable stage, to recover their exercise function. While the patients need to be supplemented with medication as well to inhibit the production of inflammatory factors. Atorvastatin calcium (a derivative of Atorvastatin) is reported as component in Liprimar. However, there are only few studies available on the treatment of COPD by Liprimar. The current study investigates the therapeutic value of aerobic resistance exercise, combined with Liprimar, in treating COPD patients and attempts to provide a basis for the treatment of COPD. *Methods:* The author(s) recruited a total of 147 patients diagnosed with COPD and were hospitalized at Internal medicine department, Third Clinical Medical College, Xinjiang Medical University (Cancer Hospital) and the study period was between October 2015 and June 2019. 120 patients were selected as subjects of this experiment on a voluntary basis. Aerobic resistance exercise therapy, Liprimar and combination therapy were provided to the patients. The patients' physical fitness indicators, levels of inflammatory cytokines and cardiopulmonary function were observed to evaluate the treatment plan. *Results:* The COPD patients who received aerobic and obstructive exercise treatment, in combination with Liprimar, showed improvement in the indicators related to physical fitness, decreased body fat percentage, waist-to-hip ratio, BMI, blood sugar, Hba1c content, blood lipid, low levels of inflammatory factors (such as IL-8, IL-6, TNF- α), and notable recovery in cardiopulmonary function. *Conclusions:* A combination of aerobic and obstructive exercises with Liprimar can treat COPD patients in a better way. It can improve the exercise function and cardiopulmonary function of the patients. However, the clinical application of this treatment plan should be verified with more sample size. Further, the clinical application should also adjust the plan appropriately, according to individual differences.

Key words: aerobic resistance exercise; Liprimar; Chronic obstructive pulmonary disease (COPD)

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is an umbrella term which is used to denote a group of lung conditions that cause breathing difficulties. It includes emphysema, which damages the air sacs in the lungs and chronic bronchitis, in which the airways undergo long-term inflammation. The main symptoms

of COPD are increasing breathlessness, particularly when patients experience persistent chesty cough with phlegm. Few patients tend to neglect this symptom as just a 'smoker's cough'. The other symptoms include frequent chest infections and persistent wheezing [1-2]. The damage caused by COPD to the lungs is irreversible while the treatment can help in mitigating the progression of the condition. Though aerobic

exercise is a common pulmonary rehabilitation training method, the studies inferred that the patients with COPD tend to be affected by skeletal muscle atrophy. This is also one of the important factors in the decline of patients' quality of life [3]. Over time, aerobic exercise can help in decreasing the heart rate and blood pressure, and improve breathing since the heart need not work hard alike during exercise. Aerobic exercises include walking, jogging, jumping rope, bicycling (stationary or outdoor), cross-country skiing, skating, rowing, and low-impact aerobics or water aerobics.

Several kinds of medications are used to treat the symptoms and inhibit the progress of COPD complications. Bronchodilators and glucocorticoids are often used in the clinical treatment of COPD. Liprimar, an HMG-CoA reductase inhibitor, is used to reduce cholesterol and prevent cardiovascular-related disease. Recent studies have shown that Liprimar, a commonly-used lipid-regulating drug in clinical practice has anti-inflammatory, antioxidant and immunomodulatory effects [4-5]. **Atorvastatin calcium** (a derivative of Atorvastatin) is reported as a component in Liprimar. However, there are only few studies available on the treatment of COPD by Liprimar. The current study investigates the therapeutic value of aerobic resistance exercise, combined with Liprimar, in treating COPD patients and attempts to provide a basis for the treatment of COPD.

Methods and Materials

Ethical permission

The authors attained the approval and ethical permission to conduct the study from The research ethical board, Third Clinical Medical College, Xinjiang Medical University (Cancer Hospital), Xinjiang, China. Hospitalized COPD Patients at the Internal medicine department in the hospital were enrolled for the study. The study period was between Jan 2017 and December 2020. The patients were randomly assigned to observational group and the control group. COPD was diagnosed according to Chinese medical association's guidelines for the diagnosis and treatment of COPD (2007 revision) [6].

Selection criteria

The inclusion criteria for the study is as follows: Those COPD confirmed patients who volunteered for observation, and those who had not taken statins for two weeks prior to the onset, and exhibited no track record of severe liver and kidney dysfunction were enrolled in this study. It was observed that all these patients recorded high levels (3-5 times above normal level) of serum creatine kinase and alanine transaminase. Those patients diagnosed with myalgia were considered only if their drug treatment during medication can be stopped or otherwise they were excluded from the study.

Treatment

In the current study, the exercises were prescribed to the patients with COPD based on their pathological causes, willingness and their physical characteristics. The exercises prescribed were aerobic and resistance-based ones such as taijiquan and jogging. In line with the interest of the patient and mastery degree, the researchers found the aerobic and resistance exercise based on the formula, oxygen consumption $X\% = \text{Hrrest} + (\text{HRMax} - \text{Hrrest}) \times X\%$ oxygen consumption calculation. As per this formula, the oxygen consumption lies in the range of 40-60% for the observational group exercise which is confined to moderate intensity heat rate.

The exercises were prescribed based on the guidance from professionals. The standard gradients of resistance training were defined to be 45%, 50%, 55% and 60% of the maximum strength while three groups of resistance exercises were conducted with 25, 20, 15 and 10 times respectively. In case of control group, they followed their existing exercise regimen without any medication.

Determination of Interleukin 4 (IL 4), interleukin 6 (IL-6) and interleukin 10 (IL-10). Fasting venous blood was collected from the patient prior to the treatment and after a period of six months once the treatment is over. The blood samples were then processed for Enzyme Linked Sandwich Immunoassay (ELISA) with the help of a kit procured from Immunology department, Fourth military medical university. The researcher conducted the physical fitness test as well as measured four indices of blood lipid. The body density was determined with the help of a formula, body fat percentage (%) =

$(4.570/\text{body density} - 4.142) \times 100$ calculated densities. In this formula, the total fat is calculated by multiplying body weight and body fat percentage. Fat loss weight (lean weight) denotes the weight excluding the total fat weight. Being the blood glucose and glycosylated-hemoglobin indicators, the concentrations of Fasting Blood Glucose (FBG) and HbA1c were determined using a blood glucose meter manufactured by Novo Nordisk and a Boehringer Mnnhelm kit from Germany, respectively. The researcher then analyzed the low-density lipoprotein (LDL), high-density lipoprotein (HDL), Serum cholesterol (Tch) and triglyceride (TG) using 721 spectrophotometer.

Lung function measurement: Spirometry is inclusive of pulmonary mechanic tests including measurements of FVC, FEV₁, FEF values, forced inspiratory flow rates (FIFs), and MVV. These tests assess the ability of lungs to move huge volumes of air quickly through the airways so as to identify the airway obstruction. The measurements were taken using the spirometry device and were plotted as a pneumotachograph. This graph can help in assessing the lung conditions such as asthma, pulmonary fibrosis, cystic fibrosis, and Chronic Obstructive Pulmonary Disease. All the data were analyzed using SPSS 13.0 statistical software, and $P < 0.05$ was considered as statistically significant.

Result

Patients details

The study samples included a total of 105 males and 75 females with an average age of 65.7 ± 6.7 years

while the course of disease was in the range of 7.2 ± 3.7 years (table 1). There were four group Experimental group 1 (aerobic resistance), Experimental group 2 (Liprimar), Experimental group 2 (aerobic resistance + Liprimar), Control group, each having 45 patients enrolled for this study. There was no significant difference was in age among these groups.

After treating the patients with a combination of systematic moderate intensity aerobic exercise, resistance training and Liprimar treatment, the body indicators changed to different degrees. Body fat percentage, waist-to-hip ratio and BMI were compared with pre-experiment data (Figure 1). After simple exercise treatment, the above indexes got significantly reduced. However, when Liprimar was used alone in the treatment, it exhibited only less effect on these indicators. A combination of aerobic and resistance exercises with Liprimar produced superior results compared to individual treatment. Fasting Blood Glucose (FBG) concentration and HbA1c indexes of the experimental group i.e., group treated

Table 1. Demographic details of patients

	Number	age	Year
Experimental group 1 (aerobic resistance)	45	65.46 ± 2.67	8.81 ± 3.41
Experimental group 2 (Liprimar)	45	62.87 ± 3.26	8.14 ± 3.18
Experimental group 2 (aerobic resistance + Liprimar)	45	63.27 ± 2.86	7.83 ± 2.16
Control group	45	62.91 ± 2.48	7.68 ± 3.22

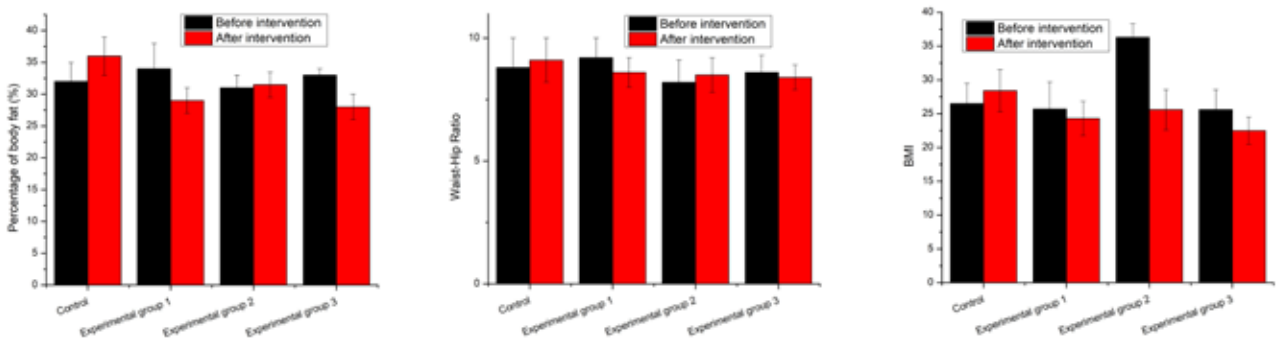


Figure 1. Changes of physical health indicators

with aerobic resistance exercise and Liprimar, were significantly lower compared to the values recorded before the treatment. However, there was no significant change in the control group before and after the experiments (Figure 2).

The current study investigated the effects of different treatment regiments upon Tch, TG, HDL and LDL in patients. The results from Observational group showed that the indicators such as Tch, TG and LDL, in the group treated with aerobic resistance exercises and Liprimar, were significantly lower than those before the experiment. However, there was no significant difference found before and after the experiment in the control group (table 4).

IL -8, IL -6, and IL-10 levels found in the group treated with Liprimar and aerobic resistance exercise after the experiment, were significantly lower than those before the experiment. However, there was no significant change before and after the control group (Figure 4). This denotes the fact that Liprimar treatment can slow down the content of inflammatory cytokines in COPD patients.

Control group patients, with FEV1 / FVC, FEV1 indicators, exhibited no significant changes before and after the experiment. But after aerobic and resistance exercises' therapy, Liprimar treatment and a combination of the above index, there was a significant increase observed (figure 5).

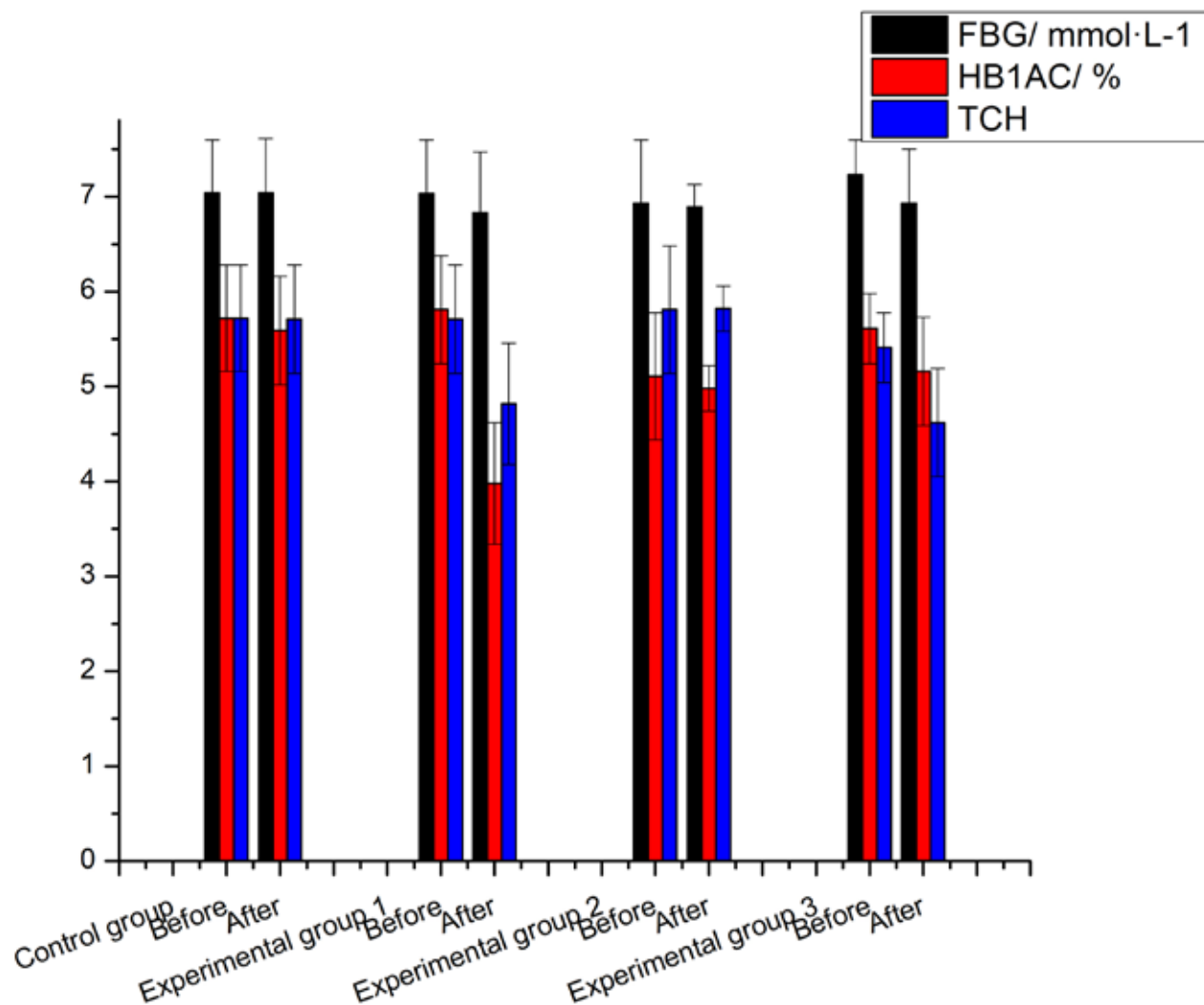


Figure 2. Changes in blood biochemical parameters in patients

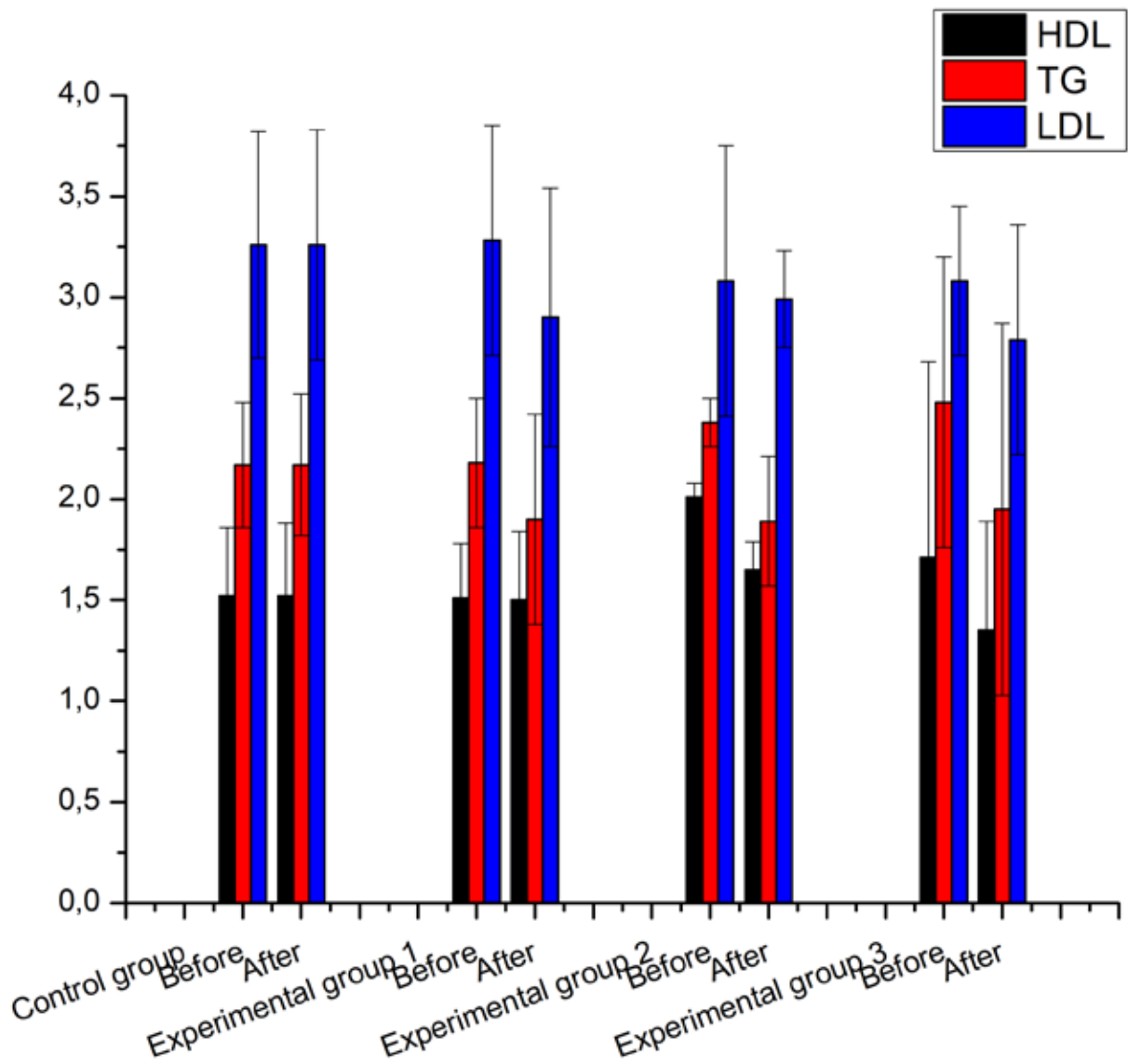


Figure 3. Changes in blood lipid profile of patients

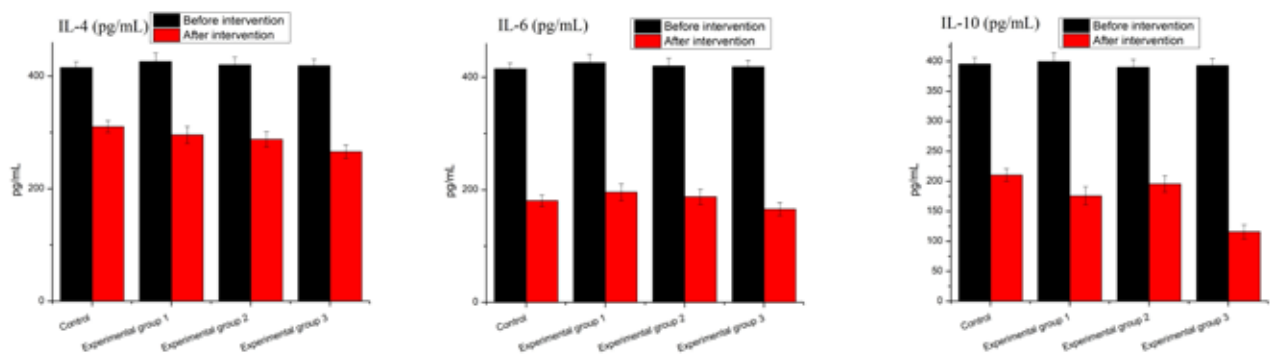


Figure 4. Effect of different treatment on patients with IL-8, IL 6 and TNF- α

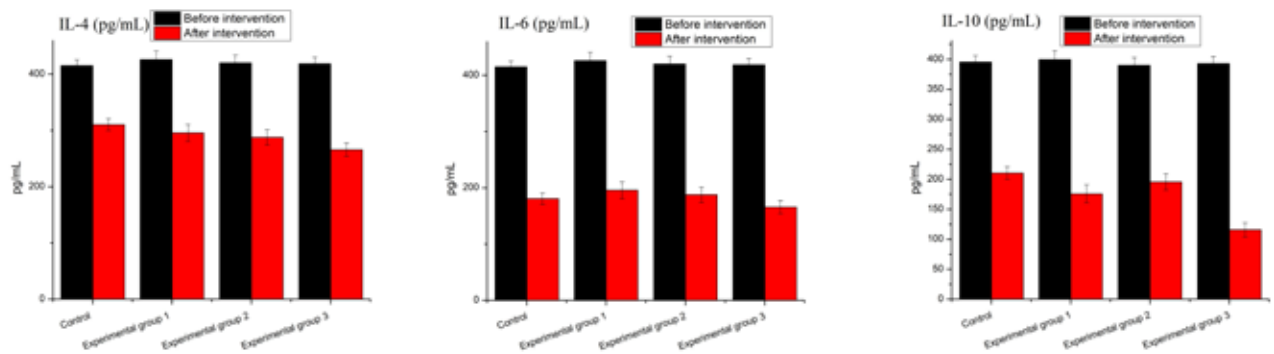


Figure 5. Effects of different treatments on patients with FEV₁/FVC and FEV₁

Discussion

Aerobic resistance exercises were prescribed in the current study as exercise treatment program. By following this treatment program, COPD patients improved their physical fitness and cardiopulmonary function. This indicates that aerobic resistance exercise can effectively treat COPD patients. Liprimar belongs to a class of reductase inhibitors and its full name is 3-hydroxy3-methyl-glutaryl coenzyme A (HMG – COA). It is commonly used in clinical lipid regulation and the prevention of cardiovascular disease. Liprimar also has anti-inflammatory, antioxidant and immune regulatory effects. In COPD patients, with smoke activated stimuli, the inflammatory cells migrate to the lung tissue and release a variety of inflammatory cytokines. Excessive amounts of inflammatory cytokines result in the accumulation of inflammatory cells in lung tissue. On the other hand, the activity of inflammatory cells keeps increasing due to which more inflammatory cytokines are secreted which gather around the inflammatory cells. This phenomenon forms a vicious circle between inflammatory cells and inflammatory cytokines which jointly damages the deep lung tissues [20-21,25-31]. The changes that occur in inflammatory cytokines among the patients, must be monitored actively to better evaluate the treatment regimen. After Liprimar treatment, the levels of inflammatory cytokines in COPD patients got significantly reduced before the experiment. The level of inflammatory cytokines could also be reduced by aerobic exercise therapy though the degree is significantly lower than that of Liprimar. When combined with aerobic resistance

exercise and Liprimar, the level of inflammatory cytokines in patients was significantly lower than before the experiment. Further, the effect was also better than the group treated with exercise alone or Liprimar alone. This indicates that a combination of these two treatment regimens had a better therapeutic effect on patients.

In the present study, a significant decrease was found in the pulmonary functions of severe COPD patients when compared with mild and moderate COPD patients and controls. The findings of the present work are consistent with those of previous studies which concluded that pulmonary function data (FEV₁, FVC, FEV₁% and PEF_R) were significantly lower in COPD patients, when compared with controls. The extent of inflammation, fibrosis and luminal exudates in the small airways is correlated with reduced values of FEV₁ and FEV₁%. The airflow limitation in COPD patients is due to the increased resistance to airflow. This is caused by smooth muscle hypertrophy, goblet cell metaplasia, degeneration of the airway cartilage and mucous hypersecretion. This indicator that the aerobic and resistance exercise therapy and Liprimar treatment can improve the patients' cardiopulmonary function. The combination therapy exerts a positive effect on the patient's health. The inflammatory cells, activated by smoke and bacteria, tend to migrate to the lung tissue and release a variety of inflammatory cytokines such as *IL* -8, *IL* -6, and *IL*-10. COPD is a lung disease with chronic inflammation in airway and lungs. Different cytokines play a role in the orchestration of inflammation in inflammatory airway diseases such as Chronic Obstructive Pulmonary Disease,

through the recruitment, activation and survival of inflammatory cells. Patients with COPD can be treated with aerobic exercise which helps them in recovering their lung function, and at the same time drug therapy inhibits the production of inflammatory factors.

Inflammatory cells, activated in COPD patients, migrate to lung tissues and release a variety of inflammatory cytokines including *IL -8*, *IL -6*, and *IL-10* levels, etc. [7, 8]. So, when changes in these indicators are monitored in patients, one can better evaluate the treatment regimen. Previous studies have shown that Liprimar can reduce the level of inflammatory cytokines in patients [9]. However, there are few studies only available on the effect of aerobic resistance exercise on inflammatory cytokines. The current study discussed the effects of aerobic resistance exercise, liprimar and a combination of both these factors upon inflammatory cytokines in COPD patients and their treatment. When patients were treated with Liprimar alone, the changes of inflammatory cytokines were significantly lower than before the experiment. After aerobic exercise treatment, the level of inflammatory cytokines got decreased and there was no significant difference found when compared with the control group. However, when the levels of inflammatory cytokines in the patients treated with aerobic resistance exercise and Liprimar were significantly lower than before the experiment and lower than the group treated with exercise alone, it can be inferred that a combination of these two treatment regimens can be more effective for the patients.

There was no significant change observed in the control group before and after the experiment. This pattern infers that the exercise prescription, adopted in this study, produced a positive effect on improving the physical conditions of patients. Further a combination of aerobic & resistance exercises and Liprimar can produce better effects than traditional methods. Fasting Blood Glucose (FBG) concentration and HbA1c indexes of the experimental group i.e., group treated with aerobic resistance exercise and Liprimar, were significantly lower compared to the values recorded before the treatment. This infers that aerobic and resistance exercises' treatment could slow down the blood glucose and Hb1Ac of COPD patients. Previous studies have concluded that aerobic resistance exercise can reduce

the blood glucose level in patients [10, 11]. However, there are only few studies available on the impact of aerobic resistance exercise on COPD. The current study not only discussed the impact of aerobic resistance exercise on COPD, but also discussed the effect of Liprimar and when both are combined in treating COPD. When patients were treated alone with Liprimar, there were no significant changes observed in these two indicators. However, when the patients were treated with combined therapy i.e., aerobic resistance exercise and Liprimar, their blood glucose and HbA1c contents got significantly reduced than before the experiment and lower than the group treated with exercise alone. One can infer that a combination of the two had a better therapeutic effect on the patients. As per the studies conducted earlier, the reduced levels of T_{ch}, TG, HDL and LDL in the blood can effectively relieve and prevent the deposition of cholesterol in the arterial wall [12]. The results from Observational group showed that the indicators such as T_{ch}, TG and LDL, in the group treated with aerobic resistance exercises and Liprimar, were significantly lower than those before the experiment. Therefore, it can be inferred that the aerobic resistance exercises can slow down the indicators such as T_{ch}, TG and LDL in COPD patients. Liprimar regulates lipid, TG and HDL levels while these values got decreased in patients treated with Liprimar alone. The effect of exercises on these indicators infers that the exercise improves the activity of lipoprotein enzymes in muscle and adipose tissues. Then, it accelerates the transfer of cholesterol and phospholipid to HDL [13]. The effect of Liprimar on these indicators may be linked with other mechanisms. After combining aerobic resistance exercise with Liprimar in the treatment of COPD patients, the studied indicators were significantly lower than those of the control group (Figure 3). This infers that a combination of the two treatments had a better therapeutic effect on patients.

In summary, a combination of aerobic resistance exercise and Liprimar can effectively improve the cardiorespiratory function and exercise endurance of COPD patients while at the same time, it can reduce the inflammatory factors too. However, the clinical application of this treatment plan should be verified with more number of samples. Further, it should be appropriately adjusted according to individual differences.

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Correspondence

Yahua liu,
The third Clinical Medical College of Xinjiang Medical University (Cancer Hospital).
nkh56851@126.com; 86-13929824417;