Effect of Planned Exercise on Serum Biomarkers in Chronic Obstructive Pulmonary Disease

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Abstract

Objectives: To study the influence of planned exercise training in COPD patients on serum biomarkers - plasma fibrinogen, CRP, albumin.

Methods: This is a hospital based randomized control trial conducted in a tertiary care teaching hospital in northern Kerala from January 2016 to September 2017. 40 patients of COPD (GOLD category C& D) who are more than 40 years of age and without any serious other systemic diseases are divided equally into intervention and control group by random allocation. Both groups are given standard pharmacological treatment and the intervention group was taught about planned exercises which include purse lip breathing and diaphragmatic breathing and lower limb exercises to increase strength and stamina 25 times a day in morning and evening 5 days a week. All patients will be followed up for one year. Plasma fibrinogen, CRP, albumin were measured every 3 months during this one year follow up during stable disease.

Results and discussion: Present study had shown a significant improvement in biomarkers that include CRP, plasma fibrinogen and albumin.

Conclusion: The study concludes that there is an improvement in level of biomarkers following planned exercises.

Keywords: biomarkers, COPD, pulmonary rehabilitation, plasma fibrinogen, CRP, albumin.

Introduction

COPD has a prevalence of 4 to 10 percent. It accounts for approximately 4.5 per cent of all deaths. Moreover, COPD is a contributory factor in another 4.3 per cent of deaths. The World Health Organization reports that 15 billion cigarettes are smoked daily worldwide and predicts that COPD will rank fifth in life-years lost to premature death and disability in 2020. Risk Factors for development are COPD are Smoking, Occupational exposures, Air pollution, Genetic factors Asthma/airway Hyper reactivity, Childhood respiratory infections, Low socioeconomic status. Because of severe exercise limitation, Patients with advanced COPD may restrict their activities to a sedentary lifestyle. This limitation leads to social isolation, depression, and skeletal muscle de conditioning which in turn restrict their activity and impair quality of life. Protein and calorie malnutrition occurs as the consequence of impaired nutritional intake caused by dyspnea. Malnutrition is augmented by increased metabolic demands caused by increased basal oxygen consumption, inefficient skeletal muscle oxygen utilization, and cachexia-producing cytokines such as tumour necrosis factor alpha. Systemic effects of COPD are explained by the systemic inflammation due to production of various inflammatory biomarkers. Pulmonary rehabilitation for patients with chronic obstructive pulmonary disease is well established intervention for enhancing standard pharmacological and other therapies in controlling and alleviating symptoms and optimizing functional capacity. The primary goal of pulmonary rehabilitation program is to restore the patient to the highest possible level of independent function. The ideal patient for pulmonary rehabilitation is one with stable moderate to severe lung disease on standard medical treatment and not associated with other serious or unstable medical conditions. Pulmonary rehabilitation has been well established as a means of

improving functional status and reducing the disability and economic burden of patients with chronic obstructive pulmonary disease.

Materials and methods

Aims and Objectives: To study the influence of planned exercise training in COPD patients on biomarkers (plasma fibrinogen, CRP, albumin).

Study design: Randomized control trial.

Study Population: Patients with COPD (GOLD CATEGORY-C & D) attending Department of pulmonary medicine in MES medical college.

Inclusion Criteria: Patients with COPD (GOLD CATEGORY-C & D) with age more than 40 years

Exclusion Criteria: People with serious other systemic diseases – bronchiectasis, interstitial lung disease, coronary artery disease, structural heart disease, chronic kidney disease, chronic liver disease and patients who previously undergone similar exercise training.

Procedure: COPD Patients attending Department of pulmonary medicine who satisfy the inclusion criteria are explained about the study and after taking written informed consent are included in the study. The selected 40 patients of COPD (GOLD category C& D) are divided equally into intervention and control group by random allocation using computer. Both groups are given standard pharmacological treatment and encouraged to ambulate and the intervention group will be taught about planned exercises which includes purse lip breathing and diaphragmatic breathing and lower limb exercises to increase strength and stamina –leg pressing, leg swinging, ankle dorsi flexion –plantar flexion and hip flexion exercises 25 times a day in morning and evening 5 days a week. All 40 selected patients will be followed up monthly for one year. The subjects included in the intervention group shall be reviewed monthly in the Pulmonary Rehabilitation Clinic to make sure they are following the planned exercises in the right manner and weekly telephonic communications shall be made to assure compliance. For all 40 subjects plasma fibrinogen, CRP, albumin shall be assessed every 3 months during this one year follow up. The Serial change in biomarkers are done during stable disease, not during exacerbation.

Statistical Analysis: Data shall be entered in MS excel and analysed using SPSS version 16. Comparison of various parameters between groups and within group over time shall be done using t Test and chi-squared test.

A total of 40 male patients are selected based on inclusion and exclusion criteria. Only male patients were willing to participate in study.

Results

A total of 40 male patients are selected based on inclusion and exclusion criteria. Only male patients were willing to participate in study. All the background characteristics like age, socioeconomic status, FEV1 are comparable in study and control group.

Table 1. Mean age of study participants

Group	Mean	SD	N	t	P
Study	67.8	6.3	20	1.18	0.245
Control	65.1	8.3	20		

The mean age of the study group was 67.8 ± 6.3 and that of the control group was 65.1 ±8.3. No significant difference was seen with respect to age between the groups (t=1.18, p=0.245).
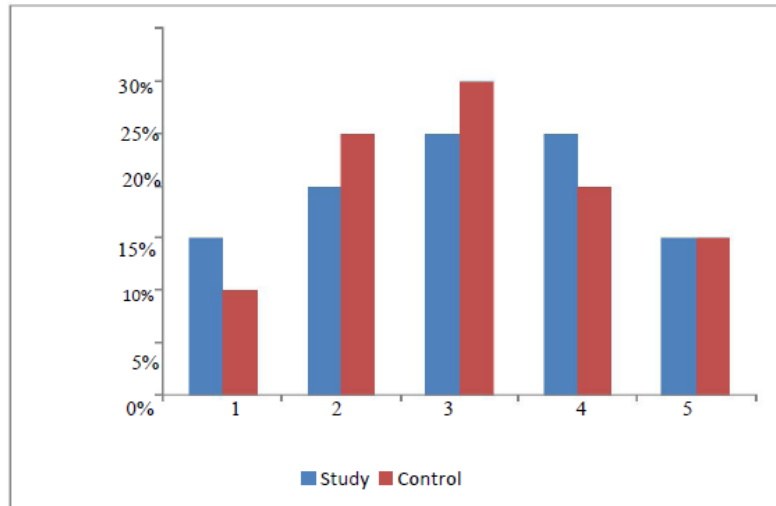
Figure 2. Comparison of BG prasad socioeconomic classification, 2014

Of the total of 40 people selected there is no significant difference with respect to the socio economic status according to the BG Prasad socioeconomic classification between study and control group (chi=0.51,p=0.972).
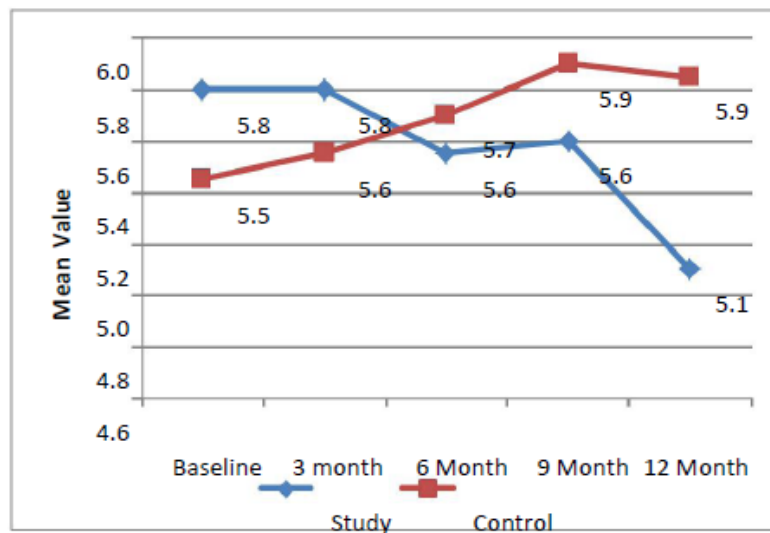

Figure. 3 Comparison of CRP based on group

* Significant at 0.05 level.

There is no significant difference in C-reactive protein values between study and control group at baseline.

Table 2. Change in CRP

Change in CRP	Study			Control			t	P
	Mean difference	SD	N	Mean difference	SD	N		
Baseline to 3 month	0.0	0.5	20	0.1	0.4	20	0.7	0.489
Baseline to 6 Month	-0.3	0.9	20	0.3	0.8	20	1.93	0.061
Baseline to 9 Month	-0.2	1.1	20	0.5	0.5	20	2.39*	0.022
Baseline to 12 Month	-0.7	0.7	20	0.4	0.5	20	5.54**	0.000
3 month to 6 Month	-0.3	0.9	20	0.2	0.7	20	1.65	0.107
3 month to 9 Month	-0.2	1.3	20	0.4	0.5	20	1.75	0.089
3 month to 12 Month	-0.7	0.7	20	0.3	0.7	20	4.81**	0.000
6 Month to 9 Month	0.1	1.1	20	0.2	0.5	20	0.53	0.597
6 Month to 12 Month	-0.5	0.7	20	0.2	0.7	20	2.65*	0.012
9 Month to 12 Month	-0.5	1.1	20	-0.1	0.5	20	1.72	0.093

**Significant at 0.01 level.

Improvement in C-reactive protein values was noted only in the study group denoted by the negative difference in the mean values. With regards to improvement in C-reactive protein values as shown in table – a significant change can be noted from 12 months.
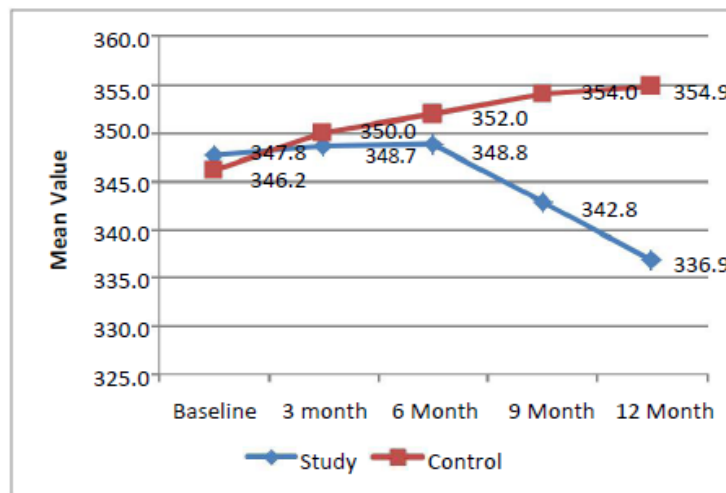

Figure 4. Comparison of fibrinogen based on group

** Significant at 0.01 level.

There is no significant difference between study group and control group in fibrinogen levels at baseline.

Table 3. Change in fibrinogen

Change in Fibrinogen	Study			Control			t	p
	Mean difference	SD	N	Mean Difference	SD	N		
Baseline to 3 month	0.9	10.5	20	3.8	5.3	20	1.08	0.286
Baseline to 6 Month	1.1	13.5	20	5.8	6.8	20	1.39	0.173
Baseline to 9 Month	-5.0	17.2	20	7.8	8.1	20	3.01**	0.005
Baseline to 12 Month	-10.9	15.2	20	8.7	10.9	20	4.69**	<0.01
3 month to 6 Month	0.2	11.1	20	2.0	6.4	20	0.65	0.523
3 month to 9 Month	-5.9	17.9	20	4.1	7.8	20	2.28	0.028
3 month to 12 Month	-11.8	16.4	20	5.0	11.2	20	3.78**	0.001
6 Month to 9 Month	-6.1	18.7	20	2.1	3.3	20	1.91	0.063
6 Month to 12 Month	-12.0	16.8	20	3.0	8.6	20	3.53**	0.001
9 Month to 12 Month	-5.9	7.7	20	0.9	7.3	20	2.87**	0.007

** Significant at 0.01 level

Improvement in fibrinogen values was noted only in the study group denoted by the negative difference in the mean values. With regards to improvement in fibrinogen values as shown in table – a significant change can be noted from 9 month onwards.
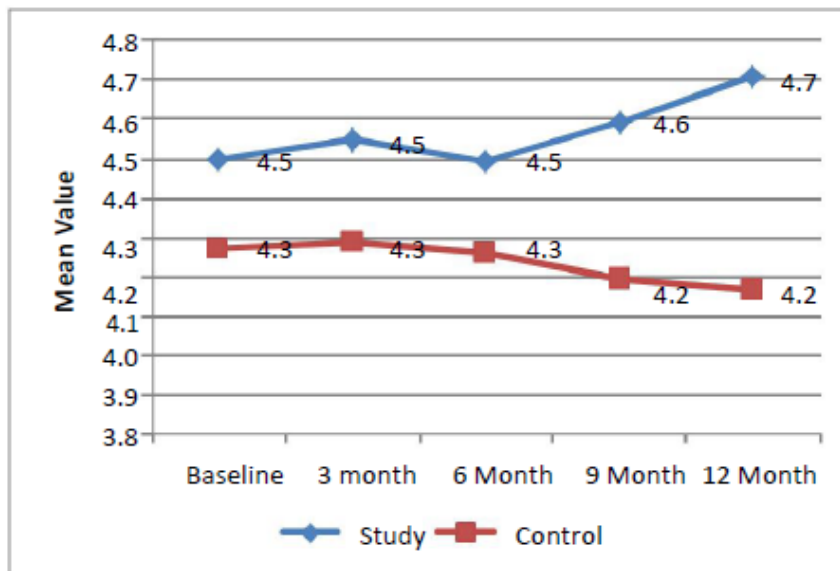

Figure 5. Comparison of albumin based on group

**Significant at 0.01 level

There is no significant difference in albumin level between study and control group at base line.

Table 4. Change in Albumin

Change in Albumin	Study			Control			t	p
	Mean difference	SD	N	Mean difference	SD	N		
Baseline to 3 month	0.1	0.2	20	0.0	0.1	20	0.66	0.515
Baseline to 6 Month	0.0	0.6	20	0.0	0.2	20	0.04	0.971
Baseline to 9 Month	0.1	0.4	20	-0.1	0.1	20	1.83	0.075
Baseline to 12 Month	0.2	0.4	20	-0.1	0.1	20	3.92**	<0.01
3 month to 6 Month	-0.1	0.6	20	0.0	0.2	20	0.23	0.822
3 month to 9 Month	0.0	0.4	20	-0.1	0.1	20	1.44	0.159
3 month to 12 Month	0.2	0.4	20	-0.1	0.1	20	3.28**	0.002
6 Month to 9 Month	0.1	0.3	20	-0.1	0.2	20	2.25	0.030
6 Month to 12 Month	0.2	0.5	20	-0.1	0.2	20	2.75**	0.009
9 Month to 12 Month	0.1	0.3	20	0.0	0.1	20	2.02	0.050

** Significant at 0.01 level

Improvement in albumin values was noted only in the study group denoted by the negative difference in the mean values. With regards to improvement in albumin values as shown in table – a significant change can be noted at 12th month.

Discussion

Chronic obstructive pulmonary disease is associated with substantial morbidity and mortality. The prevalence of Chronic Obstructive Pulmonary Disease is increasing. Chronic obstructive pulmonary disease is a leading cause of morbidity worldwide, particularly in developing countries. Chronic obstructive pulmonary disease is also associated with a significant reduction in physical activity which contributes to the patient's disability and poor health-related quality of life. Medicines have limited role in improving physical capacity of these patients. Dyspnea is one of the most frequently reported symptoms which significantly limit exercise capacity. Earlier the management of COPD has focused mainly on pharmacological treatment of the airway obstruction. However over the last two decades, growing evidence of systemic manifestations in COPD patients and their negative effects on the functioning of these patients led to the development and use of non-pharmacological treatments, such as pulmonary rehabilitation[1,2]. Pulmonary rehabilitation and pharmacological therapy should be used together for better management of chronic obstructive pulmonary disease[3].

In the present study a total of 40 patients were selected as per inclusion and exclusion criteria. All selected patients were males, as only male patients were willing to participate in study. The mean age of the study group was 67.8 ± 6.3 and that of the control group was 65.1 ± 8.3. No significant difference was seen with respect to age between the groups. There is no significant difference between the study and control group in education, occupation and socio economic status, base line FEV1, CRP, fibrinogen, albumin and BMI values.

The study showed an improvement in CRP values following planned exercises. A study by Ipek Candemir et al showed a decrease in CRP values but decrease in values was not statistically significant.[4]

After planned exercises for one year there was a significant reduction in fibrinogen values. Similarly in a study by Maria Tereza Aguiar Pessoa Morano et al there is a significant reduction in the fibrinogen values following pulmonary rehabilitation.[5]

In the present study there was an improvement in albumin values. In a study by Ugur Gonlugur et al Serum albumin level decreased with declining in pulmonary function.[6] In a study by Maria Tereza Aguiar Pessoa Morano et al there is no significant change in albumin values following pulmonary rehabilitation.[5]

Conclusion

The study concludes that there is improvement in the level of biomarkers following planned exercises training. Decline in CRP levels started at the 3 months and significant difference noted at the 12 months of study. Improvement in fibrinogen and albumin started after 6 months and significant difference noted from 9months and 12months respectively.

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