

Original Article

Dose antioxidant ascorbic acid supplementation delay lung function deterioration in stable patients with chronic obstructive pulmonary disease?

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ABSTRACT

Objective

To determine whether antioxidant ascorbic acid supplementation holdup the lung function deterioration in stable chronic obstructive pulmonary disease patients.

Patients and Methods

The single blind uncontrolled comparative clinical study was carried out at Basic Medical Sciences Research Laboratory, LUMHS, Jamshoro. Forty five enrolled patients were indiscriminately divided into two groups, group-I (n=22), getting standard treatment which included salbutamol 100 μ g and beclomethasone 50 μ g in metered-dose aerosol two times a day and group-II (n=23) receiving 500 mg of ascorbic acid twice daily along with standard treatment. Pre-treatment and post-treatment spirometry was carried out as per protocol.

Results

In group-I patients an average FEV1/FVC ratio $65.79 \pm 2.6\%$ was obtained at baseline which significantly dropped to $58.86 \pm 1.47\%$ ($P=0.026$) at the end of study. While in group-II patients mean FEV1/FVC ratio $65.99 \pm 0.943\%$ was at baseline, which non-significantly decreased to $63.59 \pm 2.1\%$ ($P=0.328$) at the end of study.

Conclusion

The response of vitamin C in delaying lung function deterioration may point out that oxidative stress is a major component in COPD pathology. So ascorbic acid could be considered as a component of recovery program. (Rawal Med J 2010;35:).

Key Words

Antioxidant, ascorbic acid, chronic obstructive pulmonary disease.

INTRODUCTION

In recent years chronic obstructive pulmonary disease (COPD) is coupled with a towering frequency of morbidity, mortality and a significant cause of declined quality of life and increased number of hospitalizations.¹⁻⁴ There is escalating confirmation for a close association among cigarette smoking and COPD that progresses gradually.^{5,6} Contemporary confirmation incriminates augmented oxidative stress as an imperative mechanism of the pulmonary inflammation⁷ which crop up in cigarette smokers.¹ Cigarette smoke restrains and creates a hefty quantity of reactive oxygen species (ROS) which facilitate pulmonary inflammation.⁸ The symmetry among the free radicals creation and exhaustion of endogenous antioxidants in the body has been postulated to play critical role in pathogenesis of COPD.⁹ Overstated free radicals congregation and exceptionally squat antioxidants accessibility put up a state of oxidative stress,¹⁰ which causes failure to repair DNA damage leading to structural alterations, deteriorations in pulmonary function and amplify pulmonary inflammatory response.¹¹⁻¹³ Access of leukocytes to site of inflammation further leads to a rise in the confined synthesis of inflammatory mediators, and ROS, ending with enhanced oxidative stress which adds to oxidative spoil¹⁴ and plays a foremost role in pathogenesis of COPD, described by low lung function¹⁵ and escalating mortality.^{16,17}

A number of management approaches which successfully attenuate and seize the oxidative load coupled with fewer adverse effects have been considered.¹⁸ Ascorbic acid, with influential scavenging action against these ROS might emerge as striking antioxidant for chronic inflammatory disorders of the lung.¹⁷ However, noticeably smaller number of studies have investigated therapeutic outcome of antioxidants in

COPD patients. The aim of this study was to explore therapeutic response of ascorbic acid supplementation with customary therapy in patients with COPD.

PATIENTS AND METHODS

This study was carried out at Basic Medical Sciences Research Laboratory, LUMHS, Jamshoro, from August 2007 to May 2009. Forty five newly diagnosed untreated patients with mild to moderate stable COPD and FEV1/FVC less than 70% were included in study. All had past history of cigarette smoking more than ten years and presently were suffering from productive cough with difficulty in breathing. They were assessed and graded for severity of dyspnea according to Medical Research Council 6-point scale¹⁹ (Table-I).

Table 1. Grades and severity of dyspnea (Medical Research Council).

Grade	Degree	Criteria
0	None	No dyspnea except by means of taxing exercise.
1	Mild	Dyspnea when walking with speed on ground or stepping up.
2	Moderate	Sluggish walking on ground due to breathlessness.
3	Slightly Sever	Suddenly stop walking due to breathlessness.
4	Sever	Abruptly bring to a halt after 100yd walking or after few minutes to take breath.
5	Extremely Severe	Much breathlessness to depart the home or with clothing or unclothing.
6	Extremely Sever	Much breathlessness to depart the home or with clothing or unclothing.

Those who had a previous history of asthma, current respiratory tract infection or other systemic disorders were excluded from the study. Demographic information including age, gender, level of education, profession, extent of illness, present and past drug history, physical examination and follow up visits were recorded. Patients were randomly divided into two groups; group I (n=22) received customary therapy which included salbutamol 100µg and beclomethasone 50µg in metered-dose aerosol two times a day; while group II (n=23) patients received ascorbic acid 500 mg twice a day along with customary therapy. Written informed consent was taken from all participants. Patients were followed monthly for nine months.

Baseline pre-treatment and post-treatment spirometry was carrying out with ML311 Spirometer Pod (The AD Instruments). At least three adequate readings from which absolute measurements of forced vital capacity (FVC), forced expiratory volume in one second (FEV₁) and FEV₁/FVC ratio were calculated. Percent predicted values were derived from prediction equation.²⁰ Data are expressed as means ± (SEM). Paired Student's t-test was used to determine significance. A p<0.05 was considered significant. Data were analyzed using SPSS 10.0 for windows.

RESULTS

Out of 45 patients, two from group-I and one from group-II dropped out of study (6.25%). The baseline characteristics of all participants are shown in Table 2. All participants had cough with sputum, dyspnea on exertion, and their FEV₁/ FVC ratio was less than 70%. None of the patients reported any drug related side effect. No abnormality was observed in complete blood pictures, renal and hepatic function tests before and after treatment program.

Table 2. Base line characteristics of study population.

Variable	Group-I Contemporary Therapy (n=22)	Group-I I Vit-C Supplementary Therapy (n=23)	P value
Age (Years)	55.33 ± 2.19	53.46 ± 1.94	0.088
Sex	Male	Male	-
Height(m)	1.74 ± 0.03	1.72 ± 0.02	0.132
Weight (Kg)	61.88 ± 0.63	62.35 ± 1.16	0.722
BMI (Kg/m ²)	20.31 ± 0.28	20.90 ± 0.53	0.338
Duration of Symptoms (Years)	3.46 ± 0.54	3.83 ± 0.65	0.668
Severity of Dyspnea (Grade)	1.60± 0.13	1.73± 0.11	0.164
Smoking History (Years)	13.26 ± 0.39	12.60 ± 0.44	0.353
No. of Cigarettes/Day	17.43 ± 1.98	20.12 ± 2.08	0.251

Values are articulated as mean ± SEM. No statistical significant among groups.

In group-I, an average FEV₁/FVC ratio 65.79±2.6% was seen at baseline which significantly dropped to 58.86±1.47 % (P=0.026) at the end of study. Similarly, baseline readings of FVC and FEV₁ showed significant decline when compared with post-treatment end of study period (Table 3).

Table 3. Therapeutic outcome in two groups.

PFT Variables	Group-I (n =22)			Group-II (n =23)		
	Pre-Treatment	Post-Treatment	P-Value	Pre-Treatment	Post-Treatment	P-Value
FVC (L) (% Pred)	0.91 ± 0.11 (50.2%)	0.53 ± 0.11 (29.4%)	0.012	1.05 ± 0.11 (57.8%)	0.99 ± 0.14 (54.6%)	0.779
FEV ₁ (L) (%Pred)	0.60 ± 0.01 (45.1%)	0.31 ± 0.01 (23.4%)	0.006	0.69 ± 0.01 (51.4%)	0.63 ± 0.01 (47.0%)	0.675
FEV ₁ / FVC %	65.79 ± 2.60 %	58.86 ± 1.47 %	0.026	65.99 ± 0.90 %	63.60 ± 2.10 %	0.328

n=Number of patients. Absolute values represent mean ± SEM (% predicted values)

On the other hand, in group-II patients, mean FEV₁/FVC ratio 65.99±0.90% was seen during the pre-treatment period, which was decreased to 63.60±2.1% (P=0.328) at the end of study. Correspondingly, post-treatment readings of FVC and FEV₁ showed non-significant change when compared with pre-treatment level.

DISCUSSION

COPD may become a chief community health threat globally in coming few years.²¹ In present study, our results in COPD treated with salbutamol and beclomethasone showed noteworthy reductions in FEV₁/FVC ratio, while a slight but non-significant drop was observed in FEV₁/FVC ratio when vitamin C was added to standard therapy. These results indicate effects of vitamin C on slowing the decline of lung function in patients with COPD and are in agreement with the study by Siedlinski et al,⁵ who observed that glutamate-cysteine ligase C (GCLC) was an original vulnerable gene for declined lung function and they postulated that this transpires due to smoking and squat vitamin C intake.

On the other hand, Wu et al had looked into the issue, and observed that vitamin C and vitamin E supplementation significantly amends the DNA spoil of white blood cells in patients.¹¹ Our results are closely consistent with the study of Tug et al who investigated the patients with COPD experiencing amplified oxidative stress and their serum concentrations of vitamin A, C and E declined.²³ Our results also indicate that use of antioxidants may be helpful in management of COPD. We did not investigate the serum levels of vitamin C in these patients and this is one of the limitations of our study.

The inhabitants with COPD are at the soaring threat of lung function limitations, because, cigarette smoke directs to chronic inflammation which well thought-out the main

pathological cause of emphysema,¹² a enduring critical bulging of airspaces finally resulting to failure of recoil function of lungs. Furthermore, vitamin C therapy aids to lessen and slow down the lung function collapse, the major component of this disorder.

CONCLUSION

We showed an efficient response of vitamin C in delaying lung function deterioration, in COPD patients. Ascorbic acid may be considered as a component of recovery program for COPD. Larger studies with use of vitamin C may further delineate role of this agent.

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