Original Article

To Study Association Between Exhaled Carbon Monoxide Levels with Disease Severity in Various Stages of Obstructive Airway Disease

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Abstract

Background. Chronic obstructive pulmonary disease (COPD) is a general name for the chronic airflow obstruction that develops most commonly due to long term tobacco smoking and other noxious gases. The aim of the present study is to check whether exhaled carbon monoxide (CO) levels had any co-relations with disease severity in various stages of COPD.

Methods. The clinical severity of asthma and COPD was determined using the criteria defined in the Global Initiative for Asthma (GINA) and Global Initiative for chronic obstructive pulmonary disease (GOLD) guidelines. Spirometry was used to confirm the presence of airway obstruction.

Results. We observed that exhaled CO levels increased with increasing severity of airway obstruction. A statistically significant negative correlation was observed between forced expiratory volume in the first second and exhaled CO ($p<0.05$).

Conclusions. We found that measuring the level of exhaled CO in patients with COPD along with spirometry forms a new approach for better understanding of the pathophysiology of COPD cases. **[Indian J Chest Dis Allied Sci 2019;61:83-86]**

Key words: Obstructive airway disease, Exhaled carbon monoxide, FEV_1, Smoking.

Introduction

Chronic obstructive pulmonary disease (COPD), a preventable and treatable disease, is characterised by chronic airflow limitation that is not fully reversible. This airflow limitation does not change markedly over several months and is usually progressive in the long term. It is associated with an abnormal inflammatory response of the lungs to the noxious stimuli, predominantly smoking. Other factors, particularly occupational exposure, may also contribute to the development of COPD. Once COPD is established, airway inflammation persists, even after many years of smoking cessation.[1]

Chronic obstructive pulmonary disease is a major cause of morbidity and mortality throughout the world. The prevalence and burden of COPD are projected to increase in the coming decades due to continued exposure to COPD risk factors and changing age structure of the world population. According to the study published by the World Bank/ World Health Organization, it is projected to rank fifth in 2020 in burden of disease caused worldwide.[2]

Several cell lines and inflammatory mediators are likely to be involved in the pathogenesis of COPD. Cigarette smoking is the notorious cause of COPD. It is associated with an abnormal inflammatory response of the lungs to noxious stimuli predominantly smoking. Hereditary deficiency of alpha-1-trypsin is one of the best documented generic risk factor.[3] Occupational dusts and exposure to biomass fuel in confined spaces are also known to cause COPD.[4,5]

The most useful test of airflow dynamic is forced expiratory spirogram. Measurement for at least three years is required to assess the rate of decline in forced expiratory volume in the first second (FEV_1) and rates >50mL per year suggest a decline. Post-bronchodilator FEV_1 is the basis of classification of severity of COPD and it is strongly predictive of subsequent mortality.[6-8]

Carbon monoxide (CO) is considered to be a major factor contaminating the Earth's atmosphere, whether outdoor or indoor.[9] It has well known toxic effects on human beings. CO is well known indoor pollutant and originate as a result of the functioning of gas cookers and some heating systems, stationary combustion equipment, ingress of exhaust fumes from an attached garage, and proximity to heavily trafficked roads.[10] Tobacco smoking active cigarette and waterpipe smoking is another important source of CO.[11,12] Moreover, CO is one of the most toxic substance present in the gas-phase of second-hand tobacco smoking.[13] Exhaled CO (eCO) measurement is simple, reproducible and non-invasive. Measuring the level of eCO in COPD cases along with spirometry forms a new approach for better understanding of pathophysiology of COPD cases.[14] Exhaled CO level is

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increased in bronchial asthma and COPD.[15] The present study was carried out to know whether eCO levels had any association with the disease severity in various stages of COPD.

Material and Methods

The present study was conducted in the Department of Tuberculosis and Respiratory Diseases, J.N. Medical College, Aligarh Muslim University, Aligarh, Uttar Pradesh, India. Informed consent was obtained in written from all the individuals enrolled in the study.

In this study, there were 150 COPD patients and 125 healthy controls. COPD patients were divided into three groups; smokers, ex-smokers and non-smokers while healthy subjects (controls) were divided into smokers and non-smokers.

The diagnosis of COPD was made by history, clinical examination, spirometric criteria and other relevant investigations as per Global Initiative for chronic obstructive pulmonary disease (GOLD) guidelines. The clinical severity of asthma and COPD was determined using the criteria (appropriate clinical and respiratory function tests) defined in the Global Initiative for Asthma (GINA) and GOLD guidelines. The diagnosis of asthma and COPD were established on the basis of reversibility of the airways obstruction with greater than 12% and less than 12% improvement in forced expiratory volume in the first second (FEV_1) after inhalation of 200μg of salbutamol from the nebuliser. Spirometry was used to confirm the presence of airway obstruction. The patient has to inhale completely before exhaling all the air and at least for six seconds. None of the patients were taking any antioxidants supplements and did not show any symptoms of upper and lower respiratory tract infection.

Demographic profile, radiological findings, pulmonary function measurements and smoking history of all the patients were recorded. Exhaled CO and carboxyhemoglobin concentration (%COHb) were measured on a portable piCO+ Smokerlyser (Breath CO monitor, Bedfont Scientific Ltd., Kent England). In this procedure, participants were to exhale completely, inhale fully and hold their breath for 15 seconds. If the participants were unable to hold their breath for 15 seconds, they were asked to hold it for as long as possible by them. Following breath holding, the participants were asked to exhale slowly into the Smokerlyser and encouraged to exhale fully. This procedure was repeated three times with one minute of normal breathing between each repetition and the mean value was used for analysis. Exhaled CO level measured by the analyser correlates closely with blood COHb concentration.[16]

Statistical Analysis

Independent t-test was used to compare the mean eCO between different groups of COPD cases and healthy controls. One-way analysis of variance (ANOVA) and post-hoc test Tukey's Honest Significant Difference test was performed to compare the mean values in four stages of airway obstructions (mild, moderate, severe and very severe) among the COPD cases. For all statistical analysis, $p<0.05$ were considered statistically significant. Data were analysed using Statistical Package for the Social Sciences (SPSS, version 20 and Microsoft Office Excel 2013 software).

Results

In this study, 150 patients with COPD, (age range 23-80 years; 122 males) and 125 healthy controls (age range 35-85 years; 92 males) were studied. Patients with COPD were divided into three groups: smokers (n=33), ex-smokers (n=82) and non-smokers (n=35). Healthy controls were divided into two groups: smokers (n=42) and non-smokers (n=83). Demographic details and smoking status (pack year) are presented in table 1.

Table 1. Demographic characteristic of COPD group

Variables		COPD Group			Controls	
		Smoker (22%)	**Non-smoker (23.3%)**	**Ex-smoker (54.7%)**	**Smoker**	**Non-smoker**
Age	Male	48.8±8.0	48.8±9.7	58.2±10.1	49.8±8.9	54.7±9.9
	Female	50.0±5.7	52.8±8.8	53.3±10.9	56.0±8.7	48.9±7.0
Total		**48.9±7.9**	**51.5±9.1**	**58.0±10.1**	**50.6±8.7**	**52.8±9.4**
Sex	Male (122)	32 (26.2%)	12 (9.8)	78 (63.9%)	36 (39.1)	56 (60.9)
	Female (28)	1 (3.6%)	23 (82.1)	4 (14.3%)	6 (18.2)	27 (81.8)
Locality	Rural (84)	17	20	47	22	51
	Urban (66)	16	15	35	20	32
Socio-economic status	Poor (89)	20	18	51	26	49
	Fair (36)	8	13	15	9	20
	Good (25)	5	4	16	7	14
Pack year	Rural	24.1±12.0	-	22.1±10.7	20.6	-
	Urban	30.0±8.1	-	29.0±13.0	19.6	-
Total		**26.9±10.3**		**25.0±12.2**	**20.2±11.0**	

Out of 75 smokers, 68 were males while in 118 non-smokers, 68 were males. Out of 82 ex-smokers, 78 were males and four females.

In COPD males, 12 were non-smokers, 78 were ex-smokers and 32 were smokers. In COPD females, 23 were non-smokers, four were ex-smokers and one was smoker. Out of 275 (150 COPD and 125 healthy controls) the socio-economic condition of 164 were poor, 65 fair and 46 were good.

Difference in the mean eCO level was found to be significant ($p<0.05$) (Table 2). The mean eCO level was decreased with improvement in disease after treatment ($p<0.05$).

Table 2. Comparison of eCO and FEV_1 in different groups of COPD

	eCO	FEV_1
Smoker with COPD (33) (22.0%)	12.6±4.5	35.09±14.19
Ex-smoker with COPD (82) (54.7%)	5.2±1.6	38.01±14.48
Non-smoker with COPD (35) (23.3%)	2.9±0.9	43.91±12.66
Stages of COPD		
I (0)	–	–
II (28) (18.7%)	4.7±2.9	60.68±6.52
III (71) (47.3%)	5.8±3.8	40.82±6.72
IV (51) (34.0%)	7.9±4.9	23.82±4.15

Figures in parentheses indicate number of patients along with percentages

Definition of abbreviations: eCO=Exhaled carbon monoxide; FEV_1=Forced expiratory volume in the first second; COPD=Chronic obstructive pulmonary disease

Discussion

Carbon monoxide levels in the air has also been associated with emergency visits of people with COPD.[17] Increased arterial COHb may relate to severity in patients with COPD because of lung and systemic inflammation and production of reactive oxygen species.[18] Elevated eCO levels might provide an early warning signal for an acute infective episode, which may lead to exacerbation of COPD.

A major limitation of eCO in COPD is the marked effects of cigarette smoking, which masks any increase that may occur because of the disease progress. With respect to exhaled breath analysis, COPD patients had higher measured eCO values than non-smokers without COPD. Among COPD patients, current smokers at the time of study had higher eCO values than ex-smokers.[19] CO is a by-product of airway inflammation. Therefore, measurement of eCO is a simple method for detecting and monitoring airway inflammation. In view of this, we have studied levels of CO in exhaled air in patients with COPD. We have found a greater than three-fold increase in the levels of eCO in ex-smokers with COPD compared to healthy non-smokers.

The prevalence of COPD is more among males than females.[20,21] We also observed the same trend in our study. The level of eCO increased with an increase in pack years among the patients with COPD and the correlation was significant ($p<0.05$). In our study, the elevated levels of eCO among smokers with COPD (12.6±4.5) when compared to healthy non-smokers (1.5±0.6) corroborates with findings described in a previous study.[22]

In our study, we found a significant association of severity of airway obstruction with the level of eCO, *i.e.* eCO level increased with an increase in the severity of the airway obstruction. The correlation between forced expiratory volume in the first second (FEV_1) and eCO was found to be negative (-0.280) and significant ($p<0.05$).

In our study we compared eCO levels of the patients with COPD and healthy controls (both smokers and non-smokers) and found it to be significant ($p<0.05$). Besides this we compared eCO in different groups of COPD with healthy controls and the difference was significant ($p<0.05$) in all the groups. In our study we also found that individuals with COPD have higher CO than healthy individuals.

With respect to exhaled breath analysis, patients with COPD had higher measured eCO value than non-smokers without COPD. Breath analysis is currently a research procedure but there is increasing evidence that it may have an important role in the diagnosis and management of the lung disease in the future.[23]

Yuvrajan[24] found that quantification of eCO along with spirometry could be a better choice than spirometry alone in the diagnosis and management of COPD cases. So measuring the level of eCO in patients with COPD along with spirometry forms a new approach for better understanding of the pathophysiology of COPD.[24]

Conclusions

We conclude that there was a negative correlation between exhaled carbon monoxide levels and FEV_1, *i.e.* eCO level increases with decrease in FEV_1. This means eCO level increases with increase in severity of the airway obstruction.

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