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Original Article

Physiology Section

Lung Transfer Factor in Middle Aged Asymptomatic Male Smokers of a City from West India: A Cross-Sectional Study

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ABSTRACT

Introduction: Smoking is an increasingly popular indulgence in India. Assessment by routine spirometry falls short of direct functional parameter like Diffusion Lung Capacity (DLC), also known as lung transfer factor (LTF).

Aim: To measure LTF amongst middle aged male smokers and to study various correlates for it.

Materials and Methods: Total of 45 asymptomatic male current smokers were enrolled for this cross-sectional study conducted at pulmonary function testing lab of Physiology Department of our college. Smoking history was evaluated and smoking index was defined by product of number smoked per day and years smoked. We used instrument Ultima PFX of Medgraphic Company. After pre syringe calibration LTF was measured by Methane mixture using protocols of ATS. Parameters measured were Dlco-uncorrected, corrected and normalized to VA (alveolar volume). Results were compared for statistical significance and significance was set as p <0.05.

Results: In case group of 45(25 bidi and 20 cigarette smokers) mean age was 30 years, mean duration was 8 years, mean smoking index was 60. We found small insignificant decline in actual LTF values than predicted which was not significantly different between bidi and cigarette smokers. Duration, age and intensity of smoking were negatively and significantly correlated with LTF value while anthropometric parameters were not.

Conclusion: Smoking adversely affects LTF in young asymptomatic current male smoker that further declines with severity of smoking and with duration regardless of type of smoking. With years to come, these alterations can largely be prevented by smoking cessation, at least theoretically.

Keywords: Cigarette, Diffusion lung capacity, Smoking

INTRODUCTION

Deleterious effect of smoking, the leading cause of chronic airflow obstruction, on lung function is well recognised [1]. India has over 100 million current tobacco smokers, accounting for approximately 20% of global tobacco-related deaths [2]. Smoke can lead to obstructive, restrictive or mixed pattern of lung diseases, smoking cessation being the only proven way of slowing down disease progression [3-5]. The single-breath diffusing capacity test is the most common way to determine DLC (diffusion lung capacity) that reflects both airway and alveolar function [6]. A diminished value for the single-breath carbon monoxide transfer factor (DLco-SB) has been reported in smokers [7]. Indian study linking lung transfer factor with smoking is so far not known.

AIM

The present study was designed to evaluate the effect of cigarette or bidi smoking on lung transfer factor and various correlates of it.

MATERIALS AND METHODS

Study Subjects

A cross-sectional study was carried out at pulmonary function laboratory, Department of Physiology, Government Medical College, Bhavnagar, Gujarat, India. The study was conducted in 45 randomly selected male subjects from Bhavnagar city with age ranging from 20 to 50 years. Subjects had Indian ethnicity and South Indian origin.

Inclusion and Exclusion Criteria

We included asymptomatic, apparently healthy male smokers, ageing 20 to 50 years, giving informed consent, smoking regularly, being smoker for more than 1 year, having smoking index less than 300 and not having any other addiction.

We excluded ex-smokers, occasional smokers and subjects having known respiratory disease, diabetes, hypertension, renal failure, cancer, AIDS, cardiac arrhythmia. We also excluded subjects doing yoga or breathing exercises, unwilling to give informed consent and taking drug affecting the autonomic nervous system, anti-platelet drugs, thrombolytic, statins.

Quantification of Smoking

We included only current smokers and excluded ex-smokers or occasional smokers as defined by WHO guidelines [8]. Smoking was quantified by the smoking index (SI). As previously published, SI was defined as number of *bidis*/cigarettes smoked in a day multiplied by number of years smoked [9]. The concept of using SI concept instead of packs per year was used for quantification of exposure to smoke because *bidi* – the hand rolled form of tobacco wrapped in the dried tendu leaf – is the most common smoking product in India [10]. The number of *bidis* per pack is variable in contrast to cigarettes since, the former is a cottage industry with lack of manufacturing standardization in its process. Previous studies have revealed that *bidis* and cigarettes impose similar risks in relation to lung cancer and while calculating time-intensity of tobacco smoke exposure, one *bidi* and one cigarette should be considered equivalent [11]. Depending on SI, subjects were categorized into the following groups [12]: Light smokers (SI=1-100), Moderate smokers (SI=101-300) and Heavy smokers (SI> 300).

Anthropometric Parameters

We measured barefooted height of subject in centimetres (sensitivity of 0.1 cm) using standiometer while subjects was standing as tall as possible with the eyes level and looking straight ahead, with feet together.

We measured weight in kilograms (sensitivity of 0.1 kg) of bare footed subject wearing light clothing having empty bladder before meal on a standardized weighing scale.

Instrument Used

Present study was carried out with the help of instrument known as ULTIMA PF with MultiGas Technology (real time diffusion) system for Diffusion lung capacity (DLCO) and computerized Software named BREEEZESUITE (Med graphics Diagnostic Company, Saint Paul, MN, USA) based on ATS & ERS with facility of exact flow sensor calibration by 3 litre syringe calibration and gas analyzer calibration before each testing. The instrument used inbuilt computerized software of Pulmonary Function Test named "BREEZESUITE".

Procedure for DLCO-Single Breath

All study group subjects were physically healthy on basis of clinical examination, devoid of any respiratory symptoms. Prior approval from institutional review board of our Government Medical College was obtained and participants were properly explained about the objectives, methodology, expected outcome and implications of the study. Written informed consent were obtained from all the subjects and all were given practice and minimum three attempts. Subject takes four time even, relaxed tidal breath, (inspire-expire)-(inspire-expire)-(inspire-expire)-(inspire) and exhales forcefully down to the RV (residual volume) level. Single, rapid inspiratory VC(vital capacity) manoeuvre is done upto 85% of VC and then breath holding for 8 to 10 sec of time (no Valsalva or Muller manoeuvres) followed by rapid exhalation rapidly to the RV level [6]. We used references set by Ayers et al., for DLCO uncorrected values and collection protocol was according to Jones-Meade et al., (ATS) [13,14].

STATISTICAL ANALYSIS

We expressed numerical data as mean ± SD and categorical data as numbers. All calculations were accomplished using Graph Pad in Stat 3 software (demo version free software of Graph Pad Software, Inc. California, USA). Observed LTF parameters were compared against predicted reference values by unpaired Student's t-test with the help of Graph pad instat3 statistical software. Correlation between LTF parameters and various factors were accomplished by Pearson's correlation test.Effect of duration of exposure was compared by subgrouping based on duration less or more than mean duration of smoking. Statistical significance was indicated by p-value < 0.05.

RESULTS

Our study included 45 young asymptomatic male smokers who had mean age 30 years, mean BSA 1.63 m^2, mean BMI 23.71 kg/m^2. Out of 45 smokers, 20 were bidi smokers and 25 were cigarette smokers which had average smoking duration 8 years and had been smoking 7 pieces per day, giving smoking index on average 60.35 were mild smokers and 10 were moderate smokers as per smoking index while there was no heavy smoker in our study group [Table/Fig-1].

Comparison of test values with predicted revealed small but insignificant difference of diffusion lung capacity–corrected, uncorrected and normalized by VA but actual alveolar ventilation was significantly lower compared to predicted values [Table/Fig-2].

Bidi smokers had comparatively lesser values of Diffusion lung capacity, VA and DL/VA as compared to cigarette smokers but none of them was statistically significant [Table/Fig-3].

With advancement of age and increase in duration of smoking, Diffusion lung capacity decreases significantly. Diffusion lung

Parameter	Value
Age (years)(Mean ±SD)	29.87±7.58
Height(cms)(Mean ±SD)	161.00±7.19
Weight(kgs)(Mean ±SD)	61.49±10.80
BSA(m^2)(Mean ±SD)	1.63±0.17
BMI(kg/m^2)(Mean ±SD)	23.71±3.88
Smoking history	
Type	**Number**
Bidi smokers	20
Cigarette smokers	25
Duration (years)(Mean ±SD)	7.71±4.97
Number per day(Mean ±SD)	6.87±3.92
Smoking index(Mean ±SD)	60.22±67.25
Intensity of smoking	**Number**
Mild smokers	35
Moderate smokers	10
Heavy smokers	0

[Table/Fig-1]: Baseline data, anthropometric data and smoking history in smokers.

Parameter	Actual (Mean ±SD)	Predicted (Mean ±SD)	p-value
DLCOuncor (ml/min/mmHg)	24.31±7.60	26.08±7.04	0.26
DLCOcor (ml/min/mmHg)	25.53±7.16	25.98±6.69	0.11
DLCO/VA (ml/min/mmHg)	7.10±3.62	6.21±0.29	0.99
VA (L)	4.13±1.47	5.57±0.56	<0.0001*

[Table/Fig-2]: Comparison of actual and predicted values of lung transfer factor in study group.
'*' indicates statistical significance

Parameter	Bidi smoker (n=20) (Mean ±SD)	Cigarette smoker (n=25) (Mean ±SD)	p-value
DLCOuncor (ml/min/mmHg)	23.36±9.09	25.06±6.26	0.46
DLCOcor (ml/min/mmHg)	23.22±8.02	23.79±7.43	0.81
DL/VA (ml/min/mmHg)	6.00±0.65	7.98±4.68	0.29
VA (L)	3.75±1.63	4.43±1.33	0.13

[Table/Fig-3]: Effect of type smoking (bidi versus cigarette) on parameters of transfer lung factor among smokers.

Parameter	Statistic	DLCOuncor	DLCOcor	DL/VA	VA
Age (in years)	r	-0.53	-0.48	-0.33	-0.53
	p	0.0002*	0.0008*	0.03*	0.0002*
Height (in cms)	r	0.16	0.15	-0.16	0.20
	p	0.31	0.31	0.29	0.19
Weight (in kgs)	r	-0.04	0.02	-0.08	-0.06
	p	0.78	0.89	0.58	0.71
BSA (m^2)	r	0.01	0.13	-0.18	-0.07
	p	0.97	0.39	0.23	0.67
BMI (kg/m^2)	r	-0.13	-0.06	-0.01	-0.17
	p	0.38	0.68	0.98	0.27
Duration (years)	r	-0.40	-0.40	-0.26	-0.43
	p	0.007*	0.001*	0.045*	0.003*
Number /day	r	-0.27	-0.30	-0.09	-0.21
	p	0.035*	0.024*	0.56	0.16
Smoking index	r	-0.37	-0.41	-0.21	-0.36
	p	0.012*	0.004*	0.16	0.016*

[Table/Fig-4]: Correlation between various factors and transfer lung factor among smokers.
'*' indicates statistical significance

Parameter	Duration≤ 5y n=25(Mean ±SD)	Duration>5 y n=20(Mean ±SD)	p-value
DLCOuncor (ml/min/mmHg)	26.98±7.44	20.96±6.53	0.007*
DLCOcor (ml/min/mmHg)	26.22±8.04	20.18±5.57	0.007*
DL/VA (ml/min/mmHg)	8.08±4.65	5.87±0.58	0.017*
VA (L)	4.75±1.34	3.34±1.31	0.001*

[Table/Fig-5]: Effect of duration of Smoking on transfer lung factor among smokers
'*' indicates statistical significance.

capacity decreases with anthropometric parameters like height, weight and BMI but without statistical significance. There was significant and negative correlation between Dlco parameters and age, duration of smoking and numbers smoked per day. When number of bidis or cigarette smoked per day were multiplied by duration of smoking, we got exposure to harmful smoke by SI which correlated negatively with transfer lung factor with statistical significance [Table/Fig-4].

Smokers with history of smoking for more than 5 years had significantly lower LTF parameters compared to those with duration of less than or equal to 5 years [Table/Fig-5].

DISCUSSION

Cigarette and bidi smoking is an increasingly popular indulgence in this country, former having higher per capita consumption today than at any time in the history of the tobacco industry and later being famous for its cheap availability and stimulant effects [15]. Picture becomes even dangerous in India where bidi, offering unfiltered smoke exposure, is 10 times more common than cigarette [16] and 24% males above age 15 smoke tobacco [17]. Smoking has an extensive effect on the respiratory function [18] and it has been clearly implicated in the etiology of respiratory diseases including bronchial carcinoma [16]. Bidi smoking is 10 times more prevalent than cigarette smoking [16] but we found 56% prevalence of cigarette smoking and that is due to sampling of subjects from urban area, majority being working men and of young age with comparatively good socio-economic status.

Spirometry is routinely done as pulmonary function test but it falls short of inferences which are of direct functional importance regarding the actual functioning of respiratory membrane across which gaseous transport takes place. Same can be measured by diffusion lung capacity also known as Lung Transfer Factor (LTF) which reflects ultimate aim of pulmonary function that is gas exchange. LTF was found to be reduced in either corrected or uncorrected form when we compared actual values against predicted values but there was no statistical significance. Even when corrected for alveolar ventilation in the form of DLCO/VA, the performance, though insignificantly, was short of actual predicted values. This indicated defect in diffusion capacity of respiratory membrane which has not yet become significant. Declined DLCO can be due to anemia effect of carboxyhaemoglobin [19], decrease in capillary blood volume or local bronchoconstriction [20]. Elevations in blood carbon monoxide content induced by smoking can reduce exercise tolerance and maximal aerobic capacity [21] which is inapparent until dsypnoea develops. Lack of significance can be attributed to young age, predominantly mild intensity of smoking, lesser duration of exposure and lesser smoking index values as compared to other studies [22-26], wherein all these risk factors were on higher side. We found, however, significantly reduced alveolar volume (AV) in smokers who were yet to show significant effect of smoking on LTF. The changes observed are resulted from reduction of the pulmonary elasticity owing to development of restrictive disorders in lung parenchyma [27]. There are studies supporting that ex-smokers have values similar to persons who never smoked [28,29] so cessation of smoking is effective more so in young aged individuals like ours to revert and stop further dysfunction.

Age was significantly and negatively correlated with all LTF parameters in line with previous studies [2,25,26]. However, we could not find much significant association, being negative, between tested parameters and anthropometric parameters like height, weight and BMI which is unlike other studies [30]. Duration and number of smokes were associated negatively and significantly with LTF parameters. Dose response relationship between smoking and declined LTF is in line with previous studies [7,25,27].

Despite the smaller amount of tobacco in bidis, they can produce more nicotine, carbon monoxide, and tar than the average manufactured cigarette due to the way users puff on them [31]. Bidi smokers had small and insignificantly reduced LTF in line with the fact that both form damages equally and filtered cigarettes are not much in use in India [32]. We found significantly declined LTF in smokers which results with longer duration of smoking (more than 5 years). This is in line with study done by Prasad R [16]. It highlights the fact that it is the number, duration and more importantly SI that combines both can quantify smoke exposure. In one previous study, we found that smoking affects significantly to decline pulmonary functions with restrictive patterns in subjects taken as controls and not exposed to prolonged vehicular pollution [33]. With years to come and with increase in intensity, these parameters can further decrease that accelerate age induced diminished LTF. Thus stoppage of smoking, before any clinically evident respiratory impairment takes place, bears potential scope for preventive programmes. This study findings suggests that there are not much early effects of smoking that can significantly hamper the function of gas diffusion in the youths but it can lead to functional impairment cumulatively. Such information can be used to illustrate the harm of smoking and should be used to encourage young people to quit or avoid smoking.

LIMITATIONS

Our study was limited by moderate sample size, use of western reference values, absence of controls and its horizontal nature. Further studies with larger size and vertical follow up to demonstrate benefits of quitting smoking are required.

CONCLUSION

In a sample of young, asymptomatic, non-obese, predominantly mild male smokers, we found declined lung transfer factor which was small significant as such compared to predicted but significantly reduced with ageing and exposure, being unaffected by type of smoking-bidi or cigarette. It suggests further study and reaffirms the notion that prevention of smoking is a potential measure that can be targeted, theoretically at least.

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