The Early Effect of Smoking on Spirometry and Transfer Factor

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Abstract

Cigarette smoking is one of the most important etiological risk factor in COPD and significantly increases progressive deterioration in lung function. When the relationship between lung function and emphysema was assessed, the best correlation was found between emphysema and transfer factor for carbon monoxide per litre alveolar volume in the lungs. The present study concerns the early effect of smoking on spirometry and transfer factor in asymptomatic smokers. This trial was carried out in a sample composed of men (39 non-smokers and 93 smokers) aged 22 to 45 years. Although the mean pulmonary function test parameters were all in the normal range, PEF, T_L,CO and K_{CO} (T_L,CO/V_A) were significantly lower in smokers than in non-smokers. A significant correlation was found between smoking pack-year and $FEF_{75\%}$ (r= -0,3153, p<0.005), T_L,CO (r= -0,2312, p<0.05), K_{CO} (T_L,CO/V_A) (r= -0,4526, p<0.001). K_{CO} (T_L,CO/V_A) was found to be under 75% of the predicted value in 22 smokers with a history of smoking over 20 pack-years. In conlusion, we hypothesize that even in normal spirometric ranges, the measurement of carbon monoxide transfer factor may be added to the laboratory tests in healthy smokers having more than 20 pack-years cigarette burden. Lower values may indicate the early destruction of the lungs and transfer factor may be used as an additional parameter to spirometry.

Key words: *cigarette smoking, spirometry, transfer factor, emphysema*

Introduction

Smoking is one of the most important etiological risk factor in COPD and significantly increases progressive deterioration of the lung function. Patients with COPD are usually diagnosed when about half of their lung function has been lost, and specialists agree that early diagnosis is important for these patients in order to improve their management (1). Smoking also effects the growth of lungs in adolescents and is found to be associated with mild airway obstruction (2). The mean rate of decline among smokers is approximately double and results in airflow obstruction around the eigth decade. However, 15 to 20% of smokers are more susceptible to smoking which causes symptomatic airway obstruction in late middle-age (3). It is difficult to seperate the parenchymatous component of COPD from its airway component. When the relationship between lung function and emphysema was assessed, the best correlation was found between emphysema and transfer factor for carbon monoxide per litre alveolar volume in the lungs (4). The aim of diagnosis is to improve

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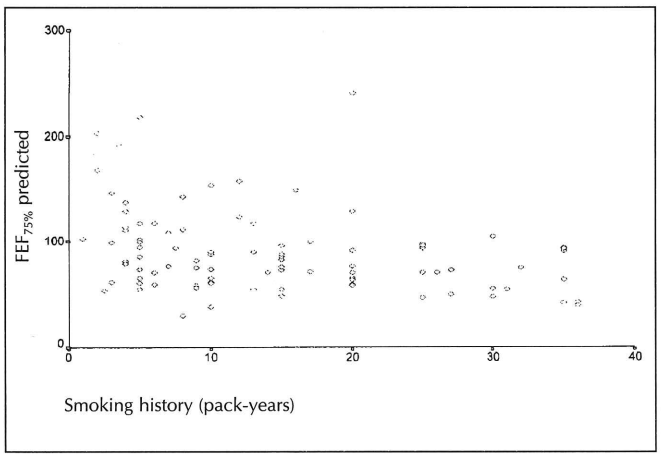

Fig. 1. The correlation between $FEF_{75\%}$ and smoking history

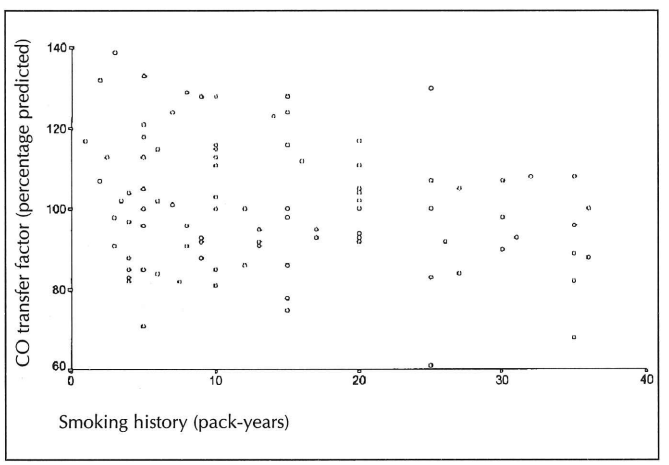

Fig. 2. The correlation between carbon monoxide transfer factor and smoking history

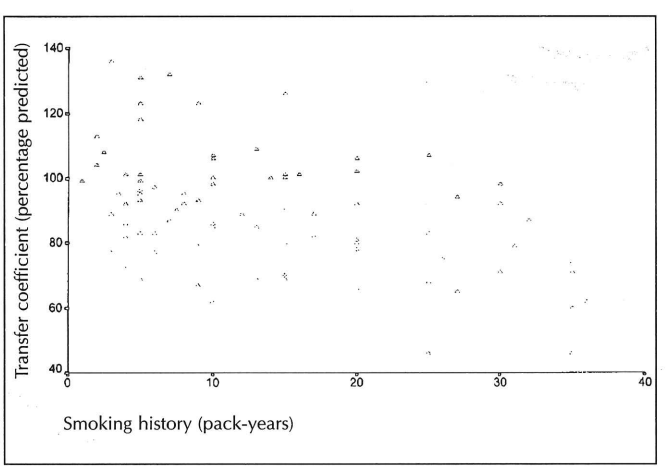

Fig. 3. The correlation between transfer coefficient and smoking history

the prognosis by effective treatment, but it is clear that non-smoking or quitting smoking is the most important measure for smoking-related diseases. The present study concerns the early effect of smoking on spirometry and transfer factor (also called diffusing capacity) for carbon monoxide in asymptomatic smokers.

Methods

This trial was carried out in a sample composed of men (39 non-smokers and 93 current smokers) aged 22 to 45 years. Subjects were selected according to the normal standard spirometric test values (FVC, FEV_1, FEV_1/FVC) in asymptomatic healthy current smokers/non-smokers who are free of respiratory, hematological and acute or chronic symptoms or diseases based on answers to a standardized questionnaire and x-ray findings. Subjects exposed to harmful environmental factors were not included in the study. Measurements were performed with a rolling-sealed, computer-based pulmonary function analyser (Sensormedics BV System 2400) and were in accordance with the test procedures recommended by the American Thoracic Society (5). The test gas was 0.3% CO, 10% helium, and the rest balanced with nitrogen. Spirometry and CO diffusing capacity measurements were performed while the participants were seated, wearing noseclips. Maneuvers with a breath holding time <9 or >11 seconds, or with an inspiratory capacity less than 85% of measured vital capacity were excluded. No correction was made for hemoglobin (Hb), but smokers were asked not to smoke for at least 4 hours prior to their clinic visit. FVC, FEV_1, FEV_1/FVC, $FEF_{25-75\%}$, $FEF_{50\%}$, $FEF_{75\%}$, PEF, T_L,CO and K_{CO} (T_L,CO/V_A) percentage predicted results were compared among the smoker and non-smoker subjects. Predicted values were determined according to Morris-Polgar. The data in the text, tables and figures are presented as means SD. Student's t-tests and Pearson correlation coefficients were used to examine the significance of differences and the correlation between groups. Statistical significance was assumed at $p<0.05$.

Results

The features of the study samples and pulmonary function test results are listed in table 1. Although the mean pulmonary function test parameters were all in normal range, PEF, T_L,CO and K_{CO} (T_L,CO/V_A) were significantly lower in smokers than in non-smokers. As shown in table 2, the PFT parameters tend to decrease as the

Table 1. Demographics of the study group and PFT parameters as percent predicted

	Non-smoker (n=39)	Current smoker (n=93)	p
Age (Year)	33.317.64	35.127.02	NS
Smoking history pack-year	-	14.369.99 pack-year	-
FVC	105.113.12%	104.5310.1%	NS
FEV_1	109.113.63%	106.5510.1%	NS
FEV_1/FVC	105.16.48%	102.957.12%	NS
$FEF_{25-75\%}$	108.6927.13%	103.3628.79%	NS
$FEF_{50\%}$	109.1829.81%	104.9427.48%	NS
$FEF_{75\%}$	94.6726.65%	89.6139.3%	NS
PEF	104.5917.61%	97.3316.71%	p<0.05
T_L,CO	124.5626.11%	100.7315.75%	p<0.00001
K_{CO} (T_L,CO/V_A)	109.4922.39%	88.1717.73%	p<0.00001

Abbreviations: FVC: forced vital capacity, FEV_1: forced expiratory volume in one second, FEV_1/FVC: forced expiratory volume in one second as fraction of forced vital capacity, $FEF_{50\%}$: forced expiratory flow when 50% of forced expiratory vital capacity has been exhaled, $FEF_{75\%}$: forced expiratory flow when 75% of forced expiratory vital capacity has been exhaled, T_L,CO: transfer capacity of the lung for carbon monoxide, K_{CO}: carbon monoxide transfer coefficient (T_L,CO/V_A), V_A: Alveolar volume, NS: Nonsignificant,

cigarette burden increases and the most effected parameters are T_L,CO and T_L,CO/V_A. A significant correlation was found between smoking pack-year and $FEF_{75\%}$ (r= -0,3153, p<0.005), T_L,CO (r= -0,2312, p<0.05), K_{CO} (T_L,CO/V_A) (r= -0,4526, p<0.001) as shown in figure 1, 2 and 3. K_{CO} (T_L, CO/V_A) was found to be under 75% of predicted value in 22 smokers with a smoking history of 20.72±11.25 pack-year.

Discussion

Chronic obstructive pulmonary disease is characterized by the presence of chronic bronchitis and/or emphysema which are mostly due to cigarette smoking. Small airways and parenchyma are primarily effected regions showing the pathologic changes in the lungs. Spirometric decline, diffusing capacity for carbon monoxide is also found to be related to the severity of emphysema (6,7). Although prevalence of impaired lung function is related inversely to pack-years of smoking in elderly men and women, smokers who quit smoking have a better ventilatory function than current smokers even over 60 years. Smokers who quit smoking under age 40 years have a similar decline in FEV_1 value of non-smokers (8). The assessment of emphysema by chest HRCT was shown to be in good correlation with the pathologic changes in the lungs and pulmonary function tests (9). Although we do not correlate spirometry and diffusing capacity with histopathologic findings and HRCT, there was a significant correlation between smoking history and T_L,CO decline. The correlation between smoking history and $FEF_{75\%}$ T_L,CO and K_{CO} (T_L,CO/V_A) may be due to early effect of smoking on small airways. Although the mean percentage of PFT parameters were in the normal range, the lower percentage of transfer factor for carbon monoxide in smokers in comparison to non-smokers might be related to the pathologic progression of a lung disease such as COPD. More convincing results may arise from the longitudinal studies and there are some limitations in the cross sectional studies. However, KCO (T_L,CO/V_A) was found to be under 75% of the predicted value in 22 smokers, therefore transfer coefficient was considered to be more specific than the others. Chronic cigarette use increases inflammatory changes in the bronchiolar walls and subsequently bronchiolar fibrosis are evident in older smokers. These lesions occur independently of emphysema and may be responsible of physiologic alterations observed in smokers (10). However, another factor for lower T_L,CO may be due to carboxyhemoglobin levels of smokers and limitations of our study include the lack of Hb and COHb measurements. Each cigarette smoked causes 0.5-2.6 mg CO to be inhaled, which contributes to the increase in COHb levels, therefore diffusion gradient decreases (11). It is increasingly clear that the single-breath T_L,CO may be abnormal when there is no evidence of airflow obstruction and that it may worsen more rapidly than the airway function tests, even when they do become abnormal. On the other hand, airway obstruction that is associated with decreased T_L,CO usually reflects the presence of significant anatomic emphysema (12). According to the article published recently (13), the predictors of longitudinal change in diffusing capacity over 8 years has been evaluated and it was found that there was more rapid decline in T_L,CO in patients who had also excessive FEV_1 declines. Smoking cessation contributes to a rapid improvement in carbon monoxide diffusing capacity but it remains unchanged in some subjects who may have irreversible changes due to smoking (14).

Table 2. PFT parameters of the study group according to severity of smoking history

	Non-smoker (n=39)	Current smoker (1-5 pack-years) (n=24)	Current smoker (6-20 pack-years) (n=49)	Current smoker (>20 pack-years) (n=20)
Age (Year)	33.317.64	30.046.60	34.736.06	42.152.87
Smoking history pack-year	-	3.921.18 pack-year*	12.984.64 pack-year	30.254.35 pack-year
FVC	105.113.12 %	102.429.07%	105.2911.26%	105.207.99 %
FEV_1	109.113.63 %	106.969.5%	106.2910.49%	106.7010.21 %
FEV_1/FVC	105.16.48 %	105.256.26%	102.067.44%	102.356.97%
$FEF_{25-75\%}$	108.6927.13%	113.4227.38%	100.9629.02%	97.1528.17%
$FEF_{50\%}$	109.1829.81%	110.9227.63%	102.9426.25%	102.6530.52%
$FEF_{75\%}$	94.6726.65%	110.5446.58%	87.2436.74%	70.3021.91%*
PEF	104.5917.61%	94.8314.56%*	97.0013.52%*	101.1524.69%
T_L,CO	124.5626.11%	104.0817.69%*	101.6514.48%*	94.4515.29%*
K_{CO} (T_L,CO/V_A)	109.4922.39%	97.8317.23%*	88.5915.74%*	75.5515.83%*

* $p<0.05$ (compared with nonsmokers)

In conclusion, we hypothesize that even in normal spirometric ranges, the measurement of transfer factor for carbon monoxide may be added to the laboratory tests in healthy smokers having more than 20 pack-years cigarette burden. Lower values may indicate the early destruction of the lungs and transfer factor may be used as an additional parameter to spirometry.

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