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Original Article

Clinical Characteristics of Smoking Asthmatics

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Background: The smoking prevalence in asthma patients are similar to those in the general population. Asthma and active cigarette smoking can interact to create more severe symptoms, an accelerated decline in lung function and impaired therapeutic responses. Accordingly, asthmatics with a history of smoking were examined to define the clinical characteristics and lung function of smoking asthmatics.

Methods: The medical records of 142 asthmatics with a known smoking history were reviewed. The patients were divided into three groups according to their smoking history - current smokers, former smokers and non-smokers. The clinical characteristics, lung function, and annual declines of the forced expiratory volume in one second (FEV_1) were compared.

Results: Fifty-three of the 142 patients (37%) were current smokers, 24 were former smokers (17%) and 65 were non-smokers (45%). The patients with a hospital admission history during the previous year included 16 current smokers (30%), 4 former smokers (17%) and 7 non-smokers (11%) (p=0.02). The mean FEV_1 (% predicted) was 76.8±19.8%, 71.6±21.1% and 87.9±18.7% for current smokers, former smokers and non-smokers, respectively (p< 0.001). The FEV_1/forced vital capacity (FVC) (ratio, %) values were 63.6±12.6%, 59.3±14.9% and 72.1±11.8% in current smokers, former smokers and non-smokers, respectively (p<0.001). The corresponding mean values for the individual FEV_1 slopes were not significant (p=0.33).

Conclusion: Asthmatic smokers demonstrated higher hospital admission rates and lower lung function. These findings suggest that the smoking history is an important predictor of a poor clinical outcome in asthma patients.

Key Words: Smoking; Asthma; Respiratory Function Tests; Diseases Progression

Introduction

Because cigarette smoking is an established risk factor for chronic obstructive pulmonary disease (COPD), the majority of asthma studies have been carried out on non-smokers to avoid the effects of smoking. About 17～35% of adult asthmatics are active cigarette smokers in developed countries, and smoking prevalence rates among asthmatics are similar to those of the general population[1]. An additional number of adult asthmatics are former smokers with prevalence rates ranging from 22% to 43%[1]. According to the Korean National Statistical office[2], the smoking prevalence rate in Korean adults was 27.3%, and the proportion of smokers among asthmatics was considered as nearly the same.

Adults with asthma who smoke cigarettes exhibit more severe asthmatic symptoms and demonstrate a more rapid decline in pulmonary function[3-6]. Asthmatic smokers are also more likely to require hospital care than asthmatic non-smokers[7-10]. Furthermore, asthma-related morbidity and mortality is higher among smokers

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than non-smokers[3,11].

Corticosteroids, especially inhaled corticosteroids, are currently the best anti-inflammatory therapy available for the treatment of asthma, and their use is recommended by the Global Initiative for Asthma (GINA)[12]. However, in recent clinical trials, active cigarette smoking was found to impair the efficacy of inhaled corticosteroids in mild asthma and short-term high dose oral corticosteroid treatments in chronic asthma[13,14].

Accordingly, it appears to be illogical to exclude smokers from asthma studies. Above all, to the best of our knowledge, there have been few Korean studies establishing the clinical impact of smoking in asthmatics including decline of lung function.

So the aim of this study is to compare clinical characteristics and assess lung function and annual changes in forced expiratory volume in one second (FEV_1) of asthmatic smokers and non-smokers.

Materials and Methods

1. Patients and methods

The medical records of 142 asthma patients with a known smoking history were reviewed. Subjects were categorized as current smokers, former smokers, and non-smokers. Current smokers were defined as those who smoked more than five packs of cigarettes per year; former smokers as those who had not smoked during the year prior to the study, but had previously smoked more than five packs of cigarettes per year[15]; and non-smokers as those who had never smoked. Smoking status was determined based on self-reports from medical records.

All subjects had clinical asthma with evidence of at least one of the three GINA criteria[12]. These criteria include: 1) the degree of reversibility in FEV_1 from the pre-bronchodilator value is $\geq$12% (and 200 mL), 2) the response to methacholine is expressed as a concentration causing a 20% decline in FEV_1 (PC_{20}), with a concentration of $<$8 mg/mL, and 3) the diurnal variation in the peak expiratory flow (PEF) is greater than 20%.

We compared the proportion of patients who were admitted to hospital for an asthma attack during the previous year, the number of patients that made an unscheduled visit to the hospital to treat recently aggravated asthma symptoms such as cough, dyspnea, and wheezing during the previous three months, the proportion of patients that received oral corticosteroids for the treatment of an asthma attack regardless of hospital admission, and the number of days subjects used oral corticosteroids during the previous year aside from hospital visits.

Measurements of forced expiratory volume in one second (FEV_1, % predicted), forced vital capacity (FVC, % predicted), and FEV_1/FVC (ratio, %) were taken during a forced expiratory maneuver using a spirometer approved by the American Thoracic Society (ATS)[16].

All spirometry results were obtained during a stable state of asthma. When a patient performed spirometry several times, the best FEV_1 measurement was selected for analysis.

Annual changes in FEV_1 for the 62 patients who performed spirometry at least twice over a period of more than one year were analyzed. The relationship between FEV_1 as a dependent variable and time (in years) as an independent variable was evaluated with simple linear regression analysis to obtain individual slopes of FEV_1 versus time[17]. The study was approved by the institutional review boards of Korea University Anam Hospital.

2. Statistical analysis

Data are expressed as the mean$\pm$standard deviation (SD) unless otherwise indicated. Statistical significance was assessed using one-way ANOVA for continuous variables. Post hoc analysis was based on Duncan's multiple comparison. Categorical variables were analyzed using Chi-square test. Multiple regression analysis was performed to evaluate the relationships between lung function and other independent variables, including age, sex, and smoking status. The standardized β coefficient was used to compare the influence of each independent variable. p-value of $<$0.05 was considered significant. SPSS version 13.0 for Windows (SPSS Inc., Chicago, IL, USA) was used throughout.

Results

1. Demographic and clinical characteristics of subjects

One hundred forty-two subjects were enrolled in this study with a demographic makeup of 89 men (63%) and 53 women (37%). Fifty-three subjects were current-smokers (37%), 24 were former smokers (17%), and 65 were non-smokers (46%). There were 45 men in the current smoker group (85%), 22 in the former smoker group (92%), and 22 in the non-smoker group (34%) ($p<0.001$). Mean group ages were 52±17.5, 61±14.5, and 53±15.1 years, respectively (p=0.06). The current smoker group smoked an average of 26.9±19.9 pack-year whereas the former smoker group smoked an average of 33.7±17.0 pack-year ($p<0.001$). Former smokers used more theophylline than non-smokers and current smokers (38% vs. 14% and 28%) (p=0.03), and current smokers used more leukotriene modifiers than non-smokers and former smokers (36% vs. 11% and 17%) (p=0.02) (Table 1).

Sixteen patients were admitted to the hospital for an asthma attack during the previous year in the current smoker group (30%), four in the former-smokers group (17%), and seven in the non-smoker group (11%) (p=0.02). Thirty-seven patients in the current smoker group (70%) made an unscheduled outpatient visit to the hospital for the treatment of aggravated asthma symptoms within the previous three months, 17 in the former smoker group (71%), and 41 in the non-smoker group (63%), but these percentages demonstrated no significant differences (p=0.63). Thirty-six current smokers (68%) received oral corticosteroids for the treatment of an asthma attack (excluding admission to hospital), as did 12 former smokers (50%), and 50 non-smokers (77%), but these differences were not significant. Comparisons of the mean number of days an oral corticosteroid was used during the previous year (excluding hospital admission) revealed that current smokers used oral corticosteroids 13±16 days/year, former smokers 16±29 days/year, and non-smokers 17±18 days/year. There were no significant differences (Table 2).

2. Lung function

Mean FEV_1 (% predicted) values in the three groups were 76.8±19.8% for current smokers, 71.6±21.1% for former smokers, and 87.9±18.7% for non-smokers ($p<0.001$). The FEV_1 of non-smokers was found to be significantly different from those of the other two groups. Furthermore, mean FEV_1/FVC (ratio %) values were 63.6±12.6% for current smokers, 59.3±14.9% for for-

Table 1. Patient characteristics*

	Smoker		Non-smoker	p-value
	Current	Former		
Patients, No.	53	24	65	
Mean age, year	52±17.5	61±14.5	53±15.1	0.06
Sex, No. (%)				
Female	8 (15)	2 (8)	43 (66)	<0.001
Male	45 (85)	22 (92)	22 (34)	
Smoking intensity, pack-year	26.9±19.9	33.7±17.0	0	<0.001
Use of medication, No. (%)				
Anti-cholinergics	2 (4)	1 (4)	0 (0)	0.26
Theophylline	15 (28)	9 (38)	9 (14)	0.03
ICS	6 (11)	4 (17)	14 (22)	0.36
ICS+LABA	46 (87)	21 (88)	50 (77)	0.21
LT modifier	19 (36)	5 (17)	9 (11)	0.02

*Data represent the mean±SD unless otherwise indicated.
ICS: inhaled corticosteroid; LABA: long acting beta agonist; LT: leukotriene.

Table 2. Hospitalizations and prior oral corticosteroid use during previous year

	Smoker		Non-smoker (n=65)	p-value
	Current (n=53)	Former (n=24)		
No. of patients with admission history within the previous year, No. (%)	16 (30)	4 (17)	7 (11)	0.02
No. of patients that made an unscheduled hospital visit in previous three months, No. (%)	37 (70)	17 (71)	41 (63)	0.63
No. of patients that received oral steroids within the previous year, No. (%)	36 (68)	12 (50)	50 (77)	0.06
No. of days on oral steroids during the previous year, days	13±16	16±29	17±18	0.518

Data are presented as the mean±SD otherwise indicated.

Table 3. Pulmonary function test results

	Smoker		Non-smoker (n=65)	p-value
	Current (n=53)	Former (n=24)		
FEV_1,% predicted*	76.8±19.8†	71.6±21.1‡	87.9±18.7†,‡	<0.001
FVC, % predicted	90.8±15.6	88.8±15.6	92.5±15.6	0.60
FEV_1/FVC ratio, %*	63.6±12.6†	59.3±14.9‡	72.1±11.8†,‡	<0.001

Data are presented as the mean±SD.
FEV_1: forced expiratory volume in one second; FVC: forced vital capacity.
*,†,‡Same letter indicates significant differences based on Duncan's multiple comparison.

Table 4. Multiple regression analysis of variables associated with pulmonary function

Factor	FEV_1 (% predicted)		FEV_1/FVC (ratio, %)	
	β*	p-value	β*	p-value
Age	0.038	0.67	−0.328	<0.001
Sex	−0.033	0.75	−0.212	0.03
Current smoking	−0.242	0.01	−0.239	0.01
Hospital admission	−0.197	0.03	−0.130	0.13

FEV_1: forced expiratory volume in one second; FVC: forced vital capacity.
*Standardized beta coefficient.

mer smokers, and 72.1±11.8% for non-smokers. The FEV_1/FVC of non-smokers also differed significantly from those of the other two groups ($p<0.001$) (Table 3). In order to determine the role of smoking as an independent variable, the current smoker group was compared to the non-smoker group. Through multiple regression analysis, it was determined that smoking status and hospital admission for an asthma attack were significant independent variables for FEV_1. For FEV_1/FVC, sex, age, and current smoking were the effective independent variables (Table 4).

3. Annual changes in lung function

Mean values of the individual FEV_1 slopes were as follows: 0.018±0.35 L/yr (current smokers), 0.13±0.26 L/yr (former smokers), and −0.02±0.35 L/yr (non-smokers) (p=0.33) (Table 5).

Discussion

In the present study, clinical characteristics, such as lung function and the number of hospital admissions related to an asthma attack, were compared between asthma patients who were current smokers, former smokers,

Table 5. Annual changes in FEV_1

	Smoker		Non-smoker (n=65)	p-value
	Current (n=53)	Former (n=24)		
Change in FEV_1 (L/year)	0.018±0.35	0.13±0.26	−0.02±0.35	0.33

Data are presented as the mean±SD (range).
FEV_1: forced expiratory volume in one second.

and non-smokers. Our study reveals that lung function is more impaired and hospital admission rates are higher for asthmatic smokers than asthmatic non-smokers.

Current and former smokers represented 37% and 55% of the patients enrolled in this study, which is similar to findings of previous studies[11]. Furthermore, smoking intensity was greater for former smokers than current smokers, presumably because they were older, and had, as a result, smoked cigarettes for a longer period of time.

On the other hand, the study unexpectedly determined that oral corticosteroid use during the previous year was not significantly different among the three study groups. As has been found in previous studies[13,14], oral steroid consumption was expected to be higher in asthmatic smokers. Our results may have occurred because asthmatics with mild to moderate attacks were treated with oral steroids at outpatient clinics instead of the hospital. It reflects that there was no significant difference in the occurrence of mild to moderate attacks in the three study groups. Hospital admission rates for severe attacks, however, were higher in asthmatic smokers than asthmatic non-smokers. There was no significant difference in the number of patients who made unscheduled outpatient clinic visits for treatment within the previous three months, which is a gauge used to determine the recent aggravation of asthma symptoms. This differed from previous results possibly for reasons similar to the results obtained for oral corticosteroid use[3,5].

In the present study, current and former smokers used significantly more medication (i.e., leukotriene and theophylline) than non-smokers (p=0.03, p=0.02) presumably because smokers need more medication to control asthma symptoms.

Current smokers with asthma had significantly lower FEV_1 values, despite their younger age, indicating greater lung function impairment in current smokers. In addition, FEV_1/FVC values were lower than 70% in current smokers, which implied the presence of airway obstructions, a finding that also occurs in previous studies[7,8,15]. Smoking status was a common independent variable after adjusting for sex, age, and asthma severity (based on hospital admissions) using multiple regression analysis for FEV_1 and FEV_1/FVC.

Changes in lung function were examined using annual FEV_1 changes. Greater FEV_1 declines in smokers than in non-smokers and in subjects with asthma than in subjects without have previously been reported[4]. Furthermore, the combination of asthma and cigarette smoking has been reported to synergistically reduce FEV_1[18]. Our findings, however, contradict the results of previous studies on FEV_1 reduction in adult asthmatics[4,17,18]. In the present study, no significant differences were observed among the study groups regarding FEV_1 decline. We attribute this finding to the diminutive size of the study groups, short-term follow-ups, and the retrospective nature of our study.

In conclusion, we observed the clinical characteristics of asthmatic smokers and determined that they demonstrate higher hospital admission rates for the treatment of asthma, consume more asthma-related medication, and have greater impairment of lung function as well as the increased presence of airway obstructions than in non-smokers with asthma. These findings suggest that smoking history is an independent factor that ad-

versely impacts treatment response and prognosis in adult asthmatics.

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